Medical and Biological sciences

Articles

Materials of the Conferences

COMMON AND CEREBROSPINAL IMMUNITY IN PANTROPIC VIRUS INFECTIONS

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We are offering and developing a hypothesis on common and transbarrier (hystohematogenous barriers) cerebrospinal immunity in pantropic virus infections. Common humoral and cellular immunity does not make improbable the penetration of virulent neurotropic viruses, such as tick-borne encephalitis pathogen, through hematoencephalitic barrier and the development of acute virus infection or virus persistence with the formation of chronic or slow infection process. Makers of specific antivirus vaccines should take this possibility into account.

Background

There is proof of pantropic character of tick-borne encephalitis (TBE) reproduction as well as similar diseases in inner organs and central nerve system (CNS) (1, 2).

The experience in vaccine prophylaxis against the diseases, caused by these viruses, testifies on high epidemic efficiency of TBE inactivated cultural vaccine, especially in western hotbeds of infection circulation area (3-7). Nevertheless vaccinated subjects show TBE slight clinical course, which is the evidence of virus penetration into CNS organs through hematoencephalitic barrier. We revealed chronic slow course TBE in some vaccinated subjects after aparalytic TBE or being healthy in half a year, a year or more after TBE inoculation. Poliomyelitic form, Kojewnikoff's (cortical) epilepsy, amyotrophic lateral sclerosis syndrome are among these forms (2, 8-9).

We are offering and developing the conception of common, barrier (hystohematogenous barriers) and transbarrier (cerebrospinal) specific immunity in pantropic virus infections (10, 11). Common immunity is being formed under natural immunization or vaccination apart from CNS up to hystohematogenous (hematoencephalitic) barrier, but this does not protect target-organs. Cerebrospinal immunity starts to develop only after virus or virus antigen penetration into CNS organs and tissues.

The efficiency of TBE specific prophylaxis is based on the following: antigen and immune gen activity of specific antivirus vaccines; the ability of wild virus population to penetrate into CNS organs from introduction point; the intensity of reproduction in extraneural system; penetration through hematoencephalitic barrier; tropism to nerve tissue (12,13).

Materials and methods

In our tests we used BALB/C white mice weighing 8 to 10 gram from Rapolovo nursery (Leningradskaya oblast), adult Macacus rhesus, delivered by plane from India, who were in quarantine and passed adaptation in vivarium of virology laboratory for at least 30 days. Virus indication and titration was produced on mice in intracerebral infection. We used TBE highly virulent strains (Sofyin, Pan and Absettarov) and naturally slowed Elantzev strain (15 - 20/ 3 clone).

Immunization was performed by inactivated vaccine (producer – M.P.Chumakov Poliomyelitis and Virus Encephalitis Institute of Russian Academy of Medical Sciences) and/ or naturally slowed Elantzev strain (15 - 20/ 3 clone), were inoculated in 4.0 - 4.4 lg LD_{50} concentration to macaques hypodermically or

into head brain (left thalamus). In 1 to 2 months after the immunization the injections were repeated into left thalamus: virulent strains or Sofyin (5.7 - 7.8 lg LD_{50}) or Pan (6.7 - 7.7 lg LD_{50}) or Absettarov (3.9 - 8.0 lg LD_{50}).

Table 1. The results of many days monitoring for virus accumulation in different organs and tissues in white mice of BALB/ C line, inoculated hypodermically with Absettarov highly virulent strains of TBE virus.

Name of organ, tissue	Day after inoculation			
	1st	3rd	5th	7th
	Number of the virus in lg LD_{50}/0,03 ml.			
Brain	1.0	3.5	5.5	7.2
Spleen	2.5	4.5	4.0	2.5
Lymph nodes	3.5	3.5	4.5	3.6
Liver	2.5	2.5	4.0	1.7
Intestine	2.5	2.0	4.0	1.5
Subcutaneous tissue	2.5	3.5	2.3	3.2
Blood	3.0	4.0	4.2	2.3

Results

The tests for mice of BALB/ C line with high virulent strains of TBE virus (Sofyin, Pan and Absettarov and others) resulted in the same characteristics of the given strains (2). So, in 3 days after hypodermic inoculation, the number of virus in mice brain reached 3.5 lg LD_{50}/ 0.03 ml. During the first three days the number of the virus in inner organs was relatively higher, than in brain. The most concentration of the virus in inner organs blood was marked up to the moment of clinical symptoms development in mice (the 5th day after inoculation). Before the death (the 7th day after inoculation) there was considerable lowering of virus concentration in inner organs and blood. In head brain it increased greatly from 5.5 up to 7.2 lg LD_{50}/ 0.03 ml (Table 1). At all the stages viremia was tense. The curve of virus content in blood corresponded to the one in organs, rich with reticulo endothelium cells.

Table 2. The results of many days monitoring of virus accumulation in different organs and tissues in white mice, inoculated hypodermically with TBE virus Elanzev strain.

The name of organ, tissue	Day after inoculation					
	1st	3rd	5th	7th	9th	12th
	The number of virus in lg LD_{50}/0,03 ml.					
Brain	0	0.7	3.0	5.3	3.8	2.2
Spleen	1.6	1.2	2.3	1.5	1.0	0.7
Lymph nodes	2.2	2.2	2.5	3.2	2.7	1.9
Liver	1.5	1.2	1.0	1.2	0.7	0
Intestine	1.2	1.5	1.0	2.5	1.2	0.9
Subcutaneous tissue	0.7	1.7	1.2	0	0	0
Blood	1.5	1.7	1.7	0.7	0.7	0.7

Dynamics of accumulation and distribution of naturally slowed Elantzev strain (15 - 20/ 3 clone) in hypodermically inoculated white mice of BALB/ C line had its own peculiarities.

In a day after the inoculation the virus was marked in all examined inner or-

gans and tissues excluding head brain in white mice. The majority was isolated from organs, rich with reticulo endothelium elements: spleen, lymph nodes (Table 2).

In three days after inoculation the virus was marked in all the examined organs and tissues. It was few in head brain as compared to inner organs. Even in 5 days after inoculation the number of the virus in head brain was 100 times less in Elantzev strain than in Absettarov strain in the same period. From the 9th to 12th day in survived mice there was considerable lowering of virus concentration in both CNS and extraneural organs.

We studied the dynamics of prevalence and accumulation of TBE virus in BALB/C mice, inoculated with inactivated vaccine and naturally slowed Elantzev strain (15 - 20/ 3 clone) in different types of tests.

a) Twofold intraperitoneal immunization with inactivated vaccine with 7 to 8 days interval. Then hypodermic inoculations in 14 to 15 days with Sofyin, Pan, Absettarov and others virulent strains (Table 3).

The accumulation of virulent virus in the mice, inoculated by 2-times inactivated vaccine, differed greatly from non-immunized ones. Virulent virus penetrated into animal head brain, protractedly reproduced and persisted.

b) Twofold intraperitoneal immunization of mice of BALB/ C line with inactivated vaccine with 7 to 8 days interval. Then in 14 to 15 days hypodermic inoculation with 10 000 LD_{50}/ ml with naturally slowed Elantzev strain (Table 4).

Table 3. The results of many days monitoring for virus accumulation in different organs and tissues in BALB/C white mice, inoculated twice with inactivated vaccine and injected hypodermically with 10 000 LD_{50}/ ml Absettarov strain virulent virus.

The name of organ, tissue	Day after inoculation							
	1st	3rd	5th	7th	9th	12th	15th	30th
	The number of virus in lg LD_{50}/0.03 ml.							
Brain	0	0	1.9	2.7	1.9	2.2	1.4	1.7
Spleen	0.7	1.2	1.6	1.0	1.0	0	0.7	0
Lymph nodes	1.9	2.2	2.0	1.6	0.7	0.7	0	0.7
Liver	1.0	0.7	0	0	0	0	0	0
Intestine	0.7	1.2	0.7	0	0	0	0	0
Subcutaneous tissue	0.7	1.2	0.7	0	0	0	0	0
Blood	1.1	1.4	0	0	0	0	0	0

During multiple tests we revealed very rarely the penetration of naturally slowed Elantzev strain into mice brain, mainly in 9 days after hypodermic inoculation. The reproduction of virus was not marked during 30 - days monitoring.

In tests for Macacus rhesus after extraneural inoculation (hypodermic, intravenous) with both naturally slowed Elantzev strain and highly virulent Sofyin and Pan and Absettarov we didn't registered the disease. Highly virulent strains reproduced actively in inner organs, penetrating into CNS, where we marked their protracted persistence (Table 5).

We didn't found virus penetration into CNS organs in macaques, inoculated extraneurally with high concentrations of naturally slowed Elantzev strain (4.0 - 7.7 lg LD_{50}/ ml) (Table 6).

Table 4. The results of many day monitoring for virus accumulation in different organs and tissues in BALB/ C white mice, inoculated twice with inactivated vaccine and injected hypodermically with naturally slowed Elantzev strain

Name of organ, tissue	Day of inoculation							
	1st	3rd	5th	7th	9th	12th	15th	30th
	The number of virus in lg LD_{50}/ 0.03 ml.							
Brain	0	0	0	0	0.7	0	0	0
Spleen	1.2	0.7	0	0.9	0	0	0	0
Lymph nodes	1.7	1.9	1.7	0	0	0.7	0	0
Liver	1.2	0	0	0	0	0	0	0
Intestine	1.2	0	0	0	0	0	0	0
Subcutaneous tissue	0	0.7	0.7	0	0	0	0	0
Blood	0.7	0.9	0	0.7	0	0	0	0

Table 5. The results of many days monitoring of virus accumulation in macaques, inoculated intravenously with TBE virus Sofyin strain (in lg LD_{50})

The name of organ, tissue	Day after inoculation					
	1st	8th	15th	30th	60th	90th
Cerebral cortex	1.2	2.2	1.0	0.9	0	0.7
Subcortical nodes	1.4	2.2	1.3	1.1	0.9	0.9
The 3rd ventricle	1.0	1.8	1.1	0.7	0	0
Pons	0	1.9	1.3	0	0	0
Cervical	1.1	1.9	0.7	0.9	0.7	0.7
Pectoral	1.3	2.4	1.4	1.3	0.9	0.9
Lumbar	1.0	1.5	1.3	1.3	1.1	0.6
Liver	1.4	2.0	0.9	0	0	0
Intestine	1.1	1.3	0.7	0	0	0
Spleen	2.0	2.8	1.9	1.1	1.3	0.7
Lymph node	1.5	2.2	1.6	1.1	0	0.5
Blood	0.5	0.9	0.7	0	0.7	0

Macaque extraneural inoculation (immunization) with both TBE virus high virulent and naturally slowed strains lead to intensive production of specific virus neutralizing and antihemagglutinating antibodies. But repeated inoculation for macaques head brain with VE virus high virulent strains didn't protect against mortal encephalitis in 7 to 10 days after inoculation.

After initial inoculation to the left thalamus with Absettarov, Pan or Sofyin strain, severe panencephalitis was developed with macaques death on the 7th to 10th day with intensive virus reproduction in different CNS organs (Table 7).

In macaques, dissected on the 3rd, 8th, 15th and 30th day after intracerebral inoculation with Elantzev strain, we marked its weak reproduction in CNS organs (Table 8).

All macaques, momentary immunized with naturally slowed Elantzev strain into the left thalamus and then in 1 to 2 months inoculated into head brain with large concentrations of TBE highly virulent viruses, were not ill during 30 days of monitoring and farther.

Table 6. The results of many days monitoring of virus accumulation in macaques, inoculated intravenously with TBE virus Elantzev strain (in lg LD_{50})

The name of organ, tissue	Day after inoculation					
	1st	8th	15th	30th	60th	90th
Cerebral cortex	0	0	0	0	0	0
Subcortical nodes	0	0	0	0	0	0
The 3rd ventricle	0	0	0	0	0	0
Pons	0	0	0	0	0	0
Cervical	0	0	0	0	0	0
Pectoral	0	0	0	0	0	0
Lumbar	0	0	0	0	0	0
Liver	0.7	0.9	0.5	0	0	0
Intestine	0	0.7	0	0	0	0
Spleen	1.5	1.9	1.1	0	0	0
Lymph node	1.2	1.6	0.7	0	0	0
Blood	0.5	0.7	0.7	0.7	0	0

Table 7. The number of virus in lg LD_{50}/ml on the level of clinical signs on the 7th day after inoculation of macaques into left thalamus with (M±m) strains.

The name of organ, tissue	Sofyin	Pan	Absettarov
Cerebral cortex	4,6±0,16	5,1±0,30	4,25±0,18
Subcortical nodes	4.7±0.13	4.8±0.19	4.45±0.25
The 3rd ventricle	4.4±0.41	4.2±0.38	4.00±0.60
Pons	3.2±0.27	3.8±0.24	3.6±0.35
Cervical	4.2±0.25	3.7±0.21	3.9±0.40
Pectoral	4.8±0.11	4.5±0.36	4.5±0.10
Lumbar	3.9±0.24	3.5±0.13	4.25±0.18
Liver	1.2±0.12	1.8±0.19	1.6±0.5
Intestine	1.7±0.14	1.5±0.24	1.5±0.15
Spleen	0.8±0.11	1.3±0.17	1.25±0.2
Lymph node	1.2±0.13	1.4±0.13	1.1±0.25
Blood	0.5±0.10	0.7±0.08	0.85±0.12

In animals, immunized into head brain with Elantzev strain and then repeatedly inoculated by Sofyin, Pan or Absettarov strains on the 8th, 15th and 30th day after virulent strain inoculation, there were neither slowed, nor virulent TBE viruses being determined in CNS and inner organs.

In Macacus rhesus, immunized into head brain (left thalamus) with inactivated vaccine against tick-borne encephalitis or naturally slowed Elantzev strain, there was pericyte proliferation around capillaries and precapillaries with the formation of perivascular ferrule. Cells are located as lines, forming the gathering, clearly confined from the rest of brain tissue. They show clear mitosis pictures. In the structure of perivascular ferrule there are large cells of reticular type with friable cytoplasm, nuclear and pirocytophilic neucleolus as well as the cells of lymph histocytic type, plasmoblasts and “ripe” plasma cells.

Table 8. The results of many day monitoring for virus accumulation in macaques, injected into left thalamus with Elantzev strain (clone 15-20/ 3) TBE virus(in lg LD_{50})

Name of organ, tissue	Day after inoculation										
	3rd			8th			15th			30th	
	Macaque's (test) number										
	11	12	15	16	17	18	41	45	46	47	58
Cerebral cortex	0	1.2	0	0.7	0.5	0	0	0	0	0	0
Subcortical nodes	0	0	0	0	0	0.7	0	0.7	0.7	0	0
The 3rd ventricle	0	0	0	0.7	0.7	0	0	0	0	0	0
Pons	0	0	0	0	0	0	0	0	0.7	0	0
Olives	0.7	0	0.7	0	0.5	0.7	0	0	0.7	0.7	0
Cerebellar cortex	0.7	0	0	0	0	0	0	0	0	0.7	0
Spinal cord	0	0	0	0	0	0	0	0	0	0	0
Cervical	0	0	0	0	0	0	0	0	0	0	0
Pectoral	0	0	0	0	0	0	0	0	0	0	0
Lumbar	0	0	0.7	0	0	0.7	0	0	0	0	0
Liver	0	0	0	0	0	0	0	0	0	0	0
Intestine	0	0	0	0	0	0	0	0.7	0	0	0
Spleen	0	0.7	0	0	0	0	0	0	0	0	0
Lymph node	0	0	0	0	0	0	0	0	0	0	0

Rather similar morphological formations were marked in lymph nodes during the first ten days after extra neural immunization in macaques. We found plasmatic cells of transition type in medullated cords. They are large polygonal cells with pyrononinophilic cytoplasm, oval-shape light nucleus with basophilic neucleolus, appeared as a result of reticular cells transformation. Later monitoring (30 to 54 days after TBE virus inoculation) showed ripe plasmatic cells in cortical and cerebral layers of lymph nodes on the level of plasmoblasts. In some cases the last were bedded abundantly in medullated cords, replacing lymphoid tissue. Free phagocytes were often revealed in follicle sinuses and reactive centers.

So, we showed that immunity morphology in peripheral lymph nodes is similar to one in CNS as a result of perivascular ferrules formation in infection process. This is the basis of the assumption, that perivascular ferrules in CNS play the role of morphofunctional lymph nodes.

Conclusion

We revealed two independent types of immunity formation in neurotropic virus infection: common (extraneural) and off - hematoencephallic barrier (cerebral spinal). Both immunities develop independently only after the penetration of virus or virus antigen into target organs. Common immunity leads to the lowering of reproduction activity of virus virulent populations, but it does not provide its complete elimination in CNS organs. This forms the conditions for virus persistence, leading in some cases to chronic or slow forms of the disease.

Extraneural common immunity, being induced by inactivated vaccine against TBE does not provide reliable blockade against virus virulent populations in extraneural system and does not stop its penetration through hematoencephalitic barrier, which leads to virus persistence in CNS organs and tissues and slows TBE in some cases.

At the same time the immunity, induced with inactivated vaccine, is enough for the blockade of naturally slowed viruses penetration from extraneural system to CNS organs and tissues. On grundimmunity background, created by inactivated vaccine with further introduction of live vaccine, the reliable protection against TBE virus virulent populations is provided. In this connection the necessity to turn to combinatory vaccination appears again, as well as the creation of grundimmunity by inactivated vaccine with final immunization by safe but highly immunogenic live vaccine against TBE, which surely protects from western and eastern genotypes of TBE virus, and TBE complex agents.

References:

1. Pogodina V.V., Frolova M.P., Erman B.A. Chronic tick-borne encephalitis. - Novosibirsk, 1986.- 233 p.

2. Smorodintsev A.A., Dubov A.V. Tick-borne encephalitis and its prevention. - Leningrad: Medicina, 1986. - 231 p.

3. Vorobyova M.S., Rashchepkina M.N. The history of the creation and development of tick-borne encephalitis vaccine production in Russia and abroad// The Far Eastern Journal of Infections Pathology.-2007. - N11. - P.21 - 27.

4. Zlobin V.I. Epidemiological conditions and the problems of tick-borne encephalitis elimination in Russian Federation// Bulletin Sib. Med. - 2006. - V.5. – Suppl.1. - P.16 - 23.

5. Leonova G.N., Pavlenko E.V., Krylova N.V. Tick-borne encephalitis vaccine prophylaxis. - Vladivostok, 2006. - 100 p.

6. Barret P.N., Schoba-Bendixen S., Erlich H.J. History of TBE vaccine // Vaccine 21. -2003. - S1/41-S1/49.

7. Kunz C. TBE vaccination and Austrian experience // Vaccine 21. - 2003 -S1/50-S1/55.

8. Kuimov D.T., Dubov A.V. Amyotrophic lateral sclerosis as a syndrome of tick-borne encephalitis // Jour. for neuropathology and psychiatry - 1958.-№ 3. - P.282 - 287.

9. Shapoval A.N. Tick-borne encephalitis chronic forms. - Leningrad: Medical Science, 1978. - 176 p.

10. Dubov A.V. Immune prophylaxis: common and cerebrospinal immunity// Siberia Medical Journal. - 2004.-№ 2. - V.19. - P.56-57.

11. Dubov A.V. Transbarrier cerebrospinal immunity in tick-borne encephalitis/ The Far Eastern Journal of Infections Pathology.- 2007. – N 11.-P.132.

12. Dubov A.V. Common and cerebrospinal immunity in vaccine process genesis // The proceedings of the conference «The problems of health protection and development in the North and Siberia population. - Krasnoyarsk, 2007. – Edit.6. - P.99 - 100.

13. Timofeev A.V., Karganova J.J. Tick-borne Encephalitis Vaccine: from Past to Future. - M., 2003.

14. Guirs B.K., Grigoryeva L.V., Koshukov S.D., Dubov A.V. Pathomorphological changes in the vessels of the central nerve system of monkeys after intracerebral inoculation of different strains of tick-borne encephalitis.// Trying out experience of the live vaccine against tick-borne encephalitis. - Tyumen, 1971. - P.102-111.

INTERNATIONAL RANKING SYSTEMS FOR UNIVERSITIES AND INSTITUTIONS: A CRITICAL APPRAISAL

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Ranking of universities and institutions has attracted wide attention recently. Several systems have been proposed that attempt to rank academic institutions worldwide.

We review the two most publicly visible ranking systems, the Shanghai Jiao Tong University 'Academic Ranking of World Universities' and the Times Higher Education Supplement 'World University Rankings' and also briefly review other ranking systems that use different criteria. We assess the construct validity for educational and research excellence and the measurement validity of each of the proposed ranking criteria, and try to identify generic challenges in international ranking of universities and institutions.

None of the reviewed criteria for international ranking seems to have very good construct validity for both educational and research excellence, and most don't have very good construct validity even for just one of these two aspects of excellence. Measurement error for many items is also considerable or is not possible to determine due to lack of publication of the relevant data and methodology details. The concordance between the 2006 rankings by Shanghai and Times is modest at best, with only 133 universities shared in their top 200 lists. The examination of the existing international ranking systems suggests that generic challenges include adjustment for institutional size, definition of institutions, implications of average measurements of excellence versus measurements of extremes, adjustments for scientific field, time frame of measurement and allocation of credit for excellence.

Naïve lists of international institutional rankings that do not address these fundamental challenges with transparent methods are misleading and should be abandoned. We make some suggestions on how focused and standardized evaluations of excellence could be improved and placed in proper context.

Background

The evaluation of the performance of universities and institutions is an attractive concept. In theory, objective and accurate evaluations of institutional excellence may help allocate funding rationally, prioritize research and educational investment, inform the public, guide the burgeoning market of candidate students and junior researchers, and help institutions in internal self-evaluation and improvement. International ranking of universities and institutions has received wide attention in the last few years within higher education, administrators, as well as in the broader public. In Google the words *university ranking* return 42700000 hits.

The purpose of the current manuscript is to examine critically the most popularized existing international ranking systems, assess their validity and derive insights for specific issues that need to be addressed, if international ranking of institutions is to be reliable and useful in measuring and promoting excellence. Our appraisal focuses primary (but not exclusively) on the international ranking sys-

tems that have drawn the greatest attention on the web, the Shanghai Jiao Tong University [1] 'Academic Ranking of World Universities' and the Times Higher Education Supplement [2] 'World University Rankings'. We focus on these two ranking systems because they already have a history of producing lists of institutions and they are very popular based on their appearance in web searches. In contrast to this huge public impact, there is still a dearth of peer-reviewed scientific publications on international ranking methods. Raw data and several key details about the methodology still remain unavailable to public scrutiny. We discuss issues of construct validity and measurement validity for each of the items that have been proposed as components of excellence in the ranking process. Finally, we use this information to make a list of the generic challenges that need to be met in international rankings of institutional excellence.

Methods *Sources of data*

We focus on systems that use explicit criteria to rank universities around the world in terms of excellence, regardless of whether other institutions (e.g. non-university research institutes) are also ranked or not. The information for the discussed ranking systems is obtained from perusal of their web sites [1,2] and any associated peer-reviewed publications. We performed a search of PubMed and the Web of Science (search term 'university* AND ranking*', last search December 2006) that showed that of the two most popularized international ranking systems, only one has been described in the peer-reviewed literature [3,4] and this was only after it had already received fierce criticism [5]. No other international ranking systems have had their methods described in peerreviewed publications as of December 2006, but we also consider briefly other systems that use different criteria, based on their web description. The concordance between the two main ranking systems was evaluated in terms of their agreement for the top 200 universities based on their publicized 2006 rankings.

Validity assessment methods and generic issues

We assessed each of the proposed criteria for excellence in terms of construct validity and measurement validity. Construct validity refers to whether an indicator measures what it is intended to measure (i.e. excellence). We considered separately excellence in education and excellence in research. Other parameters of excellence may also matter (e.g. societal contribution, provision of healthcare), but may be even more difficult to measure. Measurement validity refers to the errors that may ensue in the measurement process.

Literature searches in the Web of Science were made focused on specific criteria to try to identify evidence that would be pertinent to the construct and measurement validity of each item. For research indicators, we used the databases of the Thomson ISI Web of Knowledge (as of December 2006), including the Web of Science, Essential Science Indicators, ISI Highly Cited, and Journal Citation Reports. Information on affiliation of Nobel Prize winners and authors of the most-cited papers was derived from the Nobel Prize website with perusal of the listed curricula vitae and autobiographies [6] and the perusal of the recent publication record in the Web of Science, respectively.

For the rating of validity for each item/criterion, we used a 4-point rating scale (poor, low/modest, good, very good) for all items. Poor means that the specific criterion is unlikely to be useful as a valid measure of excellence. Low/modest means that the specific criterion has some correlation with excellence, but this is either weak or very indirect. Good means that the specific criterion has considerable potential for capturing excellence. Very

good means that the specific criterion has a strong potential for capturing excellence. We used a consensus approach for rating with iterative discussion among the authors (led by JPAI) after the evidence on the validity of each criterion had been collected and shared.

Based on the experience obtained from scrutinizing the proposed criteria and the evidence regarding their construct and measurement validity, we generated, through discussion among the authors, a list of generic issues that should be addressed in current or future efforts to rank institutions for excellence internationally.

Results

Description and validity of existing international rankings

Brief description of Shanghai and Times rankings The Shanghai ranking [1] uses a weighted composite sum. Shanghai appraises education and faculty based on Nobel- and Fields-winning alumni/faculty and highly-cited researchers. It measures research by counting non-review articles in *Nature* and *Science*, and the total number of published articles. Also, a weighted average of these indicators is adjusted for institutional size and contributes 10% to the final sum.

The Times ranking [2] is also a composite system. The ranking assigns much weight (40% of total) to an expert opinion survey. Additional components address the rating from graduate recruiters, recruitment of international faculty, the enrollment of international students, the student to faculty ratio, and total citation counts.

Validity of Shanghai ranking

Nobel and Fields awards clearly measure research excellence, even if they don't cover all fields. However, it is unclear why universities with Nobel- or Fields-winning alumni are those that provide the best education. As for faculty, Nobel- and Fields-winners typically have performed their groundbreaking work elsewhere. We found that of 22 Nobel Prize winners in Medicine/Physiology in 1997–2006, only seven did their award-winning work at the institution they were affiliated with when they received the award (Table 1). Therefore, this measurement addresses the ability of institutions to attract prestigious awardees rather than being the site where groundbreaking work is performed. Finally, the vast majority of institutions have no such awardees. Thus, such criteria can rank only a few institutions.

The determination of scientists with the highest impact has also good construct validity for research excellence, but highly-cited status has some measurement problems. It is based on a database [7] that counts raw citations. Ten citations in a single-authored paper or in a paper as, for example, 342nd author from 865 others, counts as the same [8]. There is no widely accepted alternative on how to adjust citation indices for the number of co-authors; weighting the exact contribution of an author in a paper remains elusive. The database also tries (appropriately so) to separate scientific fields, but this is unavoidably imperfect. Scientists with more multidisciplinary work have more difficulty passing the highly-cited threshold in any one field. Within the same field, scientists in sub-fields with higher citation densities have an advantage. For example, all 'Clinical Medicine' (including 1790 journals and over 1500000 author names in the last decade) [9] is treated as a single field. Approximately 250 scientists are selected per field regardless of the denominator (all authors), but there are 21 times more author names in 'Clinical Medicine' than in 'Space Science' [9]. Finally, highly-cited status is based on two decades of citations (1981–1999), a distant surrogate of current work [10]. We found that among the corresponding authors of the 10 most-cited articles published as recently as 1996–1999 and 2000–2003, 5/10

and 2/10, respectively, had changed institutions or were deceased by 2006 (Table 2) [9].

Counting the names and affiliations of authors in each non-review paper in *Nature* and *Science* is easy and carries negligible measurement error. Construct validity is more problematic. Overall, these two journals publish 22% of the most-cited articles across all scientific fields, but this varies from 54% in 'Immunology' to less than 7% in eight of a total of 21 scientific fields [11]. Moreover, reviews are often more-cited than any 'original' article [12,13] and their exclusion may not be justified.

Finally, the number of articles is influenced by the database used, and says nothing about their impact [14]. Rewarding the publication of more papers regardless of impact may end up reinforcing bulk science, salami publication and least publishable unit practices [15,16].

Table 1. Nobel winners in Medicine/Physiology for 1997–2006: affiliation at the time they did the award-winning work and at the time they were given the Nobel Prize

Name	Year	Affiliation (Nobel work)	Affiliation (Nobel award)
Fire AZ	2006	Carnegie Institute, Washington	Stanford University
Mello CC	2006	University of Massachusetts	Same
Marshall BJ	2005	Royal Perth Hospital, Australia	University of Western Australia, Nedlands
Warren JR	2005	Royal Perth Hospital, Australia	Perth, Australia (private address)
Axel R	2004	Columbia University	Same
Buck LB	2004	Columbia University	Fred Hutchinson Cancer Research Center
Lauterbur PC	2003	SUNY Stony Brook	University of Illinois
Mansfield P	2003	University of Nottingham	Same
Brenner S	2002	MRC Molecular Biology Unit, Cambridge	Molecular Science Institute, Berkeley
Horvitz HR	2002	Cambridge University	MIT
Sulston JE	2002	MRC Molecular Biology Unit, Cambridge	Sanger Institute, Cambridge
Hartwell LH	2001	Cal Tech	Fred Hutchinson Cancer Research Center
Hunt RT	2001	Cambridge University	Imperial Cancer Research Fund, London
Nurse PM	2001	University of Edinburgh	Imperial Cancer Research Fund, London
Carlsson A	2000	University of Lund	Göteborg University
Greengard P	2000	Yale University	Rockefeller University
Kandel ER	2000	Columbia University	Same
Blobel G	1999	Rockefeller University	Same
Furchgott RF	1998	SUNY, Brooklyn	Same
Ignarro LJ	1998	Tulane University	UCLA
Murad F	1998	University of Virginia	University of Texas
Prusiner SB	1997	UCSF	Same

Validity of Times ranking

If properly performed, most scientists would consider peer review to have very good construct validity; many may even consider it the gold standard for appraising excellence. However, even peers need some standardized input data to peer review. The Times simply asks each expert to list the 30 universities they regard as top institutions of their area without offering input data on any performance indicators. Research products may occasionally be more visible to outsiders, but it is unlikely that any expert possesses a global view of the inner workings of teaching at institutions worldwide. Moreover, the expert selection process of The Times is entirely unclear. The survey response rate among the selected experts was only <1% in 2006 (1600 of 190000 contacted). In the absence of any guarantee for protection from selection biases, measurement validity can be very problematic. The opinion of graduate recruiters probably has poor construct validity for academic excellence, while it does measure the market impact of education; measurements are provided by a sample of 736

recruiters with undisclosed response rate and selection process.

Table 2. Corresponding authors of the 10 most-cited papers published in 1996–1999 and the 10 most-cited papers published in 2000–2003 (citations as of end of 2006)

Name	Year	Affiliation (most-cited paper)	Current affiliation
Altschul SF	1997	NLM/NCBI	Same
Otwinowski Z	1997	University of Texas	Same
Brunger AT	1998	Yale University	Stanford University
Jeanmougin F	1997	IGBMC, INSERM	No publications 1998-present day
Ross R	1999	University of Washington	Deceased
Perdew JP	1996	Tulane University	Same
Banchereau J	1998	Baylor Research Institute	Baylor Institute for Immunology Research*
Kalnay E	1996	NCEP	University of Maryland
Posada D	1998	Brigham Young University	University of Vigo
Botstein D	1998	Stanford University	Same
Lander ES	2001	Whitehead Institute for Biomedical Research	MIT**
Berman HM	2000	Rutgers University	Same
Cleerman JI	2001	NHLBI	Same
Venter JC	2001	Celera Genomics	J Craig Venter Institute
Hanahan D	2000	UCSF	Same
Roussouw JE	2002	NHLBI	Same
Spek AL	2003	University of Utrecht	Same
Spergel DN	2003	Princeton University	Same
Tuschl T	2001	Max Planck Institute	University of Basel/ Rockefeller University
Kumar S	2001	Arizona State University	Same

*No change in affiliation; change in the name of the same institution. **No change in affiliations, but change in preference for which affiliation is listed more prominently in Essential Science Indicators records.

The international character of an institution is an interesting aspect, but its construct validity for determining excellence is unknown. International character probably reflects resource, administrative and legislation issues. Institutions offering competitive packages may recruit more international faculty from those with limited resources. International faculty and student enrollment may also be dictated largely by local or national regulations (e.g. allowed teaching languages). Enrollment of students from foreign countries in particular may often reflect the tuition system or the wealth of recruited international students (e.g. if foreigners pay higher fees) rather than true diversity, let alone excellence. In general, student applications and recruitment are determined by a complex array of factors that only distally reflect excellence [17], and sometimes they may be negatively correlated with excellence in research (e.g. at least one study in Canada has found that high research output of a university discourages student applications [18]). The optimal student to faculty ratio is difficult to generalize across different disciplines and settings. Finally, the quality of the measurements for such international data is also not transparent.

The total number of citations has much better construct validity for addressing scientific impact than total number of papers. Even though citations are not always reflective of approval of a scientific work, they do reflect its contribution to scientific debate. However, one should carefully adjust for scientific field. Moreover, differences across citation databases, errors in automated citation counts [19], self-citation, different citation rates across scientific fields [14], and non-standardized handling of group authorshi papers [20], pose some measurement error limitations Using citation databases requires careful cleaning of th raw data and there is no hint that Times undertakes an such cleaning.

Agreement in international rankings

In 206, the Shanghai and Times lists shared only 133 uni versities among their top 200s. Some discrepancies ar notorious (Figure 1): four of the top 50 on the Shangha list did not even make the top 500 of the Times list, an several top Times choices disappeared on the Shangha list (Table 3). Some of the discrepancies reflect the fac that The Times does not consider institutions that have n undergraduate education (e.g. UCSF and Rockefeller) However, discrepancies extend well beyond this differ ence (Table 3).

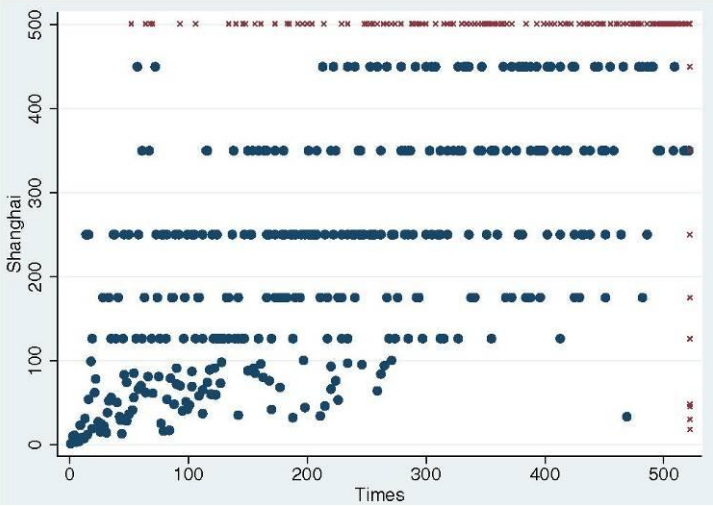

Figure 1. Correlation between Shanghai and Times ranking systems.
Data are considered for the top 500 universities in the Shanghai and Times systems. Cross marks denote universities ranked outside illustrated rank positions in either system. Note that for Shanghai it is common for several universities to have the same aggregate score and thus share the same rank (the median value of the span of ranks involved).

As both systems claim to measure institu tional excellence (even with different indicators), the lac of better concordance is disquieting.

Other options

A brief discussion of some other rankings may offer addi tional insights. Some ranking systems evaluate institu tional web presence [21]. However, web connectivity doe not necessarily reflect educational or research excellence and it is search-engine dependent. Moreover, any effort t appraise the relevance, quality, source, or purpose of we links is difficult. At best, cyber-presence is an experimenta ranking method.

Table 3: Examples of marked discrepancies in Shanghai vs Times rankings

Institution	Rank
Institutions in the top 70 of the Shanghai list not making the top 500 of the Times list	
University of California San Francisco	Shanghai rank = 18
Rockefeller University	Shanghai rank = 30
Universite Paris 06	Shanghai rank = 45
Karolinska Institutet	Shanghai rank = 48
Institutions in the top 70 of the Times list not making the top 500 of the Shanghai list	
Fondation des Sciences Politiques	Times rank = 52
Ecole Polytech Fed Lausanne	Times rank = 64
Indian Institutes of Management	Times rank = 68
School of Oriental and African Studies	Times rank = 70

Institutions are also ranked on research funding. This is more popular for national-level rankings, e.g. in Canada 'RESEARCH Infosource' publicizes a list whose highlight is 'The $100 Million Club' [22]. Comparisons of institutions in countries with different opportunities are unfair and different disciplines attract very

different funding [23]. Even within the same country, high funding could actually signal low quality, if not accompanied by proportional achievements. A fundamental question is whether funding is a means to a goal or the goal itself. In addition, attribution of funding entails decisions on whether funding to affiliated hospitals or research institutes should be attributed to the main institution/university, whether all sources of funding should count or just competitive sources, and how to count collaborative multi-institutional grants.

Hybrid systems have also emerged. Newsweek [24] published its own set, largely amalgamating the Times and Shanghai rankings. Such high-visibility hybrids prove the attractiveness of ranking exercises, but also their glaring sloppiness. Table 4 summarizes the extent of problems in construct and measurement validity for various components of the systems discussed above.

Generic issues in institutional rankings

Adjustment for size

Most of the ranking indicators discussed above depend on institution size. Larger institutions may have more papers, citations, award-winning scientists, students, web-links and funding. Size plays a minor role in the calculations used for the Shanghai and Times lists. For the Shanghai list, 10% of the weight addresses institutional size. For the Times list, only citations are adjusted for faculty numbers.

Normalization is potentially conceivable for analyses at the country level [25], where adjustments can be made for population or wealth indices that are well standardized internationally. Conversely, there are no internationally standardized data on 'size' of institutions. It is unknown how exactly the Shanghai and Times lists make adjustments (raw data are not publicly available).

Table 4. Construct validity for excellence and measurement validity of discussed ranking systems

	Construct validity for excellence		Measurement validity
	Research	Education	
Shanghai			
Alumni, Nobel/Fields	-	-	++
Faculty, Nobel/Fields	+++	+	++
Faculty, highly-cited	++	+	+
Nature/Science articles	++	-	+++
Number of articles	-	-	+
Size	-	-	-
Times			
Peer opinion	+++	+++	-
Graduate recruiter opinion	-	+	-
International faculty	+	+	?
International students	-	+	?
Student-faculty ratio	-	+	?
Citations per faculty	++	-	+
Other rankings			
Web presence	+	+	+
Funding	+	-	+

-, Poor; +, low/modest; ++, good; +++, very good; ?, unknown (insufficient detail provided on the reliability of databases).

Even if one assembles faculty quotas worldwide, definitions differ. Definitions vary even across schools in the same university. Harvard lists 10674 medical faculty staff, but only 2497 faculty staff for all other schools combined [26]. Comparisons across institutions in different countries are tenuous. Finally, excellence is not necessarily linearly proportional to number of faculty, but may be also affected by availability of support staff and infrastructure. Redundancy, attainment of critical mass and multiplicative effects of collaboration are difficult to model.

Defining the institutions

Definition of the institutions to be ranked is not always straightforward. The size and nature (types of scientific fields included and their relative representation) of an institution varies depending on whether it is split or not to subunits and affiliates. For example, the University of California or the University of Illinois comprise many campuses each, and there are a large number of Max Planck Institutes. For medicine in particular, hospitals are the main components of a university, but not all hospital work originates from university faculties. Merging (or not) hospitals with their universities unavoidably changes rankings. The same applies to affiliated research institutes and spin-offs.

Averages and extremes

Any institution is a conglomerate of schools, departments, teams, and single scientists working in very different fields. An aggregate ranking may not do justice to the constituent parts. This is a form of the well-known ecological fallacy: the average misrepresents its components. If an institution is comprised of two departments with grades of 10/10 and 0/10, the average (5/10) grossly misrepresents both departments.

Some indices measure either the overall performance (e.g. number of papers or citations – either total or average per faculty), while others focus on the extremes of the distribution (e.g. Nobel winners, highly-cited researchers, top 1% most-cited papers). Both types of information may be useful, depending on what we want to know. Finally, the description of extremes may need to consider not only the best extremes, but also the worst extremes (e.g. researchers convicted of fraud, faculties with no or minimal citations, uncited papers).

None of the existing international ranking systems aims at quantifying the intra-institutional diversity in performance. This is a loss of significant information that would be more helpful in providing constructive feedback to institutions. Diversity becomes even larger when we consider between-scientist variability within the same institution.

Adjustment for field

Many indices depend on the scientific field. For example, according to the Thomson ISI classification of fields (n = 21) [9], 'Clinical Medicine' journals publish 20 times more papers that cumulatively receive 50 times more citations than 'Economics/Business' journals [9]. Only 0.15% of papers in 'Mathematics' receive over 100 citations within a decade from their publication, while this happens to 10% of papers in 'Molecular Biology' [9].

The Shanghai list recently developed a system for separate rankings in each of five fields [1]. This highlights the problems with superficial field adjustments. Grouping is arbitrary: Natural Sciences and Mathematics, Engineering/ Technology and Computer Sciences, Life and Agricultural sciences, Clinical Medicine and Pharmacy, and Social Sciences; Arts and Humanities and Psychology/Psychiatry are excluded. Ranking criteria are similar to the overall ranking, with some modifications, e.g. consideration of number of articles in 'top' high-impact journals per field, instead of articles in *Nature*/*Science*. 'Top' journals are determined based on impact factors, but

these are not comparable across the many disciplines amalgamated into the five larger fields. For example, the discipline of 'Agriculture, Soil Science' (highest journal impact factor 2.414) is merged into the same large field as 'Immunology' (highest journal impact factor 47.400) [9]. Moreover, the distribution of citations for articles in any journal is left-skewed, with 20% of the articles taking 80% of the citations, so impact factor is a modest correlate of specific article impact [27].

How many scientific fields are there? Each of the 21 fields of Thomson ISI [9] includes many sub-fields that are occasionally quite different among themselves. Other classifications get somehow different results. Based on citation network analyses, W Bradford Paley and colleagues recently described 23 main fields that contain 776 different scientific discipline nodes [28]. Even once we agree on how to split fields, there is still no consensus on how exactly to adjust for field in conglomerate appraisals of complex institutions.

Furthermore, in existing conglomerate rankings, institutions focusing in only one or a few fields only are under-ranked, even though this focus may be inherent in their mission. Finally, some indicators are rather meaningless for select fields (e.g. number of journal publications or journal citations for arts and humanities).

Measurement time frame

Many useful indices, such as citation impact, require a time distance to be determined. As we discussed above, if this time distance is long, the measurement may be largely irrelevant to the current status of an institution. This is probably less of a concern for very large institutions with long traditions. The recruitment or loss of a few influential scientists or teams will not change their overall picture much. Mathematical sociology simulations show that large groups persist for longer, if they are capable of dynamically altering their membership, while smaller groups thrive when their composition remains unchanged [29]. For the majority of smaller institutions, modest changes may have a major impact over time.

Credit allocation

The time frame is one of the parameters influencing what institution should get credit for what. As we showed above, credit allocation for prestigious award winners and influential scientists depends on whether we focus on where they did their work vs where they work currently. Another major issue is how to assign credit for tasks that require collaboration between multiple scientists and institutions. For example, among two equally-cited papers, a paper authored by investigators in 100 institutions counts 100 times more in the Times calculations than a paper from a single institution. There is no consensus on whether this imbalance should be corrected and, if so, how. Credit allocation is also be influenced by institutional definition (discussed above).

Table 5 summarizes the extent of problems arising from issues of average vs extremes focus, field adjustment, measurement time frame and credit allocation in Shanghai and Times.

Discussion

Current international rankings reflect a naive wish to summarize in a convenient way processes that are very interesting to study, but also extremely complex. Excellence is important to define, measure, interpret and improve. However, wrong appraisals may lead to inappropriate characterizations and corrective actions. The serious limitations of these exercises should be recognized. Current international rankings seem too poor to carry serious scientific credibility.

As ranking exercises acquire influence for funding, institutions and scientists may seek to excel in the specific criteria requested for excellence. The exist-

ing ranking criteria could actually harm science and education. For the Shanghai list, most institutions will be unable to attract more Nobel and Fields awards or top highly-cited scientists or even increase their presence in *Nature* and *Science*, while inflating publication numbers with junk science is easy. For the Times list, some of the 'international character' criteria would encourage global brain drain [30]. All criteria that fail to properly adjust for institutional size favor the creation of mega-size universities with unknown consequences. Large centers of excellence may accelerate some research with the accumulation of global talent, but may drain academic institutions where they are more badly needed as vehicles for social improvement and innovation [31].

Some of the same problems exist even for country-level appraisals [32], but measurement problems are more manageable. Detailed discussion of national evaluation systems is beyond our intention. Nevertheless, for some countries, evaluation agencies accumulate relatively standardized, clean information and some also use adjustments – with the caveats discussed above. Still, several popular national ranking systems have major impact despite clearly spurious methods. One example is US News and World Reports, whose highly visible rankings have been criticized repeatedly [33-36]. Even national systems with more careful methods and meticulous (even burdensome) data collection have been attacked [18,36].

Table 5. Focus on extremes of excellence vs averages, appropriate field adjustment, time frame of measurement and credit allocation problems of Shanghai and Times ranking systems

	Focus*	Field adjustment	Time frame of measurement	Credit allocation
Shanghai				
Alumni, Nobel/Fields	Very extreme excellence	Not all fields represented	Typically very remote	Problematic
Faculty, Nobel/Fields	Very extreme excellence	Not all fields represented	Typically remote	Problematic
Faculty, highly-cited	Extreme excellence	To some extent	Remote (1981–1999)	Problematic
Nature/Science articles	Extreme excellence	Uneven per field	Recent (last 5 years)	Reasonable***
Number of articles	Average excellence	None	Very recent (last year)	Reasonable***
Size	Not applicable**	None	Sources unclear	Straightforward
Times				
Peer opinion	Varies per expert	To some extent	Varies per expert	Varies per expert
Recruiter opinion	Not applicable**	None	Varies per recruiter	Varies per recruiter
International faculty	Not applicable**	None	Sources unclear	Straightforward
International students	Not applicable**	None	Sources unclear	Straightforward
Student-faculty ratio	Not applicable**	None	Sources unclear	Straightforward
Citations per faculty	Average excellence	None	Recent (last 5 years)	Reasonable***

*Whether excellence is appraised based on the extremes or the average of the distribution of performance.

**Indicators pertain to the whole institution, so they are average indicators, but as per Table 4 they are unlikely to be more than low/modest indicators of excellence.

***Decisions need to be made regarding allocation of credit for multi-authored papers, variable credit according to authorship position etc

Conclusion

Despite the failure of current international ranking systems, reliable information on specific performance indices may be useful, if properly analyzed and interpreted. In general, validity may decrease as we move from appraising single scientists, to appraising teams, departments, schools, and whole institutions, and problems are maxi mized when we cross national boundaries.

Therefore, we think that focused appraisals of single scientists and teams should take precedence over overarching appraisals of institutions. For international institutional appraisals, information can be improved by global collaboration to standardize data on key aspects of universities and other institutions. However, remaining deficits in the quality and unavoidable inconsistencies in the definitions of the collected information should be transparently admitted and their possible impact should not be underestimated. Evaluation exercises should aim at describing accurately the existing diversity rather than force spurious averages and oversimplified rankings. All performance indices should be interpreted strictly for what they stand. Finally, as probably no measurement has perfect construct validity for the many faces of excellence, efforts to improve institutions should not focus just on the numbers being watched.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

The original idea was generated by JPAI. All authors discussed the concepts involved and the protocol for evaluations and analyses and all authors collected data. JPAI wrote the first draft of the manuscript and all authors reviewed it critically. All authors have approved the submitted version.

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References:

1. Academic Ranking of World Universities – 2006 [http:// ed.sjtu.edu.cn/ranking.htm]
2. Education news & resources at the Times Higher Education Supplement [http:// www. thes. co.uk/worldrankings/]
3. Cheng Y, Liu NC: A first approach to the classification of the top 500 world universities by their disciplinary characteristics using scientometrics. Scientometrics 2006, 68:135-150.
4. Liu NC, Cheng Y, Liu L: Academic ranking of world universities using scientometrics – a comment to the "Fatal Attraction". Scientometrics 2005, 64:101-109.
5. Van Raan AFJ: Fatal attraction: conceptual and methodological problems in the ranking of universities by bibliometric methods. Scientometrics 2005, 62:133-43.
6. Nobel Prizes [http://nobelprize.org/nobel_prizes/lists/all/]
7. ISI highlycited.com [http://isihighlycited.com]
8. Slone RM: Coauthors' contributions to major papers published in the AJR: frequency of undeserved coauthorship. AJR Am J Roentgenol 1996, 167:571-9.
9. Thomson Scientific Essential Science Indicators module, Web of Knowledge [http://portal.isiknowledge.com.ezproxy.library.tufts.edu/portal.cgi?DestApp=ESI&Func=Frame]. (available with subscription).
10. Van Raan AFJ: Comparison of the Hirsch-index with standard bibliometric indicators and with peer judgment for 147 chemistry research groups. Scientometrics 2006, 67:491-502.
11. Ioannidis JP: Concentration of the most-cited papers in the scientific literature: analysis of journal ecosystems. PLoS One 2006, 1:e5. doi:10.1371/journal.pone.0000005.
12. Patsopoulos NA, Analatos AA, Ioannidis JP: Relative citation impact of various study designs in the health sciences. JAMA 2005, 293:2362-6.
13. Bhandari M, Swiontkowski MF, Einhorn TA, Tornetta P 3rd, Sche-mitsch EH, et al.: Interobserver agreement in the application of levels of evidence to scientific papers in the American volume of the Journal of Bone and Joint Surgery. J Bone Joint Surg Am 2004, 86-A:1012-6.
14. Garfield E: The history and meaning of the journal impact factor. JAMA 2006, 295:90-3.
15. Schein M, Paladugu R: Redundant surgical publications: tip of the iceberg? Surgery 2001, 129:655-61.
16. Kostoff RN, Johnson D, Rio JA, Bloomfield LA, Shlesinger MF, et al.:Duplicate publication and 'paper inflation' in the Fractals literature. Sci Eng Ethics 2006, 12:543-54.
17. Heller DE: Student price response in higher education – An update to Leslie and Brinkman. J Higher Educ 1997, 68:624.
18. Drewes T, Michael C: How do students choose a university? An analysis of applications to universities in Ontario, Canada. Res Higher Educ 2006, 47:781-800.
19. Tomlinson S: The research assessment exercise and medical research. BMJ 2000, 320:636-9.
20. Dickersin K, Scherer R, Suci ES, Gil-

Montero M: Problems with indexing and citation of articles with group authorship. JAMA 2002, 287:2772-4.

21. World Universities' ranking on the Web [http://www.webo metrics.info]

22. Research infosources [http:// www. researchinfosource.com]

23. Giles J: Plan to rank universities fails to impress. Nature 2006, 441:917.

24. The Top 100 Global Universities (Newsweek: International Editions – MSNBC.com) [http://www.msnbc.msn.com/id/ 14321230]

25. King DA: The scientific impact of nations. Nature 2004, 430:311-6.

26. Harvard at a glance [http:// www. news. harvard.edu/glance/]

27. Garfield E: Citation Indexing : Its Theory and Application in Science, Technology and Humanities Philadelphia: ISI Press; 1979.

28. Map of Science [http:// wbpaley. com/ brad/mapOfScience/ index.html]

29. Palla G, Barabasi AL, Vicsek T: Quantifying social group evolution. Nature 2007, 446:664-7.

30. Ioannidis JP: Global estimates of high-level brain drain and deficit. FASEB J 2004, 18:936-9.

31. Ioannidis JP, Ahmed T, Awasthi S, Clarfield AM, Clark J, et al.: Open letter to the leader of academic medicine. BMJ 2007, 334:191-3.

32. Dill DD, Soo M: Academic quality, league tables, and public policy: A cross-national analysis of university ranking sys-terns. Higher Educ 2005, 49:495-533.

33. Green RG, Baskind FR, Fassler A, Jordan A: The validity of the 2004 U.S. News & World Report's rankings of schools of social work. Soc Work 2006, 51:135-45.

34. McGaghie WC, Thompson JA: America's best medical schools: a critique of the U.S. News & World Report rankings. Acad Med 2001, 76:985-92.

35. Butler D: Academics strike back at spurious rankings. Nature 2007, 447:514-5.

36. Banatvala J, Bell P, Symonds M: The Research Assessment Exercise is bad for UK medicine. Lancet 2005, 365:458-60.

A META-ANALYSIS OF N-ACETYLCYSTEINE IN CONTRAST-INDUCED NEPHROTOXICITY: UNSUPERVISED CLUSTERING TO RESOLVE HETEROGENEITY

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Meta-analyses of N-acetylcysteine (NAC) for preventing contrast-induced nephrotoxicity (CIN) have led to disparate conclusions. Here we examine and attempt to resolve the heterogeneity evident among these trials.
Two reviewers independently extracted and graded the data. Limiting studies to randomized, controlled trials with adequate outcome data yielded 22 reports with 2746 patients.
Significant heterogeneity was detected among these trials (I^2 = 37%; p = 0.04). Meta-regression analysis failed to identify significant sources of heterogeneity. A modified L'Abbé plot that substituted groupwise changes in serum creatinine for nephrotoxicity rates, followed by model-based, unsupervised clustering resolved trials into two distinct, significantly different ($p < 0.0001$) and homogeneous populations (I^2 = 0 and $p > 0.5$, for both). Cluster 1 studies (n = 18; 2445 patients) showed no benefit (relative risk (RR) = 0.87; 95% confidence interval (CI) 0.68–1.12, p = 0.28), while cluster 2 studies (n = 4; 301 patients) indicated that NAC was highly beneficial (RR = 0.15; 95% CI 0.07–0.33, $p <$ 0.0001). Benefit in cluster 2 was unexpectedly associated with NAC-induced decreases in creatinine from baseline (p = 0.07). Cluster 2 studies were relatively early, small and of lower quality compared with cluster 1 studies (p = 0.01 for the three factors combined). Dialysis use across all studies (five control, eight treatment; p = 0.42) did not suggest that NAC is beneficial.
This meta-analysis does not support the efficacy of NAC to prevent CIN.

Background

Since its development, meta-analysis has become a powerful tool for informing clinical practice. Performed correctly, meta-analysis is superior to a purely narrative approach of summarizing medical research. As such, robust conclusions may sometimes be reached from serial, otherwise underpowered small studies [1,2]. Nonetheless, there are substantial limitations and pitfalls in meta-analysis. Publication bias, reliance on subjective summary results rather than individual patient data and the mishandling of important heterogeneity can all lead to erroneous conclusions [1-8]. This possibility is underscored by the occasional lack of concordance between meta-analyses and subsequent large randomized, controlled trials [3,9].

Over the past decade, the efficacy of N-acetylcysteine (NAC) for preventing contrast-induced nephrotoxicity (CIN) has been explored in more than 60 clinical studies [10-71], 12 meta-analyses [72-83] and two comprehensive analyses of published meta-analyses [84,85]. Of the meta-analyses, some declared that NAC is beneficial [72-78] while others determined that the data are inconclusive [79-83]. Significant heterogeneity was detected in all of the meta-analyses that specifically tested for it and meta-regression and other approaches have failed to resolve or pinpoint the cause of the heterogeneity. This much-studied example, where meta-analysis may have increased rather than decreased clinical ambiguity, provides an opportunity to better understand and dissect complex heterogeneity problems in meta-analysis.

We assembled a meta-analysis of NAC efficacy in preventing CIN. Like previous attempts, we encountered significant heterogeneity that was not explained using a comprehensive meta-regression approach. A modified L'Abbé plot [86] followed by the application of a model-based, unsupervised clustering algorithm [87] resolved the trials into two significantly different populations. Clinical practices aimed at preventing CIN are discussed and recommendations are made regarding future trials of NAC.

Methods

This meta-analysis was completed in accordance with the Quality of Reporting of Meta-analyses (QUOROM) statement [2].

Literature search

We searched MEDLINE (PubMed and Dialog), EMBASE, International Pharmaceutical Abstracts, Derwent Drug File, Adis R&D Insight, Adis Clinical Trials Insight, Biological Abstracts and CINAHL (OVID), the Web of Science and The Cochrane Library. Searches included: controlled vocabulary for acetylcysteine, contrast media/adverse, toxic and poisoning effects; free text for acetylcysteine and contrast; and MeSH terms acetylcysteine and contrast media. Retrieved records from the Cochrane CENTRAL file were re-checked in Web of Science to identify subsequent publications. Search dates were from the inception of the databases until September 30, 2004. Conference proceedings from the American Society of Nephrology, National Kidney Foundation, American Heart Association, American College of Cardiology, Society of Interven-tional Radiology, Radiologic Society of North America and International Society of Nephrology were also reviewed over the past five years. There were no restrictions on language or publication status. Over 450 citations and abstracts were screened by two authors to assemble a preliminary set of possibly relevant reports. New publications after September 30, 2004 were periodically monitored using the same search criteria up to March 1, 2007.

Selection criteria

Studies were limited to prospective, randomized, controlled trials (PRCTs) investigating the efficacy of NAC in preventing CIN. Trials with confounded, non-concurrent or otherwise improperly constructed control groups were prospectively excluded from further analysis. Outcome data were solicited from the authors if not found in the publication. Trials that still lacked outcome data necessary for planned analyses were excluded.

Quality assessment, data retrieval and clinical endpoints

Two of the authors evaluated each trial using the Jadad scoring device, under unmasked conditions [88]. Each PRCT included in the analysis scored at least 1 on the five-point scale, with higher scores indicating greater trial quality. Data were extracted independently into a standardized form. Results were compared and disagreements were resolved by discussion. The primary outcome measures were the development of CIN as defined in the studies [10-31] and change in creatinine (ΔCre). The occurrence of acute kidney injury requiring dialysis was recorded. When not reported in the publication, we contacted the authors for post-contrast dialysis information.

Meta-analysis and heterogeneity testing

Treatment effects were quantified by relative risk (RR) using a random-effects model (Comprehensive Meta-Analysis, Biostat Inc, Englewood, NJ). Statistical heterogeneity was assessed by means of a Mantel-Haenszel derived Cochran's Q statistic and associated I^2 value. Cochran's Q is used to test the null hypothesis that all treatment effects are equivalent [89]. Calculated from the Q-statistic and degrees of freedom, I^2 repre-

sents the proportion of treatment effect variation owing to trial heterogeneity, rather than simple sampling error [4,89,90]. Statistical heterogeneity is present when this variation in results exceeds the amount expected from chance alone. The quantitative pooling of such studies may lead to erroneous conclusions [4].

Publication bias and meta-regression analysis

Evidence of publication bias was formally tested using multiple methods including those of Begg and Mazumdar [6], Egger *et al*. [5] and Higgins and Thompson [4]. Standard meta-regressions of the effect size expressed as log RR were performed against trial factors including publication date, size and Jadad score. Well-known patient-related risk factors associated with increased rates of CIN were also evaluated by meta-regression including mean age, diabetes mellitus (%), gender (% female), mean contrast volume and mean baseline creatinine concentration [91-94]. Likewise, total NAC dose was examined for its relationship with outcome. A separate meta-regression examined the log odds of developing CIN in the treatment *versus* the control groups. This was used to detect whether NAC efficacy was affected by the rate of CIN in the control population [95,96]. All meta-regressions were weighted by the inverse variance of each study.

Jackknife-k *sensitivity analysis, modified L'Abbé plot and unsupervised clustering: detection of trial subpopulations*

A sensitivity analysis for heterogeneity was completed by means of a jackknife-*k* [97] procedure in order to detect studies that contributed most to heterogeneity. A pre-specified *p*-value greater than 0.2 for Cochran's *Q* statistic and an I^2 of less than 10% indicated homogeneity. Every possible one-, two- and three-study combination was removed.

The method of L'Abbé *et al*. [86] was used to visualize heterogeneity in our set of trials. As originally described, the L'Abbé plot graphs the control group outcome rate along the *x*-axis and the treatment group outcome rate along the *y*-axis for each trial. To correct for differences in the definition of CIN across studies, we modified the L'Abbé plot by substituting ΔCre, a continuous variable, for the CIN rate. Compared with a standard L'Abbé plot (data not shown), the modified plot was similar, but was better at separating studies that were low and high contributors to heterogeneity.

We then analyzed our modified L'Abbé plot using an unsupervised, model-based clustering method that creates a best-fit Gaussian model and finds the number of clusters that maximize the Bayesian information criterion. All members of the data set are then classified using iterative expectation-maximization methods and group membership likelihoods are calculated [87]. The study and patient characteristics of each cluster were then compared using Wilcoxon rank sum tests. The decomposed Breslow-Day test was used to determine whether the identified clusters had significantly different treatment effects.

Results *Trial flow*

The literature search identified 45 clinical studies investigating NAC to prevent CIN (Figure 1). Ten studies were retrospective [32-41]. Three studies were prospective but not randomized [42-44]. Five studies were removed owing to a lack of placebo controls [45-49]. Three studies were excluded because CIN was not clearly defined [50-52]. One abstract was excluded because discrepant outcome results reported in the abstract and a subsequent meta-analysis could not be resolved [53].

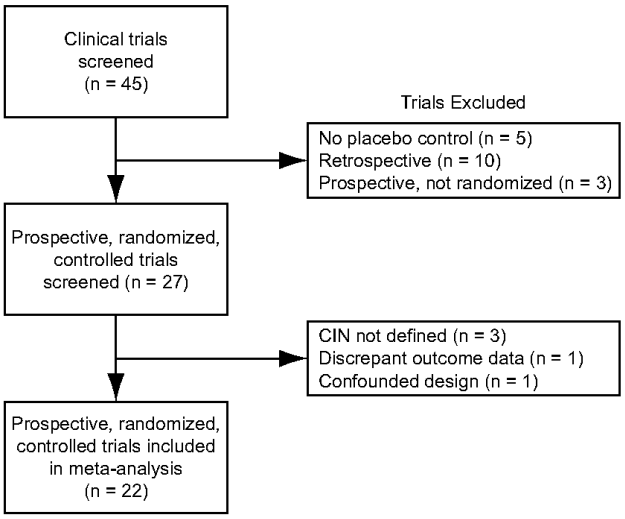


Figure 1. Study selection flow diagram.

One study was removed owing to a confounded design, where treated patients received more fluid compared with controls[54].

Additional information required for analysis was requested from trial authors; when unsuccessful in the case of one abstract [18], data were extracted from other meta-analyses. We included the more complete, updated data from manuscripts that were published after our cutoff date [55-57] if these studies had been available in the form of abstracts [19-21] before September, 2004.

Table 1 lists the characteristics of the 22 trials meeting our prospective selection criteria [10-31]. Figure 2 shows a forest plot ordered by time of publication, with RR and confidence intervals (CIs) of developing CIN if treated with NAC. A summary statistic is not shown owing to the significant heterogeneity (I^2 = 37%; p = 0.04) that precluded the pooling of these trials.

Publication bias and meta-regression analysis

Although non-significant ($p \leq 0.11$, but $p > 0.05$ when applying any one of the three methods used for analysis), a visual inspection of a funnel plot suggested publication bias with four studies [10, 11, 14, 25] contributing most to the apparent asymmetry (shown with open circles on the left-hand side of Figure 3). An extensive meta-regression analysis of patient and study characteristics found no study-specific characteristic (publication date, size, quality as measured by Jadad score or total NAC dose) or patient-related characteristic (age, diabetes, gender, contrast volume, baseline creatinine or CIN event rate in the control group) that significantly co-varied with NAC efficacy (Table 2).

Sensitivity analysis

A jackknife-*k* sensitivity analysis [97] identified 10 studies that decreased heterogeneity when individually removed (right-hand side of Figure 4). Removal of any one of the remaining 12 studies increased heterogeneity (left-hand side of Figure 4). The four small studies [10,11,14,25] that individually contributed the most to heterogeneity are shown as open circles in Figure 4 (circle size is proportional to inverse variance).

Removal of any single study or all possible two-study combinations failed to adequately resolve heterogeneity.

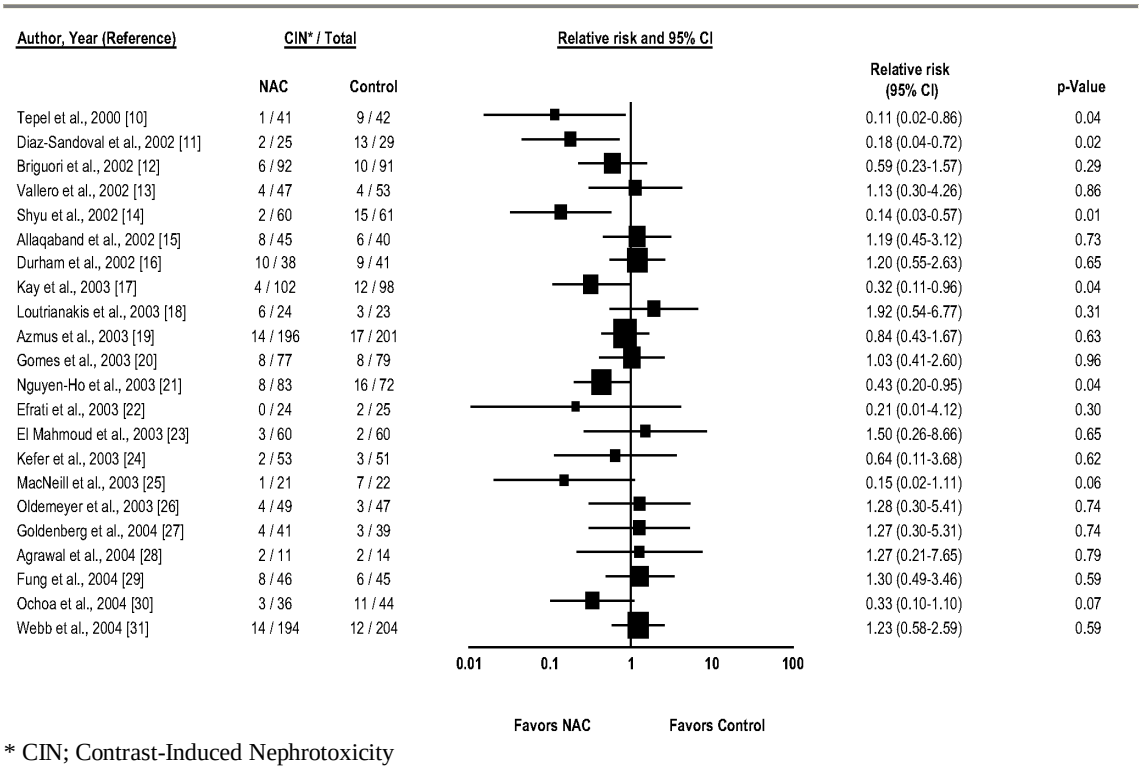
Table 1. Study Patient Characteristics

Authors (reference)	Pub. Date	Average patient age (years)	Per cent Male	BSCr (mg/dl)	Diabetes (%)	Contrast volume (ml)	Jadad Score	End point (SCr rise)	Contrast procedure	NAC regimen	Hydration regimen
Tepel *et al.* [10]	*07/00*	*65*	NA	*2.5*	*32.5*	*75*	*1*	*0.5 mg/dl 48 h*	*CT*	*600 mg tablet bid × 4*	*0.45% 1 ml/kg/h 12 h before, 12 h after*
Diaz-Sandoval *et al.* [11]	*02/02*	*73*	*80%*	*1.6*	*38.9*	*184*	2	*0.5 mg/dl or 25% 48 h*	*LHC*	*600 mg liquid in ginger ale bid × 4*	*0.45% 1 ml/kg/h 2–12 h before, 12 h after*
Briguori *et al.* [12]	07/02	64	86%	1.5	37.8	197	1	25% 48 h	LHC and/or PA and/or PCI	600 mg tablet bid × 4	0.45% 1 ml/kg/h 12 h before, 12 h after
Vallero *et al.* [13]	09/02	62	NA	1.0	23.0	205	1	0.5 mg/dl or 33% 48 h	LHC and/or PCI	600 mg tablet bid × 4	0.45% 1 ml/kg/h 1–2 h before, 24 h after
Shyu *et al.* [14]	*10/02*	*70*	*68%*	*2.8*	*63.5*	*117*	*1*	*0.5 mg/dl 48 h*	*LHC ± PCI*	*400 mg powder bid × 4*	*0.45% 1 ml/kg/h 12 h before, 12 h after*
Allaqaband *et al.* [15]	11/02	70	NA	2.1	48.3	122	3	0.5 mg/dl 48 h	LHC ± PCI or PA + PCI	600 mg liquid in cola bid × 4	0.45% 1 ml/kg/h 12 h before, 12 h after
Durham *et al.* [16]	12/02	71	66%	2.3	48.1	81	3	0.5 mg/dl 48 h	LHC	1200 mg liquid in orange juice bid × 2	0.45% 1 ml/kg/h ≤ 12 h before, ≤ 12 h after
Kay *et al.* [17]	02/03	69	62%	1.3	37.5	125	5	25% 48 h	LHC and/or PCI	600 mg tablet bid × 4	0.9% 1 ml/kg/h 12 h before, 6 h after
Loutrianakis *et al.* [18]	03/03	67	NA	1.9	36.0	147	1	0.5 mg/dl 120–168 h	LHC	600 mg bid × 4	0.45% 1 ml/kg/h
Azmus *et al.* [19]	07/03	67	59%	1.3	49.6	126	5	0.5 mg/dl or 25% 24–48 h	LHC or PCI	600 mg powder in water bid × 5	0.9% 1 L pre, 1 L post, or none
Gomes *et al.* [20]	10/03	65	59%	1.3	51.9	103	4	0.5 mg/dl 48 h	LHC or PCI	600 mg bid × 4	0.9% 1 ml/kg/h 12 h before, 12 h after
Nguyen-Ho *et al.* [21]	11/03	70	NA	1.4	67.5	347	4	25% 48–72 h	LHC or PCI	2000 mg liquid in juice bid × 2 or 3	0.45% 75 ml/h ≥ 24 h from enroll
Efrati *et al.* [22]	12/03	67	90%	1.5	52.9	140	2	25% 24–96 h	LHC	1000 mg liquid in cola bid × 4	0.45% 1 ml/kg/h
El Mahmoud *et al.* [23]	12/03	67	81%	1.9	30.0	177	2	25% 24–48 h	LHC	600 mg orally bid × 2	0.9% 1 ml/kg/h
Kefer *et al.* [24]	12/03	62	77%	1.1	12.5	199	1	0.5 mg/dl or 25% 24 h	LHC and/or PCI	1200 mg in 0.9% saline IV over 60 min, 12 h pre 0 h post	0.9% 1 ml/kg/h
MacNeill *et al.* [25]	*12/03*	*73*	*86%*	*1.9*	*46.5*	*110*	*4*	*25% 72 h*	*LHC ± PCI*	*600 mg liquid in juice/soda bid ×5*	*0.45% 1 ml/kg/h 12 h or 2 ml/kg/h 4 h before, 75 ml/h 12 h after*
Oldemeyer *et al.* [26]	12/03	76	55%	1.6	44.9	131	2	0.5 mg/dl or 25% 48 h	LHC	1500 mg liquid in soda bid × 4	500 ml D5 20 ml/h 12 h before, 12 h after
Goldenberg *et al.* [27]	02/04	70	83%	2.0	43.9	116	5	0.5 mg/dl 48 h	LHC ± PCI	600 mg liquid in soda tid × 6	0.45% 1 ml/kg/h

Table 1. Study Patient Characteristics *(Continued)*

Agrawal *et al.* [28]	04/04	63	68%	1.7	47.8	178	2	0.5 mg/dl or 25% 48 h	LHC and/or PCI	800/600/600 mg liquid in soda 12/2 h pre/6 h post	0.45% 1 ml/kg 12 h ± 250 ml bolus before, 12 h after
Fung *et al.* [29]	05/04	68	70%	2.3	52.8	128	3	0.5 mg/dl or 25% decrease in GFR 48 h	LHC or PCI ± PA	400 mg powder tid × 6	0.9% 100 ml/h 12 h before, 12 h after
Ochoa *et al.* [30]	06/04	71	43%	2.0	55.5	144	4	0.5 mg/dl or 25% 48 h	LHC and/or PCI	1000 mg liquid in diet cola bid × 2	0.9% 150 ml/h, ≥ 500 ml 12 h before, ≥ 1000 24 h after
Webb *et al.* [31]	09/04	70	NA	1.7	34.9	120	5	0.5 mg/dl 48–192 h	LHC or PCI ± PA	500 mg in D5NS IV for 15 min, 1 h pre	0.9% 200 ml before, 1.5 ml/kg/h 6 h or discharge (<6 h) after

SCr, serum creatinine; BSCr, baseline serum creatinine; CT, computed tomography; LHC, left heart catheterization; PCI, percutaneous coronary intervention; PA, peripheral angiography; Jadad score, measure of study design quality (0 is the weakest, 5 is the strongest); NAC, N-acetylcysteine; NA, not applicable; bid, twice daily; tid, three times daily; IV, intravenous; h, hour; D5NS, 5% dextrose plus normal saline; 0.9%, normal saline; 0.45%, half-normal saline.



* CIN; Contrast-Induced Nephrotoxicity
NAC; N-acetylcysteine

Figure 2. Forest plot of twenty-two studies meeting inclusion criteria for meta-analysis.

Studies are ordered by date of publication. Lines represent 95% CIs. Box sizes represent the weight (by inverse variance) of each trial. Note a trend over time towards no effect. No summary statistic is shown owing to excessive heterogeneity.

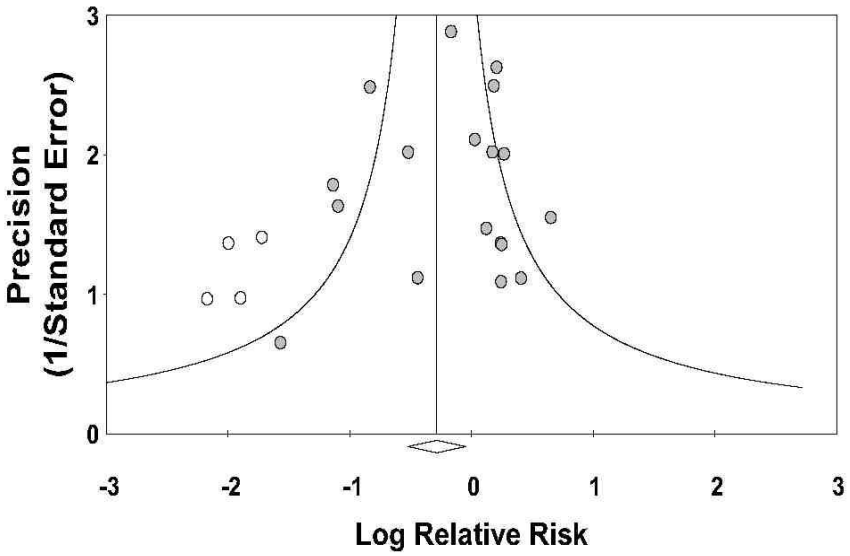


Figure 3. Funnel plot of precision versus log RR.
Log RR of developing CIN is plotted versus precision for each of the 22 studies in this meta-analysis. Four studies later identified as contributing most to heterogeneity are noted with open circles and are seen to produce asymmetry in the plot. The summary log RR for all 22 studies is denoted by the open diamond.

Table 2. Meta-regression of study and patient factors

	Characteristic	*r**	*p*-value
Study-related	Publication date (months after first)	0.36	0.1
	Study size (number of patients)	0.14	0.54
	Jadad score (1–5)	0.07	0.75
	Total NAC dose (mg)	-0.26	0.25
Patient-related	Age (years)	-0.13	0.56
	Baseline Creatinine (mg/dl)	-0.01	0.96
	Diabetes mellitus (%)	-0.23	0.31
	Female (%)	0.1	0.72
	Contrast volume (ml)	-0.27	0.24
	CIN event rate in control group (%)	0.21	0.35

*A negative correlation coefficient implies more benefit as the tested independent variable increases.

In contrast, the removal of multiple three-study combinations (combinations [11,14,25] [10,11,14] [11,14,21] and [11,14,17]) reached our pre-defined target for homogeneity (after the removal of any one of the three-study groups above, $I^2 \leq$ 9.5% and $p \geq 0.34$). These four three-study groups represent only 7.9%, 9.4%, 12.0% and 13.7% of the entire study population, respectively. *Modified L'Abbé plot and unsupervised clustering analysis*

A modified L'Abbé plot of creatinine change in controls versus creatinine change in NAC-treated subjects for all 22 studies is shown in Figure 5A. The no-effect line is plotted for reference. Most trials grouped together symmetrically around the no-effect line, with the exception of four very beneficial, relatively small studies [10,11,14,25].

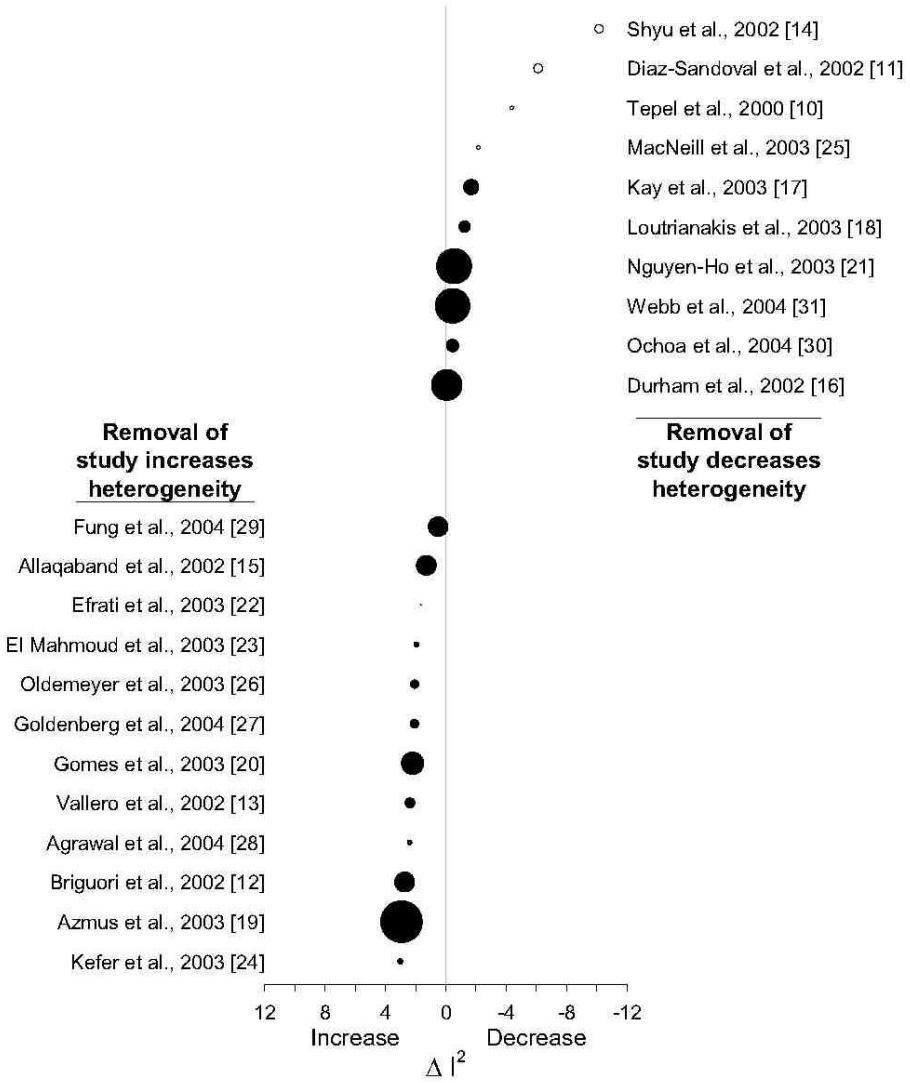


Figure 4. Jackknife sensitivity analysis.

Studies are ordered from top to bottom by their effect on heterogeneity when removed one at a time from the set of 22 studies. Removing any of the 10 studies at the top of the plot decreases heterogeneity, while removing any of the 12 studies at the bottom of the plot increases heterogeneity. The four studies that individually contributed the most to heterogeneity are shown as open circles. Circle size is proportional to the inverse variance.

These same four studies had caused the appearance of asymmetry in the funnel plot and were associated with heterogeneity by jackknife-*k* analysis. As suggested by the L'Abbé plot, a box plot (Figure 5B) of creatinine change clearly shows that these four studies have relatively large creati-nine increases in control patients ($p = 0.02$; open boxes on the left-hand side) and relatively large creatinine decreases in NAC-treated patients ($p = 0.07$; open boxes on the right-hand side).

Using a model-based, unsupervised clustering approach [87], our modified L'Abbé plot defined two different subpopulations of trials within the overall meta-analysis (Figure 6A). Dividing the 22 PRCTs based on their assignment to cluster 1 (18 studies, 89% of patients) [12,13,15-24,26-31] or cluster 2 (four studies, 11% of patients) [10,11,14,25], these two sets of trials were found to have significantly different treatment effects ($p < 0.0001$) and both were internally homogeneous (Figure 6B).

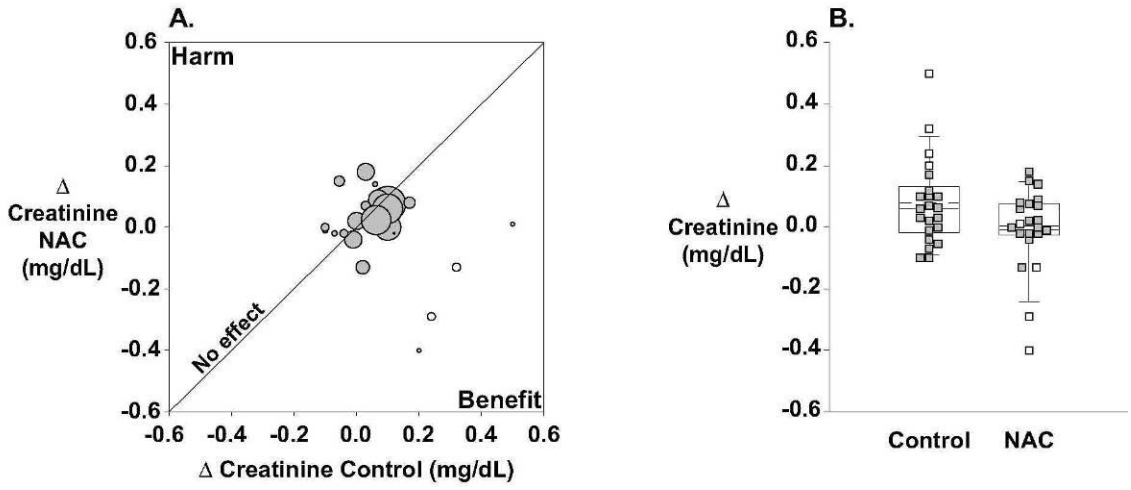


Figure 5. Changes in creatinine across all trials.

A: Modified L'Abbé plot of change in creatinine from baseline to study endpoint in the control arm (*x*-axis) versus NAC treatment arm (*y*-axis) of each study. Studies are weighted by inverse variance (i.e. larger symbols represent larger studies with less variability). Open circles denote cluster 2 studies [10, 11, 14, 25].

B: Box plot of change in creatinine from baseline to study endpoint in the control arm and NAC treatment arm of each study. Boxes represent the 25th, 50th and 75th percentiles. Whiskers are 5th and 95th percentiles. Dashed lines show the mean of each group. Open squares denote cluster 2 studies.

Group membership likelihoods were greater than 90% for the 18 studies assigned to cluster 1 and greater than 99% for the four studies assigned to cluster 2. Cluster 1 studies (2445 patients) showed no benefit from NAC administration to prevent CIN (RR = 0.87; 95% CI 0.68–1.12, $p = 0.28$). Cluster 2 studies (301 patients) indicated a large benefit from NAC treatment (RR = 0.15; CI 0.07–0.33, $p < 0.0001$). The four highly beneficial trials in cluster 2 all employed oral NAC at low or moderate doses and in this regard were not different in design from some larger trials that grouped with cluster 1. Likewise, cluster 2 patients received iopromide, ioxilan or iopamidol, contrast agents which did not appear to explain the large apparent benefit of NAC in these studies. However, cluster 2 studies were published earlier, are smaller in size and of lower quality as measured by Jadad scores (Table 3; $p = 0.01$, three study characteristics combined). Notably, control subjects experienced more CIN in cluster 2 compared with cluster 1 trials (31% ± 10% versus 12% ± 6%; $p = 0.03$). These increased episodes of CIN in cluster 2 were not associated with any consistent pattern of patient-related characteristics that increase risk for CIN (Table3).

Power analysis

A power analysis was performed using the point estimate of the treatment effect in cluster1 trials (RR = 0.87) to provide the most conservative estimate of the size of a trial necessary to show a significant effect. A single PRCT comparing NAC treatment with control subjects, in a balanced design, would need to enroll 32 200 patients in order to have an 80% chance of showing a significant benefit of NAC to prevent CIN at the $p < 0.05$ level. This assumes that the diagnosis of CIN would be based on similar cutoff values for a change in creatinine [10-31].

Dialysis events after contrast

The occurrence of dialysis was examined in the 22 trials meeting our inclusion criteria ($n = 2746$). A total of 13 patients received dialysis post-contrast (control $n = 5$, NAC-treated $n = 8$; $p = 0.42$) with no difference in the use of dialysis in cluster 1 (control $n = 4$, NAC-treated $n =$

8; p = 0.26) and cluster 2 (control n = 1, NAC-treated n = 0; p = 1.0) between the two treatment arms. NAC treatment showed no evidence of being protective using the clinical endpoint of dialysis events (RR = 1.42; CI 0.46–4.39, p = 0.54).

Table 3. Comparison of cluster 1 and cluster 2 studies (mean ± SD)

	Characteristic	Cluster 1	Cluster 2	p-value†
Study-related	Publication date (months after first)	38 ± 8	22 ± 17	0.05
	Study size (number of patients)	136 ± 106	75 ± 35	0.23
	Jadad score (1–5)	2.9 ± 1.5	2.0 ± 1.4	0.24
	All three factors combined	34 ± 13	50 ± 9	0.01
Patient-related	Age (years)	68 ± 4	70 ± 3	0.24
	Baseline creatinine (mg/dl)	1.6 ± 0.4	2.2 ± 0.6	0.09
	Diabetes mellitus (%)	43 ± 13	45 ± 13	0.93
	Female (%)	31 ± 14	22 ± 9	0.31
	Contrast volume (ml)	158 ± 61	122 ± 46	0.11

† Wilcoxon rank sum test

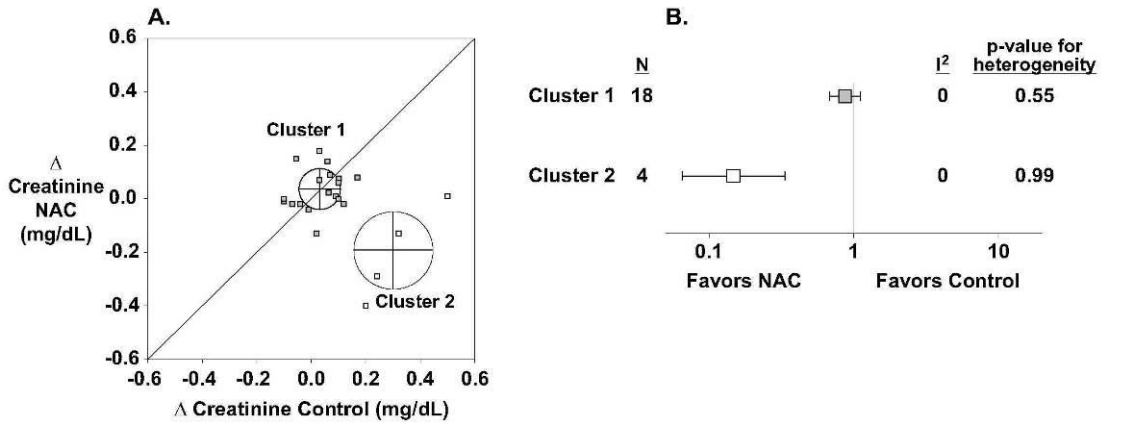


Figure 6. Cluster analysis based on changes in creatinine.

A: Modified L'Abbé plot showing the results of model-based, unsuper-vised cluster analysis. Unlike Figure 5A, studies are unweighted for easier visualization. Cluster analysis (see the Methods section) applied to the 22 studies found two distinct populations of trials. Crosshairs and circles denote the mean ± SD of each cluster.

B: Aggregate NAC treatment effect and heterogeneity analysis of each cluster. The entire group of 22 studies had unacceptable heterogeneity (I^2 = 37%; p = 0.04) making the summary point estimate unreliable (not shown). Cluster 1 (n = 18; 2445 patients) is homogeneous and shows no benefit (RR = 0.87; 95% CI 0.68-1.12, p = 0.28). Cluster 2 (N = 4; 301 patients) is also homogeneous and indicates that NAC is very beneficial (RR = 0.15; 95% CI 0.07-0.33, p < 0.0001).

Examination of new studies published after our cut-off date

From September 30, 2004 to March 1, 2007, 14 clinical trials of NAC in CIN were published [58-69]. Nine studies [58-64,70,71] met our prospective inclusion criteria. Like our meta-analysis of 22 PRCTs, these nine trials (1151 patients) had significant heterogeneity (I^2 = 56.0%; p = 0.03). When the nine studies were added to our meta-analysis, significant heterogeneity was again observed (I^2 = 40.9%; p = 0.01). Our model-based, unsupervised clustering approach showed that eight of these trials [58-63,70,71] grouped with cluster 1 with a probability of group membership of more than 94% for each trial. This updated cluster 1 (26 studies, 3268 patients) had low, non-significant heterogeneity (I^2 = 8.3%; p = 0.34) and showed no benefit of NAC for preventing CIN (RR = 0.90; 95% CI 0.72–1.12, p = 0.35). Cluster 1 and 2 treatment effects

remained significantly different (p < 0.0001).

One study of both high- and low-dose intravenous NAC in patients with acute myocardial infarctions [64] did not group strongly with either cluster (probabilities of group membership: low-dose arm, 39% for cluster 1 and 61% for cluster 2; high-dose arm, 49% for cluster 1 and 51% for cluster 2). Based on these results, this study [64] was found to be an outlier (p < 0.05; Dixon test) [98] compared with other trials assigned to either cluster 1 or 2.

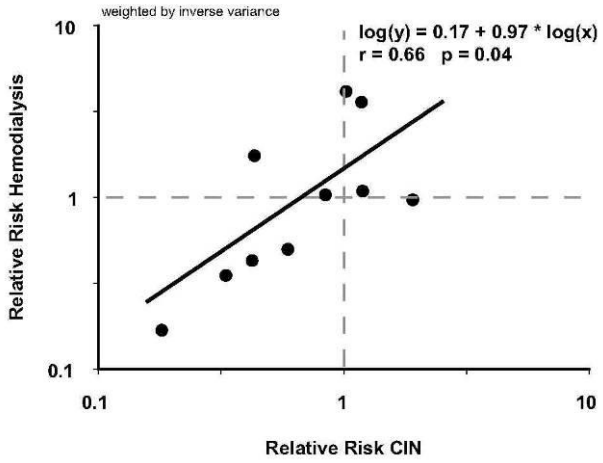


Figure 6. Hemodialysis risk model.

Relative risk of developing CIN is plotted versus RR of needing hemodialysis, based on hemodialysis data available from nine studies. Axes are in logarithmic scale. The RR of CIN would have to be less than 0.67 in order for the RR of hemodialysis not to be on the side of harm (RR < 1).

Hemodialysis risk model

We tested for a correlation between CIN and the clinically more rigorous outcome of dialysis. The correlation was weighted by the inverse variance of each study. Of the 22 trials in our meta-analysis and the nine more recent studies, hemodialysis events occurred in a total of nine trials [12,15,16,18-21,58,64]. Figure 7 shows that the RR of CIN, as defined in each trial, is positively correlated with the RR of requiring dialysis post-contrast (r = 0.66; p = 0.038). However, the regression equation is shifted upwards from the line of identity. For the RR of dialysis to be on the side of benefit (RR < 1.0), the RR of CIN would need to be substantially below one (RR < 0.67 for CIN). In fact, observing a RR of CIN this low in any future clinical trial is unlikely based on our cluster analysis, because it lies outside the 95% CI for cluster 1. A trial enrolling 32 200 patients, as described in the power analysis, would also have a moderate likelihood of showing a harmful effect of NAC on the need for post-contrast dialysis (RR = 1.29).

Discussion

The limited ability of meta-analysis to address unexplained heterogeneity has been explored in a well-known data set that has been subjected to a large number of previous investigations. CIN is a common and important complication of diagnostic imaging that has a substantial impact on morbidity and mortality [91-94]. While hydra-tion is clearly beneficial in preventing CIN [99,100], NAC has been investigated in many trials and subsequent meta-analyses with no consistent answer as to its efficacy. This meta-analysis of 22 studies, like previous meta-analyses [72-83], has demonstrated significant heterogeneity. The inconsistency across studies was systematically explored. Funnel plots [4-6] and a reiterative sensitivity analysis

[97] both identified subsets of studies that appeared to be most strongly associated with this problem. However, a standard meta-regression approach [1,2,84] failed to identify a single study or patient-related characteristic that correlated with or fully explained variability in the NAC treatment effect. Ultimately, a modified L'Abbé plot [86] that substituted change in creatinine, a directly measured continuous endpoint, for CIN event rates, an all-or-nothing outcome that was variably defined across trials, indicated the possibility of distinct trial subpopulations within the overall results. Borrowing from our experience in functional genomics research, unsupervised, model-based clustering [87] was applied to demonstrate that the data set represented two homogeneous, significantly different trial populations. This novel approach allowed us to directly compare trials that populated each of the two dissimilar clusters and provided a reliable aggregate point estimate for performing a formal power analysis.

NAC prophylaxis for the prevention of CIN was first introduced in 2000 [10] and although definitive proof of efficacy has been elusive, the use of NAC prophylaxis has become widespread. NAC trials have mainly been conducted in stable patient populations with at least one risk factor for the development of CIN [10-68]. Small doses of NAC given orally have been the most frequently investigated regimen despite evidence that the drug is poorly absorbed and undergoes significant first-past metabolism [101]. Although vigorous hydration has been demonstrated as an effective preventive strategy [99], NAC trials have typically been conducted using no more than maintenance infusions (1 ml/kg/h) of half-normal or normal saline [10-31]. Whether the small, non-significant benefit of NAC in cluster 1 of our meta-analysis would persist if hydration were individually optimized is questionable. Importantly, a large PRCT of unselected patients undergoing elective coronary angiography found that normal compared with half-normal saline reduced the incidence of CIN almost threefold [100]. Merten *et al.* [102] reported a negligible incidence of CIN in subjects treated with a sodium bicarbonate infusion at 3 ml/kg/h before contrast followed by 1 ml/kg/h after contrast. These studies suggest that fluid administration regimens have a large impact on CIN risk. It is worth noting that all four highly beneficial studies in cluster 2 of our meta-analysis [10,11,14,25] employed protocols specifying half-normal saline infusions at 1 ml/kg/h.

Changes in serum creatinine levels have invariably been used to diagnose CIN in trials of NAC. However, serum creatinine is a poor surrogate marker for glomerular filtration rate (GFR) because creatinine is influenced by diet, endogenous production, renal filtration, secretion and reabsorption [103,104]. Contrast agents themselves may decrease creatinine secretion and thereby raise serum creatinine levels, independently of changes in GFR [105]. Conversely, NAC in the absence of contrast has been shown to decrease serum creatinine levels in normal volunteers [106] and patients [66]. Hoffmann *et al.* [106] detected significant NAC-induced decreases in serum creatinine that were not associated with similar changes in cystatin C. As cystatin C is not secreted by renal tubule cells it may be a more accurate indicator of GFR [107,108]. Interestingly, in our meta-analysis, three out of the four cluster 2 studies [10,11,14] and one cluster 1 study [17], shown by sensitivity analysis to make a relatively large contribution to heterogeneity, all reported substantial NAC-induced decreases in serum creatinine. This response to NAC may be a drug effect independent of changes in GFR.

The four highly beneficial studies (cluster 2) represent only 11% of patients

in our meta-analysis. These trials were significantly different from cluster 1 studies in that they had early publication dates, were small in size and of low quality. Furthermore, cluster 2 studies uniformly employed an inferior hydration regimen that may have exaggerated any effects of NAC treatment. Cluster 2 studies were characterized by relatively large serum creatinine increases in control patients and similarly large creatinine decreases in NAC-treated patients.

A power analysis of cluster 1 studies indicated that 32 200 patients would be needed in a single PRCT to have an 80% chance of detecting benefit using definitions of CIN based on serum creatinine. Importantly, dialysis use was not decreased by NAC treatment across the 2746 patients in our meta-analysis. The large PRCT just proposed would have a moderate likelihood of demonstrating harm as measured by the more rigorous clinical endpoint of dialysis. Based on this investigation, low-dose oral NAC has not been shown to prevent CIN and should not be routinely recommended.

Eight of the nine new trials published since we closed our meta-analysis [58-63,70,71] were found to group with cluster 1 and support our overall findings. One of the trials was an outlier and not only reported significant reductions in CIN rates, but also decreases in dialysis use and mortality [64]. In this study, very ill patients with acute myocardial infarctions were treated with intravenous NAC boluses during angioplasty [64]. As noted by the authors, these single-center results require confirmation. As survival improved in their trial, Marenzi *et al*. speculated about possible benefits of NAC beyond the simple prevention of CIN [64]. Alternatively, the relatively high mortality in control subjects might also be explained by hidden imbalances created during randomization. In contrast to this highly beneficial trial, other studies in high-risk patients undergoing coronary bypass [109] or abdominal aortic surgery [110] did not find that intravenous NAC reduced the incidence of postoperative renal dysfunction or mortality.

Conclusion

Our meta-analysis does not support the use of NAC for reducing rates of acute kidney injury due to intravascular iodinated contrast. In several overly influential trials showing large beneficial effects, NAC decreased serum cre-atinine levels, suggesting possible drug effects independent of true changes in GFR. Dialysis use across all studies occurred infrequently, but did not indicate that NAC was efficacious. Future clinical trials of therapies to prevent CIN should incorporate primary endpoints other than change in creatinine.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

RLD, KJN and DAG conceived of the study protocol. PCS, KJN, SJK, DAG and RLD were responsible for collecting and assembling source data. KJN, SJK and SB provided statistical expertise. RLD, SJK, SB, DAG, CN and KJN were responsible for analyzing and interpreting data. All authors read and approved the final manuscript.

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References:

1. Smith GD, Egger M: Meta-analysis: unresolved issues and future developments. *Br Med J* 1998, 316:221-225.

2. Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF:Improving the quality of reports of meta-analyses of ran domised controlled trials: the QUOROM statement. Quality of reporting of meta-analyses. *Lancet* 1999, 354:1896-1900.

3. Noble JH Jr: Meta-analysis: methods, strengths, weaknesses, and political uses. *J Lab Clin Med* 2006, 147:7-20.

4. Higgins JP, Thompson SG: Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002, 21:1539-1558.

5. Egger M, Davey Smith G, Schneider M, Minder C: Bias in meta-analysis detected by a simple, graphical test. *Br Med J* 1997, 315:629-634.

6. Begg CB, Mazumdar M: Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994, 50:1088-1101.

7. Easterbrook PJ, Berlin JA, Gopalan R, Matthews DR: Publication bias in clinical research. *Lancet* 1991, 337:867-872.

8. Egger M, Smith GD: Misleading meta-analysis. *Br Med J* 1995, 311:753-754.

9. LeLorier J, Gregoire G, Benhaddad A, Lapierre J, Derderian F: Discrepancies between meta-analyses and subsequent large randomized, controlled trials. *N Engl J Med* 1997, 337:536-542.

10. Tepel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W: Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med* 2000, 343:180-184.

11. Diaz-Sandoval LJ, Kosowsky BD, Losordo DW: Acetylcysteine to prevent angiography-related renal tissue injury (the APART trial). *Am J Cardiol* 2002, 89:356-358.

12. Briguori C, Manganelli F, Scarpato P, Elia PP, Golia B, Riviezzo G, Lep-ore S, Librera M, Villari B, Colombo A, Ricciardelli B: Acetylcysteine and contrast agent-associated nephrotoxicity. *J Am Coll Cardiol* 2002, 40:298-303.

13. Vallero A, Cesano G, Pozzato M, Garbo R, Minelli M, Quarello F, Formica M: Nefropatia da contrasto in cardiologia interventis-tica: assenza di vantaggi con impiego profilattico di N-Acetilcisteina. *G Ital Nefrol* 2002, 19:529-533.

14. Shyu KG, Cheng JJ, Kuan P: Acetylcysteine protects against acute renal damage in patients with abnormal renal function undergoing a coronary procedure. *J Am Coll Cardiol* 2002, 40:1383-1388.

15. Allaqaband S, Tumuluri R, Malik AM, Gupta A, Volkert P, Shalev Y, Bajwa TK: Prospective randomized study of N-acetylcysteine, fenoldopam, and saline for prevention of radiocontrast-induced nephropathy. *Catheter Cardiovasc Interv* 2002, 57:279-283.

16. Durham JD, Caputo C, Dokko J, Zaharakis T, Pahlavan M, Keltz J, Dutka P, Marzo K, Maesaka JK, Fishbane S: A randomized controlled trial of N-acetylcysteine to prevent contrast nephropa-thy in cardiac angiography. *Kidney Int* 2002, 62:2202-2207.

17. Kay J, Chow WH, Chan TM, Lo SK, Kwok OH, Yip A, Fan K, Lee CH, Lam WF: Acetylcysteine for prevention of acute deterioration of renal function following elective coronary angiography and intervention: a randomized controlled trial. *JAMA* 2003, 289:553-558.

18. Loutrianakis E, Stella D, Hussain A, Lewis B, Steen L, Sochanski M, Leya F, Grassman E: Randomized comparison of fenoldopam and N-acetylcysteine to saline in the prevention of radiocontrast induced nephropathy. *J Am Coll Cardiol* 2003, 41:327A.

19. Azmus A, Manica A, Manica JL, Duro K, Bulcao L, Lima C, Frey M, Gottschall C: Efeito da acetilcisteina sobre a funcao renal de pacientes sumetidos a cateterismo cardiaco – resultados finais. *Arq Bras Cardiol* 2003, 81:7.

20. Gomes VO, Caramori P, Lasevitch R, Brizolara AA, Nery P, Araujo A, Hemesath M, Brito FS Jr: Prevention of contrast-induced nephropathy with N-acetylcysteine in patients undergoing coronary angiography: a randomized multicenter trial. *Circulation* 2003, 108:IV-460.

21. Nguyen-Ho P, Dzavik V, Seidelin P, Daly P, Ross J, McLaughlin P, Ing D, Barolet A, Schwartz L, Miner SE: N-acetylcysteine does not prevent long-term clinical events despite reducing periproc-edural contrast-associated nephropathy. *Circulation* 2003, 108:IV-445.

22. Efrati S, Dishy V, Averbukh M, Blatt A, Krakover R, Weisgarten J, Morrow JD, Stein MC, Golik A: The effect of N-acetylcysteine on renal function, nitric oxide, and oxidative stress after angiog-raphy. *Kidney Int* 2003, 64:2182-2187.

23. El Mahmoud R, Le Feuvre C, Le Quan Sang KH, Helft G, Beygui F, Batisse JP, Metzger JP: Absence of nephro-protective effect of acetylcysteine in patients with chronic renal failure investi-gated by coronary angiography. *Arch Mal Coeur Vaiss* 2003, 96:1157-1161.

24. Kefer JM, Hanet CE, Boitte S, Wilmotte L, De Kock M: Acetyl-cysteine, coronary procedure and prevention of contrast-induced worsening of renal function: which benefit for which patient? *Acta Cardiol* 2003, 58:555-560.

25. MacNeill BD, Harding SA, Bazari H, Patton KK, Colon-Hernadez P, DeJoseph D, Jang IK: Prophylaxis of contrast-induced nephrop-athy in patients undergoing coronary angiography. *Catheter Cardiovasc Interv* 2003, 60:458-461.

26. Oldemeyer JB, Biddle WP, Wurdeman RL, Mooss AN, Cichowski E, Hilleman DE: Acetylcysteine in the prevention of contrast-induced nephropathy after coronary angiography. *Am Heart J* 2003, 146:E23.

27. Goldenberg I, Shechter M, Matetzky S, Jonas M, Adam M, Pres H, Elian D, Agranat O, Schwammenthal E, Guetta V: Oral acetylcysteine as an adjunct to saline hydration for the prevention of contrast-induced nephropathy following coronary angiography. A randomized controlled trial

and review of the current literature. *Eur Heart J* 2004, 25:212-218.

28. Agrawal M, Wodlinger AM, Huggins CE, Tudor GE, Pieper JA, O'Reilly KP, Denu-Ciocca CJ, Stouffer GA, Ohman EM: Effect of N-acetylcysteine on serum creatinine concentration in patients with chronic renal insufficiency who are undergoing coronary angiography. *Heart Drug* 2004, 4:87-91.

29. Fung JW, Szeto CC, Chan WW, Kum LC, Chan AK, Wong JT, Wu EB, Yip GW, Chan JY, Yu CM, Woo KS, Sanderson JE: Effect of N-acetylcysteine for prevention of contrast nephropathy in patients with moderate to severe renal insufficiency: a randomized trial. *Am J Kidney Dis* 2004, 43:801-808.

30. Ochoa A, Pellizzon G, Addala S, Grines C, Isayenko Y, Boura J, Rem-pinski D, O'Neill W, Kahn J: Abbreviated dosing of N-acetyl-cysteine prevents contrast-induced nephropathy after elective and urgent coronary angiography and intervention. *J Interv Cardiol* 2004, 17:159-165.

31. Webb JG, Pate GE, Humphries KH, Buller CE, Shalansky S, Al Shamari A, Sutander A, Williams T, Fox RS, Levin A: A randomized controlled trial of intravenous N-acetylcysteine for the prevention of contrast-induced nephropathy after cardiac catheterization: lack of effect. *Am Heart J* 2004, 148:422-429.

32. Raven Q, Walton T, Howe A, Macon E: Role of acetylcysteine in the prevention of contrast-media-induced nephrotoxicity. *Am J Health Syst Pharm* 2003, 60:2232-2235.

33. Pai DY, Denny DF, Shanahan AJ, Ruddy MC: The effect of acetyl-cysteine on renal function in elderly high-risk patients exposed to arteriographic contrast dye. *Am J Hypertens* 2003, 16:255A.

34. Nicholson D, Haas GJ, Carnes CA, Abraham WT, Feldman DS: Lack of efficacy of N-acetylcysteine in attenuating contrast induced nephropathy in patients with severe systolic heart failure. *J Card Fail* 2004, 10:S131.

35. Erickson CW, Erickson JE, Wilsker G, Brunner L: A retrospective analysis of oral acetylcysteine intervention to prevent radio-graphic contrast-induced nephropathy in patients undergoing coronary angiography with elevated serum creatinine. *Am J Kidney Dis* 2002, 39:A16.

36. Adamian M, Mehran R, Moussa I, Dangas G, Mintz GS, Lansky AJ, Adamyan Y, Ibrahim M, Fahy M, Cioara C, *et al.*: Mucomyst administration in percutaneous coronary interventions in patients with impaired renal function: a matched comparison. *Am J Cardiol* 2002, 90:H144.

37. Rasty S, Sierra M, Salmon A: N-acetylcysteine versus N-acetyl-cysteine plus fenoldopam in the prevention of contrast induce nephropathy. *Crit Care Med* 2003, 31:A108.

38. Rezkalla SH, Benz M: Effectiveness of acetylcysteine on preventing renal dysfunction in patients undergoing coronary procedures. *Wis Med J* 2004, 103:38-41.

39. Kanderian AS, Abdelhadi RH, Bhatt DL, Schneider J, Chung MK: Hydration versus N-acetylcysteine for protection of renal function in patients with renal insufficiency undergoing percutaneous coronary intervention. *J Am Coll Cardiol* 2003, 41:63A.

40. Gill NK, Piccione EA, Vido D, Clark BA, Shannon RP: The role of acetylcysteine in preventing contrast-induced nephropathy following cardiac catheterization in patients with acute and chronic renal failure. *J Am Coll Cardiol* 2003, 41:23A.

41. Casterella PJ, Mason SM, Doing T, Burke JL, Revenaugh JR, Sorensen SG, Horne BD, Pearson RR, Anderson JL, Muhlstein JB: N-acetylcysteine and fenoldopam do not significantly reduce the incidence of contrast-induced nephropathy. *Am J Cardiol* 2002, 90:H143.

42. Boccalandro F, Amhad M, Smalling RW, Sdringola S: Oral acetyl-cysteine does not protect renal function from moderate to high doses of intravenous radiographic contrast. *Catheter Cardiovasc Interv* 2003, 58:336-341.

43. Tadros GM, Mouhayar EN, Akinwande AO, Campbell B, Wood C, Blankenship JA: Prevention of radiocontrast-induced nephrop-athy with N-acetylcysteine in patients undergoing coronary angiography. *J Invasive Cardiol* 2003, 15:311-314.

44. Nogareda GJ, Ricci DR, Penn IM, Huckell V, Fox R, Chow J, Eichman A, Buller CE: Oral N-acetylcysteine administered immediately prior to routine percutaneous coronary procedures ameliorates contrast-induced nephrotoxicity. *J Am Coll Cardiol* 2003, 41:62A-63A.

45. Briguori C, Colombo A, Violante A, Balestrieri P, Manganelli F, Paolo Elia P, Golia B, Lepore S, Riviezzo G, Scarpato P, *et al.*: Standard vs double dose of N-acetylcysteine to prevent contrast agent associated nephrotoxicity. *Eur Heart J* 2004, 25:206-211.

46. Bader BD, Berger ED, Rossmann S, Risler T, Erley CM: Prevention of contrast media-induced acute renal failure in patients with severe impaired renal function – theophylline versus N-acetylcysteine. *J Am Soc Nephrol* 2002, 13:447A.

47. Briguori C, Colombo A, Airoldi F, Violante A, Castelli A, Balestrieri P, Paolo Elia P, Golia B, Lepore S, Riviezzo G, *et al.*: N-acetylcysteine versus fenoldopam mesylate to prevent contrast agent-associated nephrotoxicity. *J Am Coll Cardiol* 2004, 44:762-765.

48. Huber W, Eckel F, Saur D, Sennefelder A, Hennico R, Schenk C, Schmelz R, Fritsch R, Weiss W, Classen M, Heemann U: Prophylaxis of contrast-induced nephropathy: acetylcysteine, theophyl-line or both – a randomized study. *Intensive Care Medicine* 2002, 28:S139.

49. Pelliccia F, Pristipino C, Pasceri V, Granatelli A, Speciale G, Roncella A, Richichi G: A pilot randomized study on the safety and efficacy of the association fenoldopam-acetylcysteine for preventing contrast-induced renal failure. *Am J Cardiol* 2004, 94:176E-177E.

50. Drager LF, Andrade L, Barros de Toledo JF, Laurindo FR, Machado Cesar LA, Seguro AC: Renal effects of N-acetylcysteine in patients at risk for contrast nephropathy: decrease in oxi-dant stress-mediated renal tubular injury. *Nephrol Dial Transplant* 2004, 19:1803-1807.

51. Rashid ST, Salman M, Myint F, Baker D, Agarwal S, Hamilton G: N-Acetylcysteine for the prevention of nephropathy induced by radiographic contrast media in vascular patients undergoing angiography: a randomised, double-blind, controlled trial. *Br J Surg* 2004, 91:139.

52. Ray DS, Srinivas V: Role of N-acetyl cysteine in prevention of contrast nephropathy in patients of diabetic renal failure: a prospective study. *Nephrol Dial Transplant* 2003, 18:664.

53. Kahlon JPS, Moser L, Rosman H, Nordstrom C, Zafar A, Khairullah Q, Schreiber T, LaLonde T, Gardin J, Yamasaki H: Effectiveness of N-acetylcysteine for the prevention of radiocontrast-induced nephropathy: is the jury still out? *Circulation* 2002, 106:691-692.

54. Baker CS, Wragg A, Kumar S, De Palma R, Baker LR, Knight CJ: A rapid protocol for the prevention of contrast-induced renal dysfunction: the RAPPID study. *J Am Coll Cardiol* 2003, 41:2114-2118.

55. Azmus AD, Gottschall C, Manica A, Manica J, Duro K, Frey M, Bulcao L, Lima C: Effectiveness of acetylcysteine in prevention of contrast nephropathy. *J Invasive Cardiol* 2005, 17:80-84.

56. Gomes VO, Poli de Figueredo CE, Caramori P, Lasevitch R, Bodanese LC, Araujo A, Roedel AP, Caramori AP, Brito FS Jr, Bezerra HG, *et al.*: N-acetylcysteine does not prevent contrast induced neph-ropathy after cardiac catheterisation with an ionic low osmolality contrast medium: a multicentre clinical trial. *Heart* 2005, 91:774-778.

57. Miner SE, Dzavik V, Nguyen-Ho P, Richardson R, Mitchell J, Atchison D, Seidelin P, Daly P, Ross J, McLaughlin PR, *et al.*: N-acetylcysteine reduces contrast-associated nephropathy but not clinical events during long-term follow-up. *Am Heart J* 2004, 148:690-695.

58. Balderramo D, Verdu M, Ramacciotti C, Cremona L, Lemos P, Orias M, Eduardo MJ: Renoprotective effect of high periprocedural doses of oral N-acetylcysteine in patients scheduled to undergo a same-day angiography. *Rev Fac Cien Med Univ Nac Cor-boda* 2004, 61:13-19.

59. Gulel O, Keles T, Eraslan H, Aydogdu S, Diker E, Ulusoy V: Prophylactic acetylcysteine usage for prevention of contrast neph-ropathy after coronary angiography. *J Cardiovasc Pharmacol* 2005, 46:464-467.

60. Kotlyar E, Keogh A, Thavapalachandran S, Allada C, Sharp J, Dias L, Muller D: Prehydration alone is sufficient to prevent contrast-induced nephropathy after day-only angiography procedures – a randomised controlled trial. *Heart Lung Circ* 2005, 14:245-251.

61. Coyle L, Rodriguez A, Jeschke R, Simon-Lee A, Abbott K, Taylor A: Acetylcysteine In Diabetes (AID): a randomized study of acetylcysteine for the prevention of contrast nephropathy in diabetics. *Am Heart J* 2006, 151:1032.e1039-e1012.

62. Sandhu C, Belli A, Oliveira D: The role of N-acetylcysteine in the prevention of contrast-induced nephrotoxicity. *Cardiovasc Intervent Radiol* 2006, 29:344-347.

63. Carbonell N, Blasco M, Sanjuan R, Perez-Sancho E, Sanchis J, Insa L, Bodi V, Nunez J, Garcia-Ramon R, Miguel A: Intravenous N-acetylcysteine for preventing contrast-induced nephropathy: a randomised trial. *Int J Cardiol* 2007, 115:57-62.

64. Marenzi G, Assanelli E, Marana I, Lauri G, Campodonico J, Grazi M, De Metrio M, Galli S, Fabbiocchi F, Montorsi P, *et al.*: N-acetylcysteine and contrast-induced nephropathy in primary angi-oplasty. *N Engl J Med* 2006, 354: 2773-2782.

65. Ng TM, Shurmur SW, Silver M, Nissen LR, O'Leary EL, Rigmaiden RS, Cieciorka M, Porter LL, Ineck BA, Kline ME, Puumala SE: Comparison of N-acetylcysteine and fenoldopam for preventing contrast-induced nephropathy (CAFCIN). *Int J Cardiol* 2006, 109:322-328.

66. Macedo E, Abdulkader R, Castro I, Sobrinho AC, Yu L, Vieira JM Jr: Lack of protection of N-acetylcysteine (NAC) in acute renal failure related to elective aortic aneurysm repair-a randomized controlled trial. *Nephrol Dial Transplant* 2006, 21:1863-1869.

67. Sochman J, Krizova B: Prevention of contrast agent-induced renal impairment in patients with chronic renal insufficiency and heart disease by high-dose intravenous N-acetylcysteine: a pilot-ministudy. *Kardiol Pol* 2006, 64:559-564.

68. Rashid ST, Salman M, Myint F, Baker DM, Agarwal S, Sweny P, Hamilton G: Prevention of contrast-induced nephropathy in vascular patients undergoing angiography: a randomized con-

trolled trial of intravenous N-acetylcysteine. *J Vasc Surg* 2004, 40:1136-1141.

69. Huber W, Eckel F, Hennig M, Rosenbrock H, Wacker A, Saur D, Sen-nefelder A, Hennico R, Schenk C, Meining A, *et al.*: Prophylaxis of contrast material-induced nephropathy in patients in intensive care: acetylcysteine, theophylline, or both? A randomized study. *Radiology* 2006, 239:793-804.

70. Khalili H, Dashti-Khaidaki S, Tabifar H, Ahmadinejad N, Ahmadi F: N-acetylcysteine in the prevention of contrast agent-induced nephrotoxicity in patients undergoing computed tomography studies. *Therapy* 2006, 3:773-777.

71. Ozcan EE, Guneri S, Akdeniz B, Senaslan O, Aslan O, Badak O: Prospective randomized study of sodium bicarbonate, N-acetyl-cysteine, and saline for prevention of radiocontrast-induced nephropathy. *Eur Heart J* 2006, 27:83.

72. Birck R, Krzossok S, Markowetz F, Schnulle P, van der Woude FJ, Braun C: Acetylcysteine for prevention of contrast nephropa-thy: meta-analysis. *Lancet* 2003, 362:598-603.

73. Isenbarger DW, Kent SM, O'Malley PG: Meta-analysis of randomized clinical trials on the usefulness of acetylcysteine for prevention of contrast nephropathy. *Am J Cardiol* 2003, 92:1454-1458.

74. Alonso A, Lau J, Jaber BL, Weintraub A, Sarnak MJ: Prevention of radiocontrast nephropathy with N-acetylcysteine in patients with chronic kidney disease: a meta-analysis of randomized, controlled trials. *Am J Kidney Dis* 2004, 43:1-9.

75. Kshirsagar AV, Poole C, Mottl A, Sholham D, Franceschini N, Tudor G, Agrawal M, Denu-Ciocca C, Magnus Ohman E, Finn WF: N-ace-tylcysteine for the prevention of radiocontrast induced nephropathy: a meta-analysis of prospective controlled trials. *J Am Soc Nephrol* 2004, 15:761-769.

76. Pannu N, Manns B, Lee H, Tonelli M: Systematic review of the impact of N-acetylcysteine on contrast nephropathy. *Kidney Int* 2004, 65:1366-1374.

77. Guru V, Fremes SE: The role of N-acetylcysteine in preventing radiographic contrast-induced nephropathy. *Clin Nephrol* 2004, 62:77-83.

78. Bagshaw SM, Ghali WA: Acetylcysteine for prevention of contrast-induced nephropathy after intravascular angiography: a systematic review and meta-analysis. *BMC Med* 2004, 2:38.

79. Misra D, Leibowitz K, Gowda RM, Shapiro M, Khan IA: Role of N-acetylcysteine in prevention of contrast-induced nephropa-thy after cardiovascular procedures: a meta-analysis. *Clin Car-diol* 2004, 27:607-610.

80. Nallamothu BK, Shojania KG, Saint S, Hofer TP, Humes HD, Moscucci M, Bates ER: Is acetylcysteine effective in preventing contrast-related nephropathy? A meta-analysis. *Am J Med* 2004, 117:938-947.

81. Liu R, Nair D, Ix J, Moore DH, Bent S: N-acetylcysteine for the prevention of contrast-induced nephropathy. A systematic review and meta-analysis. *J Gen Intern Med* 2005, 20:193-200.

82. Duong MH, Mackenzie TA, Malenka DJ: N-acetylcysteine prophylaxis significantly reduces the risk of radiocontrast-induced nephropathy: comprehensive meta-analysis. *Catheter Cardiovasc Interv* 2005, 64:471-479.

83. Zagler A, Azadpour M, Mercado C, Hennekens CH: N-acetyl-cysteine and contrast-induced nephropathy: a meta-analysis of 13 randomized trials. *Am Heart J* 2006, 151:140-145.

84. Biondi-Zoccai GG, Lotrionte M, Abbate A, Testa L, Remigi E, Burzo-tta F, Valgimigli M, Romagnoli E, Crea F, Agostoni P: Compliance with QUOROM and quality of reporting of overlapping meta-analyses on the role of acetylcysteine in the prevention of contrast associated nephropathy: case study. *Br Med J* 2006, 332:202-209.

85. Bagshaw SM, McAlister FA, Manns BJ, Ghali WA: Acetylcysteine in the prevention of contrast-induced nephropathy: a case study of the pitfalls in the evolution of evidence. *Arch Intern Med* 2006, 166:161-166.

86. L'Abbé KA, Detsky AS, O'Rourke K: Meta-analysis in clinical research. *Ann Intern Med* 1987, 107:224-233.

87. Fraley C, Raftery A: Model-based clustering, discriminant analysis, and density estimation. *J Am Stat Assoc* 2002, 97:611-631.

88. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ: Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996, 17:1-12.

89. Cochran WG: The combination of estimates from different experiments. *Biometrics* 1954, 10:101-129.

90. Higgins JP, Thompson SG, Deeks JJ, Altman DG: Measuring inconsistency in meta-analyses. *Br Med J* 2003, 327:557-560.

91. Sharp SJ, Thompson SG: Analysing the relationship between treatment effect and underlying risk in meta-analysis: comparison and development of approaches. *Stat Med* 2000, 19:3251-3274.

92. Eichacker PQ, Parent C, Kalil A, Esposito C, Cui X, Banks SM, Ger-stenberger EP, Fitz Y, Danner RL, Natanson C: Risk and the efficacy of antiinflammatory agents: retrospective and confirmatory studies of sepsis. *Am J Respir Crit Care Med* 2002, 166:1197-1205.

93. Levy EM, Viscoli CM, Horwitz RI: The effect of acute renal failure on mortality. A cohort analysis. *JAMA* 1996, 275:1489-1494.

94. McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW: Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. *Am J Med* 1997, 103:368-375.

95. Pannu N, Wiebe N, Tonelli M: Prophylaxis strategies for contrast-induced nephropathy. *JAMA* 2006, 295:2765-2779.

96. Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, Mintz GS, Lansky AJ, Moses JW, Stone GW, *et al.*: A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention. *J Am Coll Cardiol* 2004, 44:1393-1399.

97. Miller R: The jackknife – a review. *Biometrika* 1974, 61:1-15.

98. Dixon WJ: Analysis of extreme values. *Ann Math Stat* 1950, 21:488-506.

99. Eisenberg RL, Bank WO, Hedgock MW: Renal failure after major angiography can be avoided with hydration. *AJR Am J Roentge-nol* 1981, 136:859-861.

100. Mueller C, Buerkle G, Buettner HJ, Petersen J, Perruchoud AP, Eriksson U, Marsch S, Roskamm H: Prevention of contrast media-associated nephropathy: randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angi-oplasty. *Arch Intern Med* 2002, 162:329-336.

101. Fishbane S, Durham JH, Marzo K, Rudnick M: N-acetylcysteine in the prevention of radiocontrast-induced nephropathy. *J Am Soc Nephrol* 2004, 15:251-260.

102. Merten GJ, Burgess WP, Gray LV, Holleman JH, Roush TS, Kowal-chuk GJ, Bersin RM, Van Moore A, Simonton CA III, Rittase RA, *et al.*: Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized controlled trial. *JAMA* 2004, 291:2328-2334.

103. Hoffmann U, Banas B, Fischereder M, Kramer BK: N-acetylcysteine in the prevention of radiocontrast-induced nephropathy: clinical trials and end points. *Kidney Blood Press Res* 2004, 27:161-166.

104. Toprak O: Interactions between serum creatinine, volume status, N-acetylcysteine, and contrast-induced nephropathy. *Ren Fail* 2006, 28:265-266.

105. Brautigam M, Persson PB: Do iodinated contrast media interfere with renal tubular creatinine secretion? *Radiology* 2006, 240:615.

106. Hoffmann U, Fischereder M, Krüger B, Drobnik W, Krämer BK: The value of N-acetylcysteine in the prevention of radiocontrast agent-induced nephropathy seems questionable. *J Am Soc Nephrol* 2004, 15:407-410.

107. Perlemoine C, Beauvieux MC, Rigalleau V, Baillet L, Barthes N, Der-ache P, Gin H: Interest of cystatin C in screening diabetic patients for early impairment of renal function. *Metabolism* 2003, 52:1258-1264.

108. Laterza OF, Price CP, Scott MG: Cystatin C: an improved estimator of glomerular filtration rate? *Clin Chem* 2002, 48:699-707.

109. Burns KE, Chu MW, Novick RJ, Fox SA, Gallo K, Martin CM, Stitt LW, Heidenheim AP, Myers ML, Moist L: Perioperative N-acetylcysteine to prevent renal dysfunction in high-risk patients undergoing CABG surgery: a randomized controlled trial. *JAMA* 2005, 294:342-350.

110. Hynninen MS, Niemi TT, Poyhia R, Raininko EI, Salmenpera MT, Lep-antalo MJ, Railo MJ, Tallgren MK: N-acetylcysteine for the prevention of kidney injury in abdominal aortic surgery: a randomized, double-blind, placebo-controlled trial. *Anesth Analg* 2006, 102:1638-1645.

DEPRESSION IN MULTICULTURAL AUSTRALIA: POLICIES, RESEARCH AND SERVICES

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Depression is one of the leading causes of disability in Australia. The cultural and linguistic diversity of the Australian population poses a significant challenge to health policy development, service provision, professional education, and research. The purpose of this study is to explore the extent to which the fact of cultural and linguistic diversity has influenced the formulation of mental health policy, the conduct of mental health research and the development of mental health services for people with depression from ethnic minority communities.
The methods used for the different components of the study included surveys and document-based content and thematic analyses.
Policy is comprehensive but its translation into programs is inadequate. Across Australia, there were few specific programs on depression in ethnic minority communities and they are confronted with a variety of implementation difficulties. The scope and scale of research on depression in Ethnic minority communities is extremely limited.
A key problem is that the research that is necessary to provide evidence for policy and service delivery is lacking. If depression in Ethnic minority communities is to be addressed effectively the gaps between policy intentions and policy implementation, and between information needs for policies and practice and the actual research that is being done, have to be narrowed.

Background

Depression, one of the leading causes of disability worldwide, [1-3] will be the second largest cause of disability in Australia by the year 2020 [3]. Suicide, often related to depression, is the fourth largest cause of mortality in Australia [3]. The Australian Government recognises the need to address the issue of depression [4-7] and several initiatives are under way, the most notable being *beyondblue: the national depression initiative* [8]. The approach of *beyondb-lue* is to foster sustainable partnerships among organisations, agencies, service providers, community and government sectors, individuals, consumers and caregiv-ers, to promote coordinated activities and to build on existing strengths in order to address the problem of depression in the Australian community. The purpose of *beyondblue* is reduce the burden of depression. However, it is not clear whether these and other activities will deal effectively with depression in a multicultural and multilingual population. An adequate response to depression in this context will rely on three broad components: a body of mental health and services research to guide policy and practice, relevant policies, and resources for services that translate good policies into practice. This study reports findings from a national examination of policy, research and service delivery in relation to depression in ethnic minority communities in Australia.

Australia is home to many ethnic, religious and language groups. Broad indicators of diversity show that 28% of the population was overseas-born (15% in a non-English speaking country) at the time of the 2001 Census and 16% of the population spoke a language other than English at home. Ethnic minority communities vary substantially with respect to mean age, time of migration, language, religion, type of immigration, along many other variables. There is also significant social

and economic diversity within any particular ethnic minority community. Diversity poses a significant challenge in the areas of health service policy, service provision, professional education and research.

Despite Australia's adoption of multiculturalism as national policy over the past 35 years, it is only in the last decade that mental health services have attended to the issue of linguistic and cultural diversity. Some important developments are the inclusion, as part of the National Mental Health Strategy, of cultural diversity as an important component of the National Standards for mental health service delivery [9], the establishment of specialist state transcultural mental health centres, specialist services for refugees, and the establishment of a national tran-scultural mental health network [10]. New models of care are being explored, for example bilingual clinical services [11,12]. Such developments have occurred in the context of the major reform of mental health systems with the closure of large psychiatric hospitals and the development of community-based services and more recently, a concentrated effort to engage general practice in mental health care.

In view of the composition of the Australian population it is important that mental health services adequately respond to the complexity created by the interactions between culture, language and mental health. Cultural factors play a significant role in depression (and other mental disorders), particularly in how the illness is experienced, the personal meaning of the illness, clinical manifestations, how it affects help-seeking and pathways to care, and in issues such as adherence and responsiveness to treatment [13-20]. In multilingual settings, additional concerns relate to the problems of translation and the dynamics of the interpreting process, and the increased probability of diagnostic error and poor treatment outcomes [17,21-24].

Attention to cultural and linguistic diversity is an important consideration in tackling the problem of depression in Australia. The aim of this study was to examine the current status of policy, research and service provision in Australia in relation to depression and ethnic minority communities. We explore the extent to which an appropriate policy framework has been developed, the extent, nature and usefulness of Australian-based research, and the existence of service programs for depression that are responsive to the needs of ethnic minority communities.

We do not here advocate for any particular response to the challenges presented to the mental health system by the cultural and linguistic diversity of the Australian population. (For example, we do not argue for or against ethno-specific mental health services.) Our purpose is to examine the developments in the areas of policy, research and services that have occurred in response to the reality of cultural and linguistic diversity since the beginning of the national mental health strategy.

Methods *Policy Analysis*

Major Commonwealth and State/ Territory mental health policies and related documents were examined for their relevance to mental health system responses to depression in Ethnic minority communities. The policies examined are listed in Table 1. Content analysis (described in the Results) was used in examining them.

Research Analysis

Publications

Medline and Psychinfo searches were undertaken for publications by Australian researchers, including all publications where any of the authors had an affiliation to an Australian institution. Search terms were combinations of the following: depression and/or suicide and

cultural and/or ethnic and/or language and/or immigrant and/or refugee groups. The search was limited to publications in the period 1990 – the starting point for the national mental health strategy – to 2002, when the data collection was concluded. Only original research was included. Papers were summarised for details related to depression or suicide.

Higher Degree Theses

Research theses from 1990 onwards were sought. An internet search was conducted of 30 Australian tertiary institution libraries using 'advanced' key word search facilities, where available, for the terms depression or suicide and thesis. We counted relevant theses as those describing in their title a focus on immigration or, ethnic or language minority groups in Australia.

Table 1. List of Commonwealth/National and State Policies examined

LOCATION	MENTAL HEALTH POLICY TITLE
Commonwealth	National Mental Health Policy, 1992 [66]
Commonwealth	Mental Health Statement of Rights and Responsibilities, 1991 [67]
Commonwealth	National Standards for Mental Health Services, 1996 [9]
Commonwealth	Second National Mental Health Plan, 1998 [68]
Commonwealth	Mental Health Promotion and Prevention National Action Plan Under the Second National Mental Health Plan: 1998–2003, 1999 [69]
Commonwealth	National Action Plan for Promotion, Prevention and Early Intervention for Mental Health, 2000 [4]
Commonwealth	Youth suicide in Australia: the national youth suicide prevention strategy, 1997 [70]
Commonwealth	National Action Plan for Depression, 2000 [6]
Commonwealth	Life – A framework for prevention of suicide and self-harm in Australia, 2000 [7]
Australian Capital Territory	The future of Mental Health Service in the Australian Capital Territory – Moving Towards 2000 and Beyond – A Whole of Territory Strategic Plan 1998–2001, 1998 [71]
New South Wales	Caring for Mental Health – A Framework for Mental Health Care in NSW, 1998 [72]
	Caring for Older People's Mental Health – A Strategy for the Delivery of Mental Health Care for Older People in NSW, 1998 [73]
	Caring for Mental Health in a Multicultural Society – A Strategy for the Mental Health Care of People from Culturally and Linguistically Diverse Backgrounds, 1999 [28]
	Getting in Early – A Framework for Early Intervention and Prevention in Mental Health for Young People in NSW, 2001 [74]
Tasmania	Tasmanian Multicultural Policy, 2001 [75]
	Rural Mental Health Plan, 2001–2004, 2001 [76]
	A Plan for Now and the Future – Strategic Plan for 1999–2002, 1999 [77]
Western Australia	Making a Commitment – The Mental Health Plan for WA, 1996 [78]
	Transculturally Orientated Mental Health Services, 2001 [26]
Queensland	Queensland Health non-English speaking background mental health policy statement, 1995 [27]
	Ten year mental health strategy of Queensland, 1996 [79]
	Queensland Health Multicultural Policy Statement, 2000 [80]
South Australia	A New Millennium – A new beginning, 2000–2005 – Mental Health in South Australia, 2000 [81]
Victoria	Victoria's Mental Health Services: Framework for service delivery, 1996 [31]
	Improving services for people from a non-English speaking background, 1996 [29]
	New Directions for Victoria's Mental Health Services: The next five years, 2002 [82]

Databases

The Social Science and Data Archives (SSDA) [25] held by the Australian National University, provides information regarding Australian databases available for secondary analysis. Databases were screened to identify those with information potentially relevant to depression or suicide and ethnic minority communities. Further information was sought from the websites of the Australian Bureau of Statistics (relating to the Australian Survey of Mental Health and Wellbeing and the National Health Surveys) and the Department of Immigration and Citizenship (DIAC) (formerly the Department of Immigration, Multicultural and Indigenous Affairs), relating to the Longitudinal Sur-

veys of Immigrants to Australia. Sixty-nine databases were admitted to more detailed content analysis of their abstracts and variables.

Research Funding

Major Australian funding organisations, including the National Health&Medical Research Council (NH&MRC), Australian Research Council (ARC), VicHealth, HealthWay, and Australian Rotary Health Fund were asked to provide information on their funding priorities and currently funded projects. Websites and annual reports were inspected for relevant information. Documentation was sought for the five years prior to the time of our assessment. All materials were interpreted and relevant content aggregated on priorities and currently funded projects.

Current Research Activities

Two hundred and seventy-seven relevant university departments and research organisations were identified through university websites and directories and were surveyed to supply information on relevant research. Heads of organisations/departments were invited to send the questionnaires we supplied to any researchers known to be conducting relevant work. The questionnaire asked about the nature of the research; funding support; collaborations; research team size and disciplines; involvement of ethnic communities, caregivers and consumers; location of the work; current status of the work; and publications.

Service Programs and Projects

A nationwide survey was conducted in capital cities and major regional towns to identify specific services addressing depression in ethnic minority communities. Questionnaires were sent to 1480 organisations including ethnic community organisations, mental and general health service providers, Divisions of General Practice, public health units, Local Governments, Migrant Resource Centres, transcultural mental health services, refugee and other services. Those identifying a relevant program on a screening questionnaire were invited to provide more detailed information about potentially relevant programs or projects. All survey responses were examined as to whether the programs were specific to mental health, depression and the level of focus on ethnic minority communities. Relevant programs were analysed in relation to reported strategies and activities, barriers, supports, perceived role in depression in ethnic minority communities, partnerships and program involvement of ethnic communities, caregivers and consumers.

Results *Policies*

Preliminary examination indicated that specialised State 'transcultural mental health' policies [26-29] provided comprehensive policy coverage of issues relevant to mental health and ethnic minority communities. It should be noted that policies were almost invariably concerned with broad issues of mental health and illness and did not focus specifically on depression. Key topics (Table 2) were identified from these policies and used to content analyse each of the major Commonwealth and State/Territory mental health policies. The examination of the policies indicated a highly variable degree of attention to issues relevant to ethnic minority communities.

Against the topics covered by the transcultural mental health policies, Commonwealth policies provided a relatively comprehensive coverage of issues. Areas that were unrepresented or underrepresented included: Providing information which supports access; Interpreters/language services; Coordination of care; Support for ethnic community workers; Data collection; and Service utilisation. More recent policies (since 1995) have tended to include a clearer focus on ethnic minority communities and call for improvement of the evidence base for all

forms of mental health activity in relation to ethnic minority communities.

Table 2. List of issues addressed by State Transcultural Mental Health Policies

- access and equity
- effectiveness and efficiency
- coordination, continuity of care
- mental health services/service providers
- staff development/education/training
- planning which meets the community's needs
- collaborations and partnerships with ethnic minority communities, consumers and caregivers
- delivering culturally sensitive services
- community education/support
- providing information which supports access
- interpreters/language services
- general practice
- support for ethnic minority community workers
- assuring quality
- data collection
- research
- service utilisation
- monitoring and evaluation
- the role of specialised transcultural mental health services
- mental health promotion
- special target groups

At the time of the study there was no single policy at the Commonwealth level dedicated to the mental health of ethnic minority communities. Reference to ethnic minority communities in mainstream policies has been at the most general level, and strategies advocated for the 'special needs groups', including immigrants and refugees, were often separated from the main strategy. Approximately half of the policies examined contain a brief mention of ethnic minority communities, often as an 'afterthought', once the general policy model for the mainstream community has been developed.

All of the State mainstream mental health policies make reference to ethnic minority communities but Victoria, New South Wales, Western Australia and Queensland (referred to as 'active states' below) have sections dedicated to ethnic minority communities. These same States have explicit Transcultural Mental Health policies and have had active involvement with the Australian Transcul-tural Mental Health Network, now operating as Multicultural Mental Health Australia. They also fund specialist Transcultural Mental Health services that are dedicated to mental health service improvements relating to ethnic minority communities. These policies give clear indications of how services may be modified to respond appropriately and effectively to the needs of ethnic minority communities.

More than the Commonwealth policies, State policies consider the strategies by which improvements in service provision are to be pursued. These strategies are intended to support the work of local area-based mental health services in improving services to ethnic minority communities. Less well covered areas in the State mental health policies in relation to ethnic minority communities are issues of: Effectiveness and efficiency; Planning based on community needs; Community

education and support; and Data collection, monitoring and evaluation.

Within the active States the specialist transcultural mental health policies represent a comprehensive statement of the range of required service improvements and directions. Apart from offering clear direction to mental health services, they focus on community engagement, development, and education in relation to mental health, and the inter-linking of mental health services with community-based organisations. The specialist transcultural policies also take advantage of State-based knowledge and resources in developing local service improvements.

Despite the existence of a well-developed policy environment in Australia in relation to mental health and ethnic minority communities, there remain substantial problems in policy implementation [30]. *Victoria's Mental Health Services – The Framework for Service Delivery* [31] identifies this problem as one of motivation for reform: "...the general lack of service response to persons from different cultural backgrounds comes not so much from a lack of knowledge about what should be done but more perhaps from a lack of will to do it....it is long past the time when health providers did not have to ensure that their services are able to be provided in a culturally sensitive manner." (p. 28)

Research

Publications

Research on depression within ethnic minority communities in Australia is predominantly in three areas: research on refugees and asylum seekers (10 studies); studies related to the post-partum period (6 studies); and research on suicide (6 studies). Additional papers dealt with a range of relevant issues, but not specifically on depression in ethnic minority communities (8 studies).

In the period surveyed the most developed program of depression-relevant research was that on refugees [32-37]. This work has explored pre- and post-migration factors associated with psychological morbidity in addition to information on depression, anxiety and post-traumatic disorders. The second consistent area of work has been on post-natal depression [38-43], but limited to Arabic-speaking and Vietnamese-speaking groups. The subject of suicide received some attention [44-48], but this work has been entirely based on suicide rates in various birthplace populations and no work has been done on psychosocial factors in suicide, suicide risk and behaviours.

The remaining eight studies [49-56] cover different issues, including levels of depression, correlates of depression, epidemiology as part of the National Survey of Mental

Health and Wellbeing, general practitioner and patient agreement on mental health status, depression in general practice patients, effectiveness of training community workers, depression in women with young children, adolescents, and international students.

Higher Degree Theses

Examination of the 228 identified theses on depression in Australia since 1990 revealed only five theses (2.2 percent) addressing issues relevant to ethnic minority communities [57-61].

Databases

Examination of accessible databases indicated that few were relevant for the purposes of secondary analyses in relation to ethnic minority communities and depression. More common were databases that included information on immigrants' living conditions in Australia, including social contacts, family structure, employment, housing, perceived prejudice, physical health and a range of migration and settlement factors. These factors could be useful to analyse in as far as they can be considered as determinants (risk and protective factors) or correlates of depression.

Most of the data however are old and may be of more theoretical value than providing a picture of contemporary issues confronting immigrants. The Longitudinal Surveys of Immigrants, developed by DIAC, may also give some indication of causal pathways through the possible examination of associations of variables across several follow-up data collections, but these data provide information only for recent arrivals to Australia.

Research Funding

The assessment of funding priorities and funded projects revealed that most funding bodies provided some scope within their statements of priority to for grant submissions for mental health research on ethnic minority communities. Currently funded projects included NH&MRC projects examining suicide trends, refugee psychiatric status and service utilization, and the risk factor profile of the New South Wales Vietnam-born community; an ARC grant to study the narratives of migrants in cultural transition; and a HealthWay grant to examine depression and mental health promotion within ethnic minority and indigenous groups. The VicHealth funding round of 2001 was exceptional, supporting eight projects focusing on selective prevention activities, exploring the building of social capital and connectedness in recently arrived communities. While not specifically addressing mental disorders, this funding was based on the concept of mental wellbeing, and is essentially indistinguishable methodologically, from the over $30 million annual investment in settlement support programs funded by DIAC, for which evaluation with respect to mental health is lacking.

Overall, with respect to In the funded research identified there was a strong focus on recently arrived groups, especially refugees. There is little continuing work on the longer-term resident immigrant communities, including follow-up work from studies that have demonstrated higher rates of suicide in certain immigrant groups [44-46,48,62].

Current Research Activities

The final component in assessing Australian research was a survey of university departments and research groups. The response rate was 33%. From 277 surveyed institutions, only nine relevant projects were identified. Again there was a continuation of work on existing themes of peri-natal depression and asylum seekers. A few studies on health promotion and mental illness literacy and pathways to care could potentially contribute much needed information.

Research Activities Summary

Collectively, the body of research published and the work currently conducted is very limited in scale and scope. Little is known about the prevalence of depression, risk factors and protective factors, cultural concepts of depression and attitudes to depression, pathways to care, and uptake and effectiveness of existing interventions in relation to ethnic minority communities. For depression in ethnic minority communities there is effectively no evidence-base to support mental health policy development and service design, and there is virtually no evidence concerning effectiveness of services currently provided or regarding particular treatment approaches and models of service.

Service Provision

The response rate to the services survey was 28%. Overall, 101 programs were reported to us as being relevant to ethnic minority communities (from 97 organisations out of the 422 that responded to the survey). Among these programs, the focus on depression or mental health and ethnic minority communities was variable. We classified programs according to their relevance in addressing depression in ethnic minority communities (Table 3). Six programs directly addressed this issue while 40 were more broadly focused on mental health in ethnic minority commu-

nities. Only three mainstream mental health programs and two depression-focused programs reported cultural adaptations to respond to the particular needs of ethnic minority groups. Most organisations targeted multiple communities with the same program with little evidence of adaptation. The most frequently targeted communities were Chinese, Vietnamese, Spanish-speaking, Italian and Greek – all of which represent large and longer-term resident ethnic minority communities in Australia. This service focus contrasts sharply with the research focus, which is very much on recently arrived groups.

We reduced the wide range of information provided for the 101 programs that were reported to us by thematic/ content analysis. Programs were analysed in terms of barriers, strategies and required supports, role in addressing depression in ethnic minority communities, and involvement of ethnic minority consumers and caregivers and other ethnic minority community members. Five key themes – *Information Needs, Need for Organisation and Integration, Resource Needs, Process Barriers*, and *Program Focus* – were identified through progressive analytical coding refinements carried out by one researcher in regular consultation and review with the other researchers.

Various *Information Needs* were reported by services, including the need for research that could inform their work. The most frequent aspect of information needs was the need for *local* data, both on communities and on resources related to mental health, including information regarding demography, social conditions, epidemiology of depression, mental health issues within ethnic minority communities, the availability of services and supports, 'best practice' in service delivery to ethnic minority communities, 'working' models that involve ethnic minority communities, available ethnic and bilingual service providers, and cultural issues and community understandings of depression.

Need for Organisation and Integration involved the establishment and maintenance of collaborative links, e.g., between mainstream health and mental health services and ethno-specific community organisations. This included ethno-specific organisations providing assistance in the development of culturally appropriate programs, and mainstream organisations assisting ethnic community organisations with acquiring funds for their activities and promoting mental health activities initiated by ethno-specific organisations. Ethno-specific organisations saw a role in advocating on behalf of ethnic minority communities in relation to mental health services, program development and implementation. Despite the expressed need for collaborative work, ethno-specific services felt that they were not recognised ass having a 'legitimate place' within the health care system. On the other hand, mental health services reported a lack of coordination in their attempts to reach ethnic minority communities with their programs. There was the stated need for some 'external process' to organise and support partnership processes, particularly between ethno-specific organisations and mainstream mental health services.

General Practice was seen as not sufficiently involved with the broader community-based initiatives to deal with mental health issues and there was a stated need for general practitioners to be more effectively linked to broader community strategies for mental health. Bilingual medical professionals were considered important for this (together with bilingual allied mental health workers and specifically psychologists).

There was also an expressed need for greater involvement of consumers, caregivers and other community members from ethnic backgrounds to provide input into programs. Current input, where it oc-

curred, was predominantly through informal consultation.

Table 3. Program types and number of programs described

Program Types	Number
Type A. Ethnic minority group programs that address depression specifically	6
Type B. Ethnic minority group programs that address mental health issues with no specific focus on depression	40
Type C. Ethnic minority group programs which addressed community development issues but not directly mental health problems and depression	13
Type D. Mainstream depression program with adaptation for ethnic minority communities	5
Type E. Mainstream depression program stating ethnic communities are not excluded but there was little to suggest program adaptation for including ethnic communities	2
Type F. Mainstream mental health programs where there is a specific adaptation for including ethnic communities	3
Type G. Mainstream mental health programs, stating ethnic communities are not excluded but there was little to suggest program adaptation for including ethnic communities	22
Type H. Mainstream community development stating ethnic communities are not excluded but there was little to suggest program adaptation for including ethnic communities	10

Resource Needs included calls for increased general funding and project-specific funding to support activities within programs, and for the development and dissemination of translated materials in languages other than English. Several respondents considered linkages with State transcultural mental health centres to be useful in supporting their programs and for accessing multilingual mental health information. Several respondents expressed a need for bilingual workers and workers within the mental health system with cultural awareness or knowledge of particular ethnic minority communities. Lack of culturally appropriate services for referral or collaborative casework was considered to be a problem by several community-based organisations.

The main *Process Barriers* identified by ethno-specific services included language barriers; high caseloads preventing workers from participating in community development; lack of bilingual staff; threats to program continuity; and low literacy levels in some communities affecting program reach. Limited program reach within particular communities and subgroups within a community (e.g. men) was emphasised by mainstream mental health programs. Lack of program funding was a common concern. Barriers within mainstream organisations (as described by ethno-specific organisations) included attitudinal issues, e.g., mainstream health service staff were considered 'uncooperative' and mental health workers were described by some as lacking specific commitment to the issues of mental health of ethnic minority communities. Some respondents suggested an 'action plan' to reduce racism within the hospital and community health system. Lack of long-term funding was thought to lead to short-term planning and incapacity for longer-term activities, which were perceived as more effective for ethnic minority communities. In relation to research barriers, community-based programs emphasised difficulties in working collabora-tively with university-based researchers due to conflict over project ownership and intellectual property. Further, funding bodies were perceived as not having a commitment to prioritising the issues of mental health in ethnic minority communities.

Mainstream organisations expressed the view that ethnic minority communities 'did not trust' them and they perceived this as presenting a 'cultural barrier' to providing services. It was considered that some communities 'had different understandings of the service delivery system' and 'a lack of awareness regarding treatments', such

as counselling and psychotherapy, which diminished access to services. Several responses indicated the need to develop promotional materials in languages other than English, to participate in ethnic community events and to encourage ethnic minority community volunteer participation in their service programs.

Program Focus relates to activities and roles, either carried out or intended. There was a call to address issues of 'racism, stereotyping and discrimination' through community education or media campaigns. Mass media, ethnic media and direct information and education sessions were the main suggested forms for information provision outside direct contact through casework. This activity was seen as a means of preventing the circumstances that may contribute to depression in members of ethnic minority communities. Within ethnic minority communities, community education was seen as a key strategy for a number of outcomes, including reducing stigma associated with depression (and other mental illness), increasing knowledge and recognition of depression, and increasing community understanding of relevant health services and other available support generally, thereby improving access to care. Further, education addressing the lack of English proficiency was seen as an important strategy for improving access to a variety of supports, services, employment and information.

Education was also seen to be important in the mainstream health system, for primary care workers as well as for mental health professionals. In the view of respondents, such education should provide training on cross-cultural or cultural issues in general. Ethno-specific organisations and ethnic primary care workers were seen to require training on mental health issues in order to facilitate more effective working arrangements in relation to mental health problems. Another form of training was to 'skill' caregivers from ethnic minority communities in developing supports for their compatriot peers. At the same time, caregivers were considered as a group 'at risk' due to their highly demanding role, and in need of additional attention by services. Responses suggested the need to develop ethno-specific carer support groups, and to provide information, material assistance, respite services, counselling and referral services.

General practice was also seen as a target for training on cultural issues, although the one program attempting this indicated disappointing attendance by general practitioners.

Supporting the 'settlement' of the recently arrived was seen as an important strategy to prevent depression. There was also a repeated suggestion to link members of ethnic minority communities to social support activities, community cultural events and recreation programs. Programs developed for elderly persons from ethnic minority communities were aimed at relieving their isolation and at providing direct assistance such as referral to aged care and social services.

Direct clinical services, such as counselling, psychotherapy, psychiatric case management, psychological rehabilitation, day activity programs, self-help and mutual support groups for those with mental disorders, were all reported by mainstream mental health organisations. These were regarded as available to the whole of the community with no particular adaptations of programs to accommodate the varied needs of ethnic minority communities. Following 'best practice' was seen as a means of improving the quality of such services to members of ethnic minority communities, although there was a stated need to identify what constitutes 'best practice' in this context.

Beyond direct and supportive services and education activities, many organisations, particularly ethnic minority

community services, were perceived as having a role in advocating on behalf of the community, in contributing to the planning, development and implementation of programs and services, and in working towards the development and implementation of policy.

Discussion

The analysis of policies revealed that, collectively, they provide comprehensive direction for service reform and practice in relation to ethnic minority communities. Australian States with longer-term commitment to addressing the problems of ethnic minority groups have specialised transcultural mental health policies and a range of strategies in place. Policy and policy implementation should be judged in the context of the broader reforms undertaken in the Australian mental health system [63]. There have been substantial competing priorities in the context of broadly under-funded mental health services [64], particularly as they have moved from hospital-based to community-based services. Moreover, the emphasis initially under the National Mental Health Strategy was strongly interpreted as addressing 'severe' mental disorders to the near exclusion of the common mental disorders [65]. Along with these changes there has been a shift in the structure and skills in the mental health workforce. The level of attention to population diversity issues is better appreciated within the broader context of the very substantial systemic reforms that have occurred in mental health services in the past decade.

Nevertheless there is clearly a need to integrate the disparate policy statements from Commonwealth and State and Territories governments into a more coherent strategy. It is our view that policy documents should be framed with diversity considered as a core characteristic of the Australian community, rather than a special issue requiring later ('afterthought') adjustments of mainstream models of care. A key barrier to policy reforms is that information on mental health, service delivery, and effectiveness of services in relation to Australia's ethnic minority communities is lacking. The promotion of research is of course essential in formulating evidence-based policies, strategies and programs.

The scale and diversity of research on ethnic minority communities and depression in Australia is extremely limited. Research is needed in order to develop a systemic approach to depression in ethnic minority communities and to create an evidence-base for the design and targeting of interventions in accordance with Commonwealth and State policy intentions. The low level of research on ethnic minority communities is surprising given the multicultural composition of the Australian community. The currently available research provides limited information on some ethnic minority communities and often this information is not relevant to the development of mental health strategies. The information needed includes population prevalence of common mental disorders, knowledge of common risk and protective factors affecting incidence and chronicity of disorders, mental health literacy and pathways to care, the community-general practice interface, effectiveness of mental health promotion approaches, and evaluation of integrated mental health care models that include both public and private specialist mental health services and the primary care system.

In addition, the multicultural composition of the community affords opportunities for theory-driven research into the interaction between culture and psychopathology, migration and psychopathology, and cultural factors affecting treatment efficacy and effectiveness (including pharmacological approaches).

There is a significant gap between the information needs as expressed by

service providers and the scope and focus of the research that is being done. Failure to carry out the research that is needed perpetuates population health inequalities and inequities in mental health service provision.

With respect to services and programs five key themes were identified in the responses to the survey. These were *Information Needs*, *Need for Organisation and Integration*, *Resource Needs*, *Process Barriers*, and *Program Focus*. These are summarised above and need not be repeated here. Addressing the variety of issues covered under these themes requires approaches that constructively address the issues and particular agendas of a number of key players: ethno-specific welfare and social services organisations, policy makers and program funding bodies, primary care and general practice, specialist mental health services, consumer, carer and community organisations, research groups and education and training organisations. There is no simple way to integrate such a range of agendas. Such integrated approaches are being promoted and pursued by state transcultural mental health centres and by the national network Multicultural Mental Health Australia.

Conclusion

In Australia considerable policy attention has been devoted to the problem of mental illness in, and provision of services to, a multicultural population. Several key problems remain. The first is that the fundamental reality of the cultural and linguistic diversity of the population has not found its way into the consciousness of policymakers, so that the problems of ethnic minority communities (and other population sub-groups) are generally tacked on in 'special needs' sections of the policy in question. Suggested solutions are then inevitably add-ons after key policy decisions are made. The issue of population diversity is simply not a significant consideration in the framing of policy directions. The second is that policy implementation lags far behind policy intentions. Much of what policy documents state about necessary changes in the structure and operations of mental health services in relation to ethnic minority communities has not, and will not, see the light of day. The issue of accountability for policy implementation requires considerable attention in this as in many other areas. The third, and in many ways the most fundamental, problem is the lack of systematic rigorous evidence for policy and practice. The research base is extremely limited. Innovative services approaches are almost never evaluated. From the perspective of service development and reform one of the more wasteful and negligent practices is the failure by governments to scale up innovative services that have been demonstrated to be effective.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

IHM contributed to the conception and design of the study, securing research funding, interpretation of results and writing. SK contributed to the design of the study, securing research funding, interpretation of results and writing. RK managed the process of data collection and analysis, with input throughout from IHM and SK, and wrote early drafts of study results. Minas completed the final version of the paper.

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References:

1. Ustun TB, Ayuso-Mateos JL, Chatterji S,

Mathers CD, Murray CJL: Global burden of depressive disorders in the year 2000. British Journal of Psychiatry 2004, 184:386-392.

2. Murray CJL, Lopez AD: The Global Burden of Disease: a Comprehensive Assessment of Mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Cambridge , Harvard University Press; 1996.

3. Mathers CD, Vos ET, Stevenson CE, Begg J: The Australian burden of disease study: measuring the loss of health from diseases, injuries and risk factors. Medical Journal of Australia 2000, 172:592-596.

4. Mental Health and Special Programs Branch (Commonwealth): National Action Plan for Promotion, Prevention and Early Intervention for Mental Health 2000. Canberra , Mental Health and Special Programs Branch, Commonwealth Department of Health and Aged Care; 2000.

5. Mental Health and Special Programs Branch (Commonwealth): Promotion, Prevention and Early Intervention for Mental Health 2000 - A Monograph. Canberra , Mental Health and Special Programs Branch, Commonwealth Department of Health and Aged Care; 2000.

6. Depression Drafting Group (Commonwealth): National Action Plan for Depression. Canberra , Mental Health and Special Programs Branch, Commonwealth Department of Health and Aged Care; 2000.

7. Commonwealth Department of Health and Aged Care: Life: a framework for prevention of suicide and self-harm in Australia. Canberra , Mental Health and Special Programs Branch, Commonwealth Department of Health and Aged Care; 2000.

8. Beyondblue - The National Depression Initiative: [http://www.beyon dblue.org.au].

9. Mental Health Branch (Commonwealth): National Standards for Mental Health Services. Canberra , Commonwealth Department of Health and Family Services, Commonwealth of Australia; 1996.

10. Multicultural Mental Health Australia: [http://www.mmha.org.au].

11. Mitchell P, Malak A, Small D: Bilingual professionals in community mental health services. Aust N Z J Psychiatry 1998, 32(3):424-433.

12. Ziguras S, Klimidis S, Lewis J, Stuart G: Ethnic matching of clients and clinicians and use of mental health services by ethnic minority clients. Psychiatric Services 2003, 54(4):535-541.

13. Marsella AJ, Sartorius N, Jablensky A, Fenton FR: Cross-cultural studies of depressive disorders: an overview. In Culture and Depression: Studies in the Anthropology and Cross-Cultural Psychiatry of Affect and Disorder Edited by: Kleinman A, Good B. Berkley , University of California Press; 1985:299-324.

14. Kirmayer LJ: Cultural variations in the clinical presentation of depression and anxiety: implications for diagnosis and treatment. J Clin Psychiatry 2001, 62 Suppl 13:22-8; discussion 29-30.

15. Draguns JG: Disorders of clinical severity. In Handbook of Cross-Cultural Psychology Psychopathology Volume 6. Edited by: Triandis HC, Draguns JG. Boston , Allyn & Bacon; 1980:99-174.

16. Yap PM: Mental diseases peculiar to certain cultures: a survey of comparative psychiatry. Journal of Mental Science 1951, 97:313-327.

17. Westermeyer J, Janca A: Language, culture and psychopathol-ogy: conceptual and methodological issues. Transcultural Psychiatry 1997, 34:291-311.

18. Westermeyer J: Psychiatric Diagnosis across cultural boundaries. American Journal of Psychiatry 1985, 142:798-804.

19. Kleinman A: Depression, somatization and the new cross-cultural psychiatry. Social Science and Medicine 1977, 11:3-10.

20. Parker G, Gladstone G, K.T. C: Depression in the planet's largest ethnic group: the Chinese. The American Journal of Psychiatry 2001, 158:857-864.

21. Altarriba J, Santiago-Riviera: Current perspectives on using linguistic and cultural factors in counselling the Hispanic client. Professional Psychology: Research and Practice 1994, 25:388-397.

22. Del Castillo LR: Effects of interpreters on the evaluation of psy-chopathology in non-English speaking patients. American Journal of Psychiatry 1970, 136(2):171-174.

23. Marcos LR, Alpert M, Urcuyo L: The effect of interview language on the evaluation of psychopathology in Spanish-American schizophrenic patients. American Journal of Psychiatry 1973, 130:549-553.

24. Marcos LR: Effects of interpreters on the evaluation of psycho-patology in non-English speaking patients. American journal of Psychiatry 1979, 136:171-174.

25. The Social Science and Data Archives (SSDA). : The Social Science and Data Archives (SSDA). [http://assda.anu.edu.au/].

26. Mental Health Division Department of Health Government of Western Australia: A Transculturally Orientated Mental Health Service for Western Australia. Perth , Mental Health Division, Department of Health, Government of Western

Australia; 2001.

27. Mental Health Branch (Queensland): Non-English Speaking Background Mental Health Policy Statement. Brisbane , Mental Health Branch, Queensland Health; 1995.

28. NSW Health Department: Caring for Mental Health in a Multicultural Society - A Strategy for the Mental Health Care of People from Culturally and Linguistically Diverse Backgrounds. Sydney , NSW Health Department; 1999.

29. Psychiatric Services Branch (Victoria): Improving Services for People from a Non-English Speaking Background. Melbourne , Victorian Department of Human Services; 1996.

30. Ziguras SJ: Implementation of ethnic health policy in community mental health centres in Melbourne. Aust N Z J Public Health 1997, 21(3):323-328.

31. Psychiatric Services Division (Victoria): Victoria's Mental Health Service: The Framework for Service Delivery: Better Outcomes through Area Mental Health Services. Melbourne , Psychiatric Services Division, Victorian Government Department of Health and Community Services; 1996.

32. Steel Z, Silove D, Bird K, McGorry P, Mohan P: Pathways from war trauma to posttraumatic stress symptoms among Tamil asylum seekers, refugees, and immigrants. Journal of Traumatic Stress 1999, 12(3):421-435.

33. Steel Z, Silove DM: The mental health implications of detaining asylum seekers. Med J Aust 2001, 175(11-12):596-599.

34. Steel Z, Silove D, Phan T, Bauman A: Long-term effect of psychological trauma on the mental health of Vietnamese refugees resettled in Australia: a population-based study. Lancet 2002, 360(9339):1056-1062.

35. Sultan A, O'Sullivan K: Psychological disturbances in asylum seekers held in long term detention: a participant-observer account. Medical Journal of Australia 2001, 175(3):593-596.

36. Silove D, Steel Z, McGorry P, Mohan P: Trauma exposure, postmi-gration stressors, and symptoms of anxiety, depression and post-traumatic stress in Tamil asylum-seekers: comparison with refugees and immigrants. Acta Psychiatr Scand 1998, 97(3):175-181.

37. Silove D, Sinnerbrink I, Field A, Manicavasagar V, Steel Z: Anxiety, depression and PTSD in asylum-seekers: assocations with pre-migration trauma and post-migration stressors. British Journal of Psychiatry 1997, 170:351-357.

38. Matthey S, Barnett BE, Elliott A: Vietnamese and Arabic women's responses to the Diagnostic Interview Schedule (depression) and self-report questionnaires: cause for concern. Aust N Z J Psychiatry 1997, 31(3):360-369.

39. Matthey S, Silove D, Barnett B, Fitzgerald MH, Mitchell P: Correlates of Depression and PTSD in Cambodian women with young children: a pilot study. Stress Medicine 1999, 15:103-109.

40. Stuchbery M, Matthey S, Barnett B: Postnatal depression and social supports in Vietnamese, Arabic and Anglo-Celtic mothers. Social Psychiatry and Psychiatr Epidemiology 1998, 33(10):483-490.

41. Barclay L, Kent D: Recent immigration and the misery of motherhood: a discussion of pertinent issues. Midwifery 1998, 14(1):4-9.

42. Nahas V, Amasheh N: Culture care meanings and experiences of postpartum depression among Jordanian Australian women: a transcultural study. Journal of Transcultural Nursing 1999, 10(1):37-45.

43. Barnett BE, Matthey S, Boyce P: Migration and motherhood: a response to Barclay and Kent (1998). Midwifery 1999, 15(3):203-207.

44. Taylor R, Morrell S, Slaytor E, Ford P: Suicide in urban New South Wales, Australia 1985-1994: Socio-economic and migrant interactions. Soc Sci Med 1998, 47(11):1677-1688.

45. Burvill PW: Migrant suicide rates in Australia and in country of birth. Psychological Medicine 1998, 28:201-208.

46. Burvill P: Suicide in the multiethnic elderly population of Australia, 1979-1990. International Psychogeriatrics 1995, 7:319-333.

47. Domino G, Niles S, Raj SD: Attitudes towards suicide: a cross-cultural comparison of Singaporean and Australian university students. Omega 1993, 28:125-127.

48. Morrell S, Taylor R, Slaytor E, Ford P: Urban and rural suicide differentials in migrants and the Australian-born, New South Wales, Australia 1985-1994. Social Science and Medicine 1999, 49:81-91.

49. Oei PS, Notowidjojo F: Depression and loneliness in overseas students. The International Journal of Social Psychiatry 1990, 36:121-130.

50. Williams H, Carmichel A: Depression in mothers and behaviour problems with their preschool children. J Paediatr Child Health 1991, 27(2):76-82.

51. Klimidis S, Stuart G, Minas IH, Ata AW: Immigrant status and gender effects on psychopathology and self-concept measures in adolescents: A test of the migration-morbidity hypothesis. Comprehensive Psychiatry 1994, 35:393-404.

52. Mildred H, Paxton SJ, Wertheim EH: Risk

factors for eating disorders in Greek- and Anglo-Australian adolescent girls. International Journal of Eating Disorders 1995, 17:91-96.

53. McLennan W: Mental Health and Wellbeing: Profile of Adults, Australia 1997. Canberra , Australia Bureau of Statistics; 1998.

54. Comino EJ, Silove D, Manicavasagar V, Harris E, Harris MF: Agreement on symptoms of anxiety and depression between patients and GPs: the influence of ethnicity. Family Practice 2001, 18:71-77.

55. Knox SA, Brit H: A comparison of general practice encounters with patients from English-speaking and non-English speaking backgrounds. Medical Journal of Australia 2002, 177:98-101.

56. Tse T: Islamic community worker program for the management of depression. Australian e-Journal for the Advancement of Mental Health 2002, 1(2): [http://www.auseinet.com/journal/vol1iss2/ index.php].

57. Alarcon H: Psychological analysis of unemployment, self-esteem and depression among professional migrants. In Faculty of Education Melbourne , Monash University; 2001.

58. Croft S: Depression in Vietnamese adolescents. In Dept not indicated Sydney , University of Sydney; 1990.

59. Kapelus S: Levels of depression and anxiety in a sample of South African migrants: a measure of adaptability. In Psychology Department Sydney , Macquarie; 1997.

60. Small R: Mothers in a new country (MINC): an Australian study of Vietnamese, Turkish, Filipino women's experience of maternity care and of maternal depression after childbirth. In Centre for the Study of Mothers' and Children's Health Melbourne , LaTrobe University; 2000.

61. Von Treuer K: Prevalence, social and biological risk factors between Australian-born Australian women and Vietnamese-born Australian women with post-natal depression. In Department of Psychology Melbourne , LaTrobe University; 1999.

62. McDonald B, Steel Z: Immigrants and Mental Health: An Epide-miological Analysis. Sydney , Transcultural Mental Health Centre; 1997.

63. Commonwealth Department of Health and Aged Care: National Mental Health Report 2000: Sixth Annual Report. Changes in Australia's Mental Health Services under the First National Mental Health Plan of the National Mental Health Strategy. Canberra , Commonweatlh of Australia.; 2000.

64. Andrews G, Hall W, Teesson M, Henderson S: The Mental Health of Australians. Canberra , Commonwealth Department of Health and Aged Care; 1999.

65. Betts V, Thornicroft G: International Mid-term Review of the Second National Mental Health Plan for Australia. Canberra , Mental Health and Special Programs Branch, Commonwealth Department of Health and Aged Care; 2001.

66. Australian Health Ministers: National Mental Health Policy. Canberra , Commonwealth Department of Health and Community Services; 1992.

67. Australian Health Ministers: Mental Health Statement of Rights and Responsibilities. Canberra, Commonwealth Department of Human Services and Health; 1991.

68. Australian Health Ministers: Second National Mental Health Plan. Canberra , Mental Health Branch, Commonwealth Department of Health and Family Services; 1998.

69. Mental Health Branch (Commonwealth): Mental Health Promotion and Prevention National Action Plan under the Second National Mental Health Plan: 1999-2003. Canberra , Promotion and Prevention Section, Mental Health Branch, Commonwealth Department of Health and Aged Care; 2000.

70. Mental Health Branch (Commonwealth): Youth Suicide in Australia: the National Youth Suicide Prevention Strategy. Canberra , Mental Health Branch, Commonwealth Department of Health and Family Services; 1997.

71. ACT Department of Health and Community Care: The Future of Mental Health Services in the Australian Capital Territory -Moving Towards 2000 and Beyond - A Whole of Territory Strategic Plan 1998-2001. Canberra , ACT Department of Health and Community Care, Australian Capital Territory Government; 1998.

72. NSW Health Department: Caring for Mental Health - A Framework for Mental Health Care in NSW. Sydney , NSW Health Department; 1998.

73. NSW Health Department: Caring for Older People's Mental Health - A Strategy for the Delivery of Mental Health Care for Older People in NSW. Sydney , NSW Health Department; 1998.

74. NSW Health Department: Getting in Early - A Framework for Early Intervention and Prevention in Mental Health for Young People in NSW. Sydney , NSW Health Department; 2001.

75. Tasmania Department of Health and Human Services: Tasmanian Multicultural Policy. Hobart , Tasmania Department of Health and Human Services; 2001.

76. Tasmania Department of Health and Human Services: Rural Mental Health Plan 2001-2004. Hobart , Tasmania Department of Health and Human Services; 2001.

77. Tasmania Mental Health Services: A Plan for Now and the Future - Strategic Plan for 1999-2002. Tasmania , Mental Health Services; 1999.

78. Smith G, McCavanagh D, Williams T, Lipscombe P: Making a Commitment: The Mental Health Plan for Western Australia.Perth , Health Department of Western Australia; 1996.

79. Queensland Health: Ten Year Mental Health Strategy for Queensland. Brisbane , Queensland Health; 1996.

80. Queensland Health: Queensland Health Multicultural Policy Statement. Brisbane , Queensland Health; 2000.

81. Mental Health Services (South Australia): A New Millenium - A New Beginning - Mental Health in South Australia. Adelaide , Mental Health Services, Department of Human Services; 2000.

82. Psychiatric Services Branch (Victoria): New Directions for Victoria's Mental Health Services: the Next Five Years. Melbourne , Victorian Department of Human Services; 2002.

ANALYSING NSW STATE POLICY FOR CHILD OBESITY PREVENTION: STRATEGIC POLICY VERSUS PRACTICAL ACTION

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There is increasing worldwide recognition of the need for government policies to address the recent increases in the incidence and prevalence of childhood obesity. The complexity and inter-relatedness of the determinants of obesity pose a genuine policy challenge, both scientifically and politically. This study examines the characteristics of one of the early policy responses, the NSW Government's *Prevention of Obesity in Children and Young People: NSW Government Action Plan 2003–2007* (GAP), as a case study, assessing it in terms of its content and capacity for implementation.
This policy was designed as an initial set of practical actions spanning five government sectors. Most of the policy actions fitted with existing implementation systems within NSW government, and reflected an incremental approach to policy formulation and implementation.
As a case study, the *NSW Government Action Plan* illustrates that childhood obesity policy development and implementation are at an early stage. This policy, while limited, may have built sufficient commitment and support to create momentum for more strategic policy in the future. A more sophisticated, comprehensive and strategic policy which can also be widely implemented and evaluated should now be built on this base.

Introduction

Childhood obesity has emerged as a major public health issue only recently. To date the public discourse has focused on the magnitude of the problem and relatively narrow debates about causes and solutions. Both the public debates and initial policy responses belie the complex causal determinants of childhood obesity and the considerable policy and investment challenges facing governments.

Using the NSW Government's *Prevention of Obesity in Children and Young People: NSW Government Action Plan 2003–*

2007 (GAP) [1] as a case study, this paper illustrates the argument that childhood obesity policy is still in its infancy and facing significant challenges in delivering the complex changes that will be necessary to achieve positive outcomes.

Background

Over the past two decades there has been a significant increase in the proportion of overweight and obese children in NSW and in Australia. This is part of a worldwide trend. The most recent NSW estimate, in 2004, found that the prevalence of overweight and obesity among boys was 26% and among girls was 24% [2]. This is a significant increase from 1985 when the prevalence among boys and girls was 11–12% [2]. The increases in the proportion of children who are overweight or obese have profound social, cultural, emotional, medical and economic consequences. For these reasons, childhood obesity prevention has become a topic of community concern and media debate, as well as policy development.

Public policy

The term 'policy' refers to a procedure or guide to action to achieve intended goals and, purportedly or actually, functions to set priorities and guide resource allocation. While policy can take the form of a formal statement, that is explicit and open to comment and accountability, this is not a necessary aspect, and policy can remain unwritten [3]. 'Public policy' refers to policy at any level of government [4].

It is widely understood that the policymaking process is influenced by social factors including cultural norms, stake-

holder interests, power relations, ideological beliefs and organizational cultures, as well as scientific knowledge [5].

Policy implementation has been less extensively researched. Stated simply, it involves putting proposed actions into effect. However, policies vary in the ease with which they can be implemented; and jurisdictions vary in their capacity to implement new policies. Disjunctions between policy and implementation are commonplace. Furthermore, differences in what politicians and the public expect, and what the infrastructure can deliver, are common in public health [6].

Childhood obesity prevention policy

In Australia the first policy response to the emerging problem of obesity came from the National Health and Medical Research Council (NH&MRC), which in 1997 produced the report *Acting on Australia's weight: a strategic plan for the prevention of overweight and obesity* [7]. The report focused on promoting physical activity and healthy diet in key settings, acknowledged that increased prevalence of overweight and obesity in the population was due to lifestyle and environmental factors, and singled out children and adolescents as a target group. Despite the report's strengths, its recommendations were largely ignored at that time [8].

Five years later, in 2002, the NSW Government held the NSW Childhood Obesity Summit in the NSW Parliament [9], putting childhood obesity on the political and public agenda, at least at that time. While the precise circumstances and impetus which led to the government convening this summit have not been documented, the interplay of social factors and competing interests at the Summit has been reported elsewhere [8]. The NSW Summit did provide recognition that childhood obesity was an emerging population health problem and that there were multiple stakeholders involved in creating the problem and, potentially, in addressing it.

The 2002 Summit marked the beginning of a planned, formal and serious response to childhood obesity in NSW and Australia. Action in NSW was followed by the formulation of a national approach by the National Obesity Taskforce [10] and policies in other states and territories [11]. It also coincided with the development of policies internationally, such as in Europe and North America (for example, *Preventing Childhood Obesity: Health in the Balance* [12]).

Childhood obesity prevention policy challenges

Child obesity policies have had to deal with three fundamental issues:

- The complexity of causal determinants which imply that a broad range of potential interventions will be required.
- The lack of a well-developed body of evidence on the effectiveness of interventions.
- The fact that many of the necessary responses are outside the direct ambit or control of the health sector.

Complex causal explanations of population health problems pose genuine policy challenges [13], and this is the case for the prevention of childhood obesity. Debates about the relative contributions of different determinants, as well as the difficulties of proving that interventions are effective, add to the contestability of policy options. For example, the food industry rejects calls for reforms in that sector by shifting the blame for childhood obesity onto the lack of exercise [14].

Most of the multiple determinants are the responsibility of sectors other than health, so that many non-health sectors must be engaged in formulating and implementing the policy responses that will be necessary for effective solutions [15]. In recognition of the complexity of childhood obesity prevention, the International Obesity Task Force (IOTF) has empha-

sised the importance of a comprehensive public health approach and developed a list of principles and recommendations to guide policy formulation [9].

While it is expected by the population health sector that policy be based on research-derived evidence of effectiveness, this is not always the case or even possible. The complexity of determinants and responses makes the accumulation of evidence about effective interventions particularly difficult [16,17]. In some cases, evidence points to actions that are politically unacceptable, and evidence is more passionately contested. The contested nature of policy means that policy analysis studies often focus on the dynamics of each step in policymaking.

Alternatively, the focus of policy analysis can be on features of the policy itself, such as:

- Was it the right policy? For example, this form of analysis may take account of whether policy was evidence-based, and whether it was appropriate to the target group and social context.
- Was the scope and scale adequate? Was the scale and intensity of effort sufficient to achieve the policy goals?
- Was the policy effective? Did the policy achieve stated or intended goals or performance indicators? Were there any unintended consequences?
- Was it feasible? That is, did the available resources and infrastructure enable the policy to be implemented?

These questions were considered in this study on the implementation of childhood obesity prevention policy in New South Wales.

Preventing obesity in children and young people: the NSW Government Action Plan 2003–2007 (GAP)

In response to the 2002 Summit, childhood obesity prevention became a NSW Government priority, and the NSW Government launched the *Prevention of Obesity in Children and Young People: NSW Government Action Plan 2003–2007* (GAP) [1]. This plan represented initial policy steps recommended by participants at the Summit (a combination of population health and clinical experts, industry/sectoral representatives, community representatives and politicians) to address the social, economic, environmental and behavioural factors contributing to the problem of childhood obesity.

The GAP identified 34 actions that NSW Health Department, NSW Department of Education and Training, NSW Department of Community Services, NSW Department of Sport and Recreation and NSW Roads and Traffic Authority agreed to implement in order to expand their contributions to the prevention of obesity in children and young people. The priority areas comprised:

- Healthy Schools
- An Active Community
- Supporting Parents
- Healthy Child and Out-of-School Care
- Community Understanding
- Increasing Our Knowledge
- Governments and Industry and the Community Working Together.

Methods

This paper describes a systematic analysis of the implementation of the NSW GAP policy, with specific attention being given to the content, scope and feasibility for implementation. The analysis did not cover the policy development process, or the effectiveness of the policy in achieving specific outcomes, as information about these was not available at the time of the study.

Policy guides published by the IOTF and World Health Organization (WHO), and written by international experts, provided appropriate and internationally authoritative benchmarks against which to assess the quality and implementation of the GAP. The IOTF's principles and recommended actions outline the key fea-

tures of a public health approach to obesity prevention [16] and provide reference points against which to assess scope and content of the actions proposed in the GAP. The WHO Stepwise Framework for Chronic Disease Prevention Policy implementation steps (see Table 1) provides criteria against which to assess the scope and scale of policy implementa tion [18,19]. It distinguishes core actions that can be implemented with existing resources and structures, from those that require an expanded level of resources and those that would require substantial new resources. Its application to the GAP explicitly links the availability of resources with the different stages of policy implementation.

Table 1. WHO Stepwise Framework for Chronic Disease prevention – policy implementation steps

Policy implementation steps	Description
Implementation Step 1 **CORE**	Interventions that are feasible to implement with existing resources in the short term
Implementation Step 2 **EXPANDED**	Interventions that are possible to implement with a realistically projected increase in, or reallocation of, resources in the medium term.
Implementation Step 3 **DESIRABLE**	Evidence-based interventions which are beyond the reach of existing resources.

(World Health Organization 2005)

Based on benchmarks derived from the documents noted above, the authors defined criteria to guide the policy analysis. The benchmarks were used in order to minimise arbitrary judgements, and provide legitimacy and credibility, to ensure that the evaluation was acceptable and useful to policymakers.

The assessment of the GAP was conducted by one of the authors (CT), who reviewed documentation and interviewed stakeholders in each of the agencies responsible for policy implementation. The findings were checked by another author (LK) and reviewed by the interviewees. All authors were involved in discussion and interpretation of the findings to ensure the rigour and credibility of results.

Results

Scope and potential to prevent childhood obesity

Table 2 presents a summary of how the actions correspond to the IOTF principles and recommendations. Overall, the proposed actions displayed features that correspond to IOTF recommendations and principles. A number of relevant government departments were involved, actions were taken and program managers did respond to the issue and link their actions to the prevention of childhood obesity. However, the policy fell short of the IOTF recommendations, in terms of breadth, sustainability of changes, and scale of actions to be implemented.

GAP did reflect a collaborative approach between government agencies beyond the health sector, but did not extend to include all relevant sectors, such as urban or transport planning, or agriculture. The focus of the policy was on programs and specific, existing initiatives, rather than an overall strategic approach. Most of the actions that had been taken were not sustainable. Half of the 34 proposed actions fitted within agencies' core business, while others involved an extension of existing roles (Table 3). Importantly, GAP did not define specific outcomes or set evaluation indicators, so that there was no precise way to measure its effectiveness.

Table 2: Analysis of GAP actions according to IOTF recommended actions and principles

IOTF Recommended Action (1 to 5)	Comments
1. Address both dietary habits and physical activity patterns of the population.	Overall, actions cover both physical activity and nutrition, but tend to be identified and implemented separately, in different settings and jurisdictions and different target groups. Information-dissemination actions were the only actions that addressed physical activity and food consumption in an integrated way.
2. Address both societal and individual level factors.	The *GAP* contains a mix, with the majority of actions directed at social and environmental factors in specific settings (e.g. school canteens).
3. Address both immediate and distant causes	Focus is on behaviours in everyday settings, rather than social, cultural factors
4. Address multiple focal points and levels of intervention (i.e. national, regional, community and individual levels)	While there is a mix of local and state level action, in many cases the local projects are limited to a small number of sites and unlikely to achieve widespread reach or population effect, unless they were implemented on a major scale across the state, or there is a clear process for staged dissemination and statewide implementation.
5. Build links between sectors that may be otherwise viewed as independent.	The *Action Plan* brings together programs across key portfolios and creates a significant cross-sectoral agenda and basis for collaboration. However, there are a number of factors that are not addressed, including transport, safety, media and food supply.
6. Include both policies and programmes.	The *GAP* is weighted more towards program implementation, rather than policy development. Only three actions relate to changing policy. However, some of the programs have a basis in existing policy, such as earlier commitments to build off-road cycleways.
IOTF PRINCIPLES (1 to 10)	
Principle 1. Education alone is not sufficient to change weight-related behaviours. Environmental and social interventions are also required to promote and support behavioural change.	While the majority of actions include environmental interventions, many are small scale and local.
Principle 2. Action must be taken to integrate physical activity into daily life, not just to increase leisure time exercise.	Seven actions within the *Plan* fit this principle.
Principle 3. Sustainability of programmes is crucial to enable positive change in diet, activity and obesity levels over time.	The *GAP* is primarily concerned with initiating discrete actions, and does not emphasise structural changes or sustainability.
Principle 4. Political support, intersectoral collaboration and community participation are essential for success.	*GAP* was initiated with the significant political support and community participation associated with the 2002 Childhood Obesity Summit
Principle 5. Acting locally, even in national initiatives, allows programmes to be tailored to meet real needs, expectations and opportunities.	Many of the *GAP*'s actions support local initiatives. While this approach can support appropriate and tailored approaches, it is important to note that many areas and communities will not be recipients of local initiatives, as actions have only been implemented in selected locations and not universally across NSW
Principle 6. All parts of the community must be reached – not just the motivated healthy.	Many *GAP* actions adhere to this principle through adopting a targeted or local approach. However, as this occurred in the context of small projects, they did not reach wide sections of the population.
Principle 7. Programmes must be adequately resourced.	While NSW Treasury did not directly allocate additional resources, NSW Health allocated additional funding, totalling $12 million over three years (2004/5 to 2006/7). These funds were concentrated on two new initiatives, the Healthy Schools Canteen Strategy and the establishment of the Centre for Overweight and Obesity. The recent investment of $7.5 million over 5 years by NSW Health and Hunter New England Area Health Service for a large Area-wide, intensive demonstration project (Hunter New England child obesity prevention program), represents a major investment by NSW Government.
Principle 8. Where appropriate, programmes should be integrated into existing initiatives.	This principle is central to the *GAP*'s design, as 50% of actions were identified as core actions for existing agencies.
Principle 9. Programmes should build on existing theory and evidence.	*GAP*'s actions are based on best available evidence, as well as health promotion theory. Note that there was limited evidence regarding effective interventions.
Principle 10. Programmes should be properly monitored, evaluated and documented. This is important for dissemination and transfer of experiences.	The *GAP* did not specify any impact (e.g. children's eating and physical activity behaviours) or outcome (e.g. population weight status) indicators for reporting and monitoring purposes. The complexity of multiple determinants influencing children's weight status makes it difficult to measure and attribute the direct impact of the actions listed in the *Plan*. This is particularly true for analysing the contribution of actions that have obesity as a secondary objective.

Table 3: Classification of GAP proposed actions as core and expanded

Core implementation actions (Interventions that are feasible to implement with existing resources in the short term)	Expanded Implementation Actions (Interventions that are possible to implement with a realistically projected increase in, or reallocation of, resources in the medium term)
HEALTHIER SCHOOLS	
School Sport Foundation	Healthy School Canteens Strategy – policy
Revitalization of secondary school sports program	Healthy School Canteens Strategy – information
Support materials for teachers to implement and supervise sport programs	NSW Health will increase funding for NSW School Canteen Association
Professional support for teachers to implement new Years 7–10 Personal Development, Health and Physical Education syllabus	
Distribute resources about school based strategies for getting students active	
Rock Eisteddford Challenge and Croc Rock Festivals	
AN ACTIVE COMMUNITY	
Modify the Active Communities Grants Scheme to increase the focus on preventing childhood obesity	Funding for Public Health Policy Officer position in Local Government Association
Work with members of the Active Communities Network to strengthen the understanding of childhood obesity issues	
The promotion of walking and cycling through community based initiatives like Bike Week.	
Building off-road cycleways	
Support local government to develop and construct local cycleway networks.	
Provide financial assistance and expertise for local government to develop Pedestrian and Access Mobility Plans.	
SUPPORTING PARENTS	
The Early Intervention Program and Flexible Child Care and Family Service projects	Additional funding to NSW Branch of the Australian Breastfeeding Association
Support and information to parents about healthy weight through Families First (early intervention, home visiting program)	Development and dissemination of NSW Breastfeeding policies
	Expert Taskforce on O&O support and treatment services
HEALTHY CHILD AND OUT-OF-SCHOOL CARE	
Nutrition information and advice on good practice in physical activity for children services and out-of-school hours programs	Active Out-of-School Hours Care pilot programs: ◦ Trialling of various ways of providing physical activity ◦ Development and trialling of a training program for OSHC staff ◦ Development and trialling of a start-up package for Centres ◦ Trialling of physical activity policy guidelines for OSHC centres ◦ Evaluation of the key elements of success.
Nutrition and physical education training programs for child care professionals	Develop and trial a physical activity training package for staff working in out-of-school hours care (OSHC) centres; based on the competencies identified in the Certificate IV 'Train the Trainer' Physical Activity for Children and Youth.
COMMUNITY UNDERSTANDING	
NSW Health will develop and maintain the overweight and obesity website	State-wide community education campaign Publish an easy to use compendium of nutrition and physical activity related information and resources on NSW Health's Childhood Obesity Website. Develop a user-friendly, online training program providing information on physical fitness, nutrition and healthy lifestyle options for children
INCREASING OUR KNOWLEDGE	Establishment of Centre for Overweight and Obesity and Australian Child and Adolescent Obesity Research Network (ACAORN) to support research. Schools Physical Activity and Nutrition Survey
GOVERNMENTS, INDUSTRY AND COMMUNITY WORKING TOGETHER	Not specified – Government, Industry and Community Working Together

Discussion

The GAP's array of seven priority topic areas, five responsible agencies and 34 actions represented cross-sector commitment to action. The identified actions were clearly designed to be implemented within the constraints of existing resources in the short-term, or with small increases in resources in the medium term. However, the small scale on which some of the actions were implemented (for example, community based projects in only a small number of communities) suggests that the likelihood of achieving any population level changes in behaviour, environment or weight status was low. On the other hand, such interventions may contribute to evidence of efficacy that may, in turn, be useful in arguing for greater investment and a more sustained, large-scale response in the future.

It can be argued that this modest policy, with a mix of core and expanded actions, was appropriate in the early years of a government-led response to a major population health problem for which there is limited evidence upon which to base investment in major new interventions. In 2002, when the NSW Childhood Obesity Summit was held, there was limited evidence in relation to effective interventions to address childhood obesity, and to guide decisions about interventions with the greatest potential to produce health benefits. The practical approach that was adopted by GAP can be perceived as staking out a place for obesity prevention on the public policy agenda and harnessing existing infrastructure.

However, the focus on a narrow set of practical actions linked with existing core business, rather than strategic policy, remains open to critique. The GAP presented a list of actions that were based on Summit recommendations, which the relevant government departments agreed to complete by 2007. The Summit resolutions themselves have been critiqued as being potentially diluted and narrow because they emerged from negotiations between competing stakeholders, including food industry groups [8].

The GAP was not a strategic response, in the sense of providing a long-term vision, specific goals or a broadly inte-grative or sustainable approach, although this is what the IOTF has recommended. GAP provided a starting point for action, rather than a fully developed policy that tackled fundamental challenges related to the complexity of causes, building large scale cross-sector initiatives or testing new interventions. While a comprehensive response that involved community, government and private industry sectors was required to tackle childhood obesity, GAP concentrated on practical activities in a limited number of government sectors. The activities can be seen as avoiding controversial political manoeuvres, and, as often occurs in health promotion, only minimally responding to the policy challenges [20]. As Lewis [21] recognises, policy solutions that are deemed acceptable and feasible or that have gone through 'a softening up process', may be preferred, as they avoid confrontation and have greater likelihood of being implemented.

As with program evaluation, policy analysis ideally draws upon a mix of information sources and analytic tools to examine the content, implementation process and outcomes. The use of explicit criteria in this analysis, to assess the breadth and infrastructure for obesity prevention policy, proved to be an acceptable and constructive approach to this study. The tools gave direction and authority to the process of identifying strengths and weaknesses in the content and implementation of GAP. However, these tools could not provide a basis for assessing the achievement of outputs or outcomes. The generic and flexible nature of each of the analytic frameworks also meant that they

did not provide a basis for checking if the implemented initiatives actually produced outcomes. Even if the policy could be shown to have met the criteria more completely, this would not itself guarantee the achievement of specific outcomes.

Conclusion

This case study revealed that the implementation of the GAP contributed to the development of infrastructure and resources for childhood obesity prevention. In addition, the process of implementing GAP has lead to significant cross sector collaboration, which is important, as many of the causal determinants of obesity lie outside the health sector. Flagship actions, such as the Healthy Schools Canteen Strategy, also provided a valuable symbol for the cultural and behavioural changes needed as part of the long-term process of slowing current trends in childhood obesity. Nevertheless, it is important not to under-estimate the range and extent of further changes and resources that will be required to reverse increasing rates of childhood obesity.

This analysis can be used to guide the next stage of public policy. Childhood obesity prevention continues to form an important public health goal, and has successfully captured media and political attention in Australia and spurred governments to hold summits and develop policies. It is critical that attention is now directed to formulating more comprehensive responses, which tackle the issue on a scale appropriate to the problem. A more strategic response needs to include a wider range of government sectors and recognise the links between health, obesity and economic levers, social infrastructure, and human capital and productivity. Policy leadership will be critical to extending the GAP activities evaluated in this case study, into a more integrated and strategic policy approach in the future.

Competing interests

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References:

1. NSW Government: Prevention of Obesity in Children and Young People: NSW Government Action Plan 2003–2007 Sydney: NSW Health; 2003.
2. Booth M, Okely AD, Denney-Wilson E, Hardy L, Yang B, Dobbins T: NSW Schools Physical Activity and Nutrition Survey (SPANS) 2004: Full Report 2006 [http:// www. coo. health. usyd. edau/research/ completed_projects.php]. Sydney: NSW Department of Health & NSW Centre for Overweight and Obesity [Accessed 14 November 2006]
3. Lin V, Gibson B, (Editors): Evidence-based Health Policy: problems and possibilities Melbourne Oxford University Press; 2003.
4. Milio N: Public policy as the cornerstone for a new public health: local and global beginnings. Family & Community Health 1988, 11(2):57-71.
5. De Leeuw E: Health policy, epidemiology and power: the interest web. Health Promotion International 1993, 8(1):49-52.
6. Tiernan A: Building capacity for policy implementation. Presentation to ANZSOG Project Management and Organisational Change Conference, Canberra 2006 [http://anzsog-research. anu. edu.au/ presentations/Anne%20tiernan.ppt]. [Accessed 29 October 2007]
7. National Health Medical Research Council: Acting on Australia's weight: a strategic plan for the prevention overweight and obesity Canberra: Commonwealth of Australia; 1997.
8. Nathan SA, Develin E, Grove N, Zwi AB: An Australian childhood obesity summit: the role

of data and evidence in 'public' policy making. Australia and New Zealand Health Policy 2005, 2(1):17.

9. NSW Health: NSW Childhood Obesity Summit Draft Program. Committee NSWCOSO. Sydney: NSW Department of Health; 2002.

10. Commonwealth of Australia: Healthy Weight 2008. Australia's Future. The National Action Agenda for Children and Young People and their Families Canberra: Department of Health and Ageing; 2003.

11. National Obesity Taskforce: December 2005 Overview Canberra: Department of Health and Ageing; 2005.

12. Koplan JP, Liverman CT, Kraak VI, (Eds): Preventing Childhood Obesity: Health in the Balance Washington DC: The National Academies Press; 2005.

13. Stone D: Causal stories and the formation of policy agendas. Political Science Quarterly 1989, 104(2):281-300.

14. Four Corners, 17 October 2005, Edited transcript of interview by Ticky Full-erton with Dick Wells, Chief Executive of the Australian Food and Grocery Council [http://www.abc.net.au/4corners/content/2005/s1480673.htm]. Downloaded 20/11/06

15. Blackburn GL, Walker WA: Science-based solutions to obesity: what are the roles of academia, government, industry, and health care? Am J Clin Nutr 2005, 82(1 Suppl):207S-210S.

16. Kumanyika S, Jeffery R, Morabia A, Ritenbaugh C, Antipatis VJ: Obesity prevention: the case for action. International Journal of Obesity 2002, 26:425-436.

17. Swinburn B, Bell C, King L, Magarey A, O'Brien K, Waters E, Primary Prevention Group of the Australian Childhood Obesity Research Network: Obesity prevention programs demand high quality evaluations. Aust N Z J Public Health 2007, 31(4):305-307.

18. World Health Organization: Preventing Chronic Disease: A Vital Investment Geneva: WHO; 2005.

19. Epping-Jordan JE, Galea G, Tukuitonga C, Beaglehole C: Preventing chronic diseases: taking stepwise action. Lancet 2005, 366:1667-71.

20. McGinnis JM, Williams-Russo P, Knickman JR: The case for more active policy attention to health promotion. Health Aff (Millwood) 2002, 21(2):78-93.

21. Lewis JM: Evidence-based policy: A technocratic wish in a political world. In Evidence-based Health Policy: problems and possibilities Edited by: Lin V, Gibson B. Melbourne Oxford University Press; 2003.

CHALLENGES IN AUSTRALIAN POLICY PROCESSES FOR DISINVESTMENT FROM EXISTING, INEFFECTIVE HEALTH CARE PRACTICES

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Internationally, many health care interventions were diffused prior to the standard use of assessments of safety, effectiveness and cost-effectiveness. Disinvestment from ineffective or inappropriately applied practices is a growing priority for health care systems for reasons of improved quality of care and sustainability of resource allocation. In this paper we examine key challenges for disinvestment from these interventions and explore potential policy-related avenues to advance a disinvestment agenda.

We examine five key challenges in the area of policy driven disinvestment: 1) lack of resources to support disinvestment policy mechanisms; 2) lack of reliable administrative mechanisms to identify and prioritise technologies and/or practices with uncertain clinical and cost-effectiveness; 3) political, clinical and social challenges to removing an established technology or practice; 4) lack of published studies with evidence demonstrating that existing technologies/ practices provide little or no benefit (highlighting complexity of design) and; 5) inadequate resources to support a research agenda to advance disinvestment methods. Partnerships are required to involve government, professional colleges and relevant stakeholder groups to put disinvestment on the agenda. Such partnerships could foster awareness raising, collaboration and improved health outcome data generation and reporting. Dedicated funds and distinct processes could be established within the Medical Services Advisory Committee and Pharmaceutical Benefits Advisory Committee to, a) identify technologies and practices for which there is relative uncertainty that could be the basis for disinvestment analysis, and b) conduct disinvestment assessments of selected item(s) to address *existing* practices in an analogous manner to the current focus on *new* and *emerging* technology. Finally, dedicated funding and cross-disciplinary collaboration is necessary to build health services and policy research capacity, with a focus on advancing disinvestment research methodologies and decision support tools.

The potential over-utilisation of less than effective clinical practices and the potential under-utilisation of effective clinical practices not only result in less than optimal care but also fragmented, inefficient and unsustainable resource allocation. Systematic policy approaches to disinvestment will improve equity, efficiency, quality and safety of care, as well as sustainability of resource allocation.

Background

The term *disinvestment* in health care is gaining prominence internationally. It relates to the processes of (partially or completely) withdrawing health resources from any existing health care practices, procedures, technologies or pharmaceuticals that are deemed to deliver little or no health gain for their cost, and thus are not efficient health resource allocations. The goal of reducing the use of ineffective technologies or practices has been central to Evidence-Based Medicine (EBM) for well over a decade. In the early 1990s claims were made that in all areas of health care, "30–40% of patients do not receive treatments of proven effectiveness" [1], and, "20–25% of patients have treatments that are unnecessary or potentially harmful" [2]. Since then, advances have been made in Australia, and internationally, to improve primarily the safety of health care, but also clinical and cost-effectiveness. Improvements have been achieved through the collaborative work of national and regional health departments, health care institutions, professional colleges, academia and numerous

organisations. In Australia these include but are not limited to the National Institute of Clinical Studies (NICS), the Australian Commission on Safety and Quality in Health Care – formerly the Australian Council for Safety and Quality in Health Care, the Australasian Association for Quality in Health Care (AAQHC), Effective Healthcare Australia (EHA), and the National Health and Medical Research Council (NHMRC). Furthermore, health technology assessment consultancy groups such as Adelaide Health Technology Assessment (AHTA) are increasingly involved in supporting current policy processes.

Considerable effort and resources have been invested in Australia in developing well-defined criteria and evidence-based policy processes for assessing *new* and *emerging* health technologies, surgical procedures and pharmaceuticals to gauge their safety, effectiveness and cost-effectiveness [3,4]. Reimbursement approval (and therefore universal access through Australia's Medicare system) for these new services, as well as the withdrawal of reimbursement for existing services, rests with the Australian Government Minister for Health and Ageing under advice from the Medical Services Advisory Committee (MSAC) and, for pharmaceuticals, the Pharmaceutical Benefits Advisory Committee (PBAC). The MSAC and the PBAC employ stringent review processes based on the existence of quality data and evidence that are available at the time of assessment. Underpinning the disinvestment movement, however, is a recognition that these stringent assessment methods are relatively novel, and that the processes to date have focused overwhelmingly on new and emerging practices, technologies and pharmaceuticals and not on existing services (even though this is within the mandate of the MSAC). Australia therefore, like other countries, suffers from a legacy whereby many currently implemented health care interventions were in use prior to well-defined standards of cost-effectiveness becoming a criterion for reimbursement. Thus there is concern that health services of limited effectiveness may still be in practice nation-wide. The Chief Executive Officer of Australia's National Institute of Clinical Studies (NICS) has stated,

We do not know how much of the total healthcare Australians receive is based on the best available evidence; studies of a number of specific conditions show that there are gaps between what is known and what happens in practice [5].

While processes such as clinical practice guidelines development and implementation continue to tackle aspects of this problem, disinvestment focuses on a complementary but parallel facet by examining practices that should be reduced or in some cases eliminated completely. We classify the principal challenges for disinvestment as follows:

1) Lack of dedicated resources by key stakeholders to build and support disinvestment policy mechanisms

2) Lack of reliable administrative mechanisms to identify and prioritise technologies and/or practices with relative uncertainty as to their clinical and cost-effectiveness

3) Political, clinical and social challenges to removing an established technology (including challenges to limiting coverage to specific patients, institutions, or providers)

4) Lack of published studies that clearly demonstrate that existing technologies/practices provide little or no benefit

5) Inadequate resources to support a research agenda to advance disinvestment methods

Discussion

The following discussion will examine some of the elements involved in addressing these challenges. The discussion

will highlight what is occurring currently with implications for what ought to occur in order to support effective disinvestment. We will present two brief case studies to illustrate several complexities with accompanying recommendations.

1) Lack of dedicated resources by key stakeholders to build and support disinvestment policy mechanisms

The bearer of financial risk for the cost of healthcare perhaps has the greatest incentive to drive a disinvestment agenda. In the USA this might include public and private payers, purchasers or large employers. Whereas in government managed or mixed-model health care systems it could be the national insurer and/or the private health insurance industry. In Australia, the MSAC faces issues in its current policy processes and capacity to support effective disinvestment. While for new devices or pharmaceuticals the burden for proving effectiveness lies with the sponsor, for potentially obsolete technology or practices, the opposite occurs. The regulator or payer (the Australian government with advice from the MSAC) firstly has to identify or be made aware of a doubtful practice, to commission reviews, and then to mount a compelling argument for ineffectiveness and/or cost-ineffectiveness. For illustrative purposes this may be described as somewhat analogous to standards of law. That is, adding an item to the schedule of benefits (or its equivalent in international terms) is beholden to a 'balance of probabilities' standard whereas removal of an item requires a standard of evidence that is 'beyond reasonable doubt'. As will be discussed further, this identification and appraisal process is in itself complex, but even if it were not, the MSAC has a full agenda with applications for new and emerging technologies and hence has limited capacity to address existing services. This is evident in communications with the MSAC members that highlight their workload, and the focus of that work. At a recent meeting of the MSAC, the 22 committee members were faced with 700 pages of documentation to consider. All of that material was for *new* and *emerging* technologies and practices; none was for *existing*, potentially ineffective health care. In Australia we therefore appear to be 'stuck with the old and overwhelmed by the new'. Irrespective of the successes the Australian policy model has had in assessing new and emerging technologies, there appears to be a lack of capacity to address both new and existing practices. Or arguably the capacity exists but is not being appropriately harnessed at present, which may reflect a lack of political will. In any case disinvestment is limited. This limitation in capacity may be, in part, a result of the political and professional complexities associated with disinvesting existing practices (discussed further below). It also points to the growing need for a political paradigm shift in order to foster policy-driven disinvestment capacity.

2) Lack of reliable administrative mechanisms to identify and prioritise technologies and practices for which there is relative uncertainty as to clinical and cost-effectiveness

Disinvestment may be easier with pharmaceuticals and/or when adverse events occur. The process is more complex when individual are not harmed by existing practices but over-treated or ineffectively treated. That is, subjected to diagnosis or treatment that is safe but of little or no meaningful clinical benefit (i.e. supported by the existence of compelling clinical- and cost-effectiveness evidence). A register for 'ineffectively-treated' does not exist in the same way as an adverse event register exists for pharmaceuticals, or an adverse event register within tertiary care settings. Further compounding this issue is the limited number of groups in Australia (or indeed elsewhere) with a clear directive and sufficient resources or

incentive to seek out, identify and investigate potentially redundant/ineffective procedures. Wilensky has recently intimated that similar limitations (and potential for improvement) exist in the United States of America (USA) [6]. This reflects a view that substantial additional investment is required to support evidence-based review of not only new and emerging but also existing health care technologies, including comparative studies examining new versus existing practices.

In Australia the incentive pendulum supports diffusion and not retraction or 'disinvestment'. The current MSAC model appears geared (and effectively so) toward controlling the tap as it is turned on, not toward neutralizing the flow through active disinvestment. It is interesting for example, that old technologies or practices are not formally de-commissioned as new items are approved. Instead, the range of options grows ever larger. And although some (including at least one of the current authors) purport that many practices simply fade away or die a slow death, the question remains whether this represents a sound policy approach to resource allocation and clinical excellence in health care.

Currently the MSAC provides advice on whether a proposed new service is as or more safe, effective and cost-effective than a comparator. There is nothing to stop the MSAC from recommending the removal of one service as it recommends addition of another service to the reimbursement schedule should the new service have demon-strably better cost effectiveness for a given indication. That the comparator is not automatically removed from the schedule highlights a challenging issue for a disinvestment programme. The new service (even if superior) may take time to diffuse into practice and become accepted by the medical profession. Premature disinvestment of the comparator may disadvantage patients where the new service was not yet available and thereby raise issues of access and equity. The evidence supporting the new technology may not go as far as assessing the cost-effectiveness of disinvestment of its comparator (in terms of capital investment, training, and changes to clinical workflow). Decision-making in disinvestment must take account of these factors.

3) Political, clinical and social challenges to removing an established technology (including challenges to limiting coverage to specific patients, institutions, or providers)

For existing technologies or practices there are complexities that do not beset those that are new or emerging.

These relate to their entrenched status and include for example:

• Resistance to change due to established clinical training and practice paradigms

• Multiple clinical, consumer and political interests

• Clinical and consumer influence and preferences, and supplier-induced demand

• Incentive and disincentive mechanisms

• The sunk costs of human and physical capital which would thereby become obsolete

Schon describes how social systems work hard to resist change, a phenomenon he labels 'dynamic conservatism' [7]. Research and applied decision making in this area must therefore include analysis of the evidence for safety, effectiveness and cost-effectiveness as well as social, ethical and political analyses to explain why ineffective health care practices persist. Only then is there scope to address how ineffective practices can be disinvested.

For the clinician there is often concern that disinvestment represents a blunt instrument of rationing, one that may restrict clinical autonomy and reduce patient choice. But can continued investment in

health care occur without thoughtful, measured disinvestment? There is an economic imperative to do so for the sake of sustainability. There is also an ethical imperative for the delivery of quality health care and a best practice imperative for clinical purchasers and providers. Disinvestment will free up resources for those practices that have demonstrated effectiveness. Furthermore, disinvestment should not be seen as an all or nothing approach. Removing a reimbursement item number from the Schedule of Medical Benefits (or the equivalent action in international terms) would be an extreme example of successful disinvestment. There may well be a policy-guided process of measured retraction including restricting the indications for particular services.

Important in any disinvestment policy model is recognition and consideration of perceived threats that may be raised by disinvestment. We have included a case study involving Assisted Reproductive Technologies (ART) for women over the age of 42 years to explore some potential threats and argue that these are legitimate considerations in a disinvestment analysis (See Table 1).

There is clear evidence of limited effectiveness for ART with increasing maternal age. There are also social, political and ethical considerations that any disinvestment strategy (and methodological framework) must take into consideration. The complexities involved in any potential disinvestment analysis of this issue support the need for methodological advances in this area of health services research. Such advances are required if health services such as ART are to be moved out of the 'too hard basket' and into active assessment, debate and appraisal.

Another barrier to disinvestment is the notion that medical technology has provided good value for money over time, and that regulators' efforts to restrict coverage (or disinvest) may reduce incentives for investment and innovation, thereby impeding the future flow of valuable technologies [8]. We may need to tolerate a certain level of payment for low value or relatively ineffective technologies and practices because such is the market environment that makes possible the valuable medical breakthroughs.

4) Lack of published studies that clearly demonstrate that existing technologies/practices provide little or no benefit

For many technologies and practices there is evidence supporting varying degrees of effectiveness when used in certain contexts (for example to certain patient groups with varying degrees of predictive prognoses). However, there are also examples of inappropriate application of otherwise effective technologies or procedures, culminating in ineffective care and inefficient resource allocation. Notable examples of this are presented in the work of Wen-nberg, disseminated in the Dartmouth Atlas highlighting geographic variation in the use of a range of procedures [9].

Under such conditions a degree of measured retraction of practice is desirable, with resultant disinvestment. Clinical practice modification and refinement techniques, perhaps via clinical practice guideline development and implementation, have demonstrated efficacy. As noted by Miles and co workers, *clinical practice guidelines remain, when certain conditions are met and their limitations fully understood, useful vehicles for implementing agreed changes to clinical practice and service provision. Certainly, the process of deriving and implementing clinical practice guidelines has developed into a science in its own* [10].

Table 1. Case Study 1 Assisted Reproductive Technologies (ART) for women over 42 years of age

ART does not specifically affect morbidity or mortality (with some exceptions). The debate has, and continues, to occur prominently in the broad community as well as government. In 2003, age-specific success rates of In Vitro Fertilisation (IVF) cycles using fresh oocytes were [28]:
- 27.7% for women aged 25–29
- 24.9% for women aged 30–34
- 17.1% for women aged 35–39
- 6.8% for women aged 40–44
- 2% for women aged ≥ 42 (some clinics have cited success rates of 5–10%)

This success rate for women aged 42 years or more has been cited by one Australian clinic as a reason for refusing to treat women of that age [29]. Politicians have also engaged with this debate. In April 2005 the Australian Government Minister for Health and Ageing considered limiting ART funding under Medicare to three cycles per year for women 42 and under, and to three cycles in total for women over this age [30]. Rising expenditure on ART and the low age-specific success rates were cited as justification for this policy. This proposal for reduced support was subsequently abandoned by the Australian Prime Minister in May 2005. Table 3 further explores some of the methodological issues associated with this as a potential case study in disinvestment.

However, for some technologies or practices the evidence for effectiveness is either less clear, or is negative, yet the practice persists. In these instances, partial or complete removal (from funding) may be necessary. Substantial challenges exist, particularly around adequate and timely definition and acceptable proof of inferiority. This is not only conceptually difficult but also limited by data availability and interpretation. Further complicating this is the lag that often exists in the reliable reporting of health outcomes data based on clinical practice. Table 2 (Case Study 2) presents a case highlighting potential complexities of 'evidence' in disinvestment review decisions. These, together with considerations from the ART example, are further addressed in Table 3.

Within this context there is scope for expanding the capacity to conduct primary and secondary research of stand alone and comparative effectiveness for existing as well as new technologies [11,12]. The disinvestment considerations highlighted in Table 3 require methodological advances but also time for thorough and rigorous review.

In such cases there may be potential for a 'funding with evidence generation' mechanism (also called 'only in research' in the United Kingdom (UK) and 'coverage with evidence development' in the USA). This approach is currently applied for some emerging technologies but could be adapted for existing practices. Here, payers/regulators may allow ongoing funding only for a defined period of time to allow for the generation and/or analyses of necessary evidence. Currently there is provision for use of this approach with new technologies by the MSAC.

5) Inadequate resources to support a research agenda to advance disinvestment policies and methods

The discussion thus far highlights the need for methodological advances to support disinvestment decision making. In Australia, health technology assessment groups conduct and present the synthesised, evidence-based reviews that support the MSAC and the PBAC reimbursement decisions for new and emerging technologies and pharmaceuticals. Health Technology Assessment (HTA) incorporates multidisciplinary fields of policy analysis, and has broadened, "*from primarily addressing effectiveness and safety issues to covering a broader array of issues such as psychological, organizational, ethical and legal aspects*" [13]. HTA studies the medical, social, ethical, and economic implications of development, diffusion, and use of health technologies, practices and services. HTA agencies together with health services and policy researchers generally, are well positioned to take a lead role in supporting the disinvestment of existing,

ineffective health care practices. To do this effectively requires collaborative research and recently announced funding increases from the National Health and Medical Research Council (NHMRC) for Health Services Research offers potential here. But in Australia HTA groups largely operate as contract research organisations and with relatively short-term contracts these groups tend to lack capacity to build or support a broad methodological research agenda for the disinvestment of existing, ineffective health care practices.

This phenomenon is not restricted to Australia, and as Lehoux has observed, the involvement of academic institutions in HTA has the potential to bring with it conflicting legitimacies between the production of traditionally scientific versus user-oriented knowledge [8]. With concerted capacity building and research initiatives aimed at improving linkage and exchange between policy advisors/ makers and academic researchers (HTA specialists), priority driven, contextually relevant research would be facilitated and could support decision-making processes that policy makers need. Moreover, it would contribute much-needed methodological advances and align with the four main characteristics of action research defined by Hart and Bond [14]: (1) collaboration between researchers and practitioners; (2) solution of practical problems; (3) change in practice; and (4) development of theory.

Table 2. Case Study 2 Upper airway surgical procedures for adult Obstructive Sleep Apnea (OSA)

Approximately one in five adults has at least mild OSA and one in 15 adults has OSA of moderate or worse severity [31]. The condition is an independent risk factor for substantial morbidity(ies) with implications also for mortality [32]. Currently, upper airway surgery is a second-line treatment alternative to an established non-surgical gold-standard. A recent meta-analysis of these surgical procedures reported success rates at [33]:

- 13% for Phase I procedures (including uvulopalatopharyngoplasty [UPPP], laser-assisted uvulopalatoplasty [LAUP], hyoid suspension [HS], genioglossus advancement [GA], and radiofrequency volume reduction of soft tissue [RFVR])
- 43% for advanced Phase II procedures (maxilla and/or mandible advancement (MMA) requiring up to three days Intensive Care Unit recovery).
- Two reports of patient satisfaction highlight that surgery has a high postoperative morbidity rate, a high patient-reported failure rate and a low level of satisfaction with 53% [34] and 61% [35] patient-reported 'regret' rates.
- The Cochrane review in this area [36] supports the restricted use of these operations and yet Australian Medicare data highlights that these procedures are widespread and increasing.

Despite the existence of these procedures for over a decade, debate regarding their efficacy has recently intensified, as to whether these success rates presented above represent 'highly effective treatment', sufficient enough to confer improved health outcomes [37-39]. Disagreement has occurred primarily between relevant medical specialties (i.e. surgeons and sleep medicine physicians). Importantly, there has been a lag in presentation of the necessary evidence to inform and advance such a debate, principally as no policy group has been assigned a stake in the collection or generation of such evidence, hereto it has accrued via the noble but *ad hoc* actions of clinical groups.

Collaborative models amenable to disinvestment strategies are increasingly being developed and adopted internationally, with some based on the priority setting developments described by Mooney [15,16]). The strategic 'Linkage and Exchange' and 'Participatory Action Research' programs in Canada [17-21] deal with similar issues. Recently, the UK's National Institute for Clinical Excellence (NICE) announced a formal policy agenda to *"purge from the NHS treatments that do not improve health or are poor value for money"* [22]. It is interesting to note however that subsequent to the NICE disinvestment agenda being released, a formal UK Treasury report into UK health research and funding highlighted the challenges faced:

The delivery of robust scientific appraisal for technologies is coming under increasing challenge as a result of its reliance on methodologies that, it is widely recognized, need further development, given that Health Technology Assessment (HTA) is a relatively new science. Appro-

priate research is required to address these challenges. In particular, research into methodology for... disinvestment methods ([23], page 103)

Table 3. Investigative issues associated with the chosen health care practices

Health Care Technology/Practice	Setting	Interest from methodological and policy perspectives*	Key Issues
ART ≥ 42 years of age	Clinic or Hospital	Harmful x Clinically Effective x Cost Effective ? Appropriate ? Socially Valued √ Universally Accessible ?/x Ethical ?	- Marginal clinical and cost-effectiveness (on population basis) but limiting its use poses problems: it is highly beneficial from perspective of concerned individuals - Therapy has equivocal purpose - Highly valued by recipients and potentially by society broadly - Ability to pay: user vs society - Equity of access - Medical vs social infertility - Opportunity cost
Upper airway surgery for adult OSA	Surgical Theatre	Harmful ? Clinically Effective ?/x Effective Alternative √ Cost Effective x Appropriate ? Necessary ? Socially Valued ?/√ Ethical ?	- Limiting its use should not, in theory, pose any problems, but pressures are strong from clinical interest groups - Complex practice paradigms/incentives - Small, homogeneous craft group - Equipoise/clinical uncertainty - Perspectives of patients who value the potential of a surgical 'fix' - Is this preference based on sound evidence or supplier induced demand? - Opportunity cost

*Key: ? = Unsure or in question; x = Limited or evidence in the negative; √ = Evidence in the positive

In the United States the 'Developing Evidence to Inform Decisions about Effectiveness' (DeCIDE) Research Network has been implemented to support the development of new scientific knowledge through research on the outcomes of health care items and services. This is a clear policy directive in line with Section 1013 of the Medicare Modernization Act of 2003. Wilensky has commented that a window of opportunity currently exists in the USA for the development of a Center for Comparative Effectiveness, particularly to address pharmaceuticals [6]. We believe the greater challenge is to incorporate the assessment of *existing* health care practices and technologies, as well as pharmaceuticals. Fundamental to this is an expanded process of medico-vigilance – monitoring of whether the practice/technology is not only safe but effective and cost-effective in 'real' use outside the tightly controlled environments in which initial evidence may have been collected. Beyond this the social, ethical and political complexities must be accounted for as explicit components of any disinvestment analysis.

Based on this discussion we present the following recommendations of initiatives to be implemented in Australia (and internationally where appropriate):

- Government partnerships to involve the professional colleges and relevant stakeholder groups (consumer/community) to put disinvestment on the agenda including awareness, collaboration and improved health outcome data generation and reporting (ongoing medico-vigilance).
- Dedicated funds and distinct processes (i.e. transparent legal framework) within the MSAC and where appropriate the PBAC to:
- Identify technologies and practices for which there is relative uncertainty for disinvestment analysis/review
- Conduct disinvestment assessments/reviews of the selected item(s)

This should involve an expanded capacity for these committees (or others adopting a similar model) to address existing practices in an analogous manner to their current focus on new and emerging

technologies, practices and pharmaceuticals.

- At this juncture in Australia's health policy landscape, collaborative links to advance disinvestment should be made between the relevant stakeholder bodies, including: the MSAC/PBAC, state departments of health, the Australian Commission on Safety and Quality in Health Care, the National Institute of Clinical Studies (and the NHMRC more broadly).
- For existing health care services for which there is relative uncertainty, consideration for the implementation of 'funding with evidence generation'. That is, ongoing reimbursement only agreed for a limited number of years pending evidence generation/review processes – with the possibility of extensions being considered.
- Dedicated funding and cross-disciplinary collaboration to build health services and policy research capacity with a focus on advancing disinvestment research methodologies and decision support tools for policy stakeholders.

Disinvestment from existing health care practices that offer little or no health gain is a policy challenge that requires greater attention, both for quality of care and sustainable resource allocation. Disinvestment may well depend less on the availability of resources than on the political will to support work in this area.

Summary

Australia currently has limited systems in place to support the disinvestment of currently used ineffective, or inappropriately applied, health care practices. With the growing burden of chronic health conditions, addressing this limitation should be recognised as an emerging national priority area [24]. This discussion piece is intended to stimulate further debate in this area (see also [25-27]). The potential over-utilisation of less than effective clinical practices and the potential under-utilisation of effective clinical practices not only result in less than optimal care but also fragmented, inefficient and unsustainable resource allocation. Systematic policy approaches to disinvestment will improve equity, efficiency, quality and safety of care, as well as sustainability of resource allocation. Developing health services and policy research methodologies that tackle these complexities to assist policy-makers will advance the disinvestment agenda. This is a growing area of priority setting in health care that requires national and international perspectives, debate and collaboration.

Competing interests

Adam Elshaug received funding for this project from the Faculty of Health Sciences of the University of Adelaide. Professor Hiller is director of Adelaide Health Technology Assessment (AHTA). This organisation is contracted to complete evaluations of health technologies. Assoc Prof Moss provides health technology assessments to the Australian Government Department of Health and Ageing as a consultant. Dr Tunis is the Founder and Director of the Center for Medical Technology Policy in San Francisco, where he consults with health care decision makers and stakeholders to support the rapid evaluation and effective use of new medical technologies. In all other respects the authors declare they have no competing interests.

Authors' contributions

AE conceptualised this paper, completed the first substantive draft and contributed to subsequent draft revisions. JH and JM contributed substantively to subsequent draft revisions. ST contributed an international perspective (primarily USA) and substantive editorial comments on two drafts. All authors read and approved the final manuscript.

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References:

1. White KL: Evidence-Based Medicine. Lancet 1995, 346:837-838.
2. Smith R: Where is the wisdom...? The Poverty of Medical Evidence. BMJ 1991, 303:798-799.
3. Morgan SG, McMahon M, Mitton C, Roughead E, Kirk R, Kanavos P, Menon D: Centralized drug review processes in Australia, Canada, New Zealand, and the United kingdom. Health Aff (Millwood) 2006, 25:337-47.
4. O'Malley SP: The Australian experiment: the use of Evidence Based Medicine for the reimbursement of surgical and diagnostic procedures (1998–2004). Aust New Zealand Health Policy 2006, 3:.
5. Buchan H: Gaps between best evidence and practice: causes for concern. Med J Aust 2004, 180:S48-S49.
6. Wilensky GR: Developing A Center For Comparative Effectiveness Information. Health Aff 2006. doi: 10.1377:hlthaff.25.w572.
7. Schon DA: Beyond the stable state: public and private learning in a changing society London: Temple Smith; 1971.
8. Lehoux P: The Problem of Health Technology: Policy Implications for Modern Health Care Systems New York: Taylor and Francis Group; 2006.
9. Wennberg JE: Unwarranted Variations in Health Care: The Dartmouth Atlas of Health Care. [http://www.dartmouthat las.org/index.shtm].
10. Miles A, Polychronis A, Grey JE: The evidence-based health care debate – 2006. Where are we now? J Eval Clin Pract 2006, 12:239-247.
11. Tunis SR: A clinical research strategy to support shared decision making. Health Aff (Millwood) 2005, 24:180-4.
12. Tunis SR, Pearson SD: Coverage options for promising technologies: Medicare's 'coverage with evidence development'. Health Aff (Millwood) 2006, 25:1218-30.
13. Draborg E, Gyrd-Hansen D: Time-trends in health technology assessments: an analysis of developments in composition of international health technology assessments from 1989 to 2002. Int J Technol Assess Health Care 2005, 21:492-8.
14. Hart E, Bond M: Action research for health and social care: A guide to practice Philadelphia: Open University Press; 1995.
15. Mooney G: Priority setting in mental health services. Appl Health Econ Health Policy 2002, 1:65-74.
16. Mooney G: Communitarian claims and community capabilities: furthering priority setting? Soc Sci Med 2005, 60:247-55.
17. Lomas J: Using 'linkage and exchange' to move research into policy at a Canadian foundation. Health Aff (Millwood) 2000, 19:236-40.
18. Mitton C, Donaldson C: Tools of the trade: a comparative analysis of approaches to priority setting in healthcare. Health Serv Manage Res 2003, 16:96-105.
19. Mitton C, Patten S, Donaldson C, Waldner H: Priority-setting in health authorities: moving beyond the barriers. The Calgary experience. Healthc Q 2005, 8:49-55.
20. Lee RC, Marshall D, Waddell C, Hailey D, Juzwishin D: Health technology assessment, research, and implementation within a health region in Alberta, Canada. Int J Technol Assess Health Care 2003, 19:513-20.
21. Wanke MI, Juzwishin D: International comparison and review of a health technology assessment skills program. Int J Technol Assess Health Care 2005, 21:253-62.
22. Kmietowicz Z: NICE is to root out ineffective treatments in NHS. BMJ 2006, 333:. doi:10.1136/bmj.333.7568.568-a.
23. Cooksey SD: A review of UK health research funding London : Her Majesty's Treasury; 2006.
24. Medical Services Advisory Committee: Australian Government Department of Health and Ageing. In Strengthening evidence-based health care in Australia Canberra; 2003.
25. Victorian Government Department of Human Services: Future directions for health technology uptake, diffusion and disinvestment in Victorian public health services (discussion paper). 2003 [http://www.health.vic.gov.au/newtech/newtech-workshop-discussion.pdf]. 21 March,2007
26. Jackson TJ: Health technology assessment in Australia: challenges ahead. Med J Aust 2007, 187:262-4.
27. Elshaug AG, Hiller JE, Moss JR: Exploring policymakers' perspectives on disinvestment from ineffective health care practices. Int J Technol Assess Health Care in press. accepted 21/09/2007.
28. Waters A, Dean J, Sullivan E: Assisted reproduction technology in Australia and New Zealand, 2003. Canberra: National Perinatal Statistics Unit; Australian Institute for Health and Welfare (AIHW); Cat. No. per 2006, 31:36.
29. Overington C: No age limit on IVF funds: Costello. The Australian Newspaper :3. 2 January 2006
30. Uren D: Limits on IVF access will put women at risk. The Australian Newspaper :4. 25 April 2005
31. Young T, Skatrud J, Peppard P: Risk Fac-

tors for Obstructive Sleep Apnea in Adults. JAMA 2004, 291:2013-2016.

32. Young T, Peppard P, Gottlieb D: Epidemiology of obstructive sleep apnea: A population health perspective. Am J Respir Crit Care Med 2002, 165:1217-1239.

33. Elshaug AG, Moss JR, Southcott AM, Hiller JE: Redefining success in airway surgery for obstructive sleep apnea: a meta analysis and synthesis of the evidence. Sleep 2007, 30:461-467.

34. Jones TM, Earis JE, Calverley PM, De S, Swift AC: Snoring surgery: a retrospective review. Laryngoscope 2005, 115:2010-5.

35. Hicklin LA, Tostevin P, Dasan S: Retrospective survey of long-term results and patient satisfaction with uvulopalat-opharyngoplasty for snoring. J Laryngol Otol 2000, 114:675-81.

36. Sundaram S, Bridgman SA, Lim J, Lasserson TJ: Surgery for obstructive sleep apnoea. Cochrane Database Syst Rev 2005:CD001004.

37. Phillips B: Upper airway surgery does not have a major role in the treatment of sleep apnea. Journal of Clinical Sleep Medicine 2005, 1:241-245.

38. Powell N: Upper airway surgery does have a major role in the treatment of obstructive sleep apnea: "the tail end of the dog". Journal of Clinical Sleep Medicine 2005, 1:236-240.

39. Elshaug AG, Moss JR, Southcott AM, Hiller JE: An analysis of the evidence-practice continuum: Is surgery for Obstructive Sleep Apnoea contraindicated? J Eval Clin Pract 2007, 13:3-9.

Materials of conference

ANTIBODIES TO BENZO[A]PYRENE IN WOMEN SUFFERING FROM GASTRIC AND INTESTINAL CANCER

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The serum samples of 205 women served as the research material. Among them there were 45 samples with the gastric cancer (GC) histological diagnosis, 70 – with intestinal cancer (IC) and 90 healthy samples. Every woman gave a written agreement to take part in the research. The content of antibodies (AB) to benzo[a]pyrene (BP) was determined by means of the modified by us method ELISA. The statistic treatment of the results was carried out with the help of standard methods.

In the majority of the researched serum samples we managed to find out the AB to BP of all three classes (IgA, IgM, IgG). Authentic differences were detected on the BP AB levels of the classes A and G between the healthy and GC patient women, and also between the healthy women and IC patient ones. The fact, that in the healthy women the specific gravity of serum samples, in which no BP AB of the A class were detected, turned out to be the highest one (8,3%), comes under notice. On the content of the BP AB of the M class the compared groups didn't differ.

There were no differences on the BP AB levels of all three classes detected between the patients in different stages of the tumor process, and also between the GC and IC patients.

Thus, the BP AB are formed both in the healthy and GC and IC patients. At that, the levels of BP AB of the A and G classes in the considered localizations cancer patients are higher than in healthy women.

The fact, that BP AB are detected not only in malignant tumor patients, but also in the majority of healthy women, is of great interest as well.

In our opinion, to establish a cancerogenes AB critical level, the exceedence of which could be estimated as the sign of cancerogene-protein adducts quantity increase, i.e. as the factor of an individual carcinogenic risk, is extremely important to all practical purposes. For this particular purpose we have analyzed the variational series of the A, M and G classes BP AB content in the healthy women group and on the basis of the τ criterion defined the affinity of utmost variants to the general aggregate of the factors. We relatively accepted the BP AB quantity maximum value, higher of which the aggregate variants "fall out" of the variational series on the τ criterion, for the upper limit of normal. 4,6 mcg/ml for the A class BP AB, 21,8 mcg/ml – for the G class ones, 38,7 mcg/ml – for the M class - turned out to be such limits.

It has been found that the number of women, in which the A and G class BP AB content exceeds the relative limit of norm, among the GC and IC patient ones is authentically higher (on the χ^2 criterion) than that among the healthy women. There were no differences on the M class BP AB content detected.

Conclusions

- In blood serum of healthy women there are antibodies to BP.
- In GC and IC patients the content of AB to BP is higher, than in healthy women.
- The appearance of AB to BP at GC and IC has specific isoallotypic features: at GC and IC the A and G classes' antibodies content increases preferentially.
- An increased content of AB to BP can be a sign of a high oncorisk, but the lack of AB or their low content in the serum is not the sign of a low oncorisk.
- The content of AB to BP in GC and IC patients doesn't depend on the stage of the tumor disease.

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ANTIBODIES TO BENZO[A]PYRENE IN WOMEN SUFFERING FROM BREAST CANCER

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The given research was carried out for the purpose of detecting antibodies (AB) to benzo[a]pyrene (BP) in breast cancer (BC) carriers and also revealing isoallotypic features of their appearance.

The serum samples of 310 women served as the research material. Among them there were 220 BCC and 90 healthy women.

The content of antibodies (AB) to benzo[a]pyrene (BP) was determined by means of the modified by us method ELISA. The statistic treat-

ment of the results was carried out with the help of standard methods.

In the majority of the researched serum samples we managed to find out the AB to BP of all three classes (IgA, IgM, IgG). However, in the healthy women the specific gravity of serum samples, in which no BP AB of the A class were detected, turned out to be the highest one (8,3%). The content of all three classes AB to BP is authentically higher in the BC carriers than in the healthy. There were no differences on the BP AB levels of all three classes detected between the patients in different stages of the tumor process. Thus, the BP AB are formed both in the healthy and BC patients. At that, the levels of BP AB in BC patients are higher than in healthy women.

In our opinion, to establish a cancerogenes AB critical level, the exceedence of which could be estimated as the sign of cancerogene-protein adducts quantity increase, i.e. as the factor of an individual carcinogenic risk, is extremely important to all practical purposes. For this particular purpose we have analyzed the variational series of the A, M and G classes BP AB content in the healthy women group and on the basis of the τ criterion defined the affinity of utmost variants to the general aggregate of the factors. We relatively accepted the BP AB quantity maximum value, higher of which the aggregate variants "fall out" of the variational series on the τ criterion, for the upper limit of normal. 4,6 mcg/ml for the A class BP AB, 21,8 mcg/ml – for the G class ones, 38,7 mcg/ml – for the M class - turned out to be such limits. It has been found that the number of women, in which the BP AB content exceeds the relative limit of norm, among the BC carriers is authentically higher (on the χ^2 criterion) than that among the healthy women.

As a matter of record one can suppose the following:

- BP plays a significant role in the BC pathogenesis not in all, but a part of patients;
- in some healthy women the BP adducts formation with the protein (the result of which is the BP AB appearance) exceeds a certain critical level and that is why the malignant tumor appearance risk is increased in them;
- the quantity of this or that class BP AB depends not only on individual features of the BP metabolism, but also on the immune response gene complement.

Conclusions.

- In blood serum of healthy women there are antibodies to BP.
- In BC patients the content of all three classes AB to BP is higher, than in healthy women.
- There are no isoallotypic features of AB to BP at BC revealed.
- An increased content of AB to BP can be a sign of a high oncorisk, but the lack of AB or their low content in the serum is not the sign of a low oncorisk.
- The content of AB to BP in BC patients doesn't depend on the stage of the tumor disease.

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FUNCTIONAL MORPHOLOGY OF TUMOR VESSELS IN OVARIAN CANCER

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Angiogenesis is a process of the new vessel generation from the existing vascular bed. It is typical for a tumor progression. The increase the invasiveness and metastatic activity of the neoplasm is a result of the angiogenesis.

The parameters of the vascular bed were studied based on the operational bioptic material of the primary tumor of 83 ovarian cancer (OC) patients.

It was found that in primary OC tumors vessels are distributed very irregularly. They have poorly developed junctional stroma and thin walls. Very rarely the vessels are covered directly by neoplasm. The considerable increase in number of the bundle vessels, hyperinflated and hyperemic vessels can be found in the marginal layer of the tumor.

The main amount of vessels of the tumor microcirculature is capillary vessels with the diameter more than 10 μm (Table 1).

The endothelial cover of the tumor stroma in small sinuses are represented by one or two endothelial cells the nuclei of which emerge in a vessel lumen and cytoplasmic outgrowths embrace the vessel on its perimeter forming a solid tube. At the same time the basal membrane is often not recognized or distinguished as a discrete plate. The increase of a caliber of the new-formed vessels is not accompanied by their structural alteration: even large diameter vascular walls are close to the structure of the capillary vessel walls.

Table 1. Parameters of the tumor vascular bed

Vascular parameter	M	m	V.c.	Max	Min
Volume, %	4,33	0,25	0,46	12,6	1,2
Number in 1 mm^2 of the tumor	23,7	1,1	0,38	62,2	12,1
Length in 1 mm^3 of the tumor, mm	423,3	37,4	0,72	1354,0	25,4
Wall square in 1 mm^3 of the tumor, mm^2	14,5	1,22	0,7	77,0	2,2
Diameter 5-10 μm, %	16,2	2,17	0,29	100,0	0
Diameter 11-20 μm, %	43,4	1,25	0,47	58,8	0
Diameter 21-30 μm, %	27,3	0,95	1,16	40,8,	0
Diameter 31-50 μm, %	6,8	0,3	1,57	12,8	0
Diameter 51-100 μm, %	4,1	0,18	2,77	8,5	0
Diameter 101-200 μm, %	2,2	0,08	2,95	3,9	0

Therefore, the investigation of the vascular density on 1 mm^2 of the tumor, the ratio of their diameters, volume of vessels, the length and square of vascular walls in 1 mm^3 of tumor tissue showed in average the high level of blood supply in the primary tumor knot in the ovarian cancer, though in particular cases the parameter variations were significant.

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PRIMARY SCREENING OF PIPERIDINE SERIES NEW COMPOUNDS

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One of the search ways for new medicines is studying fusion compounds' pharmacological properties among various analogues of well known and widely applied in medicine substances. The piperidine derivatives are of great interest. They are the products of piperidine reduction and are of low toxicological concern as pyridine is a part of many natural complexes (vitamin PP, Vitamin B6, nicotine and others). We have carried out the investigations of new piperidine derivatives synthesized at the Institute of Chemical Sciences named after Berkutov A.B. under the guidance of Academician Praliyev K.D.. The spasmolysants' primary screening method used is a model of isolated organs. The investigation on small intestine is the most available and, in this connection, very popular method. For the experiment animals of one species, sex, age and body mass (±10%) are selected. The purpose of our work has become the study of biological potency and toxicity of a new piperidine derivatives' range obtained at the Institute of Chemical Sciences named after Berkutov A.B., the Department of Education and Science of Kazakhstan, under the guidance of a member of the National Academy of Sciences Praliyev K.D.. The antispasmodic activity was investigated on the rats' small intestine in conditions of calcium and acetylcholine spasm. The work was carried out on the device oriented to the work with isolated organs and manufactured by the Ugo Basile Company, Italy. The acute toxicity was defined by means of a single intraperitoneal introduction of the investigated preparation to white nondescript mice weighing 19-21 g. The evaluation was made according to the LD_{50} factor. 54 new compounds have been investigated. The research results testify to the presence of antispasmodic activity of the following compounds: NA-281, NA-291, NA-309, NA-310, NA-311, NA-315, NA-320, NA-321, NA-323; the compounds NA-280, NA-294, NA-309, NA-311 blocking calcium spasm and the rest ones – both kinds of spasm. The high antispasmodic activity of the NA-311 and NA-323 compounds, blocking both producing calcium and acetylcholine spasms and with it being of low toxicological concern (NA-311 - 220 mg/kg ± 33,33; NA-323 - 210 mg/kg ± 7,07; the toxicity of no-spa - 213,8 mg/kg ±22,61), should be noted.

Conclusions: the piperidine derivatives, being close analogues of the natural compound – pyridine, - are promising for a profound search and development of new low toxicological concern medicines on their basis.

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INVESTIGATION OF NEUROGENIC MECHANISM OF DYNAMIC-BEHAVIOURAL ACTIVITY OF BENDAZOL

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Bendazol (dibazol) – derivation of benzimidazole has been widely used in medical research since the second half of the 20th century. This preparation has direct myotropic effect, it serves as anticonvulsive, immunomodulatory, antiagregate, adaptogenic, actoprotector remedy, that's why it is used in therapy, rehabilitation, prophylaxis in practical medicine. However there is not enough information in scientific literature about toxicity of the preparation. In our previous works it was proved that bendazol can be regarded as little toxic. It was also established that safe therapeutic range of bendazol covers 2 levels (from 1,25 to 40 mg/kg), that as regarding to LD_{50} forms 62-64 c.u. Toxic range of the preparation (from 160 to 640 mg/kg) corresponds to 13-15 c.u. with domination of cholinergic trophotropic effect.

The aim of our work is to investigate possible mechanism of the influence of bendazol on cholinergic structures of the central nervous system.

The experiments were carried out on 60 male-rats with the mass of 200-220 gr. The animals were kept according to the rules and the experiments were carried out keeping the rules of the International Convention on the protection of the vertebrates (Strasburg, 1986).

To ascertain availability of cholinomimetic ingredient in mechanism of bendazol's activity, we investigated its influences on M- и H-cholinoreceptive structures and its ability to change the duration of nicotine tremor and arecoline hyperkinesis that is caused by administration of the typical cholinomimetics – nicotine and arecoline. In an hour after inserting pharmacological agents, that are being used while testing, the animals got bendazol intragastrically in dozes of 5 and 160 mg/kg. The group animals used as a control one got solvent (distilled water) intragastrically in appropriate dozes.

Experiment with arecoline showed that preliminary inserting bendazol to the rats in dozes of 5 and 160 mg/kg prolonged the latent period of hyperkinesis if the doze is 5 mg/kg but shortened its beginning if the doze is160 mg/kg. At the same time the duration of hyperkinesis reduced depending on the doze.

The main H- cholinergic activity of the medication was evaluated according to its influence on the nicotine tremor, convulsive activity and depression of the inspiratory center. It was established that bendazol reduces the beginning of the nicotine tremor, increases its duration twice, stimulates the inspiratory center and shows little influence on the convulsive activity if the doze is 5 mg/kg. On the contrary if the doze is 160 mg/kg, the latent period of the beginning of tremor reduces if its duration increases by 120 %, depression of the inspiratory center increases 1,4 times ($p \leq 0,05$) and doesn't influence on the convulsive activity.

Thus, according to the results of the pharmacological analysis with the help of substances that influence just on the activity of central cholinergic systems, we can suggest that bendazol possesses H-cholinomimetic activity with the dozes 5 and 160 mg/kg and M-cholinolilitic activity with the doze 160 mg/kg.

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LASER SILICON INTUBATION DACRYOCYSTORHINOSTOMY REOPERATIONS EFFICIENCY EVALUATION

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Topicality. Endoscopic and laser processing technologies in dacryocystitis surgery has been quickly developing since the beginning of the 90-s of the XX century. The specified technologies provided the practical application of endonasal (retrograde) and transcanalicular laser endoscopic dacryocystorhinostomy (TLED). In ophthalmosurgery the transcanalicular approach to the lacrimal sac has gained the greatest extension as its main advantages, compared to the traditional external approach, are the lack of cicatrix on skin, little traumatism and bleeding and also a more simple surgery technique. According to the integrated data of scientific literature the efficiency of primary TLED varies from 58 to 85% and the success of reoperations usually doesn't exceed 50%, the application of transient stenting at reoperations allowing achieving higher positive results.

The purpose of the work – is to study the efficiency of bi-canalicular silicon intubation application at repeated TLED.

Materials and methods. The bi-canalicular silicon intubation TLED reoperations' results

analysis was carried out in 14 patients (14 eyes) because of ineffectiveness of the primary operation. There were 4 (28,6%) men and 10 (71,4%) women. The patients' age varied from 17 to 69 years old (the average age was 43,9+3,0 years). The reoperation was carried out at terms from 3 months to 1,5 years after the primarily executed interventions (in 12 (85,7%) patients during the first year after the surgery).

The operations were carried out using diode laser OME-1150 of the firm «Endo Optics» (USA) and endoscopic apparatus «Stozz» (Germany). For the intubation of lacrimal ways we used a lacrimal set of Ritleng (F.C.I., France) and a silicon stent (diameter of 0,64 cm and 30 cm long), which was set in for 3 months. All the patients were examined within long date: in 6 months-2 years (the average term for the examination was 16,4±1,9 months).

Results and discussing. During the operation a moderate bleeding was observed in two patients (14,3%). In the early postoperative period complications took place in 3 patients in 4 cases (28,6%). In the first case (7,1%) on the 2nd day after the reoperation a rather frank irritation of the eye conjunctiva mainly in the area of medial angle, which was evaluated by us as an allergic response for the silicon drainage material, that required carrying out, besides the corticosteroid (dexametason drops) therapy, non-steroid anti-inflammatory (diclof) antiallergic (cromohexal, hi-crom) ones in the postoperative period. Though the specified treatment reduced the irritation, it didn't liquidate it completely. More over, a granulation polyp (7,1%) located in the nasal cavity at the edge of the formed inosculation was detected in the specified patient in 1,5 months after the reoperation. It gave occasion to the prescheduled and constrained elimination of the silicon stent, whereafter the intubation granuloma was removed by forceps under local anaesthesia and endoscopic control.

At the stage of bi-canalicular intubation technique mastering the silicon drainage ends decoupling followed by its falling out (7,1%) was observed in 1 patient in 10 days after the reoperation, that didn't influence negatively the surgery result. In our opinion, the specified complication was caused by a reflex sneezing and coughing of the patient owing to periodic depression of free and relatively long ends of the silicon stent into the nasopharynx.

In the other case in 2 months after the surgery the breakdown of both lacrimal points and canaliculi (7,1%) followed by the adhesion of eyelids' skin and the lips of the incised canaliculi was registered.

By the day of release the functional result had been achieved in all the patients. At long date (up to 2 years) a positive effect with the recovery after the reoperation with bi-canalicular silicon intubation was registered in 11 patients or in 78,6% of the cases. The backsets of purulent dacryocystitis occurred in 11 patients (21,4%) in 2, 3 and 18 months after the reoperation accordingly, in 2 of the given three patients the backsets being connected with the silicon stent implantation. In one case the backset was observed after the lacrimal canaliculi eruption with medial migration of the intubation material, in the other one – in the patient with an allergic response to the silicon drainage and the granuloma formation in the inosculation area.

The reoperation with the use of transient drainage was executed for a third time and with a partial success in 2 patients.

Conclusions

1.In long date (up to 2 years) after the repeated transcanalicular laser dacryocystorhinostomy with transient bi-canalicular silicon intubation a positive result was registered in 78,6 % of the cases.

2.Complications in the early period of the given surgery (intubation granuloma, lacrimal points and canaliculi eruption, allergic response on the silicon drainage, stent falling out) were observed in almost 1/3 of the patients. Taking into account this fact the search for more perfect intubation materials remains topical. In our opinion, a biodegradable (resolving) drainage can be optimal in this respect.

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THE STUDY OF MECHANISMS OF OPHTHALMOPATHY DEVELOPMENT AT PERSONS WORKING UNDER CONDITIONS OF ACOUSTIC VIBRATIONS

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According to the absolute majority of experts on a labour safety, acoustic vibrations are the most sanitary dangerous factors of industrial environment. There is some information about some ocular characteristics as a result of mechanic acoustic vibration influence. However, it should be noted that preventives and correction methods of unfavourable effects of acoustic vibrations on the visual analyzer haven't been worked out yet, owing to pathogenetic mechanisms of acoustic ophthalmopathy development.

Our investigation object is to study mechanisms of acoustic ophthalmopathy development.

Materials and methods. 217 machine-building plant workers were examined. Conditions of work in the workshops: influence of infrasound, whose intensity level exceeds maximum allowable sanitary norms on 16-20 db and runs up to 96-100 db on the frequency of 8-16 Hz. The total equivalent level of noise intensity in one shift exceeds the maximum allowable level on 11-13 dbA in average.

Biomicroscopy was carried out by means of the stereobinocular microscope "Zeiss". The state of eye bottom vessels was studied using the ophthalmoscope 11750-VBI, Welch Allyn; the electroretinogram registration was conducted with A. M. Shamshinova's methodology (1998).

The results of research. The clinical observations showed that protracted influence of acoustic vibrations with pressure even within the normal range upon the human organism stimulates functional changes in the visual analyzer which lead, first of all, to visual discomfort.

Primary signs of microcirculation disorders (like aterosclerotic and hypertonic changes) were revealed by means of biomicroscopy of conjunctiva (especially at persons of 40 years and older). One part of examined (23.76%) had microaneurisms of conjunctiva vessels, more often in the area of the lower sector of limbus and in the area of the lower transitional pleat of mucous eye membrane.

The ophthalmoscopy of vessels of an eye bottom helped to bring to light arterial wall induration in the pool of the second order arterioles, venous plethora, venous glomes like Gwist's symptom, there was also revealed Salus-Gunn's symptom of the I-II degree. The frequency of exposure of vascular changes (like hypertonic, aterosclerotic and aterosclerotic-hypertonic angiopathy) in the examined group exceeds on 71.5% analogical displays of vascular pathology diagnosed in the control group.

Little decline of amplitude parameters of macular electroretinogram was observed at examined persons, both red and green stimuli. Statistic analysis allowed revealing a reliable distinction ($p<0.001$) between the groups of the amplitude of the wave A of macular electroretinogram of the green stimulus, which mainly rod cells and cones of macular area responds to.

Taking into consideration that there were no revealed significant distinction of parameters in macular electroretinogram on the red stimulus, which mainly macular area cones react to, it was possible to suppose that electrogenesis abnormality as a reliable decline of the amplitude of the wave A of macular electroretinogram on the green stimulus is conditioned, to a considerable extent, by dysfunction of rod cells, situated in the stimulated area.

Bioelectric retinal activity was also investigated at stimulation of low frequency. A reliable decline of electroretinogram amplitude for 10 Hz was revealed at examined persons in comparison with the control. Reliable extension of time interval N-P was considered to be a sign of disruption of interneuronal correlation in external layers of retina, most probably at the stage of information transmission from photoreceptors to neurons of the second level.

Thus, clinical observation of machine-building plant workers achieved that protracted influence of acoustic vibrations with pressure even within allowable level upon the human organism provokes functional changes in visual analyzer, which lead to, at the first place to visual discomfort. Ophthalmoscopy revealed vascular changes like hypertonic, aterosclerotic and aterosclerotic-hypertonic angiopathy in the group of examined persons. This angiopathy exceeds on 71.5% analogical manifestations of vascular pathology diagnosed in the control group. Bioelectric retinal activity was also analyzed. Decline of the electroretinogram amplitude for 10 Hz was displayed at persons from examined group in comparison with the control. Given investigation allowed suggesting a working classification of acoustic ophthalmopathies, which permits to work out a complex of sanitary and pharmacological measures for the prophylaxis and treatment of manifestation of acoustic vibration influence upon the eye.

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COMPLEX DIAGNOSTICS OF MYOENDOMETRIUM PATHOLOGY

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In many countries of the world the recent decades are characterizes by the incidence rate of hormonodependent tumors of reproductive organs (hysteromyoma among them), hyperplastic processes and endometrium cancer with the rejuvenescence of the sick women contingent. Numerous data allow to consider hysteromyoma as a clinical risk marker of the development of genitals' hormonodependent tumors (among them are primary-

multiple formations) in women of not only perimenopausal but also of reproductive age (J.B. Bosman, 1989; E.G Shvariov, 1993; L.M. Bershtein, 2001; N. Potischman, C.A. Swanson, L.A. Brinton et al., 1993).

In spite of the sufficient number of detection methods of myeondometrium pathology, the necessity of new ones is retained. It is stipulated by inadequate susceptibility of the existing methods, their complicacy and high cost at the screening and monitoring stages. For our research of biological material the endometrial secretion was chosen. It is stipulated by the fact, that during the usage of immunofluorescent and histochemical research methods of normal, hyperplastic and malignant endometrium tissue the ability of some enzymes and their isoforms to be accumulated in apical parts of glandular mucus was revealed (E.G. Shvariov, 1993). The biological peculiarity of endometrium is that this hormonosensitive tissue has the ability of cyclic renewal of cellular composition and is influenced by sexual hormones**,** peroxide lipid oxidation products and proteins.

No doubts that the development of various pathologic processes is associated with the so called "oxidant stress", which can be the direct cause of a disease or accompanies its development. The production of active oxygen forms increases, and the antioxidant system which regulates processes of peroxide lipid oxidation and peroxide protein destruction is involved into the process. The oxidant stress development doesn't affect the isolated disturbance of lipids, proteins or nucleic acids because of their close interaction; thus, they are to be considered as a whole complex.

The offered approach allows to carry out biochemical cytological and crystallographical research simultaneously. Diagnostically it turned out to be more effective than the detection of markers in serum, where the received indexes were rather diverse.

420 women were examined; they were divided into following groups:

1) control group, including 64 (15,2 %) women without reproductive organs pathology;

2) 208 (49,5%) women with hysteromyoma having normal structure of endometrium;

3) 84 (20,1%) women with hysteromyoma having hyperplastic processes;

4) 13 (2,86%) women with hysteromyoma in combination with atypical hyperplasia of endometrium:

5) 52 (12,4 %) women with hysteromyoma in combination with cancer of endometrium.

In these groups the content of catalase was detected. Catalase is one of the enzymes of antioxidant protection, that is malon dialdehyde, which is the secondary product of peroxide lipid oxidation and carbonil groups of protein – markers of peroxide destruction.

The meanings of catalase index and catalase number in the control group were 3,09 ± 0,18 untis and 0,8 ± 0,08 units. In women with hysteromyoma having normal endomtrium structure, the investigated parameters were 2,53 ± 0,16 units and 0.71 ± 0,05 units; in women with hystromyoma in combination with hyperplastic processes the parameters were 1,8 ± 0,33 units and 0,44 ± 0,09 units. The lowest meanings of there enzymes were registered in the group of women with hysteromyoma in combination with atypical hyperplasia of endometrium and endometrium cancer – 0,68 ± 0,2 and 0,2 ± 0,09 units ($p < 0,05$). The meanings of malon dialdehyde in the investigated groups, on the contrary, had the tendency to the increasing and were 0,37 ± 0,1 units; 0,49 ± 0,06 units; 1,68 ± 0,23 units and 3,01 ± 0,85 units. When evaluating the coefficient of correlation it was determined that there is a strong inverse connection between the investigated data ($p < 0,05$).

The determination of peroxide protein destruction was carried out according to the technique of R.L. Levine et al. (1990) in modification of E.E. Dubinina et al. (1995). The showings were evaluated in peripheral blood as well as in endometrial secretion; the most convincing data were received in endometrial secretion. The results showed the evaluation of showings of peroxide protein destruction on the level of carbonil derivatives in endometrial secretion to be one of the most sensitive showings of the oxidant stress.

The previous years in clinical medicine a new diagnostic technique was developed; it is based on the information of overmolecular level during the transition of biological liquids into the solid states (V.N. Shabalin, S.N. Shtokhina, 1999; 2001).

This information is contained in the structure of the so called facii, the microscopic investigation of which allows to receive the morphological decoding (V.N. Shabalin, S.N. Shatokhina, 2000).

The described phenomena allows the usage of the results of structural analysis of biological liquids in screening and monitoring of patients with hyperplastic processes of myoendometrium and endometrium cancer.

For the investigation of endometrial secretion, its transition into solid phase with the method of cuneate dehydration was made. The analysis of structural elements of a dehydrated drop was made with the stereomicroscope Mz-12 (Leica) and digital camera "Pixera" (USA). We investigated the samples of dried drops, i.e. facii, as well as their enlarged photographs (from x10 to x160). The coefficients appropriate the endometrium pathol-

ogy of different levels were calculated. Morphometrical showings of facii of endometrium secretion were evaluated with the help of the programme Image Tool.

During the examination of endometrial secret of hormonodependent tumors we determined 3 types of facii: radial (it is found in 48,4% of patients having hysteromyoma with the normal endometrium structure); mixed, which is found in patients with hysteromyoma in combination with hyperplastic endometrium; three-radial, which is found in patients with atypical endometrium hyperplasia and endometrium cancer.

In patients having hysteromyoma with normal endometrium structure in the samples of facii large fissures prevailed, forming special separate parts, where only isolated three-radial fissures were met. With the increasing of severity of endometrium pathology (glandular endometrium hyperplasia) the spread of three-radial fissures increased. In patients with atypical endometrium hyperplasia and endometrium cancer the structure of facii differed from that described above: in the investigated samples all over the area of facii the net of three-radial fissures was found.

To determine the power on interaction between the showings Srad and Str the tetrachorioidal coefficient of Pirson was calculated, which was increased with the severity of pathology of myemoendometrium from 0,3 to 0,8.

The main structural elements of facii are given in the table №1.

Table 1. The main Characteristics of Endometrial Facii in Myemoendometrium Pathology.

The investigated groups	The main structural elements of facii of uterus biological liquids	Srad (mm^2) (area of radiality)	Str (mm^2) (area of 3-radial fissures)
Patients without tumor pathology of reproductive system (N=64)	siteness, radial fissures, separate parts are expressed, in 10% isolated three-radial fissures can be found.	6,8 ± 0,12	0,3-0,5± ± 0,06
Hysteromyoma with normal endometrium (N=208)	siteness, radiality of fissures, separate parts, in 48,4% isolated three-radial fissures at any age are found.	5,1 ± 0,42	1,1 ± 0,08
Hysteromyoma with endometrium hyperplasia (N=84)	siteness, radiality of fissures, increasing number of separate parts, three-radial fissures.	6,1 ± 0,46	2,1 ± 0,11
Hysteromyoma with atypical endometrium hyperplasia (N=13)	clear siteness is being lost, in peripheral zone isolated radial fissures are kept, on the other part of surface there is a net of three-radial fissures.	2,23 ± 0,58	3,2 ± 0,58
Hysteromyoma with endometrium cancer (N=52)	siteness is lost, in 88% of patients radial fissures are absent, three-radial fissures are the main structural elements.	0	6,7 ± 0,6

Thus, the evaluation of structural peculiarities of endometrial secretion, some enzymes of antioxidant protection, secondary products of peroxide lipid oxidation and markers of peroxide protein destruction allows to reveal patients of high risk group with endometrium pathology at the preclinical period; it also allows to reveal forming pathologic processes of myenoendometrium, preventing the development of precancer and cancer of this localization. Nontraumatic sampling of the material, the simplicity of its processing give us large possibilities of effective dispancerization of women with the investigated pathology.

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STABILITY OF THE NATIVE AND IMMOBILIZED INULINASE TO VARIOUS DENATURIZING AGENTS

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Today enzyme inulinase (2,l-β-D-fructanfructanohydrolase, EC 3.2.1.7), which splits off fructose residues from the nonreducing end of the molecule of inuline, is of great interest in connection with the possibility of its using in the production of fructose from inuline and inuline-containing materials. When using inulinase for reducing inuline-containing materials, it has received the product-95% fructose syrup, which doesn't demand of special purified methods. Another direction of using of this enzyme is the direct fermentation of inuline into ethanol.

Endoinulinase Aspergillus awamori has been purified by ammonium sulfate precipitation, gel-chomatograhy on sephadex G-100, SDS-PAGE electrophoresis. The immobilization of inulinase by ion exchange AV-26 and AV-17-2P has been made by adsorption and glutaraldehyde methods. The effect of UV-radiation and carbamide on the stability of native and immobilized enzyme has been investigated. DRT-400 lamp has been used in UV irradiation.

It has been determined that UV irradiation in doses 75.5-151.0 J/m^2 leads to the inactivation of soluble inulinase both immobilized inulinase preparations preserve 96 % of catalytic activity in dose 151.0 J/m^{2}min. Doses 906-1400 J/m^2 cause disulfide bonds degradation and the photolysis of catalytic site as a result of amino acid radicals formation. We have observed an increase oh the adsorptively immobilized inulinase stability at the 302 J/m^2. Covalently bonded protein preserves hydrolytic activity in high doses (1300 J/m^2). Thus, covalent immobilization provides high stability for the inulinase to UV irradiation. The type of a way of binding influences significantly on the heterogeneous enzyme preparations stability.

It is shown, that the thermo stability of adsorb immobilized inulinase, bound with anionite AV-26, increases in comparison with native inulinase: the immobilized enzyme has the max catalytic activity at temperature 70°C. For immobilized and native enzymes optimums pH are practically the same, only there is a wider range of meanings pH from 4.5 to 5.0. Activity of the native preparates is preserving completely the thermo stability of covalent bound inulinase is more higher than at the adsorb immobilization. So, after heating to 100°C inulinase, immobilized by the chemical method, shows 19% of the catalytic activity of the native enzyme. The fixation of the triple structure by the multipoint interaction between active groups of the carrier and of the protein takes place after immobilization of the enzyme on anionites. It was shown, that the immobilization leads to the increasing of the activation energy (E_{act}), ΔH of the hydrolysis reaction of inulinase in comparison with diffusion difficulties of the high molecular substrate during the approaching to bounding and catalytic groups of the active center. The negative value ΔS for the hydrolysis reaction of inulinase, realized by the native enzyme, means that the breaking up of the polymeric substrate proceeds with high speed and is characterized by the high order. After the immobilization of inulinase ΔS of the enzyme breaking up of inulinase decreases, apparently at the expense of the direct interaction on of the enzyme with the substrate.

It is shown, that the incubation of soluble inulinase with carbamide in concentration 8 mol/L leads to the total denaturation of the enzyme, and its activity isn't registered. After the interaction of immobilized inulinase with the solution of carbamide in concentration 8 mol/L for 60 min with constant mixing the enzyme showed the catalytic activity (30% of activity of immobilized unmodified inulinase).

Thus, the stability of inulinase in relation to denaturizing agents has been shown to increase with the immobilization of ion exchange. The character of binding with the matrix affects greatly the stability of immobilized enzyme to physical factors.

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LOW-FREQUENCY NEUROMUSCULAR ELECTRICAL STIMULATION TRAINING OF HUMAN SKELETAL MUSCLES IN CONDITIONS OF GRAVITATIONAL UNLOADING

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A number of studies have indicated that sudden exposure to microgravity environment causes a decrease in the tone of the skeletal muscles [Kakurin et al., 1971b; Kozlovskaya et al., 1984], reduction of muscle strength [Cherepakhin & Pervushin, 1970; Kakurin et al., 1971a; Mitarai et al., 1980; Grigor'yeva & Kozlovskaya, 1985; Koryak, 1998; 2002], perceptual and coordination disorders in the neuromuscular systems [Ross et al.,

1984; Grigor'yeva & Kozlovskaya, 1985; Kirenskaya et al., 1985], shift of the spinal reflex mechanisms [Cherepakhin & Pervushin, 1970; Kakurin et al., 1971b; Kozlovskaya et al., 1982], and degradation of joint position sense [Bock et al., 1992; Bock, 1994]. It is accepted that the major factor responsible for all of these changes is the sudden elimination of the proprioceptive information from the muscle and tendon in response to absence of load-bearing. Gravitational loading appears to be necessary for the maintenance of human lower limb skeletal muscle size and force [Kawakami et al., 2000; Kubo et al., 2000; Koryak, 2001]. Studies simulating microgravity have shown that exercise countermeasures can attenuate, but not completely prevent the loss of muscle mass and force [Kawakami et al., 2001; Koryak, 2001]. The muscle groups most affected by exposure to microgravity appear to be the antigravity extensors of the knee and ankle [Akima et al., 2001]. Among these, the plantarflexors seem to be the most affected [Akima et al., 2000], likely due to their greater mechanical loading under normal gravitational conditions. Most notable after exposure to microgravity is a disproportionate loss of force as compared to that of muscle size [Akima et al., 2000; Kawakami et al., 2001], indicating that factors other than atrophy contribute to muscle weakness. The internal architecture of a muscle is an important determinant of its functional characteristics (*force–velocity* relationships, *force–length*, and maximum isometric force [Gans & Bock, 1965; Lieber & Frieden, 2000]. There is a paucity of studies on the effects of disuse [Maganaris et al., 1998] or simulated microgravity [Kubo et al., 2000; Kawakami et al., 2000] on muscle architecture.

Purpose. The purpose of the present study was to investigate the internal architecture of the triceps surae [medial (GM) and lateral (LG) gastrocnemius and soleus (SOL) muscles] in relation to the functional characteristics of the plantarflexors after 6 days of «*dry*» water immersion (DI) with exercise countermeasures [term-long low-frequency neuromuscular electrical stimulation (NMES) trainings].

Methods. To simulate microgravity the DI model has been used [Shulzhenko & Vil-Villiams, 1976]. Four subjects (men-volunteers; 22.8 ± 0.8 yr, 1.84 ± 0.1 m, and 79.3 ± 4.2 kg) gave their written, informed consent to participate in this study, after the Ethics Committee of the Institute of Biomedical Problems RAS had approved the procedures involved. All the experimental procedures were performed in accordance with the Declaration of Helsinki. NMES is applied to four muscle groups of both lower extremities. "*Dry*" electrodes (Ltd. "Axelgaard", USA) are placed on the skin above the quadriceps femoris muscles, the hamstrings, the tibialis anterior, the peroneal, and the triceps surae muscles. The synchronous stimulation of antagonistic muscle groups prevents unwanted joint movements. The NMES-training is performed during 3 hours per day with 1 s « *on* » and 2 s « *off* » trains at intensity levels of 20-30 % of maximum tetanic force and a frequency of 25 Hz and amplitude of stimulus from 0 up to 45 V. The electrical stimulus was provided by the "STIMUL LF-1" stimulator (RUSSIA). The technical equipment consists of electrode trousers carrying stimulation electrodes for the 12-channels, and 2 interconnected 6-channel stimulators caned on a belt. The NMES-training of muscles of the examinee was carried out directly in a bath. Subjects performed a series of isometric plantarflexion contractions on an isokinetic dynamometer ("Biodex", USA) at ankle angles of 0° (neutral ankle position: the footplate of the dynamometer perpendicular to the longitudinal axis of the tibia). All measurements were carried out with the knee joint flexed at 90 deg. A real-time B-mode ultrasound apparatus ("SonoSite MicroMaxx", USA) with a 7·5 MHz linear-array probe, and length of a scanning surface 60 mm and thickness of 10 mm was used to obtain sagittal images of the GM, GL and SOL at rest and at 50 % of plantarflexor MVC at the neutral ankle position. The fascicle pennation angle (Θ) was measured from the angles between the echo of the deep aponeurosis of each muscle and interspaces among the fascicles of that muscle. The length of fascicles (L) across the deep and superficial aponeurosis was measured as a straight line [Abe et al., 2000]. Shorter fascicle L fibres (ΔL_{muscle}) was determined as a delta between L and cos Θ fibres in the active comparison with the passive condition. In the present study, ultrasonic measurement was repeated three times for each subject and averaged values were used. All ultrasonic images were processed with use of the software package "Dr. ReallyVision" (Ltd. "Alliance – Holding", RUSSIA).

Results. After the 6-day DI with application by NMES-training, maximal plantar flexion torque by three subjects has increased on the average by 11.3 % (150 ± 17.3 *vs* 167 ± 6.7 N) and at one has decreased for 9.6 % (155 *vs* 140 N). After DI, in the passive condition, L fibres in the MG, and LG, and SOL has decreased for 12 (from 32 ± 2 to 28 ± 1 mm), 13 (from 36 ± 2 to 31 ± 2 mm), and 13 % (from 36 ± 3 to 32 ± 2 mm) but in the active condition by 18 (from 26 ± 3 to 22 ± 2 mm), 22 (from 36 ± 3 to 28 ± 2 mm), and 21 % (from 32 ± 2 to 26 ± 2 mm), respectively. The Θ angles, in the passive condition, was decreased by 22, 20 and 16 %; but in the active condition by 17, 22 and 17 %, respectively. Shorter fascicle lengths and

steeper fascicle angles in the active compared with the passive condition show internal shortening of fascicles by contraction. Before DI ΔL_{muscle} the MG has found 7.9 mm after has decreased and has made 7.8 mm, and in SOL 5.9 *vs* 5.6 mm. Significant increased in ΔL_{muscle} from 0.9 to 3.3 mm were found by LG.

Conclusion. This study describes, for the first time, the architecture of the human triceps surae [medial (MG) and lateral (LG) gastrocnemius and soleus (SOL) muscles] *in vivo*, both at rest and during graded (50 % MVC) isometric plantar flexions. The results obtained *in vivo* indicate that human MG, LG, and SOL architecture drastically changes both as a function of ankle joint angle at rest and as a function of the force developed during isometric contractions at a fixed joint angle. At rest, when changing the ankle joint angle from -15 to +30 deg, GM pennation angle increased from 31 to 49 deg, LG – from 20 to 28,5 deg, and SOL – from 22.8 to 34 deg; fibre length decreased from 35.5 to 26.8 mm, LG – from 46.8 to 31.2 mm, and SOL – from 39.2 to 28.2 mm. These results indicate that fibre length and pennation angle of the human triceps surae cannot be assumed to remain constant with changing muscle length [Huijing & Woittiez, 1985]. The decrease in fibre length and increase in pennation angle with increasing muscle length may be ascribed the taking up of the slack characterizing these structures [Huijing & Woittiez, 1985]. In the present study, the decrease in fibre length occurring from -15 to +30 deg of passive plantar flexion also suggests that muscle fibres became progressively slack with increasing ankle joint angles. The major findings of this study were that, after 6 day DI with of NMES-training, isometric maximal voluntary torque by the plantar flexor muscles increased. Previous studies have documented decrease of the contractile properties of skeletal muscles during DI (Grigor'yeva & Kozlovskaya, 1985; Koryak, 1998a; 2002, 2003). The present exercise training resulted small increased (~11 %) in maximal voluntary plantar flexion torque in the triceps surae muscle what is antigravitational the triceps surae muscle whereas absence of preventive actions results in decrease in MVC more than on 50 % [Grigor'eva & Kozlovskaya, 1985; Koryak, 1998a, b; 2002, 2003) and in P_o more than on 30 % (Koryak, 1998a,b; 2001, 2003].

Efficacy of NMES-training for increased the contractile properties of skeletal muscles has been suggested in previous studies [Koryak, 1995; Mayr et al., 2000; Koryak et al., 2002]. The insignificant increase in force of contraction in the present study can be assumed it is defined by slack intensity impulses.

It is well known that the smaller motoneurons innervating muscles are more readily activated than the larger cells innervating units [Henneman et al., 1965; Burke & Edgerton, 1975], as the strength of the contraction increases progressively. The smaller units consist of slow twitch muscle fibres (type I) and the larger units consist of fast twitch fibres (type II). In submaximal voluntary contractions, type I fibres the motor units are activated by the synaptic current impinging on the motor neuron. The situation is completely different in contractions triggered by NMES, because the muscle fibres of the motor units are activated by an electric current which is applied extracellularly to the nerve endings, and larger cells with lower axonal input resistance are more excitable [Blair & Erlanger, 1933; Solomonow, 1984]. In fact, when the stimulus is applied from outside the cell, the electric current must first enter through the membrane before it depolarises the cell, but the extracellular medium shunts the current, and the smaller motor units will not be activated during submaximal NMES because of their higher axonal input resistance. Therefore, the smaller motor units do not adapt to training with submaximal NMES. However when use electrical stimulation high training intensity, larger force NMES-training to be more efficient exercise [Almekinders, 1984].

Internal architecture of the GM, LG, and SOL muscle was altered and this was only partially prevented by exercise countermeasures. Both fascicle length and pennation angle were reduced after DI with NMES, this strongly suggests a loss of both in-series and in-parallel sarcomeres, respectively. The functional consequence of the decreased fascicle length was a reduced shortening during contraction. The loss of in-series sarcomeres would mean that this is likely to have implications both on the *force-length* and *force-velocity* relationships of the muscle. The observation of a smaller pennation angle during contraction after DI with NMES will partially compensate for the loss of force, because of a more efficient force transmission to the tendon. The reduced initial resting pennation angle probably, grows out reduction decreased tendon stiffness or of the muscle-tendon complex that finds confirmation in substantial growth ΔL_{muscle} of LG (with 0.9 up to 3.3 mm after DI) during contraction. This observation is consistent with the findings of Kubo et al. [2000]. In conclusion, NMES-training was partially successful in mitigating the loss of function and architecture induced by prolonged DI. Apparently, by ascending during NMES-trained a flow muscular afferentation [Gazenko et al., 1987]. In summary, from the present results, follows, first, that the architecture different lead the triceps surae muscle considerably differs, reflecting,

probably, their functional roles, second, various changes fibre length and pennation angle between different muscles, probably, are connected to distinctions in ability to develop force and elastic characteristics of sinews or muscle-tendon complex and, at last, in the third, NMES -training has preventive an effect on stimulated muscles: in part reduces loss of force of reduction of the muscles, the caused long unloading. The received data, allow concluding, that use of NMES-trained renders the expressed preventive action, essentially reduces depth and rate of atrophic processes in muscles.

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References:

1. Almekinders L.C. Transcutaneous muscle stimulation for rehabilitation. Phys. Sportsmed.,1984,12, 118-124.

2. Akima H., Kubo K., Kanehisa H., Suzuki Y, Gunji A., Fukunaga T. Leg-press resistance training during 20 days of 6° head-down-tilt bed rest prevents muscle deconditioning. Eur. J. Appl. Physiol., 2000, 82, 30-38

3. Blair E., Erlanger F.A. comparison of the characteristics of axons through their individual electrical responses. Am. J. Physiol., 1933, 106, 524-564.

4. Bock O. Joint position sense in simulated changed-gravity environments. Aviat., Space Environ. Med., 1994, 65, 621-626.

5. Bock O., Howard I.P., Money K.E., Arnold K.E. Accuracy of aimed arm movements in changed gravity. Aviat., Space Environ. Med., 1992, 63, 994-998.

6. Burke R.E., Edgerton R.V. Motor unit properties and selective involvement in movement. Exer. Sport Sci. Rev., 1975, 3, 31-81.

7. Cherepakhin M.A., Pervushin V.I. Space flight effect on the neuromuscular system on cosmonauts. Kosm. Biol. Aviakosm. Med., 1970, 4, 46-49.

8. Gans C., Bock W.J. The functional significance of muscle architecture — a theoretical analysis. Ergeb. Anat. Entwicklun., 1965, 38, 115–142.

9. Gazenko O.G., Grigoriev A.I., Kozlovskaya I.B. Mechanisms of acute and chronic effects of microgravity. Physiologist, 1987, 30 (Suppl), S1-S5.

10. Grigor'yeva L.S.,. Kozlovskaya I.B. Effects of 7-day immersion hypokinesia on characteristics of precision movements. Kosm. Biol. Aviakosm. Med., 1985, 19, 38-42.

11. Henneman E., Somjen G., Carpenter D. O. Functional significance of cell size in spinal motoneurons. J. Neurophysiol., 1965, 28, 560-580.

12. Huijing P. A., Woittiez R. D. Length range, morphology and mechanical behavioure of rat gastrocnemius during isometric contraction at the level of the muscle tendon complex. Netherlands J. Zool., 1982, 35, 505-516.

13. Kakurin L.I., Cherepakhin M.A., Pervushin V.I. Effect of brief space flight on the human neuromuscular system. Kosm. Biol. Aviakosm. Med., 1971a, 5, 53-56.

14. Kakurin L. I., Cherepakhin M.A., Pervushin V.I. Effect of spaceflight factors on human muscle tone. Kosm. Biol. Aviakosm. Med., 1971b, 5, 63-68.

15. Kawakami Y., Muraoka Y., Kubo K., Suzuki Y., Fukunaga T. Changes in muscle size and architecture following 20 days of bed rest. J. Gravit. Physiol., 2000, 7, 53-60.

16. Kawakami Y., Akima H., Kubo K., Muraoka Y., Hasegawa H., Kouzaki M., Imai M., Suzuki Y., Gunji A., Kanehisa H., Fukunaga T. Changes in muscle size, architecture and neural activation after 20 days of bed rest with and without countermeasures. Eur. J. Appl. Physiol., 2001, 84, 7-12.

17. Kirenskaya A.V., Kozlovskaya I.B., Sirota M.G. Effect of immersion hypokinesia on characteristics of programmed voluntary movements. Kosm. Biol. Aviakosm. Med., 1985, 19, 27-32.

18. Koryak Yu. Effects of surface electrostimulation on human skeletal muscle. Proc. 5th Vienna Inter. Workshop of Functional Electrostimulation, 1995, 297-300.

19. Koryak Yu. The effect of 120-days of bed rest with and without countermeasures on the mechanical properties of the triceps surae muscle in young female. Eur. J. Appl. Physiol., 1998a, 78, 128-135.

20. Koryak Yu. Electromyographic study of the contractile and electrical properties of the human triceps surae muscle in a simulated microgravity environment. J. Physiol., 1998b, 510, 287-295.

21. Koryak Yu. Electrically evoked and voluntary properties of the human triceps surae muscle:

effects of long-term spaceflights. Acta Physiol. Pharmacol. Bulg., 2001, 26, 21-27.

22. Koryak Yu. "Dry" immersion induces neural and contractile adaptations in the human triceps surae muscle. Environ. Med., 2002, 46, 17-27.

23. Koryak Yu. Contractile properties and fatiguability of the human triceps surae muscle after exposure to simulated weightlessness. In: From Basic Motor Control to Functional Recovery III. (ed. Gantchev N.), University Press, Varna, 2003, pp. 369-380.

24. Koryak Yu., Kozlovskaya I., Gratchev V., Mayr W., Rafalt D., Freilenger G., Padalka G., Avdeev S. Electromyostimulation (EMS) as a countermeasure of the negative effects of weightlessness to prolonged spaceflights. XII Conf. Space Biol. Aerospace Med., 2002, 486-487.

25. Kozlovskaya I.B., Aslanova I.F., Grigorieva L.S., Kreidich Yu.V. Experimental analysis of motor effects of weightlessness. Physiologist, 1982, 25 (Suppl.), S49-S52.

26. Kozlovskaya I.B., Grigoryeva L.S., Gevlich G.I. Comparative analysis of the effects of actual and simulated weightlessness on the strength-velocity properties and tone of skeletal muscles of man. Kosm. Biol. Aviakosm. Med., 1984, 18, 22-26

27. Kubo K., Akima H., Kouzaki M., Ito M., Kawakami Y., Kanehisa H., Fukunaga T. Changes in the elastic properties of tendon structures following 20 days bed rest in humans. Eur. J. Appl. Physiol., 2000, 83, 463-468.

28. Lieber R.L., Frieden J. Functional and clinical significance of skeletal muscle architecture. Muscle & Nerve, 2000, 23, 1647-1666.

29. Maganaris C.N., Baltzopoulos V., Sargeant A.J. Changes in Achilles tendon moment arm from rest to maximum isometric plantarflexion: observations in man. J. Physiol., 1998, 510, 977-985.

30. Mayr W, Freilinger G., Rafolt R., Bijak M., Girsch W., Lanmüller H., Reichel M., Sauermann S., Unger E., Gratchev V., Koryak Yu., Kozlovzkaya I., Grigoriev A. Functional electrostimulation as a countrermeasure – against muscular atrophy in long-term space flights. BAM, 2000, 10, 78

31. Mitarai G., Mano T, Yamazaki Y. Correlation between vestibular sensitization and leg muscle relaxation under weightlessness simulated by water immersion. Proc. 31st Congr. Inter. Astron. Fed., Pergomon Press, Oxford, 1980, pp. 1-8

32. Ross H.E., Brodie E., Benson A. Mass discrimination during prolonged weightlessness. Sci., 1984., 225, 219-221.

33. Shulzhenko E.V., Vil–Villiams I.E. Possibility of a long-term water immersion by the method of dry plunging. Kosm. Biol. Aviakosm. Med., 1976, 10, 82-84.

34. Solomonow M. External control of the neuromuscular system. IEEE Transactions on Biomedical Engineering, 1984, 31, 752-763.

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ABOUT INDICATORY ROLE OF THE BIOSUBSTRATES CRYSTALLOGENESIS

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History of the biocrystallization phenomenon scrutiny includes over 30 years [1, 3, 4], but the first mention about it had been written in 1804 [2]. There are many papers, which demonstrated diagnostic function of crystalloscopic and tezigraphic facia [4]. In that time, the unitary publications devote to ability of crystallographic methods for indication of treatment effectiveness [1, 3]. This thesis was aim of our investigations.

Materials and methods. We study the dynamics of the transformation of teziocrystalloscopic picture of some human biofluids (saliva, urine, blood serum, teardrops etc.) in the management process. Free crystallization of biomaterial (classic crystalloscopy) was examined by using the special identification table, which consist of 5 classes of crystal and amorphous structures and half-quantitive additional criteria, such as facia destruction degree [FDD], regularity [R], cellularity [C] and marginal belt [MB]. Tezigraphic facia was evaluated by complex of basic (initiation coefficient [IC]; belt coefficient [BC]) and additional parameters [1, 3]. We used two variants of tezigraphic test. There are comparative and differential teziography, which discrepant by number of the basic substances. Data were processed with statistic programs (SPSS 11.0; Primer of biostatistics 4.03).

Results. On the base of our data it was demonstrated, that the dynamics of the biofluids' teziocrystalloscopic picture correlates with patient common condition and his clinic-functional status. This thesis was verificated on patients, which have gastroenterological, neurological, traumatologinal, cardiological and nephrological diseases. We tested the dynamics of free and initiated biosub-

strates crystallogenesis on medicamental, chirurgical, balneological and physiotherapeutic management. On our opinion, the most informative and comfortable for practical using biosubstrates are saliva and urine, but informativity of the monitoring highly increase, if two or more biofluids are analysed simultaneously. It was shown, that character of the crystalloscopic specimen's changes (on the general tendency to organization or destruction of the facia) illustrates the treatment effectiveness. This conclusion with respect general tendency is formed by the analysis of crystallization rate (crystal concentration in microscope visual field), facia destruction degree, homogeneity of elements allotment, cellularity, marginal zone width etc. It is determined, that positive treatment results associate with decreasing of facia destruction degree, cellularity; increasing of facia homogeneity and normalization of crystalloscopic rate for own crystallization (initiation potential for tezigraphic test).

We composed universal algorithm of the crystalloscopic monitoring of patient functional status, which consist of the two or three control points. If we estimate short-time or unitary medical interference, it is enough to investigate the baseline and final condition. In this time the taking of biosubstrates is accomplished. For the treatment scheme, which realized in long time, the three-points investigation is most suitable.

Conclusion. So, it was ascertained, that crystallographic methods of biofluids investigation can be used for the treatment control.

References:

1. Guliaeva S. F., Martusevich A. K., Pomaskina T. V. Mathematic modeling of saliva initiated crystallogenesis as a criteria of mineral water using effectiveness // Human Ecology. – 2005. – №7. – P. 33-35. (in Russian)

2. Lovitz T. E. The demonstration of the new method of salt investigation // Technological Journal. – 1804. – Vol. 1. – Part 3. – P. 27-41. (in Russian)

3. Martusevich A. K., Ghdanova O. B., Yanchenko V. A. Pathogenic role of biological fluids crystallization investigation on alveococcosis // Annals of Surgical Hepatology. – 2006. – Vol. 11, №3. – P. 50-51. (in Russian)

4. Colomban Ph., Lasseguest J. S., Novak A. et al. Dynamics of molecular crystals. Amsterdam: Elsevier, 1991. – 269 p.

The article is admitted to the V International Scientific Conference «Present-day problems of experimental and clinical medicine», Thailand, (Pattaya), February 20-28, 2008, came to the editorial office on 03.11.07

CLIMATIC AND GEOGRAPHIC FEATURES AND DEATH RATE IN REPUBLIC SAKHA (YAKUTIA)

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The Republic Sakha (Yakutia) occupies territory in 3103, 2 thousand sq.km, that makes 18 % of all territory of the Russian Federation. Forty percent of territory is behind Polar circle, in a zone of a long-term frozen ground. In its limits three hour zones are located.

Distinctive feature of a climate - expressed anticyclone mode of weather and frequent intrusions of air masses from Arctic Ocean with very small maintenance of water steam in summer. Winter is long, cold and not snowy; on a greater part of territory temperature is varying from 40 below zero up to 50 below zero. Summer is short, droughty, and rather hot. In some days of July in the Central Yakutia the temperature reaches up to +31 - +38.

Population of Yakutia, according to census of 2002, is 949 thousand people. The indigenous population, including representatives of small nationalities, makes 50 % (45 % are Yakuts and 5 % - small in numbers people). Indigenous small in numbers people are presented with Evenks, Evens, Dolgans and Yukaghirs. The basic part of non-indigenous population is represented with Russians (41 %), and also with representatives of other people and nationalities.

Centuries-old evolution of indigenous population of the Far North has generated a lot of the adaptive morphological and functional features, allow surviving and saving health in severe conditions of an environment. However the mortality rate coefficient of the population of Yakutia constantly increases and since 1990 for 2005 he has increased in 1, 5 times (from 6, 8 up to 10, 2) whereas in Canada similar on climatic and geographic conditions this parameter in 2006 according to the data of WHO was 7, 86. For last decade (1996-2006) death rate of the population of Yakutia on the basic classes of the reasons on 100 thousand people constantly increases. Moreover the basic part of growth for this period is made by illnesses of system of blood circulation (in 1, 3 times). Only for last five –year period (2002-2006) death rate from IHD (ischemic heart disease) has increased in 1, 13 times, from a sharp heart attack of a myocardium - 1, 35, from cerebrovascular illnesses - 1, 11. It is especially necessary to emphasize fast growth of death rate from illnesses of endocrine system, frustration of a feed and a metabolism which has increased for this period in 1, 53 times, from them

from diabetes - 1, 69. Thus, statistical data show influence of urbanization on health of the population in the North which major factors are infringement of the balanced feed, decrease in physical activity, and increase of psycho emotional pressure.

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CYTOPLASMIC RNA CHANGES IN SKIN HAIR FOLLICLE EPITHELIAL CELLS OF GUINEA-PIGS AT MICROWAVE INFLUENCE

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In the available literature there are no cytophotometric data about the cytoplasmatic RNA changes in skin hair follicles' epithelial cells when affecting by thermogenous intensity microwaves. All this conditioned, especially with due account for the possibility of the obtained experimental data extrapolation for a human, the necessity to carry out our research.

The research was carried out on 65 mature guinea-pig males weighing 400-450 g, from which 35 were used in the experiment, and 30 served as the control. The experimental animals were exposed to the effect of single general microwave irradiation (length of wave - 12,6 cm, frequency – 2375 MHz, power flow density (PFD) – 60 mW/cm^2, exposure time – 10 min). Excluding the animals from the experiment and sampling the materials were done immediately, in 6 hours, on the 1st, 5th, 10th, 25th and 60th days after finishing the exposure. . The flaps of skin were taken from different areas (head (cheek), back, stomach). The photometric activity definition of the cytoplasmic RNA content was performed in 50 cells of outer root sheaths of each cut hair follicles. The hematological control (total count of erythrocytes and leucocytes) was carried out during the experiment.

Right after finishing the microwave effect the decrease, compared to the control, of cytoplasmic RNA is registered, to the maximum extent – in the stomach skin epitheliocytes – up to 86,7%, while in the head and back skin – up to 98,3% and 97,2% from the original accordingly ($p<0,05$). In the following terms after finishing the exposure to the thermogenous intensity SHF waves a further decrease of the cytoplasmic RNA content in skin cells of all localizations, especially head and stomach, is observed. Thus, on the 5th day after finishing the SHF waves exposure the cytoplasmic RNA content is maximally decreased in the specified epitheliocytes of head and stomach skin – by 23,1% and 35,8% from the control level accordingly ($p<0,05$). Beginning with the 10th day an increase of the cytoplasmic RNA content in the cytoplasm of outer root sheaths epitheliocytes of all localizations skin hair follicles is close to the original one ($p>0,05$).

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INFLUENCE OF NATURAL 1-O-ALCYLGLYCEROLS ON ANTIOXIDANT DEFENCE SYSTEM OF RATS AT ALIMENTARY DISLIPIDEMY

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In recent years a great interest has been attracted to pharmaceutical preparations of sea hydrobionts containing 1-O-alkyl-diacylglycerols (ADG). ADG at entry to digestive tract are broken down to form high activity biological compounds, when affected by lipases, - 1-O-alkylglycerols (AG), which are responsible for hemopoietic, radioprotective, antitumor properties of ADG-containing pharmaceutical preparations. In single publication there is information about antioxidant properties of the preparations rich in ADG. It is AG that are supposed to play an important role in the manifestation of antioxidant properties of the given pharmaceutical agents. The purpose of the work has been the study of 1-O-alkylglycerols' influence on the antioxidant defence system in rats at alimentary dislipidemy (DLP), the 1-O-alkylglycerols being obtained from natural ADG.

The model of alimentary DLP was caused by unbalanced fat composition nutrient budget including high-caloric products and cholesterol. The model development criterion served the cholesterol level in blood serum and liver of the rats exceeded the initial one by more than 1/3. After the development of DLP the rats were given AG intragastrically in the dosage of 0,4 g/kg from the rat's body mass for 30 days (Novgorodtseva T.P., 2007). The 1-O-alkylglycerols were obtained by the method of ADG hydrolysis from the liver lipids of Commander Squid *Berryteuthis magister*. The total antioxidant activity (TAA) of rats' blood

plasma and the catalase activity in erythrocytes were investigated. The level of initial (hydroperoxide of lipids) and final (malondialdehyde) lipoperoxidation products in blood by the spectrophotometric method was determined.

The DLP formation in rats was attended by the lipid peroxidation products accumulation and general antioxidant and catalase blood activity decrease. After using AG the catalase activity increase and the lipid hydroperoxide level decrease in blood plasma were detected in the rats, the TAA normalization and tendency to malondialdehyde concentration decrease were registered. The research findings can testify to antioxidant properties of natural AG, that gives an opportunity to extend the ADG-containing lipids' application at various pathologies attended by the decrease of antioxidant state of the body.

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EFFICIENCY OF PREVENTIVE MAINTENANCE PROGRAM IN DIABETIC FOOT PATIENTS AT OUT-PATIENT STAGE

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During 1999-2004 we have developed and implemented an organizational model of nursing aid to the patients with diabetic foot syndrome (DFS) at out-patient stage. For further research of preventive maintenance program with use of nursing teams, 386 patients have been parted in two groups.

In the first group were 137 DFS patients with mentions of the moderate and expressed restriction of mobility due to age, main and accompanying diseases. These patients were actively observed by nursing teams during one-year follow-up. The given group is designated further as group A or group of active home nursing. The second group was made from 239 DFS patients, living out of district of service of the specified clinical bases and consequently inaccessible to observation domiciliary. All of them continued to be observed under the traditional scheme within a year from including in research, periodically they were invited on reception in diabetic foot offices according to prophylactic medical examination rules. This group has been designated as group B or group of typical practice. Both groups of patients during observation received a standard complex treatment depending on type and gravity of diabetes and current form of DFS.

After comparison of sex, age, terms and features of current diabetes, there were not revealed essential differences in both groups. Authentic differences between groups consisted only in degree of mobility restriction and also in frequency of previous amputations which have appeared higher in group A.

The analysis of clinical and social efficiency of preventive actions was performed after 1 year of observation by following criteria:

– quantity and gravity reduction of purulent-necrotic and other DFS complications in observable patients;

– healing terms, depression of amputations level;

– dynamics of the basic indicators of quality of life (QoL);

– frequency and a length of hospital stay concerning DFS;

– patient's estimation of efficiency of home nursing.

The analysis of lower extremities amputations frequency for the one-year observation period has taped authentic prevalence of this indicator ($p < 0,05$) in «typical practice» group of patients - table 1.

Table 1. Comparison of amputations frequency and level in investigated groups during observation (on 100 patients).

Level of amputations	Nursing teams (group A)	" Typical practice " (group B)
Fingers and feet	5,1	7,5
Shin	-	0,8
Hip	-	3,3
The general frequency	5,1	11,7

Among the patients of group A high amputations (at shin and hip level) for the 1-year period of observation were absent, that speaks about more active observation domiciliary. At the same time variants of various operative measures and their combination at patients were various and variously influenced quality of the further life.

Considering this circumstance, the estimation of severity level of invalidism due to lower extremities amputations has been spent, the differentiated estimation of volume of an operative measure in points is thus used (P. Vorobiyov et al., 2001).

In table 2 are presented indicators of invalidism factor for the 1-year period of observation.

Table 2. Gravity of an invalidism in investigated groups during observation period.

Indicator	Nursing teams (group A, n=137)	" Typical practice " (group B, n=239)
Quantity of the patients who have transferred amputations, in the given group (absolute value)	7	28
The total quantity of points characterizing gravity of an invalidism	13	124
Factor of gravity of an invalidism	1,86	4,43

A year later at the patients consisting under observation of nursing team, invalidism severity level has appeared much lower, than at typical practice: 1,86 against 4,43.

Degree of mobility of patients was estimated in dynamics on the modified scale of gravity of the vital activity restrictions recommended by the "International Classification of Functioning, Vital Activity and Health Restrictions" (2001). The received results reflect positive dynamics of expansion of mobility of patients in group of sisterly observation where a year later the share of patients with serious restrictions of mobility ($p < 0,05$) has authentically decreased.

References:

1.Clark CM. Jr., Snyder JW, Meek RL, Stutz LM, Parkin CG.A systematic approach to risk stratification and intervention within a managed care environment improves diabetes outcomes and patient satisfaction. *Diabetes Care*. 2001 Jun; 24(6):1079-86.

2.Dedov II, Antsiferov MB, Galstyan GR et al. Diabetic Foot Syndrome. Clinical Picture, Diagnostics, Treatment and Preventive Maintenance. Moscow. 1998.

3. Pavlov YI, Kholopov AA. Nursing care in the patients with diabetic foot syndrome. *Nurse*. 1999. Jan; 1(1):23-26.

4.Kearney PM , Pryor J. The International Classification of Functioning, Disability and Health (ICF) and nursing. *Journal of Advanced Nursing*. 2004. Mar; 46(2): 162–170.

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A NEW METHOD OF TREATING STAPHYLOCOCCUS CARRIER STATES

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The aim of the investigation was to study Staphylococcus aureus carrier state on the upper respiratory mucous membrane among healthy population and to develop a new method of its correction.

Material and methods. Bacterial status was studied in 1600 healthy subjects of reproductive age, with 192 cases being registered to carry Staphylococcus aureus on their upper respiratory mucus. Comparison group composed 60 patients - Staphylococcus aureus carriers who were treated by probiotics in combination with aeroiontherapy. Nasopharyngeal microflora was studied by the conventional bacteriological method.

Results. 12% healthy subjects proved to be Staphylococcus aureus carriers. Pathogenic staphylococci were revealed in all the subjects examined.

The available methods of treating the rhinopharynx are numerous, though not always efficient and harmless (Onishchenko G.G.). The method we suggest implies administration of an enzyme probiotic having an antibacterial effect in combination with a flow of negative air ions inhaled 20 minutes daily over a period of 10 days. "Balance-naryne-F" which contains products of acidophilus lactobacillus activity was used as an enzyme probiotic with an antibacterial effect against a number of pathogenic microorganisms. Aeroionificator "Spherion" was used as a source of negative air ions flow. "Balance-naryne-F" is absolutely harmless, has no contraindications and is well tolerated. The everyday apparatus "Spherion" helps stabilize redox processes in respiratory cells; it yields a flow of negative air ions amounting up to 1000 units per 1 ml air (Hygiene Rules

2.2.4.1294-03, 2003). In the course of the study 60 subjects were treated by the new method, with Staphylococci recurrence rate being registered only in 2 cases (3%), without any allergic reactions or any other complications.

Conclusions. The method suggested for treating bacterial carrier states allows to exclude any pathogenic staphylococci in respiratory discharge in 97 % cases, as well as to prevent any possible complications in the subjects suspected to be bacterial carriers.

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RATS' BLOOD PROTEOLYTIC ENZYMES' ACTIVITY SEASONAL MANIFESTATIONS FEATURES

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There is much enough material integrating the data about the role of proteolysis. The majority of these publications has a biochemical pattern in general and gives no comprehensive idea of the proteolysis value in chrono-physiological processes.

The purpose of the present work has been the study of the blood proteolytic enzymes' activity seasonal dynamics.

White both sex non-pedigree rats weighing 200-270 g were used as the research objects. 3 sets of experiments with regularity of 10-15 days were carried out each season of the year. Every hour blood samplings were taken during the day using the decapitation method. In all the blood samples the level of general proteolytic activity of blood (GPA) and total protein amount of plasma were determined. The accumulation of free amino acids and peptides having NH_2-groups in the probes incubated within 4 hours at 37°C was considered to be the GPA level index. The findings were stated in mcg of glycin per 1 ml of plasma (or erythrocytes) for an hour of the incubation.

According to the research results the proteolytic blood system is the most active in the autumn-summer period of the year. The level of proteolytic activity of plasma enzymes in autumn makes 43,3±0,9-64,9±0,8 mcg Gly/ml/hour, in summer - 40,4±0,9-62,7±1,1 mcg Gly/ml/hour; the activity of erythrocyte proteases is 140,3±3,6-161,9±5,6 mcg Gly/ml/hour and 140,0±2,9-153,7±1,3 mcg Gly/ml/hour, accordingly. In winter and spring season the activity of proteolytic enzymes reduces considerably: in spring the level of plasma proteases makes 35,0±1,6-60,2±1,1 mcg Gly/ml/hour, in winter - 38,0±0,9-60,7±1,0 mcg Gly/ml/hour; the activity of erythrocyte proteases is 137,3±1,9-149,4±2,3 mcg Gly/ml/hour and 108,8±6-135,7±3,8 mcg Gly/ml/hour, accordingly. We have managed to determine a little difference in the dynamics of spring-winter manifestations of proteolysis activity in plasma and erythrocytes. In erythrocytes the proteolysis takes place more actively in spring, and in plasma – in winter.

The distribution of total protein amount indexes in blood plasma in different seasons of the year allowed determining the presence of the given parameter seasonal fluctuations. Thus, the total protein maximal level in plasma is registered in autumn and summer periods of the year: 73,4±3,8-95,3±4,3 g/l and 65,0±3,8-81,9±4,3 g/l, accordingly. A considerable protein reduction is registered in spring and winter periods: 51,03±0,4-73,4±1,1 g/l and 46,4±2,5-63,4±3,6 g/l, accordingly.

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CIRCADIAN DYNAMICS OF BLOOD PROTEOLYTIC ENZYMES' ACTIVITY IN RATS

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Thanks to present-day achievements of enzymology, proteolytic enzymes have become common use in medicine. Proteases play an extraordinary role in protein metabolism, klendusity (blood coagulation, clot lysis), immune responses, morphogenesis, cell-cell interactions, oncogenic transformation, virus pathogenicity, etc.

The purpose of the present work has become the study of the circadian dynamics of some physiological parameters of blood.

White both sex non-pedigree rats weighing 200-270 g were used as the research objects. Every hour blood samplings were taken during the day using the decapitation method. In all the blood samples the level of general proteolytic activity of blood (GPA), total protein concentration, the amount of erythrocytes, leucocytes, hemoglobine were determined, the plasma pH was measured. The accumulation of free amino acids and peptides having NH_2-groups in the probes incubated within 4 hours at 37°C was considered to be the GPA lev-

el index. The findings were stated in mcg of glycin per 1 ml of plasma (or erythrocytes) for an hour of the incubation. The erythrocytometry was carried out using the method of microscopy with the help of the program "Videotest" (to study blood formed elements).

The carried out research have detected the presence of distinct interrelation between the proteolysis processes and time of the day. It has been determined that plasma proteinases, like erythrocyte proteinases, manifest their maximal activity at night (from 24.oo till 05.00 in the mean). The determination of plasma total protein amount has detected the presence of two peaks of activity of the given parameter in all the probes during the day: 1st peak – from 10.00 till 14.00, 2nd peak – from 19.00 till 24.00.

A large body of circadian activity research of blood composition factors in intact rats (576 species) showed that there are no considerable fluctuations of hemoglobin, erythrocytes and leucocytes amount, and also plasma pH, during the day that testifies to the lack of distinct diurnal rhythms, which occurred while investigating blood proteolytic activity.

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Shot report

WINTER WHEAT DAMAGE CAUSED BY GAEUMANNOMYCES GRAMINIS VAR TRITICI AND RHIZOCTONIA, EFFECT OF THE ROOT ROT PATHOGENS ON GRAIN YIELD COMPONENTS

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Distribution of major pathogens casing root rot on winter wheat in Krasnodar, Stavropol and Rostov regions had been studied by KNIISH researchers during 2000-2005. Forty eight strains had been distinguished. Infestation of root system and coleoptile of various winter wheat varieties by *Gaeumannomyces graminis var. Tritici* showed that root damage varied between 63.3 and 100%, and stem base damage – between 0 and 80% depending on a variety. Infestation with *Rhizoctonia* spp. revealed that root system damage in this case varied between 36.3% and 100%, stem base damage – between 18.1 and 63.6%. *Gaeumannomyces graminis var. Tritici* reduced productive tiller number in winter wheat variety Krasnodarskaya 99 by 23.5%, plant height – by 32.3%, ear length – by 19.1%, number of spikes per ear - by 14.4% and TKW – by 45.5%. *Fusarium* fungi reduced the same figures by 18.5, 23.1, 42.2, 31.7 and 39.5% respectively; and *Rhizoctonia* – by 45.9, 15.4, 16.2, 5.6 and 19.5%.

Distribution of major pathogens casing root rot on winter wheat in Krasnodar, Stavropol and Rostov regions had been studied by KNIISH researchers during 2000-2005. Forty eight strains had been distinguished. The most pathogenic of the strains were used to evaluate winter wheat varieties' response to these pathogens.

Infestation of root system and coleoptile of various winter wheat varieties by *Gaeumannomyces graminis var. Tritici* showed that root damage varied between 63.3 and 100%, and stem base damage – between 0 and 80% depending on a variety.

Maximal level of damage was observed on the variety Deya: root system – 100%, coleoptile – 80% (at *G. gramynis* var *graminis* infestation it had minimal damage: root system – 10.5%, stem base damage – 5.0%).

The lowest level of root system damage by *Gaeumannomyces graminis var. Tritici* was observed on a durum wheat variety Leukurum 21 – 63.6% as well as on bread wheat varieties Pamyat and Fortuna – 72.7%.

Stem base damage caused by this pathogen was not observed on varieties Batko and Moskovskaya 39.

Infestation with *Rhizoctonia* spp. revealed that root system damage in this case varied between 36.3% and 100%, stem base damage – between 18.1 and 63.6%.

The highest level of damage was observed on a durum wheat variety Leukurum 21: roots – 100%, stem base – 54.5%, and on bread wheat varieties Tanya (90.9 and 63.6%), Pamyat (72,7 and 63,6%), Batko (72,7 and 54,5%).

The lowest level of root damage was observed on Deya – 36.3%, and of stem base – on Moskvich, Nota, Yubilejnaya 100, Vostorg, Ermak, Krasnodarskaya 99, PalPich, Vita and Voronezhskaya 95 – 18.8%.

In 2007 root rot pathogens naturally occurred in field in the following proportion: *Gaeumannomyces* -74, *Fusarium* -14,5 и *Rhizoctonia* -

10%. Their effect on grain yield structure is presented below.

Gaeumannomyces graminis var. Tritici reduced productive tiller number in winter wheat variety Krasnodarskaya 99 by 23.5%, plant height – by 32.3%, ear length – by 19.1%, number of spikes per ear - by 14.4% and TKW – by 45.5%. *Fusarium* fungi reduced the same figures by 18.5, 23.1, 42.2, 31.7 and 39.5% respectively; and *Rhizoctonia* – by 45.9, 15.4, 16.2, 5.6 and 19.5%.

As seeds were treated with Premis200 before sowing (0.2 l/t) the proportion of rot causing agents changed: *Gaeumannomyces* – 47,1%, *Fusarium* – 52,0%., while the reduction in yield components changed within the experimental error.

Pre-sowing treatment of the seeds with a mixture of lignogumat and Premis200 (0.2 l/t) increased root weight of winter wheat plants compared to the control variant where seeds were treated neither with disinfectants nor with bioactive substances.

As winter wheat varieties Leukurum and Moskvich were treated with Premis200 only under artificial infection conditions their root weight increase was 2-11% lower than when they were treated with both Premis200 (application rate decreased by 30%) and lignogumat. While in the varieties Vostorg and Voronezhskaya 95 application of Premis200 decreased root weight by 14-7%.

In those variants where only Premis200 was used both were observed increase in root system damage by 23.8% (variety Fortuna) and decrease by 54.6% (variety Deya). When both chemicals were used (Premis200 (application rate decreased by 30%) and lignogumat), root system damage either remained unchanged (varieties Tanya and PalPich) compared to that of the control, or decreased by 12.5% (variety Pamyat) – 60-66% (varieties Vostorg, Yubilejnaya 100, Doka).

As winter wheat varieties Tanya, Yubilejnaya 100 and Voronezhskaya 95 were treated with Premis200 only, the increase in their root weight under artificial *Rhizoctonia* infection lowered by 5-10%, while complex treatment of the seeds with both Premis200 (application rate decreased by 30%) and lignogumat caused increase of root weight by 1-5%.

In those variants where only Premis200 was used both were observed increase in root system damage by 55.6% (variety Deya) and decrease by 81.9% (variety Moskvich). After complex treatment of the seeds with both chemicals (Premis200 (application rate decreased by 30%) and lignogumat), root system damage either increased by 9 (variety Fortuna) – 36.4% (variety Pamyat) compared to that of the control, or decreased by 27.3% (variety Nota) – 72.8% (variety Moskvich).

BLOOD PLASMA FREE FATTY ACIDS COMPOSITION IN METABOLIC SYNDROME PATIENTS

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A metabolic syndrome (MS) involves a variety of systemic clinical-biochemical processes – insulin resistance, abdominal obesity, arterial hypertension, dislipidemy [8, 9]. The MS origin has been studied insufficiently; the risk factors and pathological processes leading to this syndrome development remain disputable. There are some MS development hypotheses offered, from which the leading one is the theory of insulin resistance (IR) [7, 10]. An important role in the IR development is taken by free fatty acids (FFA). The mechanisms of glucose-insulin homeostasis and FFA interconnection predetermine the necessity to study the role of FFA and their separate components in the course of the MS formation [2, 3].

The research purpose - is to study the composition of blood plasma free fatty acids in 22 metabolic syndrome patients and 11 healthy people. The MS was diagnosed according to the criteria offered by the experts of the USA National Education Program on cholesterol [1, 12]. The investigation of carbohydrate metabolism included the glucose content determination in blood serum on an empty stomach and in 2 hours after the oral glucose load, the insulin level determination by the immunoenzyme method (the sets of the firm «DRG – diagnostics», Germany); the HOMA index was calculated (insulin on empty stomach, mUnit/ml ×glucose on empty stomach, mmol/l/22,5). The lipid exchange parameters in blood serum was determined on the biochemical analyser FP- 901M of the firm “Labsystem” (Finland) using the “Labsystem” firm sets. The A and B apolipoproteins (apo-A and apo-B) content was determined (the «DiaSys» firm sets, Germany); the apo-B/apo-A ratio was calculated. The extraction of lipids from blood plasma was executed by the method of Bly and Dyer [5]. The methyl ethers of fatty acids (FA) were obtained by the method of Carreau и Duback [6], the analysis was executed on the gas-liquid chromatograph Shimadzu GC-17A. The results were stated in relative % from the total FA sum [11].

The FFA quality composition represented by 31 components of individual fatty acids, was analyzed with due consideration of glucose-insulin homeostasis changes in the MS patients: the 1st group – MS patients with no insulin resistance, the

2nd group – patients with the diagnosed IR. In the MS patients against the background of normoinsulinemia the lauric, myristic and palmitic acids level decrease was detected, 24:0, 16:0i acids (table 1). Against the saturated FA relative amount decrease the content of polyunsaturated fatty acids (PUFA) increased. The contents of linolic (18:2ω6) and α-linolenic (18:3ω3) acids increased twice ($p<0,01$), the tendency to arachidonic acid increase (20:4ω6) was registered. The sum-total fatty acids exponent Σ ω6 increased twice. The integral change exponent in fatty acids series (unsaturation index) in the first group patients compared to the control one was higher by 41% ($p<0,05$). In the second patient group with the IR available the FFA percentage change vector was analogous, but the disorders were less vivid than in the first patient group.

The findings testify that the disorder of transport in blood and the internalization by FFA precede the insulin resistance formation. It promotes the receptor dysfunction to insulin, the signal transfer secondary system and internalization by glucose cells [2-4]. The accumulation of PUFA in plasma is probably explained by the compensatory increase of unsaturated fatty acids passive internalization by the cells when their active transport is blocked. The adaptation of cells to such polyene fatty acids transport type arouses lipolysis, intensifies insulin release resulting in hyperinsulinemia [7, 10]. The endogenic insufficiency in PUFA cells leads to the fatty acid content change of phospholipids and physical-chemical properties of plasmalemmae, their liquidness decrease, functioning failure of receptors to insulin and glucose transportation systems [3]. The findings affirm that the disorders of the receptor mediated FA transport, which result in plasmalemmae's structure changes, lie in the root of IR and hyperinsulinemia formation. Thus, a significant factor of increased risk of MS development and burdening is the FFA transport failure. The diagnostics of such failures serves a signal for the MS vicious circle development beginning that includes a complex of systemic metabolic changes concerning lipidic and carbohydrate metabolism.

References:

1. Metabolic syndrome. Report of National Institute of Heart, Lungs and Blood of American Heart Association. // Clinical Pharmacology and Therapy. - 2004. – № 13. – pp. 66–68.

2. Titov V.N. Atherosclerosis as pathology of polyene fatty acids. Biological foundations of atherogenesis theory. - M., 2002.

3. Titov V.N. Atherosclerosis as pathology of polyene fatty acids. Biological foundations of atherosclerosis pathogenesis, diagnostics, prophylaxis and treatment. - M., 2002.

4. Endakova E.A., Novgorodtseva T.P., Svetashev V.I. Blood fatty acids composition modification at cardiovascular diseases. – Vladivostok, 2002.

Materials of conference

CARRYING CAPACITY LIMITER OF THE ELECTRIC CRANE

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Reliability and safety of load-lifting cranes of the bridge type which has especially fulfilled normative service life are substantially defined by a level of their equipment devices and devices of safety, major of which are carrying capacity limiters and parameters registrars of work of the crane.

Now for used in the industry noncontrollable crane asynchronous electric drives development of the carrying capacity limiters with use of modern programmed microcontrollers and indirect methods of measurement of weight of a lifted cargo is perspective on the basis of informative parameters of the asynchronous motor.

The mathematical model of the electric drive of the mechanism of rise has been developed. The opportunity of realization of the carrying capacity limiter for cranes of bridge type with use of an indirect method of measurement of cargo weight is proved on mathematical model and by experimental researchs. The informative parameter is revealed and experimentally confirmed (rotation frequency n) with which help it is possible with sufficient accuracy to determine weight m of lifted cargo on linear function or consisting of linear pieces to the characteristic $n=f(m)$ which enter in memory of the microcontroller directly on the crane, allows to take into account its specific features, such as transfer number of the mechanism, frequency rate of tackle, efficiency of the mechanism, etc. The mathematical model of the mechanism of rise of the electric crane and the carrying capacity limiter is developed and researches of their teamwork are carried out. The way of definition of rotation speed of the motor on vibration diagrams of the stator frame of motor without the speed sensor is offered and checked experimentally up, allowing to determine with sufficient accuracy rotation frequency of the motor and to calculate weight of a lifted cargo.

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PRINCIPAL AND SPECIFIC FEATURES OF DEVELOPMENT OF INTELLECTUAL AND INFORMATION SYSTEMS FOR SELECTION AND INTRODUCTION OF RENEWED ENERGY SOURCES

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The constant reduction of mineral and raw materials resources, as well as growing negative effects such as heat, chemical and radioactive contamination of environment in combination with quick reduction of easy accessible fuel deposits, put the question of great increase the usage of the renewed energy sources (RES). RES are sources of types of energy, which are getting continuously renewed in earth biosphere such as solar, ocean, wind, river hydro power and geothermal energy. RES are clean from ecological point of view and do not create additional heating of the planet (so they are often called non-supplementary).The Studies in the field of RES have intensive development. Are they Currently Significant knowledge and experience are accumulated by now in connection with introduction of these energy technologies. At the same time, there is no practically information and economic foundation in view of modern information systems, which are based on knowledge that allows to choose efficiently, design and introduce RES. The Systems, which essential principal is base of knowledge or a model of the application domain and described by super high level language that is approximated to natural, are named intellectual systems (IS). The most typical representative IS are an expert systems (ES) and ontologies. ES is IS, which is oriented at spreading out the experience of highly trained specialists in areas, where quality of decision making traditionally depends on level of the expertise. The Ontologies are knowledge bases, which can "be read" and be understood, estranged from developer and / or physically divided by their users.The Principle difference of ES kernel and knowledge base (KB) from ontology is: in that that in ontologies contents and structure of KB are specified explicitly in ontoligies, but in KB of ES - no. The Development of knowledge base both in ES, and in ontology includes conceptualization, formalization and realization. Conceptualization provides the structuring of the subject knowledge in the manner of field of the knowledge in ES and meaningful explicit model in ontology. Formalization transforms the conceptual model in formal or "computing". Finally, in process of the realization

formal model is being programmed in corresponding language of the presentation of the knowledge.Specifics of the subject knowledge on renewed source is presented by four heterogeneous components at least, which are bound between themselves to one or another extent:

-A - technical;
-B - natural-ecological;
- C - engineering-geological;
- D - economic.

For each of four formulated aspects of presentation of the knowledge, conceptualization comes to:

- building of glossary terms;
- building of classification tree of notion;
- building of binary relations diagram.

And then, dictionary of concepts, plural attribute copies and classes, as well as included trees of categorization are built for each classification tree.

Following relations between dictionary concepts could be distinguished. They are such as:

- kind_of;
- part_of;
- has;
- is_a;
- see_also and others.

The Last of given relations are being entered not declaratively, but procedurally in analogy with programming languages, supporting abstract types data.

As our studies show, a dictionary of concepts per each chosen component (A, B, C, D) contains about 1000 notions. The Typical example attribute notion in classification and included trees are following: power, developer, manufacturer, cost, completing, average month and annual wind velocity, average number of sunny days in a year, etc.

At stage of formalization, it is necessary to select the most identical classification model for presentation and processing of obtained data. As it is shown in [1], the semantic networks under frames, rule-oriented model and model of the inductive generalization are being referred to the most typical representative of such formalisms, and possible, their mixed interpretation.

Let us illustrate the reviewed stage on example of the frame-based model. We shall remind that frame is a minimum possible description of essence of some notion, event, phenomena, situation, process or object.The Frame has nearly uniform structure and consists of standard units, named slot.

Exists several ways of the reception by slot the knowledge in exoframe: by default from protoframe (default - a knowledge), through subsequent characteristic from frame, specified in slot A_kind_of, per formula, specified in slot, through joined procedure, obviously from dialogue with user (the expert) and, finally, from database. As its seen in given diagram, the most important characteristic of frame-based model is a study of features of AKO (A_kind_of) relationship.

Thereby, frame-based model, for our application domain, for component A and B particularly and C possibly, is most suitable since it supports the hierarchy inherent to classifying and including tree, which is obtained at the stage of conceptualization.

Availability of evident procedural knowledge in description of the application domain (the component D and partially component C), points out that in this case it is better to use the rule-oriented formalism, under which operational memory of program is presented by two areas - an area of facts and area of the rules - strictly product. And methods of the work with these areas is being realized on principle "identification - an action" [1].

The Recommendations on inductive generalization model use are formulated by the author in [1].

The Last stage in chain considered is a stage of the programming. Here we shall note that for programming at a level of frame-based model in semantic set, it is reasonable to use such languages as FRL, KRL or Karre frame based shell. In the event of rule-oriented model, languages of the OPS-5 group are used. And, finally, for all three models it is possible to use the object-oriented programming languages.

References:

1. Moskalenko YU.S. Presentation and processing the knowledge in training system: Training book - Vladivostok: Publishers DVGTU, 2000. - 125 p.

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NEW APPROACHES TO STUDYING SILICON MELT CRYSTALLIZATION PRINCIPLES

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The severization of requirements at the consuming end (producers of organic silicon compounds and semiconductor products) to the quality of silicon obtained at silica-containing batch materials melting process in arc furnaces makes it nec-

essary to investigate the principles of impurity elements distribution both on melt products and silicon pool.

At silica carbothermic reduction the impurity elements from silica-containing crude ore (quarts), carbonic reducing agents, carbon electrodes, furnace lining and auxiliary process materials are reduced and transform into the melted silicon. To determine the principles of impurity distribution between the products of melting process (silicon, mixed dust-gas and slag) the data on physicochemical properties of the substances entering the process are used: the temperature and heat of melting, vapors dissociation tension, constituents' activity, formation heat, Gibbs thermodynamic potential, etc. And for the obtained crystalline silicon properties forecasting (as in the case of various alloys obtaining) the knowledge of binary and ternary diagrams is of great importance. The liquid melt silicon obtained in an electric arc furnace represents a multicomponent system with 0,1-2% ballast content. At the solidification the impurity elements form various intermetallic compounds, non-metallic compounds with silicon (slag enclosures), dissolved oxygen, silicon carbide and unreacted hydrogen of reducing substances and crystal silica [2, 3]. For the multicomponent systems of any type the forecast of properties on the basis of binary and ternary components systems data is possible if their image is used according to the method of optimal projections [4]. Geometrical methods have an important advantage, which makes possible to express the quality and quantity dependence of the properties on the composition also in the case, when the algebraic expression of this function in unknown to us. More over it is common knowledge that properties vary continuously within the limits of one and the same phase existence fields and undergo sudden alternations (kinking, bending) at the given phase conversion into another one. That is why, if it is possible to restrict the crystallization region of any phase, the general regularity detection in properties alteration of the whole region is possible when oriented to comparatively inconsiderable number of datum points. Thus, it is sufficient to study experimentally the properties of three-four compositions of the system, which correspond to the specified limits, to forecast the system's properties values with some degree of certainty within the whole region [5].

The construction of binary and more complex constitutional diagrams by experimental methods or with the help of rigorous thermodynamic calculations is a labour intensive, time-taking and very often – a stubborn problem. In this connection the approximate calculation methods of constitutional diagrams construction [6] are extremely productive. Model representations of a melt composition and repeating units' interaction energy in solution and solid phases lie in their basis. The initial calculations data are comparatively easy to obtain for ideal and regular solutions models. The necessity to use approximate calculation methods is connected with the fact that a production manager, in conditions of ultimate product requirements change, needs to have the computation data forecasting the melt emerging temperature, crystallization path, comparative crystallization rate, silicon phase composition.

For the liquidus and solidus curves construction for a predetermined composition of the n-component system we accepted as the main assumption (initial approximation) the statement that these systems quite adequately satisfy the model of regular solutions. Indirectly it is proved out by the author's multicomponent oxide systems' data [4], which testify that with the complication of the system's composition, it approaches ideal solutions in its properties.

For the calculation of liquidus temperature, the solution and solid phases' composition in the field of silicon crystallization the following data are necessary: the amount and concentration of the introduced components; values of mixing energies within the binary system, eutectic temperature and also values of distribution coefficients of impurity elements in silicon melt. In the initial stage of our research the separate flux components' thermodynamic properties and silicon-based binary systems data base is formed. The data base will allow passing directly to modeling on «DIATRIS 1.2» and «MULTICOMDIA 2.0» programs' flows [7].

References:

1. Popov S.I. Metallurgy of silicon in three-phase ore-smelting furnaces. – Irkutsk, 2004, p. 237.

2. Investigations of refined metallurgical silicon impurities' phase composition // IrSTU Bulletin. Irkutsk: Publishing House of IrSTU, 2007, №2 (30), V.1, pp. 30-35.

3. Suvorova L., Nemchinova N. Application of electron-probe X-ray microanalysis method for investigation of metallurgical silicon // Materials of the 19th International Congress of X-ray Optics and Microanalysis «ICXOM 2007», 16-21 September 2007, Kyoto (Japan). – Kyoto, 2007. P. 145.

4. Berezhnoy A.S. Multicomponent oxide systems and their value for silicates technology and petrology // Experiment in the area of technological mineral formation. – M.: Nauka (Science), 1975, pp. 8-12.

5. Kurnakov N.S., Anosov V.Ya., Ozerova M.I., Fialkov Yu.Ya. Principles of physical-

chemical analysis. – M.: Nauka (Science), 1976, p. 504.

6. Suvorov S.A., Semin Ye.G., Gusarov V.V. Phase diagrams and oxide solid solutions' thermodynamics. – L.: Publishing House of LSU, 1986, p. 140.

7. Nemchinova N.V., Udalov Yu.P., Klyots V.E. Silicon-based multicomponent system crystallization field investigation // Materials of International Council "Present-day methods of complex ore processing and alternative mineral raw material" ("Plaksin Readings-2007"), Apatity, October, 1-7, 2007. – Apatity: Publishing House of Mining Institute of Kola Scientific Center RAS, 2007. – Ch.2, pp. 468-471.

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ENERGY TECHNOLOGICAL COMBINING OF BULK PETROCHEMICAL ENTERPRISES*

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The petrochemical industry performing the processing of hydrocarbon material and being in the number of fuel and energy resources consumption leaders is characterized by a relatively low efficiency of the supplied energy use.

For the petrochemical energy industry enterprises the efficiency increase main direction one can consider to be the energy saving organization based on the principles of energy–technological integration.

The search for viable solutions on the organization of energy-technological complexes – is an extremely difficult task that requires carrying out a comprehensive analysis of the original system and the one being synthesized. The accepted decisions optimization can be reached only at the implementation of mathematical models formed depending on the set task class. The following tasks can be referred to the number of them:

- the search for superfine production facilities' operating regimes interrelated with energy supply systems;
- the industrial facility's efficient management with due consideration of its infrastructure at superimposition of indignations associated with material and energy imbalances;
- the minimization of specific material and energy consumption for production;
- the efficiency analysis of the synthesized object on a selected criterion in the dynamics of its development, etc.

An instrument for searching and selecting innovative solutions is the fully formed by now integrated methodology of complex industrial systems' analysis and synthesis within the framework of the present and projected technological complexes.

The development of a universal method combining isolated methods is a topical and many-sided task.

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ETHYLENE PRODUCTION ENERGY-TECHNOLOGICAL COMPLEX ORGANIZATION

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An energy saving upcoming trend at petrochemical enterprises is the organization of energy-technological complexes created on the base of secondary energy resources complex utilization systems. The ethylene production – is a large consumer of fuel and energy resources. At that, the considered production is characterized by a considerable output of secondary energy resources. Thus, in ethylene production there are favourable conditions for the energy-technological complex organization.

The first stage in construction of an energy-technological complex is the system's work efficiency estimation by means of a system analysis including the analysis of the considered object's relations structure, the analysis of thermal and thermodynamic effectiveness. The system analysis allows detecting the dependencies between the ethylene production scheme elements, defining the optimal sequence of the scheme computation, re-rating of the elements' efficiency, determining the value of technically usable energy, evaluating the energy saving reserves and revealing the optimum alternative for the energy-technological complex construction.

The suggested energy-technological complex in ethylene production is meant for the production of industrial steam with the pressure of 0,6 MPa, cooled water with the temperature of 7°C and technological streams' heating up, warming and hot water supply load covering. The given complex allows putting into effect the utilization of secondary energy resources being formed in the same production. This is the warmth of pyrolysis furnaces' combustion gases, gas purifiers' recycled and condensed water.

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INNOVATION METHODS TO EXTEND STORAGE LIFE OF COOLED BEEF

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Meat and meat products – is a perfect nutrient medium for various microorganisms' propagation, among which molds, yeast, gram-positive and gram-negative bacteria are most common. In this connection the problem of food staples' and products' maximal preservation is of significant importance. To raise meat products' safety level is possible due to the application of various preservative agents, both of natural and synthetic origin. However, the use of any food additive should be rational, reasonable and require a comprehensive study.

In recent years the research on meat treatment with various preparations for the purpose of storage-life extension has been carried out by the scientists of research centers in our country. The storage life extension and safety of food products is possible with the help of rational and expert application of such food additives as conservatives. The choice of a conservative and the original crude quality (and it depends on the bacterial semination of meat at the stage of its being put into the refrigerator, first of all) are in direct dependence. Not less significant criteria influencing the quality of meat are the pH value, the storage temperature and after slaughtering time.

Depending on the kind of product and its state the method of meat products treatment with conservatives is chosen. The comminuted products are carefully mixed with the conservative. If the products are in the form of pieces, they are subjected to surface treatment (the product is sprinkled with the solution of the conservative or dipped into the solution).

The analysis of the information on the subject testifies that its study was carried out on some directions: the crude safety preservation while treating it with the conservatives, which, in their turn, provide the storage life extension, bacterial semination reduction; the influence of food coatings on quality retaining and cooled meat mass loss reduction; the use of physical methods of effect (ray treatment, heating, modified atmosphere) on the meat for the purpose of negative microflora inhibition.

In spite of the popularization, the research in this direction is limited, and the informative data available do not allow detecting the features of the parameters' and conservation conditions' influence on the quality of meat and its storage life.

The purpose of the present work has been the conservative selection and the cattle meat treatment technology development, which will guarantee the bacterial semination reduction and the beef storage life extension. The solution of the raised problem will allow increasing the cooled meat output and will guarantee its undamaged condition on long storage.

As a part of the study, pieces of slaughter-warm meat weighing 500 g were used. The check sample was not treated; the second sample was treated with the preparation "Desinbac super" of the 0,1% concentration; the third sample was treated with the preparation "Desinbac super" of the 0,3% concentration; the fourth sample was treated with the preparation "Desinbac super" of the 0,5% concentration; the fifth sample was treated with the preparation "Desinbac super" of the 0,75% concentration. The treated samples were hanged on stainless steel hooks and placed into the refrigerator with the camera temperature +4 ^{o}C for 23 days. The selection of intermediate investigation probes was carried out every 5 days. The pH level of the beef before the treatment was 5,8. The microbiological study results at the beef treatment with the preparation "Desinbac super" were got. The results of the investigation are represented in the table.

Table 1. - The microbiological study at the beef treatment with the preparation "Desinbac super".

Sample number	pH	Microbiological factors					Peroxidase	Acid value
		MAFAM CFU/g	Listeria	Salmonella	E. coli	Coliforms		
24 hours after starting the experiment								
1	5,8	$1,9 \cdot 10^5$	neg.*	neg.	neg.	neg.	pos.*	5,74
2	5,9	$2,2 \cdot 10^4$	neg.	neg.	neg.	neg.	pos.	5,82
3	6,1	$2,2 \cdot 10^4$	neg.	neg.	neg.	neg.	pos.	5,82
4	6,1	$2,1 \cdot 10^4$	neg.	neg.	neg.	neg.	pos.	5,81
5	6,2	$2,1 \cdot 10^4$	neg.	neg.	neg.	neg.	pos.	5,82
Results of microbiological research on the 5th day								
1		$4,3 \cdot 10^8$	neg.	neg.	neg.	neg.	pos.	5,76
2		$2 \cdot 10^4$	neg.	neg.	neg.	neg.	pos.	5,82
3		$2 \cdot 10^4$	neg.	neg.	neg.	neg.	pos.	5,84
4		$1,8 \cdot 10^4$	neg.	neg.	neg.	neg.	pos.	5,86
5		$1,8 \cdot 10^4$	neg.	neg.	neg.	neg.	pos.	5,86
Results of microbiological research on the 10th day								
1		-	-	-	-	-	-	-
2		$4,5 \cdot 10^3$	neg.	neg.	neg.	neg.	faint pos.	6,40
3		$4,3 \cdot 10^3$	neg.	neg.	neg.	neg.	faint pos.	6,40
4		$4 \cdot 10^3$	neg.	neg.	neg.	neg.	faint pos.	6,53
5		$4 \cdot 10^3$	neg.	neg.	neg.	neg.	faint pos.	6,54
Results of microbiological research on the 15th day								
1		-	-	-	-	-	-	-
2		$2,4 \cdot 10^3$	neg.	neg.	neg.	neg.	neg.	6,60
3		$2,2 \cdot 10^3$	neg.	neg.	neg.	neg.	neg.	6,60
4		$2 \cdot 10^3$	neg.	neg.	neg.	neg.	neg.	6,62
5		$1,9 \cdot 10^3$	neg.	neg.	neg.	neg.	neg.	6,62
Results of microbiological research on the 20th day								
1	-	-	-	-	-	-	-	-
2	7	$2 \cdot 10^3$	neg.	neg.	neg.	neg.	neg.	6,62
3	6,9	$1,8 \cdot 10^3$	neg.	neg.	neg.	neg.	neg.	6,62
4	6,6	$1,2 \cdot 10^3$	neg.	neg.	neg.	neg.	neg.	6,64
5	-	$1,2 \cdot 10^3$	neg.	neg.	neg.	neg.	neg.	6,65

Note: *neg. – negative, pos. – positive.

The non-treated meat was damaged on the 7th day.

Proceeding from the results of the microbiological research one can come to the conclusion that the optimal concentration for beef treatment is the 0,5% solution of the preparation "Desinbac super". As a part of the study, it was also found out that to treat a 0,5 kg piece of meat it is required 12-15 ml of the preparation "Desinbac super".

The research on the application of the new conservative will be continued for the purpose of determining functional characteristics of the meat treated with the conservative.

An economical effect from the given preparation use is formed on account of damage prevention and, respectively, loss reduction, cattle meat quality factors retaining, and also on account of increase in output and realization of high quality cooled meat.

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Shot report

INCREASING OF TOOL RESISTANCE FOR HIGH-SPEED MACHINING BY CUTTING

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The complex manufacturing techniques of cutting tool of the raised (increased) wear resistance in an interval bainite pre-transformation are submitted.

One of the most popular task of modern science of materials is searching of the such structural states that provide a high level of design strength, including wear resistance, thermal resistance and impact elasticity for cutting tool.

Practice of using of cutting tools produced from high-speed steel shows that in the most cases the reason of bad tool resistance is in its brittle fracture or scuffing of cutting edge due to law plastic properties. Different methods of bainitic hardening, which permit to increase sharply plastic properties of cutting tool, deserve an attention. However, for all that, the strength properties are reduced.

By the researches executed at Komsomolsk-on-Amur State Technical University there was established, that one of perspective methods of cutting tool wear and thermal resistances increasing is bainitic hardening within bainite pre-transformation interval, as a heating and cooling surroundings, the fluidized bed of loose materials can be used.

Maximal thermal resistance peculiar to the samples produced from R18 steel after bainitic hardening within bainite pre-transformation time interval excluding interim transformation including bainite transformation. Bainitic hardening of high-speed steel within bainite pre-transformation time interval prevents carbides isolation that stimulate increasing of wear and thermal resistances. Furthermore, the special pre-transformation state, caused by atomic bonding weakening in crystal lattice lead to structure inhomogeneity ordering and improving of the cutting tool properties produced from high-speed steel. Comparative assessment of cutting tool wear resistance while high-speed machining showed that its wear resistance increasing 1.3 – 1.7 times as much. Using of carbonitriding for such tools increases its wear resistance 3.1 times as much and machining by electro pulse influence 3.9 times as much.

The results of experiments show the prospectiveness of research works carrying out for other structural steels.

Materials of conference

INNOVATION TECHNOLOGIES OF STUDENTS' TRAINING AT TULA INSTITUTE OF MANAGEMENT AND BUSINESS

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The major task of educational space integration, on the opinion of the Bologna Declaration developers, is the increase of European and Russian educational systems quality, the educational service appeal guaranteeing due to substantial perfection, professional exchange and scientific communication channels creation. However, together with positive changes within the system of Russian Education the following recessionary features are specified: the listeners' contingent change, as the paid education allows entering higher educational institutions to the enrollees with poor educational level, that creates serious conflicts in the "teacher-student" system in some instances; the loss by the institutes of the socializing function and the transfer to the relations between the teacher and the learner according to the "delivering-getting a service" principle; the presence of ill-founded educational innovations, the application of foreign training and up-bringing methods.

The quality problem is a predominant one in the National project, which is actively being realized in the education of Russia. Certainly, the choice of specialists' training technology – is an efficient means of getting and retaining advantages in the competitive edge. The changes in curricula and programs, teaching methods, internal activity organization can be referred to purely pedagogical innovations. The sources of renovation and educational process efficiency upgrading in training students of a private educational institution of higher professional education the Tula Institute of Management and Business are the following components: creativity, humanization, and educational management. The formation of innovation directivity supposes the availability of special criteria allowing judging about the efficiency of this or that innovation. Today, besides the traditional criteria, the teachers use the student's knowledge rating estimate, which is formed by the accumulation of semestral (intrasemestral) marks at different kinds of Certifying Examinations. The announcement for the student of his rank (place), which he takes in the group, stream, course, specialty both in all and separate disciplines according to his rating serves an important psychological moment. The transfer to rating estimations, as the experience shows, increases the contentiousness of students, touches their ambition, and promotes the academic activity. Besides, the rating estimations got by the accumulation of intrasemestral ones are more objective than the results of one-time examinations and promote a methodic work during a semester. The rating system supposes a leave from a traditional four-point appraisal. It allows making the training quality control more flexible, having a constant informative feedback about the students' material adoption level and carrying out an appropriate adjustment in the discipline teaching methods in the process of training. The Institute teachers use the following innovation methods of training: the problem and project methods of teaching, analytical abstracting, task approach, research method, presentation method and others. While developing the disciplines and organizing extracurricular learning sessions the teachers orient themselves not only to training a professional, a specialist able to meet competitions, but also to the formation of moral standards and directives in students. That is why the leading principles of students' up-bringing appear: the humanization principle, i.e. the recognition of the student's personality as self-worth; the esteem of its unicity and singularity; the formation of healthy life style need; the principle of professional orientation – the acquisition of professional community ethic norms by the future specialists, the formation of responsibility for their professional activity results; the principle of consistency – the establishment of interaction relations between the subjects of extracurricular activity in the integrated educational programs implementation; the voluntary principle – gives the student the right of choice of various extracurricular activity (scientific and creative) participation forms; the stimulation principle – is based on moral and material incentives of students for their achievements in scientific (the base Institution of higher education diploma, honor certificates), academic (using different forms of resulting control for advanced students), creative (diplomas and certificates for active participation in the Institution life), sport (certificates for healthy life style achievements), social and other activities.

By the virtue of the abovementioned one can emphasize the following directions in the strategy of educational work with students:

I. Intellectual education.

Purpose: to release and use the educational potential, which lies in the knowledge, in the process of studying a block of general professional disciplines by the students.

Tasks: to perform the training of specialists on the basis of deep fundamental knowledge; to develop cogitative faculties – the ability to realize

professional situations, to find the ways for their solution, to fulfill the necessary for this operations, to make correct conclusions; to work out the creative activity skills in students, to perform the definition of objectives, analysis, planning; to form the internal need for self-education; to pay attention to solitary work organization perfection.

II. Patriotic education.

Purpose: to teach students to get to the heart of the Motherland matter covered in the spiritual life of the Nation, in traditions and customs, historical memory.

Tasks: to develop social memory; to study fundamental and applied research of patriotism phenomenon, its traditions and present-day manifestation forms on the basis of interdisciplinary interaction; to introduce social practice and scientific findings into the academic and extracurricular activities.

III. Esthetic education.

Purpose: the development of emotionally fertile and spiritually eminent relation toward the outworld, the ability to render their esthetic experience.

Tasks: to form a high culture in students; to extend their outlook in the field of Arts, to teach them how to value and understand the beautiful.

IV. Labour education.

Purpose: involving into active creative labour.

Tasks: to form working practices; to develop positive personality traits promoting the formation of professional directivity of the future specialist; to inculcate industriousness, diligence, activeness, mobility.

V. Physical education.

Purpose: “The student’s unimpaired health is the basis of excellent studies”.

Tasks: the students’ unimpaired health need updating; to put into effect the propaganda of physical culture and sport as a healthy life style component.

The main condition for the strategic tasks implementation is seen in the creation of the students’ professional-pedagogical support concept. The pedagogical support on the part of the teachers supposes the preventive and operative help to the students in their solution of individual problems connected with physical and psychic health, social and economical status and successful advance in studies, effective business and interpersonal communication, life, professional and esthetic choice. The students’ work shadowing is defined on the part of the teachers by the success situation creation mechanism. The success is, first of all, connected with a sentiment of joy and emotional rise. As the practice of the Institution faculty teachers shows, the key to the success situation creation is a mutual readiness to conduct a dialog. The dialog technologies have the following organizational structure: 1) a certain activity attitude (emotional preparation of the student for an academic problem solution); 2) the provision of the activity, its division into operations (the creation of conditions for its successful solution); 3) the comparison of the obtained results with the required ones (the dedicated academic labour result). When preparing and planning an academic dialog, the teacher should be able to: select the educational material taking into account the subjective experience of students, on the basis of which the dialog organization is possible; emphasize the backbone discussion questions; plan the model of the teacher and student intercommunication; select didactic materials promoting the dialog interaction; work with due account for the student’s subjective experience; put questions correctly and not to express negative judgements; generalize the utterances of students giving them a scientific character. Besides, for the creation of a favourable climate and creative and kindly atmosphere maintenance one has to: show a respectful attitude to and demonstrate a trust in the student; personify the encouragements for a good work and participation in the dialog; render a timely and differentiated help; manifest one’s own personal enthusiasm; stimulate the learners’ interest; render an assistance for students in working out in them a positive self-feeling. For a further higher institution’s students’ education innovation technologies introduction it is necessary to perfect the material-technical and didactics and methodical base and to raise the teachers’ competence level.

Brief

The integration of the educational space demands the increase of all learners’ categories training quality. One of the open education problems is the insufficient level of enrollees’ basis training, the lack of the ability to study independently in them, the use of non-adapted methods of professional training, which were borrowed from educational systems of other countries, by higher education institutions. For the students’ training academic process efficiency increase at the private educational institution of higher education the Tula institute of Management and Business the following work directions are used: creativity, humanization, educational management. For these tasks implementation it is necessary to work out the concept of students’ professional support.

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AN OPEN SYSTEM OF A CONTINUOUS EDUCATION AS A VECTOR OF DEVELOPMENT OF THE HIGHEST PROFESSIONAL EDUCATION

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Nowadays, an active entering of corporations into the highest professional education is observed (for example, "Modern Humanitarian University", having been founded in Russia, with 180,000 students). It is enough similar examples both in Russian system of education and abroad.

In the present state of affairs, the problem of "survival" of regional institutes of the highest education is relevant, may be they are not as massive as corporate ones but they fulfill their state, social and public roles. They are exactly regional highest institutes which play city-forming, cultural and other functions, that is why they need a mechanism, which would allow them to oppose numerous challenges to their prosperity and even existence from the direction of "mega-institutes".

The basis, which would allow regional institutes to be able to compete, may serve an open pedagogical system, with the following features (S.L. Timkin [5]):

- a formation of "a consumer for the whole life";
- a support of innovation – educational work and a formation of innovation-educational collective;
- an open interaction with others educational systems of different levels;
- supplying students and teachers with temporal and spatial mobility;
- united informational-educational environment of a continuous education.

Many researchers (A.A. Andreev [1], G.V. Majer [3], V.I. Soldatkin [1]. V.P. Tikhomirov [6] and others) point at organic bond between the conceptions of an open and continuous education and the distance one. An organic union of traditional and distance educational technologies is essential.

In 1999, V.V. Verzhbitskij and E.A. Manushin [2] surveyed 5650 respondents aging 18-45 from 22 different Russian subjects. 98% of respondents, who are interested in education, as a condition to it pointed out at the realization, at least one of the main characteristics of distance education: openness, flexibility, a possibility of combination of study and work, remotability, etc.

Essential characteristics of open system of education are listed in the work [4]. Let us sum up their main points:

1) an openness of a system supposes to take as a source a man – an origin of development but not a system in its current state;

2) an open education gives free access to informational recourses of the whole world;

3) an open education gives an opportunity to choose the education strategies;

4) an open education assumes personal directivity of the process of education.

An open system of education is to be built on the conception of "education through the life". It should be noted that continuity and openness of education are interrelated and essential features of an open system of the highest professional education. In this case it is better to indicate an open system of continuous education. The system should provide for both highly-skilled specialists' training and raising their professional skills after the diploma period.

Distance – teaching (DT) as a component of open system of continuous education may be realized in the following cases:

- pedagogical technology of a case distance teaching;
- pedagogical technology of a satellite distance teaching;
- pedagogical technology of a network distance teaching.

In the present conditions, for a wide spreading of DT it is essential to resolute a complex of problems which reflect world-outlook, theoretical-methodological, technological, legal, social, financial-economical and other aspects of this new form of education.

The main pedagogical principles of DT are: learner-centered character of educational process; practical – centered content of education and kinds of activity; module organization of education programmes; activity and independence of students as the main subjects of education; problem and dialogical character of interrelation in the educational process; self – organization of students' activity and reflexive character of this activity; independence, implying an inner motive of getting education; context of education; an electivity of education, giving to the students free choice of a goal, content, forms, methods, sources, level of educational results' assessment.

Let us point at the principles of distance teaching's organization:

- choice of synchronous and asynchronous system of distance teaching (in some cases their combination);
- inclusion of series of subsystems into the system of distance teaching;
- choice of educational methods by principle "I - myself", one to one, one to many, many to many;

- usage of regulation – educational forms in the distance teaching;
- detachment of distance educational course as the main comprehensive unit of distance teaching and specification of distance teaching's model in the models of distance educational courses;
- distribution of computer education's systems;
- presence of the following components of the process: structural, comprehensive, variable, technological, evaluative-resulting;
- realization of interactive educational technologies;
- distribution of teachers' functions who fulfill the distance teaching;
- the importance of consultations at the different stages of distance teaching.

References:

1. Andreev A.A., Soldatkin V.I. Distance education: essence, technology, organization. – M.: Publishing House MESI, 1999. – 196 p.

2. Verzhbitskij V.V., Manushin E.A. The needs in distance educational services of Russian population. [Electronic resource]. – http:/academy.odoportal.ru/documents/academ/bibl/Russia/2.html

3. Majer G.V., Demkin V.P., Mozhaeva G.V., Vimyatin V.I. Academic university in the open system of education. – Tomsk: Tomsk University publishing, 2005. – 200p.

4. The basis of open education / Andreev A.A., Kaplan S.L., Krasnova G.A., Lobachev S.L., Lupanov K.Y., Polyakov A.A., Skamnitskij A.A., Soldatkin V.I.; Edited by Soldatkin V.I. – V.1. – Russian state university of open education. – M.: Publishing House НИИЦ РАО, 2002. – 676 p.

5. Timkin S.L. Pedagogical system of the highest institute in the condition of implementation of distance educational technologies: monograph. Omsk: Publishing House OmSU, 2007. – 385p.

6. Tikhomirov V.P. Basic principles of distance teaching system's formation in Russia // Distance Teaching. - №1. – 1998. p.4-9.

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SOME PROBLEMS OF COMPUTER WORK STABILITY AUGMENTATION IN ACADEMIC PROCESS AND ITS SERVICE TERM PROLONGATION UNDER THE CONTROL OF WINDOWS VISTA OPERATING SYSTEM

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The use of present-day high quality components of electronics plays a defining role in information processing reliability in PC. The application of motherboards with the new technology Ultra Durable 2 with system logic Intel 3x, including X38, P35, G35, G33, P31 and G31, allows raising the faultless performance of a PC at the expense of solid-electrolyte board capacitors possessing ultralow losses. The MOS-transistors with ultralow opened impedance are also used in these boards. It provides a reduced energy consumption at their switching over and allows performing a higher operating speed, that implies a low heat generation.

Using a quad-core processor Intel Core 2 Quad and a display card NVIDIA GeForce 8800 SLI Direct, X10-enabled, a high work quality is provided with resource-intensive multimedia applications and graphic programs.

The deployment of the new accelerator card HD 2600 X2 constructed on the basis of two processors ATI Radeon HD 2600 XT allows reaching a burst performance of video acceleration if operating at one monitor. Such a component is rated at one PCI Express x16 slot setting and is equipped with 1 Gbyte storage space video buffer GDDR3 running on effective frequency of 1600 MHz, and clock rate of the video core is performed at the frequency of 800 MHz. There is an S-video TV-output and four DVI video-output, which is possible to connect with four monitors with resolution of 2650x1600 dots.

The card supports a high resolution video and is equipped with the HDCP content defence technology, that, in its turn, allows connecting high definition displays and panels. This card also supports an HDMI digital interface when using a special DVI-HDMI jumper. It is compatible with the computers constructed on the basis of system logic sets AMD 580X CrossFire, AMD CrossFire Express 3200, Intel 975X Express and Intel P35 Express. The card is used with the operating system Microsoft Windows Vista and works with ATI Catalyst drivers and utilities guaranteeing burst performance and work stability.

Using the new display VX1940w with 19-incher wide-screen matrix, where a super-

resolution 1680x1050 is combined with ultrahigh operating speed, the response time (grey-to-grey) 2 msec and the dynamic coefficient of contrast up to3000:1 are achieved. In the construction VX1940w several entries are supported, it guarantees wide view angles (170° horizontally and 160° vertically) and brightness 300 cd/m^2 – that makes it a perfect solution not only for games, but for DVD viewing and work with traditional applications as well.

In audio cards the sound quality can differ in various motherboards. Even using the same codec models. The quality of the used auxiliary elements, condensator, in particular; the arrangement on the card; the proximity of the components able "to admix" unwanted sounds to the signal play a role.

So, the codec ALC885 meets the requirements of Microsoft Windows Vista Premium, has the signal/noise ratio 106 dB for the digital-to-analog converter (DAC) and 101 dB for the analog-to-digital converter (ADC). Therein the 192 kHz sampling rate support, ten-channel DAC-sound, and also HD DVD support are realized.

All the computer industry last words are carried by the Raser Barracuda AC1 card. The external package of the card serves as a cooldown radiator and form for interfaces.

The eight-channel DAC AKM 4396 and operational amplifiers JRC 4580 are better in quality than in Creative X-Fi Extreme Music/Platinum/Fata1ity. The chip cards CMI878 C-Media excels by the ability to reproduce correctly the sampling rate of 44,1 kHz, apart from 48/96/192 kHz; the choice of pedestal frequency being possible to be performed manually.

The most reliable and qualitative audio card Creative X-Fi Elite Pro has more failproof DAC (Cirrus Logic CS4398) and operating amplifiers of the X-Fi-series. It has 4 DAC, two channels, dynamic range of 120 dB. For providing maximally qualitative supply there are large groups of electrolytic capacitors. The processor frequency is 400 MHz. The inputs and outputs commutation is performed with the help of electromagnetic relays, substituting electronic switches, that increases the reliability and sound transmission integrity.

Also in this card ones of the currently best amplifiers are used: JRC2114 and JRC2068. The bandpass flatness (from 40Hz to 15 kHz) makes +0,03, -0,08 dB, noise content - 103,6 dB (A), dynamic range - 103,2 dB (A), harmonic distortions - 0,0025 %, mutual penetration of channels - 104,4 dB.

Using a new laser mouse pointing device with antibacterial coating LEXMA NanoGuard one can be sure to eliminate and deactivate bacteria with 100 % efficiency factor. A potent laser unit performs the sensor's resolution ratio of 2000 DPI. The reading speed is 40 times higher than in a usual optical mouse. The programmed keys support more than 50 customizing settings. It runs on any surface including glass.

Using a new DVD-18 format (dual-sided double layer one) for standard disks of 120 mm, one can obtain the capacity of 18 Gbytes and even 51 Gbytes (for three layer disks of 17 Gbytes per side). The Blu-ray technology disks are more promising. Using double layer Blu-ray carriers the information storage capacity up to 50 Gbytes is obtained. Six layer disks of 200 Gbytes capacity have been already created. Eight layer disks of 300 Gbytes storage capacity are being developed.

The holographic principle of disk storage information appears to be a more promising and brought to the real application one. On a standard disk of 120 mm at the reading speed of 120 Mbytes/sec one can record up to 1,6 Tbytes of information.

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THE ROLE OF COLOR FACTOR IN INNOVATION EDUCATION TECHNOLOGIES

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The necessity of education process constant perfecting for a successful work of a university in the educational market makes the problem of innovation education technologies introduction into the higher education system actual. It allows offering new possibilities, flexibility in training and brand new education to students.

The innovation education technologies currently applied in Russian higher education institutions can be relatively divided into three groups: the technologies of educational information provision; the technologies of educational information delivery; the technologies of educational information storage and processing. At the realization of educational programs the educational information delivery technologies, which guarantee the educative process and its support, acquire a special value. First of all, it is referred to newly created electronic textbooks, distance teaching courses and also information knowledge bases, reference and expert systems used for educational purposes. The information presented in them, unlike the poly-

graphic one, should have an absolutely different organization and structure. It is conditioned both by psychophysiological features of information perception from the computer screen and the information access technology. In the interactive media a great attention should be paid to the image thinking promotion owing to the technologies activating the dextrocerebral, synthetic thinking. The presentation of the educational material should reproduce an idea in the form of images. Therefore, the main moment in the innovation education technologies becomes the knowledge visualization.

Video-lectures, multimedia-lectures, electronic textbooks, computer teaching and testing systems, simulation models and computer simulators, tests and video-conferences are referred to the innovation education technologies. We think that in the academic process not the information technology on its own account is important, but the fact how its application serves the achievement of educational purposes proper. The choice of teaching aids should be defined by the subject-matter, first of all, and not by the technology. It means that at the heart of the technology option the investigation of education courses content, learners' activity, their being involved into the academic process, concrete aims and expected results of education should lies.

At the present time the developing effect of new education technologies reveals itself not always; their influence on the process of information adoption is not controlled. However, without defining the most significant factors promoting optimal perception and material memorizing, the innovation teaching aids can be inefficient, and in some cases – even destructive.

The color is exceptionally significant in innovation education technologies. The topicality of the color application in the innovation teaching aids is defined, first, by the necessity of the developing education principle realization within the system of higher education; second, by the importance of the process of the information adoption by students.

The human response on the color is of a complex character and has several aspects: the *physiological* one, when the sensation from the applied color group or separate color depends on the force and spectral distribution of the emission, its exposure duration on the observer, the observing conditions; the *psychological* one, giving the color credit for an independent and active role, the associative power and the ability to color the human reaction emotionally; the *aesthetical* one, the presupposition of which is giving the color credit for the ability to harmonize the color information.

Natural sciences have collected a great experimental material about the influence of the color on the human body. The physiological component of this response has been studied most fully. Thus, according to the records of Kravkov S., the intraocular tension reduces under the influence of the green color and grows under the influence of the red one. C. Ferre, V. Shevaryova, Ye. Plotnikova and other scientists studied the influence of the color on the fitness to work. After the carried out experiments C. Ferre came to the following conclusions: at a very short-time work the red color raises the efficiency; the blue and violet ones decrease the productiveness much; the interrupted effect of the color, i.e. a rest in conditions of fair daylight after the work at another kind of illumination, increases the productivity considerably.

The color influence on the human psyche touches not only his emotions and character, but also cognitive processes, and, first of all, - thinking. The question, in this case, is not about the informative, but the energetical aspect of the color effect, and so, not about the thinking process content, but about its dynamic and energetical characteristics. From this perspective, thinking appears in front of the subject himself not as a sequence of purposeful judgements and inferences, but as a special psychic tension terminating with a satisfactory disengagement for the subject in the case of finding a solution.

The color can harmonize the learner; it is able to mobilize his resources, appease and relax. This influence comes directly into brain, penetrates all the physiological structures. The organism responses the color flow immediately. This is a true psychosomatic approach, which allows influencing effectively both on physical activity and mental states of a human being and his learning process activation using a color system.

A concrete objective, at the solution of which our project is aimed, lies in studying the color influence on the process of information adoption by the student in new educational technologies, and also in working out the given factor most effective use recommendations in higher school didactics.

Within the framework of the given project we have elaborated recommendations on the color scheme of educational Internet resources. We suppose that the possibility to carry out a simultaneous presentation of information, combining a text, video and graphic images and animation in the computer system, allows creating an academic environment affecting all the channels of perception in most different forms. First, it concerns the work with new lexis, reading, studying new information, the creation of visual impressions, associations. Second, it supposes structuring of schemes using colors bearing a special code, establishing of associative bonds of the given constructions with

the text, etc. The color vision, emerging in the eyes and mind of the human being, bears a meaning content in itself.

The *color* together with the form and type belongs to basic structural materials of web-design. The psychological effect of separate colors and their combinations is closely connected with their position in the chromatic circle. According to G. Frilling there are several color groups giving different sensations.

1. *The colors giving warmth and cold sense*. The red-yellow spectrum part colors evoke the sensation of warmth, the blue-azure spectrum part colors – the sensation of cold. The maximum of psychological warmth sense the orange color gives. A warm color draws the object nearer, makes it visually larger and more active, attracts the attention to it, whereas a cold color moves off, calms, transfers the object to the background of the composition, subjectively reduces the object in size.

2. *The colors promoting the emergence of excitement and tranquilization, activeness and passiveness*. The most exciting action is done by the red color, which is perceived as the most active one. The equilibrium falls on the green color, which combines the lightness and vivacity of yellow with the tranquility and heaviness of blue. When combining active and passive colors it should be taken into account that the first are always perceived more vividly and are better memorized, that is why for the equilibrium achievement they should be delivered in smaller doses.

3. *The colors associated with the senses of time and space*. The greatest sense of removal from a subject (i.e. the space enlargement) is created by the colors of blue-azure spectrum part. The opposite to them orange-yellow colors give the effect of approaching of subjects to the observer. The perception of time in the light f blue-azure colors slows down up to its full stop. The chromatic circle colors on either side of this sector convey the impression of time acceleration. This sense reaches its maximum in the region of yellow and orange colors.

4. *The colors giving the sense of heaviness and lightness.* The blue-azure spectrum part colors of the chromatic circle appear the heaviest ones. This sense reaches its maximum in the region of the yellow color, which looks most airy and light.

Special sensations appear when affecting by different color combinations. The polar color pairs (the colors being opposite each other in the chromatic circle) agree well, especially when they go together against the grey background or are perceived in different planes. Thus, a combination of yellow and blue causes a strong tension, a motion effect; the neighborhood of red and green is perceived optimistically; in the pair of violet and green a concealed accumulated strength is felt; the tearing energy is manifested in the combination of orange and azure.

The non-polar color pairs can give unsuspected effects while their being perceived. Thus red in combination with blue provoke excitement and thrust learners aside. The neighboring red and yellow colors are associated with joy and warmth. Red in combination with golden gives a sense of splendor and luxury. Red in pair with orange causes a sharp temper, etc. While using non-polar color combinations one should take into account that, if the neighbor colors possess approximately the same brightness and one of the colors noticeably exceeds the other on the occupied area, then it "oppresses" its neighbor drawing over its parameters. For example, dim-blue surrounded by bright-green acquires a greenish touch and becomes a little more "colored". Directly near the boundary of the two colors an opposite tendency is observed – the colors seem to push off from each other and try to stress their differences.

It is not recommended to use the colors disposed too close to each other in the chromatic circle – the dissonance between them simply beats the eyes. The directly opposed colors also seldom make harmonic pairs: green and violet or red and azure usually seem to be too heterogeneous; relatively reasonably only blue and yellow go together.

While formatting an educational site it is important to match correctly the *combination of the text and background.* They should differ on the contrast, color intensity. *Maximally convenient* at long-term reading the combination of *a black text against a white background* is. Among other color schemes providing a good readability of the text there are two groups: the one with a dark text against a light background and the one with a light text against a dark background. Thus, black letters against a yellow background, blue – against white, green – against red, etc., are well perceived by the eye. Any *dark* enough color as a background sounds reserved, noble and even mysterious. A *light* color for a text is perceived especially bright and expressive. It should be born in mind that, if a color is too dark, the eye is inclined to perceive it as black. The same is referred to white: almost any insignificant admixtures (excepting blue) cause a sense of untidiness. To make these colors sound it is necessary to support and develop a needed tincture in other element.

At color matching it is advisable to follow the *principle of unity*, which supposes the web-site formatting with limiting of the used spectrum of every composition up to four colors.

At the present time our research is going on. The novelty of the problem being solved lies in the substantiation of an integrated approach to studying the problem of color factor using in innovation education aids. The significance of the project is in its pragmatism, practical orientation – the results obtained are aimed at executive perfection of the educational process at a higher education institution.

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DATA BASES OF SPSTL SB RAS IN THE INTERNET FOR NATURAL STUDIES

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The main objective of the Department of Scientific Bibliography of the State Public Scientific-Technological Library of the Siberian Branch of the Russian Academy of Sciences (SPSTL SB RAS) is to select and systematize materials on various directions of researches.

SPSTL SB RAS has been compiling databases covering various topics of environmental research, such as “Nature and natural resources of Siberia and the Far East, their protection and rational use”, “Problems of the North”, “Ecology and natural-territorial complexes conservation in West Siberia”, “Biodiversity of Northern Eurasia”, “Sustainable development of nature and society”, “Contamination and environment protection: reference and bibliographic-information issues”. All DBs are bases of a bibliographic type generated under Windows/IRBIS system control, their documents comprise bibliographic descriptions, subject and geographical headings, annotations, translation to foreign publications.

DB “Nature and natural resources of Siberia and the Far North” numbers about 160,000 documents since 1988 on geology, climate, hydrology, soils, vegetative and animal kingdoms, landscape ecology, terrestrial and aquatic ecosystems and natural resources. A wide spectrum of ecological problems such as anthropogenic effect on different components of environment, natural resources conservation and rational use, human ecology, ecological expertise and monitoring, legal, social and economic aspects of ecology.

Multidisciplinary DB “Problems of the North” is also worth paying attention. It includes materials (above 130,000 documents) on various problems of developing Russian and foreign (European, Alaskan, Canadian) North since 1988. It covers biological, geological, geographical, ecological, cryological, social-economic, medical-biologic problems of the North. A special section in the DB is devoted to scanty northern peoples.

DBs “Sustainable development of nature and society” (nearly 35,000 documents) for 1990-2005 deal with prospects of global ecological problems, sustainable development of nature, social and urban ecology, ecologization of industrial production, ecological up-bringing and education.

DB “Biodiversity of Northern Eurasia” (2,500 documents since 1988) touches problems of biological diversity of microorganisms, soils, animals, plants, landscapes, human genome, gene fund of organisms, biodiversity economics, the place of botanical gardens and reserves in conservation of biological diversity.

DB “Ecology and protection of natural complexes in West Siberia” has information since 1988 on various aspects of ecological problems in West Siberia (about 14,000 documents).

DB of guidebooks, manuals and information-bibliographical tools “Contamination and environmental protection” counts 2,700 documents since 1985 and gives summarized data on the most important directories, dictionaries, standards, methodical materials, reviews, domestic and foreign periodicals concerning environment pollution and protection, contaminants, wastes, their disposal and utilization.

Databases are constantly renewed, one can get fresh information for education, training and research at our Internet web site www.spsl.nsc.ru.

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Materials of conference

INFLUENCE OF TEMPERAMENT ON THE SENSE OF RHYTHM AMONG FUTURE BALLET DANCERS UNDER STRESS

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The ballet art is based on unshakable traditions of the classical dance. These traditions are supported by the laws of human body biomechanics and artistic principles of harmony, logic and practicability as the classical ballet language.

A music-rhythm sense understood as the ability to "outlive music actively (reflect in motion) and consequently have a gust of emotional time variation expressiveness of music motion" is a rather complex system necessary for a dancer.

Teplov B.M. defines musicality as an individual-psychological character of a person, a synthesis of specific inclinations and abilities forming a personal psychophysiologic dominant.

A special research carried out by Voskresenskaya L.P. testifies that a highly developed sense of rhythm influences the motor activity success. If it is remembered that the music-rhythm sense is not only of motor, but also of emotional nature, one can suppose that the state of mental strain (stress) caused by participating in important concerts or examinations, for example, exercises various influence upon the activity success of future various temperament types ballet-dancers.

Of the existing four types of temperament – the choleric, sanguine, phlegmatic and melancholic types – not all are equally professionally suitable for the "ballet-dancer" specialty. It depends on the excitatory and inhibitory processes' force relation, what loading can the nervous system stand. The achievement of movement perfection depends on the force and speed of muscular responses.

Selye H. considers a stress as a nonspecific strain. It is an aggregate of physiological reactions performing an adaptive function and characterizing the entire state of the body.

The performance of any complex pas is inevitably conjugated with its amplitude, muscle tension degree analysis, direction and movement's rhythm and frequency.

The research work task was in studying out if a psychic stress influences the music-rhythm sense of different temperament properties learners.

The research hypothesis consists in the fact that a high level stress has various effects on the sense of rhythm and spatial coordination conditioned by various properties of a temperament.

The research was carried out in the Perm State Ballet School in 2006-2007, the examinees were future ballet-dancers, 60 persons, boys and girls aged 15-16 years old.

The Perm State Ballet School students have constant practice in opera and ballet theatre performances, tours, concerts.

For the investigation of temperament properties the Eysenk H. test was used, the sense of rhythm and spatial coordination were studied on the method of Ilyin developed in the laboratory of psychology of the All-Russia Research and Development Institute of Physical Culture and Sport. While studying extraversion-introversion the "unstructured pictures" method of Kettell was used. The impulsivity was investigated on the method "The proportion of reactions in easy and difficult choice". The stress level was studied on the methods of Jean Claude Dortu.

By the virtue of the essence of temperament itself the dynamic features of any human activity – labour, academic, in our case – creative one, - depend on its properties.

One of the conditions presenting exclusive standards of temperament properties is a mental strain. They are the conditions, under which the personal activity equation, conditioned by a temperament, manifests itself most distinctly.

The research findings testify that a temperament is a significant factor of the future ballet-dancers' professional activity. The temperament influence manifests itself in the following:

a) separate temperament properties can have both positive and negative effect on ballet-dancers' activity;

b) temperament properties influence the activity success not in themselves, but according to a special psychological situation (in the given case – to the stress level).

Thus, it was found out that extraverts, at a high stress level, make more mistakes in spatial coordination and also in copying the pre-existing rhythm; the speed of movement coming down at that.

Introverts, vice versa, make fewer mistakes in rhythm and spatial coordination copying; the movement speed rising.

The examinees, who have a high speed of response (impulsive ones), copy the rhythm with a great number of mistakes and slow down the work tempo. In their turn the non-impulsive ones copy the rhythm perfectly and speed up the work tempo.

It is necessary to point out that the given features are noticed only at a high stress level.

Thus, founding on the research results one can conclude:

A non-impulsive introvert, who corresponds to the phlegmatic temperament type, makes fewer mistakes while performing at a high stress level.

An impulsive introvert, who better corresponds to the choleric temperament type, is subject to the negative high stress level influence.

As affected by a stress (before an examination or a concert, for example) the rhythm sense structure and its separate components' interconnection with different properties of the temperament change. It is a high stress level, when the negative influence of temperament properties, which condition unnecessary nervousness, anxiety, inordinate charge, incoordination of movements, music-rhythm sense failure, etc. manifest itself clearly, that results finally in lowering the effect while training.

The research results can be used by teachers in the academic process individualization:

1.Taking into account the fact that a high stress level has a negative effect on the music-rhythm sense, we should promote the sense of responsibility in extraverts; control their immoderate sociability before examinations and performances.

2.We should show a more sensible attitude to introverts, avoid criticism in their address and instill self-confidence.

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PSYCHOLOGICAL HELP IN SYSTEM OF PROFESSIONAL CHOREOGRAPHY INSTRUCTION

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One of peculiarities of training at a choreographic school is that 10-year-old children enter it, learn there for 8 years and get the profession of a ballet-dancer.

A choice – is always a certain factor of personal maturity. A professional choice – is a decision, which is made consciously on the ground of a mature self-esteem of abilities, interests, and inclinations. It is impossible to require from a 10-year-old child, hence, the vocational choice for him is made by his parents in the IV grade. As a rule, parents themselves picture the peculiarity of the profession very vaguely and very often have no idea of special abilities and specific requirements of the profession of a ballet-dancer.

The perfection of choreographic education requires studying those personality factors, which influence the given professional activity acquirement success. (Vaganova A.Ya., 1935; Ulanova G.S., 1954; Lopukhov F.V., 1966; Liepa M.E., 1967; Vasilev V.Yu. and Kasatkina N.D., 1968; Tikhomirova I.V., 1971; Sergeyev K.M., 1973; Tarasov N.I., 1981). At the present time, the problem of interconnection of physical and psychomotor development on the one hand, and intellectual one on the other hand, has been studied not deeply enough. Together with that, there is a research, wherein the availability of such interconnections is indirectly proved. Besides, one can speak of a more deep and complex character influences basing on the interconnections of psychomotor and intellectual development, when task-oriented actions on the motional sphere of a person cause correlative changes in the intellectual sphere.

The psychophysiological studies have been known, wherein a favourable influence of optimal exercise stress on the central nervous system's functional status is registered. Together with that, an inhibitory action of very high and unaccustomed physical exercise on separate intellectual functions, especially on memory processes (Gorbunov G.D., Lokalova N.P., Rotanova G.A., Oya S.M. and others), has been found out.

The study of motor qualities' and intellectual processes' development interconnections in school children is of great interest (Gorbunov G.D., Stambulova N.B., Kolman L.V., Volkov V.V., Stambulov A.V., Bandakov M.P. and others). The following has been found out in the study:

– the connectivity between intellectual processes' and psychomotor system's factors in all ages;

– the connections' dynamism, and therefore, their peculiarity in every age;

– sex differences in these connections' character starting with juvenile age;

– the possibility of task-oriented influence on the intellectual processes development by means of the so-called "leading motor qualities" formation.

It is important to note that the professional activity of a ballet-dancer in a greater degree promotes the development of a nonverbal intelligence, i.e. such forms of intellectual processes, where structural units are images or actions.

Certainly, the role of intellectual processes in physical actions' regulation is great, however, emotions and will play not a less important role here.

For the motor activity fulfillment a ballet-dancer needs a serious energy supply. A human being has three main psychological mechanisms of

energy mobilization: intellectual, emotional and willed.

The emotional mechanism. The most intensive emotions emerge in a meaningful situation characterized by the uncertainty of its outcomes. A typical example here can serve the situation of specialty examination or a contest, where the emotional mechanism of energy mobilization dominates especially apparently.

The intellectual regulation is voluntary and is purposefully formed in the process of the typical ballet-dancer's physical actions acquirement. In this case, not the emotions, but the objective, the imaginative picture, which mobilize the amount of energy necessary for the motor action implementation in accustomed conditions, act as regulators.

As for *the willed regulation*, it is switched on voluntarily in the cases, when on the way to the objective achievement the obstacles or difficulties giving rise to the contradictions of the type: "must, but can't", "want, but can't", "must, but don't want", etc., emerge. In such situations an additional energy mobilization, which is exercised on the mechanism of conation, where the main role is played by verbal self-orders helping the ballet-dancer enhance his activity, sustain it at the necessary level or retard the unwished activity, is necessary. It is obvious that for the future ballet-dancers' professional training the enumerated mechanisms' optimal interaction meeting the professional demands is of great value.

As the principle directions of the emotional volition development in the activity of ballet-dancers one can detach the following:

1.The development of emotions and sentiments (rivalry, passion, dedication, responsibility, etc.) speaking in the character of the most important motives of the artistic activity.

The sentiment of joy or discontent associated with the performance or examination result gradually disappears to give place to the flutter of pleasure produced by the anticipation of the oncoming entry.

2.In the process of professional training the ability to control one's emotions and emotional states and also to use these self-regulation skills in other life spheres gets perfected.

The emotional control manifests itself not only in the skill to conceal, suppress and "lessen" undesired emotions, but also in a special development of expression – external motion expressiveness.

The development of emotions and sentiments, the development of the ability to control one's emotions is impossible without a qualified psychological aid. But who renders the psychological aid to the choreographic school students?

First of all, it is a teacher or an educational psychologist (if there is one). From this point of view, the psychological accompaniment of the professional training can be presented as the teacher's and educational psychologist's activity on rendering a psychological aid to the future ballet-dancer. (The psychological accompaniment of the future ballet-dancer's professional training has much in common with the phenomenon described by Stambulova N.B.)

The methods of the future ballet-dancer's professional training psychological accompaniment can be various kinds of psychological aid comprehended as the aid in concrete difficulties negotiation, and wider – as the aid to the learner in his professional activity.

At such comprehension of a psychological aid its main kinds will be:

– *training* – the assistance in knowledge and skills acquirement;

– *education* – the assistance in personality and individuality formation;

– *psychodiagnosis* – the assistance in self-cognition and individualization of the whole training in terms of the psychological peculiarities and development process study;

– *psychoprophylaxis* – the assistance in prevention of destructive psychic phenomena rise and development (psychic satiety, psychological barriers, chronic mental strain, motivation to avoid failure, undesired motor skills deautomation, conflicts, etc.);

– *psychocorrection* – the assistance in correction and reformation of the raised negative psychic phenomena;

– *psychological enlightenment* – the assistance in psychological knowledge acquirement necessary for self-perfection;

– *psychological counseling* – the assistance to the teacher and student in a concrete situation analysis and making a decision;

– *psychological trainings* – specially developed complexes of autogenic training, psychotechnical exercises and games helping in development of necessary psychological qualities and skills;

– *psychological preparation* – the use of all kinds of psychological aid for providing psychic readiness for classes, rehearsals, examinations, contests, concerts and performances.

In spite of the fact that all these kinds of psychological aid are closely interconnected, each of them has its own peculiarity, its general and particular technologies, the knowledge of which enhances the teacher's psychological competence essentially.

In each training phase, according to its tasks and the learners' age, there is a definite specificity both in using separate kinds of psychological aid, and in their combination.

Psychological aid peculiarities in the elementary training phase in a choreographic school.

As a rule, the children entering the school either have almost no initial idea of ballet, or their idea is perverted. Many of the children, in connection with this, are unable to evaluate their choice correctness; besides, they experience a "deception of expectations" in various ways. The mismatch of the expectations and the ideas of ballet in general and the real academic activity often leads to disappointment, motivation fall.

1. One can emphasize two aspects of the "deception of expectations", two contradictions:

a) between the idea of ballet as a "festival" (got from watching television, visiting theatre) typical of children and real "rough work";

b) between the habit of children (especially junior school students) to follow the "pleasure principle" in motor activity and the real claim to work through "I can't" and "I don't want".

2. The necessity to approve oneself positively from the first lessons at a total absence of professional training.

3. For a considerable part of the learners the problem of coping with fears, among which the most typical ones are: the "fear of the teacher", the "fear of professional examinations", the "fear to be considered not promising", is a topical one.

The elementary training phase is associated with the acquirement of the foundations of professional activity. There appear a good few of psychological hardships in the academic process: it is difficult to be concentrated during the whole period; it is difficult to understand the movements' names, which sound in French; it is difficult to overcome the fatigue and follow out all the assignments. When something goes wrong, a desire to avoid further repetitions arises very often. All this not only slows down the training process, but also can become the reason of the psychological complexes formation (fear of examinations, mates' mockeries, etc.). The first specialty examinations become the most important test for the children: there is a special atmosphere there, a special anxiety, special significance of the result, here the first experience of success and failures is acquired. The student, who has got the label of a "non-promising" one, has great chances to become "isolated" in the class.

In this connection, while developing the psychological accompaniment of the ballet-dancer's professional becoming at every training phase it is necessary to take into account both the specificity of the phase itself, and the developmental age peculiarities of children in the given period.

The psychological accompaniment should include:

1. Psychological aid subproblems in accord with its basic directions (in studies, examinations, while preparing for concerts and performances, etc.):

- the assistance in necessary motor skills and abilities acquirement, development of motor teachability;
- the assistance in professionally important qualities development – motor and psychic ones;
- the motivation formation;
- the assistance in general adjustment for the performance;
- the formation of an adequate attitude towards success and failure;
- the assistance in making contact with teachers and students;
- the assistance in preparation or adaptation for a new general mode of life;

2. General problems of these tasks realization in terms of the integrated use of all the kinds of psychological aid with due consideration of the future ballet-dancers' age-specific features.

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STRATEGIC ORIENTATIONS OF LOW LIVING STANDARDS IN RUSSIAN REGIONS

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The generalized reproduction of the low living standard of the population is ruinous in terms of its socioeconomic consequences. The low life standard leads to the Nation's health deterioration, rising death and crime rates, decline of birth, family typology change (the percentage of incomplete, childless and invalids containing families grow, etc.), economically passive population percentage rise, social psychology deformation, social stability threat and other destructive social processes. It is acknowledged by scientists that poverty is not a simple need for means of subsistence, but a formed mode of life, which is able to self-generation at the extended scale, comprising more and more of the able-bodied population. In these conditions within the system of stable socio-economic development of the regions a special place should be given to the realization of strategic orientations of the poverty localization taking into account not only sociodemographic features of its expansion, but socioeconomic determinants of human potential reproduction as well. Nowadays, in conditions of oligarchical groups' rent oriented interests prevalence over the survival interests of the population main part of the population, the release of poverty driving forces occurs. Thus, the poverty problem has already overgrown the industrial frames of a separate state and come to the level of global social organization problem, i.e. the sources of poverty one should search for not in the fullness of transfers provision, but in the fact why personal incomes don't agree with the market environment. Considering poverty as an indicator of socially oriented development, it should be taken into account that the struggle with the low living standard reproduction must bear a system character. The poverty activation factors resolve themselves into natural, economic, social, demographic and administrative groups.

The revelation of natural determinants promotes the poverty localization in districts with unfavorable location, unstable climatic and natural conditions of husbandry. For example, spatial location (rural and urban settlements), features of sectorial differentiation of labour (mountainous and mining areas), acts of God.

The part-time employment, high unemployment, low minimum monthly wage, low level of infrastructure development, lack of conditions for small and medium business development, unsatisfactory level of social sphere development, unavailability of social benefits and services for the population belong to the business factors forming a favorable framework for the poverty reproduction. Regional and sectorial determinants are also of great importance. Particularly, an insufficient level of local self-government development and regional organization impotence contribute to low investment appeal of a region. The trade union movement incompetence manifests itself in disability of the employees to assert their rights. All these and other aspects come into account in the labour market segmentation theory, within the framework of which the necessity of state interference into those spheres of market, wherein the disequilibrium is linked with social strain growth, is substantiated.

The social variables are reflected in labour power characteristics. For example, the educational and specialized professional training of labour power that is inconsistent to up-to-date requirements of labour market; age pattern of labour power, level of health, general level of satisfaction with life, low rate of market mentality formation, prevalence of dependency motivation, etc. The demographic variables are connected with the growth of incomplete, invalid and retired persons containing families, growth of pension age human population fraction in total population size.

The administrative variables consist in low efficiency of target functions realized by federal government and local authorities, limited access to common property resources, political instability and low trust level of the population to the authorities.

Certainly, the regional specific features of the poverty reproduction should be born in mind, and general factors and isolated instances of manifestation and peculiarities should be emphasized. For example, general state of economy, low level of social protection, proportional scale of taxation, high unemployment level among economically active population, etc. are referred to general manifestations of poverty. As it is known, one of the most important factors of poverty reproduction is the low level of employment among economically active population. The specified problem is being solved inside households by means of the resources, intersupport and help substitution, and in the national level – by means of the implementation of concrete programs oriented to the specified population group. The isolated instances of poverty level increase are conditioned by accidental development of certain circumstances having unstable, irregular character (natural hazards causing

mass life standard decrease and impoverishment of the population). The specific factors are conditioned by the spatial features and industry classification of the considered spatial community. For example, the specific factors at a large extent are peculiar of rural areas. In particular, the specific factor of poverty stagnant character production in rural areas is a low earning power ratio of agrarian employment, not providing a full reproduction of human resource, oriented to the predominance of hard low qualified physical labour. The influence of specific factors on the general tendencies' activity conditions the necessity of the strategic orientations realization of the struggle with the population's low life standard reproduction.

The development of scales' reduction and poverty localization strategic orientations attend any program of socioeconomic development. Thus, the poverty coping strategy in accordance with the Rostov-on-Don Strategic Plan of Socioeconomic Development for the period until 2010 includes the complex of both active and passive measures:

- the development of socially vulnerable population groups' self-employment;
- welfare payments size increase;
- increase of social protection measures financing budgetary component owing to the place budget replenishment;
- search for additional sources of targeted social assistance financing (charity and social sphere development directly on the premises).

The primary strategic orientations of poverty localization are:

- the enlargement of able-bodied population groups' income sources through employment programs, wage indexation, informal incomes legalization and transfer of non-monetary types of wages into monetary ones;
- providing of non-discriminatory access of the population to social services (education, health care) and social programs (benefits, privileges, etc.);
- qualitative refinement of social security system inclusive of new trends in social work organization.

As far as poverty is reproduced in persistent forms, its decrease potential depends on the market forces synthesis mobilization regarded as internal regulation resources and external influences on the part of administrative leverages and the application of private, state and nonprofit economy sectors' interests' accommodation mechanisms. On the part of state influence a balance between the passive function of the state in the form of direct social services and help for the needy and active regulation in the form of participation in the programs of gainfully occupied population's human assets guaranteed resource and income access leveling. Amongst the package of regulatory control action measures of the state on economic and social sides of the public life the most important ones are such strategic orientations of poverty localization as:

- guaranteeing an effective mechanism of the population's economically active part employment promotion;
- guaranteeing of an effective mechanism of the population's social protection with the correspondent set of its realization instruments in terms of the most socially vulnerable part of the population, which is not able to earn a reasonable living (one-parent families and the ones having many children, families with children, single aged, the disabled, youth, migrants);
- guaranteeing of an effective double-natured incomes taxation mechanism promoting business activity growth and exercising a fair transfer of income;
- guaranteeing of an effective monetary system functioning mechanism allowing increasing the availability of credit resources, mortgage credit lending for the purpose of living standard leveling, and particularly, for the purpose of residence improvement, getting education, medical maintenance, acquisition of durable goods.

As for the population's social support mechanism realization, in this direction it is necessary to refine the functioning system of targeted social assistance, take into account the social assistance need degree of the population and correct the mistakes of including and excluding from social programs.

The general unsteady state of Russian economy makes pay attention to the poor households' development reserves and possibilities of their own. Such an approach was dubbed a "self-reliance" one and is founded on using the socio-economic potential of families and their business activity increase. The main idea is to mobilize the economic activity and aim it at the negotiation of inactivity, dependency, indifference and uncertainty of the needy households in their own abilities. A positive example of poor and needy households' self-adaptation can serve a practical application of "From benefit to salary" program developed by the "Urban Economics Institute" Fund, the distinctive feature of which is that it not only helps the families satisfy daily living needs using monetary grants, but also provides assistance by employment of jobless able-boded family members. However, the own resources mobilization and targeted support resources attraction efficiency will be higher in the case when these measures group with the purposeful state and local council behavior focused on self-adaptation and self-

employment of the needy and poor citizens. These are such action methods:

- the development of mortgage credit and other forms of lending;
- the assistance to self-employment in the sphere of small and medium business;
- the creation of promotional tax treatment for the entrepreneurship in the sphere of social services;
- the development of informative-consultative service network concerning the adaptation to labour market conditions and advanced training, and own business organization questions;
- the development of users' cooperatives in the sphere of social services production.

In Russia the attempts to develop the nationwide poverty localization program are undertaken. A complex solution of all these problems has a strategic value and allows considering the poverty negotiation in terms of life quality improvement including: the quality of intrasocial relations (personality, people, separate social groups and civil society organizations), the labour and entrepreneurial relations system quality (work and business ethics and responsibility), the social infrastructure development quality (the degree of satisfaction with social benefits and services), the environmental quality (external effects problem solution), the satisfaction with life quality including personal security. The content of measures aimed at the poverty reduction must reflect the whole cumulative action affecting the population's consumption level increase, benefits availability, and human potential growth.

Thus, the All-Russia socioeconomic development target program focused on the poverty localization must involve the following tasks' solution:

1) the population's health improvement (lifetime and, in particular, working activity growth providing the possibility of getting a higher income level);
2) the education refinement and effective labour market formation, that guarantee people's economic opportunities adjustment mechanism;
3) the arrangement of conditions for the population's comfortable accommodation provision growth;
4) the insurance compensation desired level provision in the period of loss of wages, targeted social assistance and social service of disadvantaged groups of the population;
5) the economic growth, competitive recovery of the economics, socioeconomic distinctions' reduction between regions, cities and rural areas.

Together with the federal program, regional targeted programs of low living standard localization are being developed. It allows realizing the wide social power and the responsibility of bodies of state power of subjects of the Russian Federation for the corresponding regions' residents, taking into account those features of poverty reproduction and its stable trend manifestation, which cannot be covered by the All-Russia program. A systematic and complex approach to the specified problem solution must be based on the coordination of various level state authorities' efforts at distinct delineation of powers and functions. The current monitoring of steady poverty reproduction causes and their tension level analysis can become a practical framework for the formulation of poverty localization concept considering territorial and categorical peculiarities of their manifestation and methodological procedures of a concrete region poverty socioeconomic portrait construction.

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REGION INNOVATION EXTENDED REPRODUCTION STRATEGY

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The innovation extended reproduction allows modernizing the technological base of regional economics and providing the competitive edge of its production essentially. As an innovation infrastructure system forming component, providing the extended reproduction of a territory innovation potential, we offer the regional innovation center creation in Rostov Region (RIC). The principle RIC activity directions are:

- the analytical, informative and consultative support of the Rostov Region Authorities in the sphere of the territory's innovation development, the elaboration of socio-economic and scientific-technological development programs, holding of exhibitions, conferences, seminars, other actions;
- the entrepreneurial business extension work in scientific and technological sphere, innovation activity of higher education institutions, academic and sectorial institutions and the implementation of innovation projects aimed at the development of science, the creation and introduction of modern knowledge-consumptive competitive technologies on the shop floors of the region;
- the execution of an examination of scientific and technological projects, new technologies,

regional programs providing the creation of competitive samples of engineering and production and promoting the market saturation with the commodity produced on their base;

- the business support and new technologies and "know-how" implementation using patents;

- the entrepreneurial business subjects', domestic and foreign investors' attraction to innovation programs implementation on the competitive base.

The RIC is called to coordinate the activity of technologies' transfer center (TTC), technology and patents centers (TPC), innovation technology centers (ITC), technological parks and other innovation activity subjects financed at the regional budget expense. A high regional development effect is possessed by the regional technologies' transfer centers (TTC) performing their activity on the following directions:

- the formation of data bank on the existing innovation developments, investigations and projects;

- the non-financial economy sector's request encapsulation for the most acute problems' solution in terms of high technologies;

- the innovation projects commercialization assistance;

- the selection and evaluation of projects possessing commercial potential, the marketing research of the market and database creation;

- the creation of information channels for commodity promotion;

- the intellectual property evaluation, the search for industrial organizations interested in concrete elaborations.

The regional development innovation formation priority orientations are determined in agreement with the goals defined in the RF and Rostov Region regulatory legal acts administering the problems of socioeconomic, scientific and technological and industrial development. The creation of an integrated monitoring system of the innovation development priority orientations will guarantee their timely specification. These orientations are detailed within the framework of the Rostov Region's check list of critical technologies necessary for the effort integration on the strategic drifts and practical realization of the present innovation potential in the region.

The current market infrastructure doesn't provide an equal access to the resources and services for all the participants of the innovation process, that restricts the scientific and technological activity results' commercialization. A considerable demand for equipped office and industrial premises with low rental fee is felt by epy small high technology business. The large- and medium-sized enterprises and organizations are in special want for the access to expensive equipment and long term non-loan credits. In connection with it a further development of business incubators network, ITC, technoparks, centers of multiple access to scientific equipment, expert-consultative structures, centers of technology and patents, subsidization of part of expenditures connected with market loan interest payments is planned.

The section of new innovation companies is the major source of novations, however, the national support system is insufficiently focused on the small entrepreneurship innovation segment needs. The cooperative network "science and education – innovation small and medium business – large business" is also undeveloped, that impedes the spread of knowledge from the research and development section and their capitalization in the Don economics. The institutions stimulating relations between scientific, educational organizations and innovation firms, between large companies and small business are ill-developed. In this respect it is necessary:

- the formation and development of pecuniary institutions providing business projects financial backing continuity in all stages of the innovation cycle (innovation funds, venture companies, "business-angels");

- the industrial engineering infrastructure (technoparks, ITC, business incubators, TTC, etc.) development;

- the extension work of cooperation ties between the innovation system subjects (the development of outsourcing and subcontracting centers);

- the development of information expert-consulting and educational infrastructures of innovation activity;

Nowadays, because of high business struggle, the majority of companies are in want of innovations, but this want is in disagreement with the demand for innovations because of high risks, administrative barriers, problems of access to long term financial resources at the state-private partnership mechanisms imperfection. It results in the fact that the demand for innovations is localized in primary sector corporations, which are ill-developed in the Rostov Region (excepting coal-mining ones). That is why the regional research and development sector is cut off, to some extent, from the financed order for innovation elaborations. In this connection it is advisable to create an intermediate structure performing the interaction between the customers from other regions and local companies. These functions can be given to the regional innovation center to do.

The basic realization risks of the region's development pessimistic (inertial) scenario are conditioned by:

- the creation of well equipped industrial productions with low unearned increment instead of high-tech complexes in the territory of Russia, that will lead to the business struggle for cheap labour force attraction (first of all, in coal mining areas);

- the loss of competitive advantages associated with the research and development sphere creative potential and the development of human potential as a whole;

- the weakening of defense and "double" technologies development systems' efficiency.

Within the framework of the innovation development active scenario it is the forward development of the "knowledge generation" medium, the provision of research and development section on the priority orientations, the creation of effective innovation infrastructure and stimulation of the economic branches' wide technological modernization, that is necessary. For the active scenario realization it is required:

- the concentration of budget and off-budget resources destined for R&D and high-tech projects financing on the priority orientations;

- the provision of high technological innovations reduction for real economic section enterprises and organizations, and also information about the existing demand for them.

Within the framework of the optimistic (active) scenario the following tasks are emphasized as the prime ones:

- the creation of a competitive research and development section and conditions for its extended reproduction;

- the creation of an effective regional innovation system;

- the development of use and legal protection of the research and development results;

- the economy modernization in terms of technological innovations.

As the result of these problems' solution with the potential development and the formation of the demand adequate structure of the research and development section supply, the realization of science and technology priority orientations in the Rostov Region is supposed. Together with that the science service export and innovation activity section results value as an independent economic branch will grow. The regional economic policy orientation to the enterprises' and organizations' activity support and stimulation will allow guaranteeing the development of the research and development competitive section and conditions for its extended reproduction. It is known that only from the export of high technology products Russia can annually get 120-150 billion dollars. The Rostov Region ranking the 11th on the innovation potential among the RF subjects is able to get additionally considerable values of financial assets and raise, thereby, the interest of foreign companies in their productions and scientific laboratories distribution in the region's territory thanks to the export of high technology products. To do this it is required:

- the Don science-intensive products export merchants' support;

- the formation and financing of the conjoined regional ordering for the scientific-technological production;

- the rendering of organizational economical support to the innovation activity subjects;

- the delivery of an agreement between the Rostov Region Administration, leading higher education institutions and research institutes about the joint activity aimed at the acceleration of most advanced R&D results involving into the economical return;

- the stimulation of production modernization owing to import substituting technologies developed in the Rostov Region.

The financing of optimistic scenario realization consists of budgetary and extra-budgetary components. The budgetary component value is formed of the following sources:

- the budgetary research and development;

- the state banks' credit resources provided in the mode of development credits for technological reequipment and participating in international technological projects (up to 100-150 billion dollars annually as a whole throughout Russia);

- the subsidization of part of expenditures connected with credit and lease payments, compensation of part of expenditures for participation in shows and patent payments coverage;

- the purposeful buying of science-intensive products created within the framework of the conjoined regional ordering;

- the innovation sector development within the framework of four National projects realization;

The entrepreneurial sector is characterized by the ill-development of subcontracting networks, the small innovation business being poorly integrated into the value formation chains. In combination with bad sensitivity of large and medium-sized enterprises to innovations by virtue of their insufficiently effective managerial systems, it essentially restricts the innovation decisions inflow into the business sector. For such a situation overcoming within the framework of the active scenario realization, the following prime measures are necessary:

- the stimulation of the demand for innovations in the regional economics business sector,

technological rearmament of companies, new high-technology products issuing and export activity, creation of new high-tech firms;

- the budget tax incentives of scientific and technological activity and demands for its results;

- the extension of international technological integration of enterprises and regional organizations;

- the formation of general conditions for the development of state-private partnership in the sphere of innovation activity;

- the regional development technological forecast and science and technology priority orientations determination mechanisms system formation for a long-term outlook (foresite technology); the formation of critical technologies' and technological development priorities' catalogue;

- the regional (organizational, financial, information) support of joint research projects of enterprises and higher educational institutions within the framework of the priority development orientations;

- the provision of innovation directivity of the purchasing system for the national needs (inclusive of the conjoint regional ordering for the R&D deliverables);

- the extension and "programming" of the demand for innovations in major companies.

Thus, the innovation development active scenario realization is the most optimal option.

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COMPETITIVE ADVANTAGES DEVELOPMENT MANAGEMENT TECHNIQUE IN APPLIED SPECIALIST TRAINING PROCESS

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One of the most important tasks of the educational system currently is the training of qualified specialists, the formation of professional traits, knowledge and skills, which can guarantee a high competitiveness level in the labour market, in them. The model of the specialist is built on the ground of the education standard. Thus, the higher education standard composition represents a paramount problem in the higher education quality providing as the specialists' ability to act professionally in conditions of production.

It s the standard that creates the sample, with which the specialist's training level is compared while defining the quality of this training. The given sample determines the work objective of the whole educational system. A wrong destination specification, at no matter how ideal the work of educational institutions is, leads to the fact that the graduate's training will not correspond to up-to-date requirements of technology and economy, i.e. the graduated specialist will not be able to solve the tasks being put in front of them by the productive-economic system [1].

The quality of education standards is determined by the degree of their correspondence to the modern society's changing requirements, state-of-the-art and the requirements of economics and potential market of labour.

In conditions of growing specialist's training quality requirements, constant underfunding of the educational system and limitations in other resources for the specialist's training, the composition of such a standard, and the organization on its base of such an educative process, which could promote the maximal development of the graduate's competitiveness, acquires a special importance.

The competitive power of the graduated specialist is formed of competitive advantages. By the "competitive advantages" we will mean the graduate's training level on definite disciplines being included into the given area specialist's training system. The graduated specialist's competitive advantages development management is the passport to the formation of his competitiveness.

The graduated specialist's competitive advantages development management occurs on the following scheme: the competitive advantages provision factors definition – the graduated specialist's competitiveness estimation – the definition of weak points in the graduated specialist's training system – the development and implementation of the development of those factors optimal control program, which are able to affect the general competitive estimation of the specialist to the maximum extent.

All the variety of scientific knowledge necessary for the applied specialist's training is acquired by the last within the framework of general-theoretical, general-professional and narrowly-specialized (professional) disciplines. The intersection of these varieties gives seven main parameters applied to the specialist of any practical activity area: social disciplines, natural science disciplines, general-technological disciplines, general-engineering disciplines, technical and economic disciplines, the disciplines of a concrete specialty and concrete direction [1]. It is necessary to take

into consideration that the studied disciplines serve as the base for teaching one or several following disciplines.

The graduated specialist's competitive advantages development potential can be determined with due account for the use of the resource approach to the specialist's competitiveness estimation [2].

The use of the resource approach to the competitiveness estimation is usually restricted by the presence consideration of the resources themselves. But there are some disadvantages in such an approach. It is important to take into account the interaction between the resources or, in other words, the communicative components of the system. The degree of the resources' and the formed by them interfaces' influence on the integral system of the competitiveness estimation is not equal for various cases, and it should be overlooked.

One of the application areas of the being developed estimation system can be the specialist's training system.

Originally the influence of various factors on the graduated specialist's competitiveness through the resources reflecting them becomes formal. Then a resource matrix (1) is built, in which the diagonal elements reflect the resources, and non-diagonal – the interfaces between these elements, the relations between them and their influence on each other.

$$P = \begin{vmatrix} P_{11} & P_{12} & \dots & P_{1n} \\ P_{21} & P_{22} & \dots & P_{2n} \\ \dots & \dots & \dots & \dots \\ P_{n1} & P_{n2} & \dots & P_{nn} \end{vmatrix}. \quad (1)$$

One should bear in mind that the inequality (2) can be valid

$$P_{ij} \neq P_{ji}. \quad (2)$$

On the diagonal it is necessary to put only really used resources, which are not equal to zero. Some of the non-diagonal elements can be equal to zero. The quantity of the included into the matrix (1) resource components depends on the specialty.

Every component of the resource matrix can be characterized by its own value and dimension. On each of the components one can introduce its potential utilization coefficient, which is determined by the formula (3) and is non-dimensional

$$k_{ij} = P_{ij\,факт} / P_{ij}, \quad i, j = \overline{1,n}, \quad (3)$$

with P_{ij} – as maximally possible value of the ij matrix component potential; $P_{ij\,факт}$ – as an actual value of the ij matrix component potential.

The matrix *K* (4) composed of all k_{ij} in some way reflects the general picture of the resource use and internal measures of competitiveness

$$K = \begin{vmatrix} k_{11} & k_{12} & \dots & k_{1n} \\ k_{21} & k_{22} & \dots & k_{2n} \\ \dots & \dots & \dots & \dots \\ k_{n1} & k_{n2} & \dots & k_{nn} \end{vmatrix}. \quad (4)$$

The matrix norm can indirectly reflect the total degree of resources utilization in the training system and the competitive potential revelation on the condition of equal importance of the components forming the matrix, that is impossible in practical use of the technique.

$$\|K\| = \sum_{i=1}^{n} \sum_{j=1}^{n} k_{ij}. \quad (5)$$

If we multiply the matrix elements (4) k_{ij} by the ponderability coefficients v_{ij}, we'll get the matrix *R* (6), which will indirectly reflect the resources utilization total degree in the training system and the competitive potential revelation at various importance of the components forming the matrixes (1 and 4)

$$R = \begin{vmatrix} k_{11} \cdot v_{11} & k_{12} \cdot v_{12} & \dots & k_{1n} \cdot v_{1n} \\ k_{21} \cdot v_{21} & k_{22} \cdot v_{22} & \dots & k_{2n} \cdot v_{2n} \\ \dots & \dots & \dots & \dots \\ k_{n1} \cdot v_{n1} & k_{n2} \cdot v_{n2} & \dots & k_{nn} \cdot v_{nn} \end{vmatrix}. \quad (6)$$

The following restriction is advisable to establish:

$$\sum_{i=1}^{n} \sum_{j=1}^{n} v_{ij} = 1. \quad (7)$$

For the ponderability coefficient estimation the method of expert evidence can be used. With the help of the expert evidence method the resource matrix importance factors are defined by the ratio of the rank sum on every factor to the total rank sum on all the factors:

$$v_1 = \frac{\sum_{l=1}^{m} a_{1l}}{\sum_{h=1}^{n} \sum_{l=1}^{m} a_{hl}}; \quad v_2 = \frac{\sum_{l=1}^{m} a_{2l}}{\sum_{h=1}^{n} \sum_{l=1}^{m} a_{hl}}; \quad \dots; \quad v_h = \frac{\sum_{l=1}^{m} a_{hl}}{\sum_{h=1}^{n} \sum_{l=1}^{m} a_{hl}}, \quad (8)$$

with $v_1, v_2, \dots v_h$.- as the resource matrix components importance factors;

a_{hl} – as the h factor rank assigned by the first expert ($h = 1,n^2$; $l = 1,m$), the maximal rank is assigned to the most important component.

The importance factors ($v_1, v_2, \dots v_h$) correspond to the factors v_{ij} of the matrix (6). While calculating the ponderability coefficient the following condition should be held: $h = i \cdot j$

The ponderability coefficients calculation is performed only on the condition of experts' opinions consistency; the concordance coefficient is calculated and compared to the table one for that. On the ground of the ponderability coefficients distribution histogram constructed on the values got the components of little value are hewed off. At that, the amount of the rejected components should not exceed fifty per cent.

Under the restriction (7) the matrix norm R has the following limit

$$\lim_{\forall k_{ij} \to 1} \|R\| = \lim_{\forall k_{ij} \to 1} \sum_{i=1}^{n} \sum_{j=1}^{n} (k_{ij} \cdot v_{ij}) = 1, \quad (9)$$

which characterizes the limiting (best) state of the training system aggregate resource defining the best internal state of the factors forming the specialist's competitiveness.

Considering the matrix R norm value at some real values k_{ij} we'll get the graduated specialist's competitiveness resource estimation C (9) in the range from 0 to 1:

$$C = \|R\| = \sum_{i=1}^{n} \sum_{j=1}^{n} (k_{ij} \cdot v_{ij}). \quad (10)$$

The considered resource approach to the graduated specialist's competitiveness estimation, taking into account the influence of weight characteristics of the competitiveness factors, has definite advantages. First, the investigator gets a convenient form of the graduated specialist's competitiveness estimation value (from 0 to 1). Second, it becomes possible to determine the development potential of the specialist's competitive advantages. Third, it is possible to develop the graduated specialist's competitive advantages with maximal economical efficiency.

The last activity can be put into effect on the ground of the resources utilization matrix analysis. With the help of the matrix R one can estimate the factors revealing the graduate's resource potential absolutely. The weakest competitiveness factors are represented by the values deviating from their maximal potential (unit) in a greater or lesser degree. The factors, which work for the expression $(1–k_{ij}) – 0$ in a greater or lesser degree, one can call the most competitiveness defining.

The general competitiveness level of the graduated specialist can be increased by implementing the underused potential of weak competitiveness forming factors. However, not always the liquidation of the maximum deviation gives the most favourable results for the graduated special-

ist's competitiveness recovery. For the defining of optimal improvement sequence of the factors able to provide the graduate's competitiveness edge to the maximum it is necessary to take into account the weight of the factor in the competitiveness bulk and invest cash assets and time into the development of competitive advantages in their weight decreasing order.

References:

1.Dorobolyuk T.B., Kalachevsky B.A., Nosov A.V. Education management in quality priorities: Monograph. – Omsk: SAHI Publishing House, 2004. – p.247.

2.Porter M. Competition: Translation from English – M.: Publishing House "Williams", 2006 – p.608.

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APPROACHES TO REGIONAL SOCIO-ECONOMIC DEVELOPMENT STABILITY ASSESSMENT

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The embodiment of the idea of stability or stable socio-economic development not destroying the environment and oriented to the needs of the present and future generations can happen at all favourable conditions at a distant enough prospect. The transfer to the stable development itself should take place in the current XXI century, in its first half. The International Summit in Johannesburg (2002) affirmed that the world community goes on moving according to the unsustainable development scenario. In the UN organization documents it is emphasized that it is necessary to charge oneself with the strengthening and consolidation of the sustained development foundations – economical, social development and environment protection at local, national and regional levels. At that, every country should observe a variety of principles, implement certain imperatives and take into account the indicators established by the UN organization on the characteristics of economy, ecology, social sphere in their interaction.

In 1996 the Concept of the RF transfer to sustainable development was accepted. The sustainable development is defined there as the development "guaranteeing a balanced solution of socioeconomic problems and the problems of the environment and natural-resources potential preservation for the purpose of the present and future people generations' wants satisfaction" (1). In the Ecological Doctrine of the RF (2002) it is underlined that "the sustainable development of the Russian Federation, the high quality life and heath and also national security can be guaranteed only on the conditions of natural systems preservation and the quality conforming environment maintenance" (2).

The transfer of the RF to the sustainable development is possible only in the case of the sustainable development provided in all its regions. That is why the regional imperative of the sustainable development is in defining goals and regional development mechanisms by means of sustainable development strategy working out, that helps integrate the social, economical and ecological policies.

The regional model of sustainable development should be based on the scientific paradigm of social evolution in the eco-compatible form and involve the body of principles and requirement (imperatives) for the economy system and structure, the mode of functioning and interaction of its subsets providing the harmonization of relations in the triad "human being – natural environment – economy".

Therefore, while working out regional concepts of socioeconomic development, it is necessary to proceed from the principle of observing the main imperatives of the economic systems' stability. Among Russian regions, the Republic of Buryatia excels as the one most fully meeting socioeconomic and ecological imperatives of sustainable development. The Republic of Buryatia takes a special place due to the lake of Baikal and natural specifics in Russia. The ethno-cultural features of the folks living in the territory of the Republic are unique. In the XXI century the Republic of Buryatia will play the role of a natural geographical socio-cultural bridge connecting becoming integrated Europe and the quickly developing Asia-Pacific Region. The lake Baikal and the Baikal natural site have a special status fixed not only at the federal butt also at the world's level as the Region of the world's environmental heritage of UNESCO.

The Uniqueness of the lake Baikal sets a number of environmental requirements including the Baikal natural site ecological zoning carrying out. In the Baikal natural site there are 3 ecological zones marked:

- the central ecological zone - is the territory, which includes the lake Baikal with the islands, the contiguous water conservation zone and also natural areas of preferential protection;

- the protective ecological zone – is the territory beyond the central ecological zone including

the water-collecting area of the lake Baikal within the bounds of the Russian Federation;

- the ecological zone of atmospheric effect — the territory outside the watershed of Baikal within the bounds of the Russian Federation up to 200 km. wide to the north and northwest of the watershed where there are economic units with activity that has a negative influence on the unique ecological system of Baikal.

Depending on the sustainability of the natural complexes to man-made burdens, the ability of the environment to self-cleaning, and also the peculiarities of the formed economy and the natural environment's corresponding pollution and violation, it is supposed to introduce different water, forest utilization and farming systems in every of these zones. The limits of general maximal admissible effect of the economic complex on the natural environment are set for every ecological zone.

Proceeding from a special position of the Republic of Buryatia, to define how stable the economical system as a whole and within every ecological zone is, is very important. Unfortunately, in numerous publications devoted to the stability assessment the regional aspect of the given problem doesn't tell.

From this point of view, the works of Bobylev S.N. (4, 5), who offers to introduce the factor of environmental capacity as an effective economic sustained development criterion, which can also be used at the regional level, are of the greatest interest. The environmental capacity of economy describes the type and level of economic development very well. The environmental capacity figures can be measured at the macrolevel and branch level as well. The main advantage of the given factors is that they can be measured in dynamics or compared with other countries, regions, economical structures, technologies, etc.

The key figures computation of the environmental capacity of the economy of Buryatia on the offered method showed that for the period from the beginning of the 90-s of the last century up to the present time the natural resources costs, the contamination and waste contents per unit of GRP (Gross Regional Product) have grown, and it testifies that the ecological component of the regional economic development doesn't stand the basic requirements of stability.

The determination of natural (ecological) and production potentials comparison criteria of the territory is also referred to complex problems. In the work of Akimova T.A. and Khaskin V.V. (3) the concept of the given potentials comparison as the limitation of the production environmental capacities sum in a certain territory for a certain time and the ecologic technological capacity of the corresponding economic complex territory has been offered. The ecologic technological capacity – is the utmost endurance towards damaging technogenic effects; a generalized characteristic of the territory reflecting the self-restoring potential of the natural environment system and quantitatively equal to the maximal development pressure, which all the recipients and eco-systems of the territory can stand for a long period of time without violation of their structural and functional properties. At that, the main balance criterion is the production complex environmental capacity non-exceedance over the ecologic technological capacity of the territory. Both values can be in energy or money terms.

Lately, while comparing different countries and regions, the estimated figure "ecological trace" has been widely used. It is used while comparing territories on their economies' environmental capacity degrees and allows defining the human pressure on the regional eco-systems expressed in "territorial units".

For the regional level the factor of "true savings" offered by the World Bank is of great interest. The "true savings" – is the accumulation rate of national savings after the appropriate depletion accounting and the environmental pollution damage. In terms of practical application of the given factor as an economical imperative the ecological deprivation computation is a complex problem. It is accounted for a variety of causes. First, it is impossible to measure quantitatively a part of negative effects and give an adequate pecuniary valuation. The biological diversity disappearance can serve as the sample. Second, very often the environment pollution backlash is manifested in a long period of time and far from the emission source. Third, sometimes it is difficult to determine the true source and the polluter. All this makes the ecological deprivation computation rather approximate. For the Republic of Buryatia bearing high ecological costs compared to other regions, one of the real methods allowing estimating the size of the applied ecological deprivation, at least partially, is the definition of extra expenses, casualties and losses of opportunity due to environmental restraints applied by a special economic regime.

Thus, the existing approaches to the regional socio-economic development sustainable level determination and assessment need to be corrected and adapted to the realia of concrete territories. At that, the economic, social and environmental demands should be observed for the purpose of revelation and solution of the main priority problems of stability.

References:

1.The Concept of the RF transfer to sustainable development // The Collection of the Russian Federation legislation. 1996. №15.

2.The Ecological Doctrine of the Russian Federation. Approved by the Russian Federation Government order from August, 31, 2002 № 1225 – p.

3.Akimova T.A., Khaskin V.V. Economics of Nature and Man / Akimova T.A., Khaskin V.V. – M.: CJSC "Publishing House "Economics", 2006. – p. 334.

4.Bobylev S.N., Khodzhayev A.Sh. Economics of Nature Use: Textbook. – M.: INFRA-M, 2007. – XXVI, p. 501.

5.Indicators of sustained development of Russia (ecologo-economic aspects) / Under the editorship of Bobylev S.N., Makeyenko P.A. – M.: CPRP, 2001.

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Materials of conference

CONCEPTION OF THE EFFECTIVE UTILIZATION OF MEANS OF PRODUCTION IN THE ROAD-BUILDING IN RUSSIA

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The interpretation of the rationality from the point of view of a customer company engaged in building, exploitation and keeping transport constructions, a contractor company and a consumer differ in our time.

The questions of rational nature usage when transport constructions are used by consumers is in the sphere of the economic decisions about the place and the time of their building, about the choice of the type of constructions and the terms of their exploitation.

The same question from the point of view of the customer of building, exploitation and keeping of the transport construction is the question about the optimization of the results of its usage by consumers and expenditures necessary to accomplish the work by constructor companies.

The question of work's optimization of contractor companies touches the choice of the complex organizing and technological decisions; the part of them is the optimization of the means of labor of these companies – system of leading and auxiliary cars and gears.

Let us examine the last problem in detail.

The fulfilled investigation can be structured in the following way.

First we systematized factors influencing the effectiveness of technological and organizing decisions including the usage of cars' park. We determined the place of the cars' park among interdependent systems of different level. On the basis of the factor analyses we described the interdependence between the efficiency of the organizing and technological decisions from one side and the means of mechanization and other resources from the other side. The results of the investigation are showed in the books [13, 14].

Then we made an retrospective analyses of the system of criteria of the estimation of the effectiveness of the usage of cars' systems of building companies. As the result we established the expediency of the usage of the integral criterion of the efficiency that connects in the unity the particular indices. The criterion "Net Present Value" was also substantiated.

For showing analytically the interdependence between the efficiency of technological decisions and the resources being used we elaborated an economic and mathematical model of the choice of effective variants of technological decisions [15]. This model is characterized by the next opportunities: it allows estimating expenditures on the work and the results and conducting them under the time using a single function having a special purpose; it allows examining the organization of building work as a probabilistic system; it allows appreciating the efficiency from the point of view of customer and contractor in some functions having a special purpose [10]; it appreciates adequately the usage of new economical technologies and cars realizing them including future expenditures of the consumer (customer); it provides its large usage in the building (experimentally proved) [9].

After we described the place of the means of mechanization in the efficiency of the building manufacture as a whole we worked out an economic and mathematical model for the calculation of the effective structure of cars' park of the road-building company in modern economic conditions (fir new and for settled structures of cars' parks) [12]. This model is characterized by next peculiarities: the model corresponds to the criterion of the evaluation of the efficiency – the net present value; it takes into account that the cars in the park are interdependent and the whole work takes place in structure of the concrete car and road detachment that determines the productivity and technical and economic indices for each car; it has a possibility for tenant operations for machines, their reservation, the financial calculation of work's results; it allows evaluating the usage of new economical technologies [11].

To confirm the adequacy of this model we analyzed the process of change of the productivity of road-building cars in different intervals of work. Using the regressive analyses we investigated the influence of work on the productivity and the duration of the planning technical service and the repairs of some building cars [3, 6, 7]. As the result of the regressive analyses we created linear dependences, we determined the limits of the parameters of the regression and the dispersion of casual quantity of the productivity, the duration of planned technical services and the repair of different intervals of the work with probability 0,95, 0,99.

We also proposed some decisions in order to perfect methods for determining the rational periodicity for the repair of road-building cars [1, 5, 8].

As a result of the regressive analyses we determined the empirical dependences of the influence of the average annual duration of planned

preventive measures to the average annual duration of unplanned repairs on the example of the process of the exploitation of some types of cars [4].

Thus as a result of the investigation we proposed the methods of analyses and prediction of the significance of cars' productivity.

Then we elaborated the economic and mathematic model for the calculation of the effective structure and the composition of cars' park from the point of view of the complex examining of the systems of the productive and technical exploitation [2]. This model allows taking into account the individual productivity of each car; the expenditures of the time on the repairs of car; the condition of no surcharge changeable power of repair means; the correction of the periodicity of the technical services and repairs.

The results of the investigation were approved in some companies. The general effectiveness of the usage of cars' park increased till 46,3-54,2 %.

The methods and the general economic and mathematic model of the optimization of the usage of cars' park correspond to the conception of the rising of the effectiveness of the usage of cars' park of road –building companies. This model is characterized by the next attributive opportunities: thanks to proposed decisions we can find in the relations of the customer and the contractor a right economic motivation in the rising of the building quality , in the increasing of the terms of service of the road construction, the effective exploitation of industrial resources (including cars 'park of the company), as all these parameters are analytically connected in the elaborated model; as changeable quantities the model proposes the quantity of the car of each functional destination, type-size for all establishments and for all technological operations; the opportunity of the dynamic planning of the usage of cars' park for a long time appears, including the calculation of new orders and the work ready establishments Let us give the description of the model.

The point is to appreciate as correctly as possible the effectiveness of the usage of the means of the mechanization is possible only after examining their influence on the effectiveness of the organizing and technological decisions of the building and exploitation of the establishments during their whole life cycle including the problems of the utilization of materials that are not suitable for the exigencies of old elements of road constructions.

It is necessary to link the problems of quality provided by the means of mechanization with the effectiveness and the terms of the next exploitation of road constructions. To do it is possible by consolidating the examination of such parameters as tariff, expenditures, normative and actual terms of establishments' exploitation till the capital repair, the effectiveness during the whole investment cycle: from planning and building till exploitation of the establishment and work on its utilization.

From the other hand it is necessary to use such function that will be able to answer the main question of the optimization.

Cars' park as a mean of production is only a part of industrial resources that have properties of reciprocal partial addition, substitution and redistribution. It makes consider the effectiveness of cars' park as a part of the effectiveness of industrial program of company where the parameters of working and material resources and different expenses will be included.

Keeping these demands it is necessary in the result of calculation to make a rational choice and distribution of cars' park from the point of view of organizing and technological provision of industrial program of the company on establishments being built served and on all technological operation for the real life period of establishments.

The usage of the economic and mathematical model is possible only in the conditions of free economic relations of companies, of open competition in distribution of orders and when all the engagements are met in time.

That is why the introduction of the methods may bring the greatest effect only if to accept the conception on level of the whole region

The function having a special purpose is the total economic effect (1).from planning building of *I*-quantity of establishments and their exploitation till the capital repair considering expenses of recourses and financial results of exploitation of *K*-quantity of early built establishments. Each private annual effect can be determined on dependence (2). The annual effect from the building of *i*- establishment can be determined as a total effect on all building technological operations divided on the normative term of exploitation of this establishment.

The division of the total effect of the building on private annual effects and the division of the time of exploitation of the establishment till the capital repair of its construction on normative and real allows connecting the questions of the efficiency of exploitation of the organizing and technological decisions with the terms of service of the establishments being built. The division of the total effect of the building on private annual effects does not mean that the financing of work has to be divided on years of exploitation. But if the normative term of exploitation of establishment did not finish and the real term ended, the tariff on the building is zero (3).

The inverse situation is also possible (4). In

accordance of the limitation, till the normative term of exploitation the expenses on the building work include the expenses on the exploitation of cars, on materials, on salary and other expenses providing diminution of operational expenses. But if the normative term of exploitation of establishment finished and the real term did not end the expenses on the building in the period are zero and the tariff is the same

Thanks to these decisions a right economic motivation in the augmentation of the quality of building, of terms of service of road construction, in the effective usage of industrial recourses.

In the limitations (5, 6) you can find the expenses on the exploitation of *i*- being built and having been built establishments. These limitations are described in detail (7-35). The distribution of cars is influenced by the limitations (7-12). The model given below describes the open system of choice and destination of cars. This model is shown below:

$$Э = \sum_{n=0}^{\max(N_i^{(R)})} Э_n \to \max, \quad i = \overline{1, I}; \tag{1}$$

$$Э_n = \left[\sum_{i=1}^{I} \left(\frac{\sum_{j=1}^{J} \left[V_{ij}^{(b)} \cdot P_{ijn}^{(b)} - Z_{ijn}^{(b)} \right]}{N_i} + \sum_{l=1}^{L} \left[V_{il}^{(e)} \cdot P_{il}^{(e)} - Z_{il}^{(e)} \right] \right) + \right.$$

$$\left. + \sum_{k=1}^{K} \sum_{l=1}^{L_k} \left[V_{kl}^{(e)} \cdot P_{kl}^{(e)} - Z_{kl}^{(e)} \right] \right] \cdot \frac{1}{(1+E)^n} \to \max, \quad n = \overline{0, \max(N_i^{(R)})}; \tag{2}$$

$$P_{ijn}^{(b)} = 0, \text{ если } N_i^{(R)} < n \le N_i; \tag{3}$$

$$Z_{ij}^{(b)} = \begin{cases} W_{ij}^{(b)} + M_{ij}^{(b)} + A_{ij}^{(b)} + H_{ij}^{(b)} + Q_{ij}^{(b)} + Z_{Dij} \cdot D_{ij}, \\ i = \overline{1, I}, \quad j = \overline{1, J}, \quad \text{если} \quad n \ge N_i, \\ 0, \quad \text{если} \quad N_i < n \le N_i^{(R)}; \end{cases} \tag{4}$$

$$Z_{il}^{(e)} = W_{il}^{(e)} + M_{il}^{(e)} + A_{il}^{(e)} + H_{il}^{(e)} + Q_{il}^{(e)}, \quad i = \overline{1, I}, \quad l = \overline{1, L}; \tag{5}$$

$$Z_{kl}^{(e)} = W_{kl}^{(e)} + M_{kl}^{(e)} + A_{kl}^{(e)} + H_{kl}^{(e)} + Q_{kl}^{(e)}, \quad k = \overline{1, K}, \quad l = \overline{1, L}; \tag{6}$$

$$W_{ij}^{(b)} = \sum_{y=1}^{Y} \sum_{x=1}^{X} \left(C_{yx} \cdot n_{yxij}^{(b)} \cdot T_{CMyx} \cdot \left(T_{ij}^{(b)} - t_{yxij}^{(b)} \right) \right), \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{7}$$

$$\sum_{x=1}^{X} \left(П_{yxij}^{(b)} \cdot n_{yxij}^{(b)} \right) \ge \frac{V_{ij}^{(b)}}{T_{ij}^{(b)} - \sum_{x=1}^{X} \left(t_{yxij}^{(b)} \cdot n_{yxij}^{(b)} \right)}, \quad y = \overline{1, Y}, \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{8}$$

$$W_{il}^{(e)} = \sum_{y=1}^{Y} \sum_{x=1}^{X} \left(C_{yx} \cdot n_{yxil}^{(e)} \cdot T_{CMyx} \cdot \left(T_{il}^{(e)} - t_{yxil}^{(e)} \right) \right), \quad i = \overline{1, I}, \quad l = \overline{1, L}; \tag{9}$$

$$\sum_{x=1}^{X} \left(П_{yxil}^{(e)} \cdot n_{yxil}^{(e)} \right) \ge \frac{V_{il}^{(e)}}{T_{il}^{(e)} - \sum_{x=1}^{X} \left(t_{yxil}^{(e)} \cdot n_{yxil}^{(e)} \right)}, \quad y = \overline{1, Y}, \quad i = \overline{1, I}, \quad l = \overline{1, L}; \tag{10}$$

$$W_{kl}^{(e)} = \sum_{y=1}^{Y} \sum_{x=1}^{X} \left(C_{yx} \cdot n_{yxkl}^{(e)} \cdot T_{CMyx} \cdot \left(T_{kl}^{(e)} - t_{yxkl}^{(e)} \right) \right), \quad k = \overline{1, K}, \quad l = \overline{1, L}; \tag{11}$$

$$\sum_{x=1}^{X} \left(П_{yxkl}^{(e)} \cdot n_{yxkl}^{(e)} \right) \ge \frac{V_{kl}^{(e)}}{T_{kl}^{(e)} - \sum_{x=1}^{X} \left(t_{yxkl}^{(e)} \cdot n_{yxkl}^{(e)} \right)}, \quad y = \overline{1, Y}, \quad k = \overline{1, K}, \quad l = \overline{1, L}; \tag{12}$$

$$M_{ij}^{(b)} = K_{Fij}^{(b)} \cdot Z_{Mij}^{(b)} + \frac{Z_P + A_R}{S_O \cdot T_M} \cdot S_{Fij}^{(b)} \cdot T_{Fij}^{(b)} + Z_{TRij}^{(b)} + K_{Uij}^{(b)} \cdot Z_{Uij}^{(b)} \cdot O_{ij}^{(b)}, \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{13}$$

$$M_{il}^{(e)} = K_{Fil}^{(e)} \cdot Z_{Mil}^{(e)} + \frac{Z_P + A_R}{S_O \cdot T_M} \cdot S_{Fil}^{(e)} \cdot T_{Fil}^{(e)} + Z_{TRil}^{(e)} + K_{Uil}^{(e)} \cdot Z_{Uil}^{(e)} \cdot O_{il}^{(e)}, \quad i = \overline{1, I}, \quad l = \overline{1, L}; \tag{14}$$

$$M_{kl}^{(e)} = K_{Fkl}^{(e)} \cdot Z_{Mkl}^{(e)} + \frac{Z_P + A_R}{S_O \cdot T_M} \cdot S_{Fkl}^{(e)} \cdot T_{Fkl}^{(e)} + Z_{TRkl}^{(e)} + K_{Ukl}^{(e)} \cdot Z_{Ukl}^{(e)} \cdot O_{kl}^{(e)}, \quad k = \overline{1, K}, \quad l = \overline{1, L}; \tag{15}$$

$$Z_{TRij}^{(b)} = T_{TRij}^{(b)} \cdot P_{TRij}^{(b)}, \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{16}$$

$$T_{TRij}^{(b)} = \frac{Q_{TRij}^{(b)}}{G_{TRij}^{(b)}} \cdot \left(t_{Zij}^{(b)} + \frac{L_{TRij}^{(b)}}{X_{TR}} \right), \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{17}$$

$$Z_{TRil}^{(e)} = T_{TRil}^{(e)} \cdot P_{TRil}^{(e)}, \quad i = \overline{1, I}, \quad l = \overline{1, L}; \tag{18}$$

$$T_{TRil}^{(e)} = \frac{Q_{TRil}^{(e)}}{G_{TRil}^{(e)}} \cdot \left(t_{Zil}^{(e)} + \frac{L_{TRil}^{(e)}}{X_{TR}} \right), \quad i = \overline{1, I}, \quad l = \overline{1, L}; \tag{19}$$

$$Z_{TRkl}^{(e)} = T_{TRkl}^{(e)} \cdot P_{TRkl}^{(e)}, \quad k = \overline{1, K}, \quad l = \overline{1, L}; \tag{20}$$

$$T_{TRkl}^{(e)} = \frac{Q_{TRkl}^{(e)}}{G_{TRkl}^{(e)}} \cdot \left(t_{Zkl}^{(e)} + \frac{L_{TRkl}^{(e)}}{X_{TR}} \right), \quad k = \overline{1, K}, \quad l = \overline{1, L}; \tag{21}$$

$$A_{ij}^{(b)} = T_{Rij}^{(b)} \cdot \left(\frac{A_{\min}}{T_M} \cdot n_{\min\, ij}^{(b)} \cdot k_R \cdot k_{PRij}^{(b)} \right), \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{22}$$

$$A_{il}^{(e)} = T_{Ril}^{(e)} \cdot \left(\frac{A_{\min}}{T_M} \cdot n_{\min\, il}^{(e)} \cdot k_R \cdot k_{PRil}^{(e)} \right), \quad i = \overline{1, I}, \quad l = \overline{1, L}; \tag{23}$$

$$A_{kl}^{(e)} = T_{Rkl}^{(e)} \cdot \left(\frac{A_{\min}}{T_M} \cdot n_{\min\, kl}^{(e)} \cdot k_R \cdot k_{PRkl}^{(e)} \right), \quad k = \overline{1, K}, \quad l = \overline{1, L}; \tag{24}$$

$$H_{ij}^{(b)} = K_N \cdot A_{ij}^{(b)}, \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{25}$$

$$H_{il}^{(e)} = K_N \cdot A_{il}^{(e)}, \quad i = \overline{1, I}, \quad l = \overline{1, L}; \tag{26}$$

$$H_{kl}^{(e)} = K_N \cdot A_{kl}^{(e)}, \quad k = \overline{1, K}, \quad l = \overline{1, L}; \tag{27}$$

$$Q_{ij}^{(b)} = (k_1 + k_2 + k_3 + k_4) \cdot (W_{ij}^{(b)} + M_{ij}^{(b)} + A_{ij}^{(b)} + H_{ij}^{(b)}), \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{28}$$

$$Q_{il}^{(e)} = (k_1 + k_2 + k_3 + k_4) \cdot (W_{il}^{(e)} + M_{il}^{(e)} + A_{il}^{(e)} + H_{il}^{(e)}), \quad i = \overline{1, I}, \quad l = \overline{1, L}; \tag{29}$$

$$Q_{kl}^{(e)} = (k_1 + k_2 + k_3 + k_4) \cdot (W_{kl}^{(e)} + M_{kl}^{(e)} + A_{kl}^{(e)} + H_{kl}^{(e)}), \quad k = \overline{1, K}, \quad l = \overline{1, L}; \tag{30}$$

$$Z_{Dij} = W_{Dij}^{(b)} + M_{Dij}^{(b)} + A_{Dij}^{(b)} + H_{Dij}^{(b)} + Q_{Dij}^{(b)}, \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{31}$$

$$D_{ij} = \begin{cases} 1, & if \quad \Delta F > Z_{Dij}, \\ 0, & if \quad \Delta F < Z_{Dij}, \end{cases} \quad i = \overline{1, I}, \quad j = \overline{1, J}; \tag{32}$$

$$O_{ij}^{(b)} = \begin{cases} 1, & if\ utization\ of\ materials\ is\ necessery, \\ 0, & if\ utilization\ of\ materials\ is\ not\ necessery, \end{cases}$$
$$i = \overline{1, I}, \quad j = \overline{1, J}; \tag{33}$$

$$O_{il}^{(e)} = \begin{cases} 1, & if\ utization\ of\ materials\ is\ necessery, \\ 0, & if\ utilization\ of\ materials\ is\ not\ necessery, \end{cases}$$
$$i = \overline{1, I}, \quad l = \overline{1, L}; \tag{34}$$

$$O_{kl}^{(e)} = \begin{cases} 1, & if\ utization\ of\ materials\ is\ necessery, \\ 0, & if\ utilization\ of\ materials\ is\ not\ necessery, \end{cases}$$
$$k = \overline{1, K}, \quad l = \overline{1, L}; \tag{35}$$

$$n_{yxij} \geq 0, \quad n_{yxij} = \text{int}(n_{yxij}), \quad y = \overline{1, Y}, \quad x = \overline{1, X}, \quad i = \overline{1, J}, \quad j = \overline{1, J}, \tag{36}$$

where (b) – index for building work; (e) – index for operational work; i – number of building establishment; I – quantity of building establishments ; j – number of technological operation on building establishment; J – quantity of technological operation on building establishment; k – number of using establishment; K – quantity of using establishments; l – number of technological operation under exploitation of establishment; L –quantity of technological operations under exploitation of establishment; n – ordinal number of year; N_i – normative period of exploitation of i- establishment till capital repair ; $N_i^{(R)}$ – real period of exploitation of i-establishment; $V_{ij}^{(b)}$ – real volume of building work on i-establishment under j-technological operation; $V_{il}^{(e)}$ – real annual volume of work on l-technological operation under i-establishment; $V_{kl}^{(e)}$ – real volume of current annual work on l-technological operation under exploitation of early built k- establishment; $P_{ijn}^{(b)}$ – tariff of building work on j-technological operation on i- establishment in n-year, rub./unit of production; $P_{il}^{(e)}$ – tariff of operational work on l- technological operation on i-establishment, rub./unit of work; $P_{kl}^{(e)}$ – tariff of operational work on l-technological operation on early built k-establishment, rub./unit of work; $Z_{ijn}^{(b)}$ – expenditures on building work on j-technological operation on i- establishment in n-year; $Z_{il}^{(e)}$ – annual expenditures on l-technological operation under exploitation of i-establishment; $Z_{kl}^{(e)}$ – expenditures on current annual work on l- technological operation under exploitation of early built k-establishment; E – norm of discount; $W_{ij}^{(b)}, M_{ij}^{(b)}, A_{ij}^{(b)}, H_{ij}^{(b)}, Q_{ij}^{(b)}$ – expenditures on exploitation of cars' park, materials, salary and other expenditures under building on i-establishment on j- technological operation; $W_{il}^{(e)}, M_{il}^{(e)}, A_{il}^{(e)}, H_{il}^{(e)}, Q_{il}^{(e)}$ – expenditures on exploitation of cars' park, materials, salary and other expenditures on annual work on l- technological operation under exploitation of i- establishment; $W_{kl}^{(e)}, M_{kl}^{(e)}, A_{kl}^{(e)}, H_{kl}^{(e)}, Q_{kl}^{(e)}$ – expenditures on exploitation of cars' park, materials, salary and other expenditures on volume of current annual work on l- technological operation under exploitation of early built k- establishment; Z_{Dij} – subsidiary expenditures providing diminution of operational expenses; $W_{Dij}^{(b)}, M_{Dij}^{(b)}, A_{Dij}^{(b)}, H_{Dij}^{(b)}, Q_{Dij}^{(b)}$ – subsidiary expenditures (providing diminution of operational expenses) on exploitation of cars' park, materials, salary and other expenditures under building on i-establishment on j- technological operation, D_{ij} – changeable quantity of necessity of diminution of operational expenditures; y – functional purpose of car; Y – quantity of types of cars of park; x – type size of car; X – quantity of type sizes of cars of y- functional destination; C_{yx} – cost price of car's hour of car of-y functional destination and of x- type size; $n_{yxij}^{(b)}$ – quantity of cars of y-functional destination of x-type size on i- being built establishment, fulfilling j- technological operation; $n_{yxil}^{(e)}$ – quantity of cars y-functional destination of x- type size on l-technological operation under exploitation of i- establishment; $n_{yxkl}^{(e)}$ – quantity of cars of y- functional destination of x-type size on current annual work on l- technological operation under exploitation of early built k-

establishment; T_{CMyx} – duration of shift of car of *y*- functional destination of *x*- type size; $T_{ij}^{(b)}$ – permissible duration of building work on *i*- establishment on *j*- technological operation in shifts; $T_{il}^{(e)}$ – permissible annual duration of work on *l*- technological operation under exploitation of *i*- establishment in shifts; $T_{kl}^{(e)}$ – permissible annual duration of work on *l*- technological operation under exploitation of early built *k*- establishment in shifts; $t_{yxij}^{(b)}$ – duration of arrangement on service and repair of cars of *y*-functional destination of *x*- type size on *i*- being built establishment fulfilling *j*- technological operation in shifts; $t_{yxil}^{(e)}$ – duration of arrangement on service and repair of cars of *y*- functional destination of *x*- type size working on *l*- technological operation under exploitation of *i*- establishment in shifts; $t_{yxkl}^{(e)}$ – duration of arrangement on service and repair of cars of *y*- functional destination of *x*-type size working on *l*- technological operation under exploitation of early built *k*- establishment in shifts; $\Pi_{yxij}^{(b)}$ – middle operational productivity of cars of *y*- functional destination of *x*- type size on *i*- being built establishment fulfilling *j*- technological operation; $\Pi_{yxil}^{(e)}$ – middle operational productivity of car of *y*- functional destination of *x*-type size on *l*- technological operation under exploitation of *i*- establishment; $\Pi_{yxkl}^{(e)}$ – middle operational productivity of car of *y*- functional destination of *x*- type size on *l*- technological operation under exploitation of early built *k*- establishment; $K_{Fij}^{(b)}, Z_{Mij}^{(b)}, S_{Fij}^{(b)}, T_{Fij}^{(b)}, Z_{TRij}^{(b)}, K_{Uij}^{(b)}, Z_{Uij}^{(b)}, O_{ij}^{(b)}$ – for *i*- being built establishment and *j*-technological operation according to quantity of necessary materials, real value of materials, area occupied by materials, middle quantity of time to place materials, transport expenditures to deliver materials, quantity of materials for utilization, expenditures on utilization of unit of old materials, changeable quantity, of necessity of utilization of materials; $K_{Fil}^{(e)}, Z_{Mil}^{(e)}, S_{Fil}^{(e)}, T_{Fil}^{(e)}, Z_{TRil}^{(e)}, K_{Uil}^{(e)}, Z_{Uil}^{(e)}, O_{il}^{(e)}$ – the same but for *l*- technological operation under exploitation of *i*- establishment; $K_{Fkl}^{(e)}, Z_{Mkl}^{(e)}, S_{Fkl}^{(e)}, T_{Fkl}^{(e)}, Z_{TRkl}^{(e)}, K_{Ukl}^{(e)}, Z_{Ukl}^{(e)}, O_{kl}^{(e)}$ – the same but for *l*- technological operation under exploitation of early built *k*- establishment; Z_P – expenditures on keeping of storehouses; A_R – salary for storehouse workers; S_O – total storehouse area; T_M – quantity of work hours in month $T_{TRij}^{(b)}, P_{TRij}^{(b)}$ – с *j*- technological operation on *i*- being built establshment; $T_{TRil}^{(e)}, P_{TRil}^{(e)}$ – middle duration of transportation and cost price of usage of transport means under delivering of materials to fulfill of *l*- technological operation under exploitation of *i*- establishment; $T_{TRkl}^{(e)}, P_{TRkl}^{(e)}$ – middle duration of transportation and cost price of usage of transport means under delivering of materials to fulfill of *l*- technological operation under exploitation of early built *k*- establishment; $Q_{TRij}^{(b)}, G_{TRij}^{(b)}, t_{Zij}^{(b)}, L_{TRij}^{(b)}$ – mass of being transport materials, vehicle capacity, time of loading and unloading in one work cycle of car, middle distance of transportation of materials under securing of *j*- technological operation on *i*- being built establishment; $Q_{TRil}^{(e)}, G_{TRil}^{(e)}, t_{Zil}^{(e)}, L_{TRil}^{(e)}$ – the same but for *l*- technological operation under exploitation of *i*- establishment ; $Q_{TRkl}^{(e)}, G_{TRkl}^{(e)}, t_{Zkl}^{(e)}, L_{TRkl}^{(e)}$ – the same but for *l*- technological operation under exploitation of early built *k*- establishment; X_{TR} – middle speed of car; $T_{Rij}^{(b)}, n_{\min ij}^{(b)}, k_{PRij}^{(b)}$ –labor-intensiveness of manual labor, middle number of minimum sizes of payment in salary, coefficient considering other payments on *j*- technological operation on *i*-being built establishment;; $T_{Ril}^{(e)}, n_{\min il}^{(e)}, k_{PRil}^{(e)}$ – the same but for *l*- technological operation under exploitation of *i*- establishment;; $T_{Rkl}^{(e)}, n_{\min kl}^{(e)}, k_{PRkl}^{(e)}$ – the same but for *l*- technological operation under exploitation of early built *k*- establishment;; $A_{\min}$ – minimal month size of payment of labor; k_R – районный коэффициент к заработной плате; k_N – norm of overhead expenses, %; k_1, k_2, k_3, k_4 – coefficient considering expenses on building of temporary constructions, coefficient considering additional expenses on work in winter, coefficient considering unforeseen expenses; coefficient considering expenses on transportation of workers ΔF – economy of expenses on exploitation of establishment for real term of service.

References:

1. Ivanov V.N., Salikhov R.F. Methods of road building machines' repair rational periodicity defining // Construction mechanization - 2003. №5. – pp. 12 – 14. (Russia)

2. Ivanov V.N., Salikhov R.F. Optimization of road building machines' park structure and maintenance // Higher Education Reporter. Construction - 2002. №12. – pp. 70 – 74. (Russia)

3. Ivanov V.N., Salikhov R.F. Control and chance failure number at machines' exploitation //

Construction mechanization - 2002. №5. – pp. 28 – 29. (Russia)

4. Ivanov V.N., Salikhov R.F. Control and chance failure number at machines' exploitation // Building mechanization - 2002. №5. – pp. 28 – 29. (Russia)

5. Ivanov V.N., Salikhov R.F., Nesov K.N. Influence of construction machines' operating time on periodicity of road building machines repair // Higher Education Reporter. Construction - 2004. №4. – pp. 91 – 94. (Russia)

6. Ivanov V.N., Salikhov R.F., Nesov K.N. Bulldozer working capacity and repair time dependence on operating time // Construction mechanization - 2004. №6. – pp. 30 – 32. (Russia)

7. Ivanov V.N., Salikhov R.F., Shchukin K.V. Maintenance and operating time influence on road building machines' working capacity // Higher Education Reporter. Construction - 2003. №3. – pp. 97 – 100. (Russia)

8. Ivanov V.N., Salikhov R.F., Shchukin K.V. Criterion of road building machines' repair rational periodicity defining // Road-building machinery - 2003. №2. – pp. 29 – 30. (Russia)

9. Odintsov D.G., Ivanov V.N., Klopunov I.S. Various materials soft roof cladding installation works' production cost structure analysis // Building materials - 2001. №6. – pp. 24 - 25. (Russia)

10. Odintsov D.G., Ivanov V.N., Klopunov I.S. Choice of construction activity rational technology variant // Higher Education Reporter. Construction - 2001. №11. – pp. 71 - 73.

11. Permyakov V.B., Ivanov V.N. Road party work analysis with remixer // Higher Education Reporter. Construction - 1997.- №12. - pp. 98-101. (Russia)

12. Permyakov V.B., Ivanov V.N. Mathematical model of road builders' machine park structure // Higher Education Reporter. Construction - 1998. - №7. – pp. 93 - 96. (Russia)

13. Permyakov V.B., Ivanov V.N. Ways of machinery systems' work efficiency upgrading in road making // Higher Education Reporter. Construction - 2000. - №11. - C.82 – 86. (Russia)

14. Permyakov V.B., Ivanov V.N. Mechanical means use efficiency in construction operations: Monograph – Omsk: Publishing House of SibRTI, 2002. – p.192. (Russia)

15. Permyakov V.B., Odintsov D.G., Ivanov V.N., Klopunov I.S. Economic and mathematical model of efficiency determination of construction works' organization and technology option // Higher Education Reporter. Construction - 2001. №1. – pp. 53 - 57. (Russia)

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