Chronic Disease Prevention Research in Central Asia, the Urals, Siberia and Mongolia - Past, Present and Future

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Abstract

Central Asia, the Urals, Siberia and Mongolia cover an immense section of Asia and although relatively sparsely populated the total inhabitants number well in excess of 100 million. Furthermore, there is an increasing tendency for urbanization of the populations, which in many cases are growing. The ethnic make-up is diverse, with various degrees of admixture of Russians to the Turkish, Mongolian and other indigenous peoples of the region, and there is evidence of major variation in the burden of different cancers among the groups, although oesophageal and gastric neoplasias are relatively prevalent in common. Clearly there is a need for cooperation for cancer and other chronic disease prevention and the presence of Russian as a shared language of science, commerce and industry means that there should be no major communication difficulties. However, collaborative efforts at present are limited and the research output is low, even in the non-English literature. Here we focus on published work from the individual countries, as assessed by PubMed searches using the country name with cancer, cardiovascular, metabolic syndrome and diabetes as search terms, with an especial focus on epidemiology, environmental carcinogenicity and screening. One major aim is to identify active groups with an interest in participation in a regional meeting and collaborative research, so that a coordinated approach to granting agencies can be made to fund such a collective endeavour.

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Introduction

Central Asia, the Urals, Siberia and Mongolia cover an immense section of Asia and although relatively sparsely populated, the total inhabitants number well in excess of 100 million. Furthermore, there is an increasing tendency for urbanization of the populations, which in many cases are growing, with concomitant increase in non-communicable diseases. The ethnic make-up is diverse, with various degrees of admixture of Russians to the Turkish, Mongolian and other indigenous peoples of the region. Although there is evidence of major variation in the burden of different cancers and other chronic ailments among the groups, there would be clear advantages of a regional collaborative approach to promotion of preventive medicine and particularly research into means to reduce communicable diseases. The Asian Pacific Journal of Cancer Prevention, Vol 10, 2009, 987-988

Table 1. Major Chronic Disease Mortality Data for Russia, the Central Asian Republics and Mongolia (Data from WHO www3.who.int/mort/table1 - Rates/100,000)

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<tbody>
<tr>
<td>Males (Total)</td>
<td>1872</td>
<td>609</td>
<td>1159</td>
<td>719</td>
<td>577</td>
<td>785</td>
<td>710</td>
</tr>
<tr>
<td>Cancer</td>
<td>241 (13)*</td>
<td>82 (13)</td>
<td>142 (12)</td>
<td>47 (7)</td>
<td>40 (7)</td>
<td>65 (8)</td>
<td>124 (17)</td>
</tr>
<tr>
<td>Ischemic Disease</td>
<td>462 (25)</td>
<td>228 (37)</td>
<td>277 (24)</td>
<td>165 (23)</td>
<td>156 (27)</td>
<td>171 (22)</td>
<td>56 (8)</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>276 (15)</td>
<td>57 (9)</td>
<td>121 (10)</td>
<td>25 (3)</td>
<td>60 (10)</td>
<td>119 (15)</td>
<td>42 (6)</td>
</tr>
<tr>
<td>Females (Total)</td>
<td>1421</td>
<td>531</td>
<td>854</td>
<td>587</td>
<td>524</td>
<td>636</td>
<td>557</td>
</tr>
<tr>
<td>Cancer</td>
<td>173 (12)</td>
<td>62 (12)</td>
<td>113 (13)</td>
<td>42 (7)</td>
<td>38 (7)</td>
<td>56 (9)</td>
<td>97 (17)</td>
</tr>
<tr>
<td>Ischemic Disease</td>
<td>406 (29)</td>
<td>207 (39)</td>
<td>251 (29)</td>
<td>153 (26)</td>
<td>173 (34)</td>
<td>171 (27)</td>
<td>42 (8)</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>397 (28)</td>
<td>70 (13)</td>
<td>150 (18)</td>
<td>31 (5)</td>
<td>79 (15)</td>
<td>119 (19)</td>
<td>40 (7)</td>
</tr>
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* Percentage of total mortality

¹UICC-Asian Regional Office for Cancer Control, apocp2000@yahoo.com, ²Republican Center for Health Promotion, Bishkek, Kyrgyzstan, ³Kazakhstan Institute of Oncology and Radiology, ⁴National Centre for Problems of Healthy Lifestyle Development, Almaty, ⁵Health Department, Astana Medical University, Astana, Kazakhstan, ⁶National Cancer Center of Mongolia, ⁷Mongolian Academy of Sciences, Ulaanbaatar, Mongolia, ⁸Andijan State Medical Institute, Andijan, Uzbekistan
the burden from cancer, cardiovascular and cerebrovascular disease and diabetes mellitus type II, the major chronic diseases linked by overlapping risk factors.

To provide a base on which to build collaborative efforts, we here review the relevant literature, accessed through PubMed using the country name, cardiovascular, cancer, diabetes and disease prevention as the search items, covering papers published in English or Russian languages with Abstracts available. The most recent mortality statistics from the World Health Organization for both males and females are summarized in Table 1 for Russia and the countries of Central Asia surveyed. Unfortunately, data are not up to date in many cases and the fact that decreases have been officially noted for cancer over the last 25 years would suggest that the statistics are not necessarily accurate, with under-reporting a highly likely scenario. Latest Globocan data for cancer incidence rates are summarized in Table 2.

**Siberia**

Here we define ‘Siberia’ as stretching from the Ural mountains through to the Pacific coast, this including four Russian administrative regions (see Table 1 for populations). Approximately three quarters of the inhabitants are urban and some eleven cities have in excess of 500,000 people. For Russia as a whole, from the WHO mortality data for the year 2000, cancer accounts for about one eighth of the total, and ischemic disease approximately one quarter (see Table 1). Cerebrovascular disease continues to be important, particularly in females. Russian mortality was already high in 1991 and has increased further in the subsequent decade, in all regions, correlating strongly with underlying economic and societal factors, and especially alcohol consumption (Men et al., 2003). While cancer registration has been a major focus of attention and coverage was once reported to be 100% in some areas (Berzin and Golod, 1983), the data are not accurate.
readily accessible and therefore the provision here can not be comprehensive. From Globocan (see Table 2), both tobacco-associated and diet-linked cancers are prevalent, although data for inter-region variation are not available.

In Siberia, clearly there are major differences between native populations and the migrants from Russia. For example, comparison of mortality rates in Russia and the Republic of Altai revealed increased proportions of cancer of the trachea, bronchus, lung in males and females, as well as gastric cancers in males and of esophageal cancers in females in the latter (Volkotrub et al., 2001). Cancer incidence rates in the native peoples of the far north-east of Siberia for the years 1977-1988 were particularly high for the stomach, lung, oesophagus and cervix (Zaridze et al., 1993). A relationship between the consumption of fish preserved by various household methods and incidence of chronic gastric diseases and stomach cancer in the aborigines of the Far East has been suggested (Kustov et al., 1982), the predominance in males being attributable to complexes of unfavourable factors to which they are subject to a greater extent (Veber and Dolgintsev, 1980). Malignant melanoma morbidity was highest in patients with the light-color skin in Khabarovsk Territory in 1973-1983 (Kustov et al., 1987).

There are a number of cases of local environmental factors playing major roles. Deficiency of trace elements (iodine, copper, cobalt) in the environment in the Mountaneous-Altai has an impact on carcinoma of the thyroid gland (Neimark and Timoshnikov, 1978). Results in the Tjumen district, early showed an influence of opisthorchiasis in terms of cholangiocellular carcinoma development (Chaklin and Shain, 1976) and analysis of the morbidity among aboriginals and migrants demonstrated the latter to have higher cancer rates (Bychkov, 1977). An association between chronic opisthorchiasis and reactivation of EBV may be implicated in cancer development (Ilyinskikh et al., 2000).

While mortality trends of Krasnoyarsk Region population from oncological diseases may have dropped in 1989 as compared with 1959 (Mazharov et al., 1991), trends in other locations are unclear. What is very evident is that the industrial environment may contribute to cancer development. In a Magnitogorsk metallurgical plant, men were found to be at 1.6 fold and women at 3.2 higher risk of lung cancer as compared with the city population in general, with presumed involvement of benzopyrene in tars and carbon-black, benzol, chromium and nickel in dust, as well as carcinogenesis modifying substances like nitrogen oxide, sulfur dioxide, phenols, iron oxides and lead (Koshkina, 1991). In the Norilsk industrial region, cancer incidence rates are over two times the national and Krasnoyarsk regional levels, with a possible link to processing of ores (Dykno et al 1992). The risk of death from malignant neoplasms in workers engaged in rubber production was found to be almost five times greater than in the general city population (Volkotrub et al., 1989). Retrospective studies on cancer mortality among workers engaged in the carbon black industry demonstrated mortality rates from cancer of the lung, stomach and gastrointestinal tract to similarly be higher than in the surrounding district (Troitskaia et al., 1980).

The genetic background to cancer development in Siberia has received only scant attention, at least as viewed from the literature. The pharmacogenetic importance of genetic polymorphisms of CYPIA1, GSTM1 and P53 genes in a unique Siberian population of Tundra Nentsi has, however, been stressed (Duzhak et al., 2001) and in Tomsk, BRCA1 and BRCA2 mutations have been shown to be responsible for Russian familial breast cancer (Tereschenko et al., 2002).

An examination of awareness of health and attitudes in Novosibirsk revealed negative trends in both social and behavioral characteristics of the population, with a particular emphasis on the impact of stress (Gafarov, 2000; Gafarov et al., 2003). Widespread ischemic heart disease risk factors and a low awareness of their implications were found in the population in another Siberian study (Vorob’eva et al., 2001). In an epidemiological survey of risk factors in railroad men of West Siberia, high incidences of arterial hypertension, smoking, hypercholesterolemia, obesity, and impaired glucose tolerance, as well as a nutritional shift to food rich in fat were noted (Kudel’kina and Molokov, 2001). The need for interventions was stressed by Ziablov and Okrugin (2001), looking at acute coronary events in female residents of Tomsk. Individuals may be aware of risk factors but there may be a low trust in the public health service (Akimova et al., 1999) and physicians efforts may not be aimed at the prevention of disease complications (Nesterov et al., 1998). In Yakutsk, a comparative morphometric analysis of atherosclerosis in 1963-1968 and 1985-1988 showed accelerated development both among the native population and migrants (Alekseev et al., 2001). It has been argued that greater efforts also need to be focused on prevention of the smoking habit (Alekseeva et al., 1998).

Central Asian Republics

For the purposes of the present review, Azerbaijan has been included with Kazakhstan, Uzbekistan, Kyrgyzstan, Tajikistan and Mongolia within this central region. Data for the individual country populations and urbanization are summarized in Table 4. Major problems shared by all the countries are high rates of esophageal and gastric cancers, while those with sizeable Russian populations also demonstrate high incidences of neoplasms of the lung, breast and prostate lesions, with some correlation to diabetes mellitus. Another factor which needs to be taken into account is the widespread contamination of the environment with industrial and radioactive waste.

Life expectancy of males in the area may be as much as 13 years less than that of females, and a significant portion of the excess male mortality is caused by cardiovascular disease (Cashin et al., 2002). One major problem is that in both absolute and per capita terms, principal users of primary health care are overwhelmingly women of reproductive age and children under five, and access rates for males are very low.

Azerbaijan

In Azerbaijan (see Figure 2), WHO statistics indicate no marked change in cancer rates between 1982 and 2002, while ischemic disease has increased and cerebrovascular
Kazakhstan

The dismemberment of the Soviet Union led to considerable political and economic turmoil in Kazakhstan (see Figure 4) during its transition to an independent country and there is a continuing need to develop training programs for public health professionals. Data for relative mortality from the three major chronic diseases suggest similarities to Russia (see Table 1), and this is mirrored in cancer incidence data (Table 2). The control of esophageal cancer is one top priority (Sharmanov et al., 1996).

Regarding traditional analytical epidemiology one group have evaluated variation between plain (Kzyl-Orda Region) and mountainous (Alma-Ata Region) areas, finding an inverse association with altitude for this cancer (Akhtiamov and Kairakbaev, 1983).

In a series of papers, workers from the Atomic Bomb Disease Institute, Nagasaki, collaborating with Kazakh scientists have reported on risk associated with the Semipalatinsk Nuclear Testing Site. In the period 1982-96, there was a noticeable increase in the number of cases of Hashimoto's thyroiditis and thyroid cancer (Zhumadilov et al., 2000). A higher incidence of LOH on 9q22.3 in basal cell skin cancers from around the site further suggests involvement of chronic low-dose irradiation by fallout from the test site as a factor (Iwata et al., 2004). Analysis of alteration of the Wnt signaling-related molecules in thyroid cancer in the region may be important to gain an insight into radiation-induced thyroid tumorigenesis (Meirmanov et al., 2003). Morphological, cytogenetic and molecular biological characteristics of lung cancer in persons exposed for a long time to radionuclide radiation pollution in the Semipalatinsk region of Kazakhstan have also been examined (Kogan et al., 2002). While one study found no evidence of radiation risk for thyroid gland among schoolchildren (Hamada et al., 2003), their incidence of acute leukaemia significantly increased with increasing proximity of residence to testing areas, with some evidence of elevated numbers of brain tumours (Zaridze et al., 1994). Findings of collaboration with an American group suggested that an increased risk of leukemia among those exposed to >2 SV as compared to those exposed to <0.5 Sv, but this could have been a chance finding (Abylkassimova et al., 2000).

Earlier studies of nitrosamines and their precursors in some Kazakh foodstuffs suggested that improvements in the processing and storage of meat and meat products were
The prevalence of ischemic heart disease (IHD) in 1998-2002 showed an uptrend (Kausova, 2004), and the same may be true for diabetes. Clearly awareness of risk factors for disease is a major problem and development of a women's wellness center in Almaty should here be noted (Wilson and Jenkins, 2001).

Turkmenistan
Publications from Turkmenistan (see Figure 4) are very limited and the only paper that we could access concerned the practical importance of hormone dependent selective screening and necessity of elucidating new disease-epidemiological and laboratory risk factors for cancer of the reproductive system (Kuznesov, 1992). However, it is clear that cardiovascular disease is the greatest chronic disease problem, accounting for about one quarter of all mortality (Table 1). Rates for both cerebrovascular disease and cancer have been decreasing since 1982, at least in the official WHO statistics. Regarding cancer incidence, the oesophagus appears to be the major problem.

Uzbekistan
In Uzbekistan (see Figure 5), ischemic disease is the major cause of mortality, particularly in females, with lower prevalence for cerebrovascular disease and then neoplasia. Incidence data show rates for oesophageal cancer to be the highest among the major cancers, along with gastric cancer, and breast cancer in females. This has recently been confirmed by a preliminary study in the Andijan region (Soipova et al., 2009). A series of investigations were carried out a number of years ago with the focus on the high incidence oral and oesophageal cancers, Nass use and cigarette smoking emerging as independent risk factors for oral leukoplakia and smoking also being found to be an independent risk factor for oesophageal lesions and significantly associated with chronic oesophagitis (Zaridze et al., 1985; Zaridze et al., 1987; Evstifeeva and Zaridze, 1992). Alcohol intake was not found to be independently associated with the presence of oral and oesophageal precancerous lesions (Evstifeeva and Zaridze, 1992). Of men from whom blood was drawn for analysis, 4%, 66%, and 86% had low levels of retinol, carotene, and riboflavin, respectively, providing an opportunity and a justification for chemopreventive trials focused on precancerous lesions as end points (Zaridze et al., 1985b). Differential evaluation of different pathologies of the esophageal mucosa suggested a link between catarrhal and erosive esophagitis and vitamin B2 deficiency and atrophic esophagitis and vitamin A deficit (Zaridze et al., 1989). Furthermore, a significant decrease in the prevalence odds ratio (OR) of oral leukoplakia was observed after 6 months of treatment in men receiving retinol, beta-carotene, and vitamin E, and of risk of progression of chronic esophagitis (Zaridze et al., 1993).

Mass prophylactic examinations allowed high rate of recognition of oncological patients mainly using a fibergastroscope (Eshniiazov and Kabulov, 1977). It has been advised that paid mobile teams at regional consultative and diagnostic centers for broad-scale check-ups of rural population, with screening programs of such teams to include diagnostic ultrasound (Saifiev et al., 1991). A recent survey of eye cancers by Mouratova (2004), demonstrated a female non-local predominance.

A high prevalence of ischemic heart disease in middle-aged men in Tashkent has been reported (Makhmudov, 1986). A program of multifactorial primary prophylaxis was carried out for 5 years among the non-organized male population aged 40-59 years, but no substantial changes were discovered in the prevalence of overweight, hypercholesterolemia and low physical activity, as well as in the lethality due to coronary heart disease or in the rate of new cases of myocardial infarction (Makhmudov et al, 1990). However, in another study of secondary prophylaxis of arterial hypertension among an unorganized rural population, the mortality due to cardiovascular disease, myocardial infarction and brain stroke appeared statistically less significant in the district of intervention as compared to the reference district (Salakhitdinov and Tursunov, 1989).

Approximately one-third of all subjects in one region of Uzbekistan have been demonstrated to be centrally obese, glucose intolerance also being common (King et al., 2002). Arterial hypertension (AH) found in 38.6% of cases in Tashkent, more frequently in the non-indigenous than in the indigenous population (16.1 and 6.0%, respectively) Atherogenic effects of hypertension appear enhanced by its combination with diabetes mellitus (Abdullakhodzhaeva and Utepov, 1990).
Regarding Kyrgyzstan (see Figure 6), mortality data point to both ischemic and cerebrovascular diseases as the major killers, with cancer accounting for less than 10%. Relatively high incidence rates, however, are evident in Globocan data for most major sites as indicated also by the figures included in Cancer Incidences in Five Continents Volume 6, for the years 1986-1987. Then, stomach and lung were the predominant cancers in males, followed by oesophagus, with breast and cervical cancer being equally prevalent in females. Igisinov and co-workers have documented in a series of recent papers differences in ethnic and local populations regarding oesophageal (Igisinov et al., 2002a), breast and cervix (Igisinov, 2002) and ovarian (Igisinov and Umaralieva, 2008) cancers (see Figure 7). A link between altitude and cancer was further found (Igisinov et al., 2002). The incidence of gastric cancer also appeared much earlier to reflect the climatic-geographical zone (Saenko, 1979). Change over time has also been described, dependent on the region and ethnic make up (Igisinov, 2005). It has been stressed that mortality from malignant neoplasms of the female breast and uterus has to be given high priority in developing health policy in the coming years in Kyrgyzstan (Bozgunchievz and Ito, 2007).

The prevalence of ischaemic heart disease risk factors in males of Bishkek is very high (Meimanaliev et al., 1991). In a group exposed to active preventive intervention a decrease in the prevalence of arterial hypertension, hypercholesterolemia, smoking and low physical activity was registered after 5 years, compared to a group without active prevention. Prophylactic measures were found to lead to a positive dynamics of risk factors such as smoking, low physical activity, hypercholesterolemia, arterial hypertension in groups of active prevention. There was a decrease in death rates due to cardiovascular diseases, including myocardial infarction, stroke, among individuals with arterial hypertension, obesity, and low activity in the same group (Meimanaliev et al., 1991a; 1991b).

In the context of altitude and chronic disease, migration of lowlands residents to highlands results in decrease of serum total cholesterol and low density lipoproteins, and an increase of high density lipoproteins (Aitbaev et al 1990). The lower incidence of atherogenic dyslipoproteinemia in the Tien Shan and Pamirs mountain-dwellers correlates with much lower prevalence of coronary heart disease and its risk factors such as arterial hypertension, smoking, and obesity than with that in lowland-dwellers (Aitbaev and Meimanaliev, 1992).

Cellular nonspecific immunity was found reduced in residents of the lowlands and highlands suffering from alimentary obesity and noninsulin-dependent diabetes mellitus (NIDM), this depression augmenting with the increment of obesity degree and age of NIDM patients (Moldobaeva et al. 1994).

Tajikistan

No population-adjusted WHO mortality data are available for Tajikistan (see Figure 8), but absolute figures are in line with continued importance for circulatory disease. The oesophagus and stomach are the major sites of cancer development, but no research papers were found in the present literature search.

Mongolia

Mongolia offers a contrast to the other countries of Central Asia in that mortality from cancer is considerably greater than from ischemic or cerebrovascular disease. In the International Association of Cancer Registries 2002 meeting in Khon Kaen, representatives from Mongolia presented cancer incidence data (Munkhtaivan et al., 2002), showing liver cancer to be the most prevalent, followed by the oesophagus. Regional variation was also described. Some time ago, epidemiological studies were conducted in Mongolia on 1,263 cases of cancer compared to 2,526 healthy controls in order to uncover risk factors for cancer of the oesophagus, stomach, lungs, liver and cervix of the uterus (Dorzhgotov, 1989). Risk factors found included, consumption of large amounts of hot tea, or salted hot tea with roast flour and cereals, the habit of eating meat at the evening meals and eating half-chewed food (oesophageal cancer); meat at evening meals, eating hot...
food, hurried eating, consumption of stale foods, large amounts of hot tea, regular alcohol intake (gastric cancer); viral hepatitis, eating habits and alcohol intake (primary cancer of the liver); smoking, regular alcohol intake (alcohol drinkers tend to smoke heavily) (lung cancer); and early menarche, repeated marriages, deliveries at early ages (before 18 years of age) and repeated deliveries (cervix).

In the liver, by far the most common cancer, both HBV and HCV play major roles (Kurbanov et al., 2007) and co-infection, especially with HBV and HDV appears to have a stronger association with HCC development at younger age (Oyunsuren et al., 2006). The Mongolian infant vaccination program for hepatitis B is successfully reducing the rate of chronic carriage in the immunized generation. However, vaccine response among rural subjects is less than that among the urban population and there may be pockets of high disease prevalence that require further study (Edstam et al., 2002).

The most common neoplasm in females is undoubtedly cervical cancer, with HPV 16 involved in the majority of cases (Chimedдорж et al., 2008). It should be noted that sexually transmitted infections as defined by PCR are common, and were found in over half of female attendees of an urban STD clinic in Ulan Baatar, with clear implications for screening (Garland et al., 2002). A recent survey showed the HPV prevalence in Ulaanbaatar to higher than that detected by similar HPV testing protocols in other populations in Asia, suggesting an important, yet unquantified, cervical cancer burden (Dondog et al., 2008).

In Mongolian women, a substantial proportion of ovarian cancers or early-onset breast cancers may be due to a particular founder BRCA1 mutation, 3452delA (Elitov et al., 2002). A recent study showed central obesity and hypertension to be the most common combination (17% of all subjects) and 4% also exhibited diabetes (Suvd et al., 2002). Therefore it is likely that the future will see increase in these chronic diseases as well as the adenocarcinoma forms of cancer which presently are still rare.

Conclusions and Prospects for the Future

Because many emerging economies lack local capacity for scientific research, building the infrastructure has become a priority for many international development organizations. For this reason, it could be argued establishment of a regional coordination and training center as a core element. One recent article of interest concerns support for applied health research in Azerbaijan, one of the newly independent states of the former USSR. In 2000, environmental epidemiology training courses were conducted and several local participants received hands-on training in the planning and conduct of a subsequent cancer study as a practical extension of the training exercise (Andruchow et al., 2005). The research demonstrated that international collaboration can not only result in the successful completion of health research in countries such as Azerbaijan, but also impart research knowledge and experience to local experts. However, several practical issues were encountered in the conduct of the training activities that limited their effectiveness. The most desired result (the proposal and conduct of new research by local experts trained through these exercises) has yet to be achieved to the levels expected.

Therefore, international collaborations for consistent and continued support may be the best way forward. Comprehensive capacity building programs providing ongoing professional development, support, and an enabling environment, rather than scientific training alone, are required to achieve long-term sustainability and measurable outcomes. A regional coordination and training center, whether real or virtual, would be an appropriate investment in human, physical, intellectual and social resources. As emphasized in the study of Hopkinson et al (2004), there are important weaknesses in Central Asia in all of these areas. It is to be hoped that the beginning made with publication of the present review will contribute to cooperation across the region.

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