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A basis for translational cancer research on aetiology, pathogenesis and prognosis: Guideline for standardised and population-based linkages of biobanks to cancer registries

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Abstract Population-based cancer research is paramount for controlling cancer. Cancer research is increasingly dependent on access to biospecimens from subjects that have been followed-up for future health outcomes. This is achieved using longitudinal follow-up of cohorts and biobanks using cancer registry linkages.

All over the world, more and more large population-based cohorts and advanced biobanking facilities are established. International standardisation and networking in the linkage of cohorts and biobanks to cancer registries is required in order to enable international cancer research and comparability of research results. An international operating procedure and standard minimum dataset for linkages of biobanks, cohorts and cancer registries is proposed. An internationally comparable provision of well characterised study bases for molecular cancer research will be an essential prerequisite for the success of translational medicine.

1. Research infrastructures – a powerhouse for cancer research

The present paper will outline how cancer registries could further improve their usefulness as research infrastructures (RI) for effective cancer control, by systematic and standardised linkages to stored biospecimens. Many cancer registries already operate in this manner and there are many examples of how this has resulted in public health advances [1,15].

Facilities, resources and related services used by the scientific community to conduct research are termed RI (e.g. cancer registries, cohorts and biobanks). Although RIs may be based on regional or national materials, today's RIs need to operate on an international scale, offering services to users from different countries. An important function of RIs is also to attract young people to science and help to shape scientific communities. They can do so by acting as a hub for providing services in essential aspects of research like (i) access to high quality and standardised data, with follow-up for health outcomes (ii) access to high quality and standardised biospecimens, complete with longitudinal follow-up for health outcomes (iii) access to high performance molecular analysis platforms and/or on-demand generated molecular data (iv) development, implementation and monitoring of Best Practises and (v) education, expertise and advice.

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In other words, a good RI works as a research powerhouse – in a similar fashion as a 'research centre', with the additional advantage that it is also the custodian and builder of the necessary research materials upon which the research is based.

In order to enable comparison of health outcomes and research results from different parts of the world, it is imperative that RIs collaborate on an international scale, in particular in areas like standardisation, quality control and coordinated development. This has already been the case for cancer registries and proven possible. An international infrastructure for cancer research is a prerequisite for progress in international cancer control.

2. Research infrastructures for more effective and less expensive health services

Translational research is an essential component for delivery of effective health care and preventive services in any setting. Health services research is the study of real-life medical practise. That health services research can be carried out is essential for the quality assurance, cost-effectiveness improvements and innovation of the real-life medical practice. There is today a massive political interest in research on the comparative effectiveness of health services. The activities of Cancer Registries to monitor incidence, mortality and survival, to evaluate the effectiveness of screening and other cancer control policies is one of the best known and established traditions of health services research. A simple way to ensure that the molecular research conducted is optimally relevant for the health services, is to ensure that the biological research materials used in the molecular analyses are always linked to real-life health services data, such as population-based cancer registry data. This will not only enable characterisation of the development of disease end-points, but will also allow inferences about generalisability of studies [1].

3. Cohorts: research infrastructures for studies of health, disease aetiology and early diagnosis

Cohort studies aim to provide a reliable study base for studies of risk factors for the diseases that affect a population. Basic information about the diseases affecting the population and the risk factors that cause these diseases is the foundation for planning of preventive services. A large number of healthy volunteers in the population are asked about living conditions and life-style (such as diet, exercise, smoking and other habits), asked to donate a series of biospecimens and are then followed-up longitudinally (especially using cancer registry linkages) to determine whether they develop diseases or not. While it is well known that most cancer is caused by factors in the environment, only a minority of these factors are known. There is an increasing interest in using cohort studies with comprehensive collection of data and molecular analysis of biospecimens to identify these potentially preventable factors. The approach was well known already >30 years ago [2]. In addition to the study of disease aetiology, cohorts are immensely useful for health-related research in many other areas such as the impact of screening, quality of life of cancer patients and so on.

The building of cohorts with associated biospecimens has boomed in recent years, concomitantly with the emergence of effective and comprehensive molecular analysis resources for analysis of biospecimens. The Public Population Projects in Genomics and Society (P3G) (www.p3g.org) has a global cohort observatory that lists no less than 15 international cohort networks and 79 individual cohorts (Table 1). Many of these cohorts are extremely well funded, the most well-known example being the National Children's Study, a 200 million USD/year cohort that studies pregnant women and their children in order to identify causes of healthy childbearing and children's development (www.nationalchildrensstudy.gov).

The largest among the comprehensive cohorts is the European prospective cohort EPIC, which is designed to investigate the relationships between diet, nutritional status, lifestyle and other environmental factors and the incidence of cancer and other chronic diseases (www.epic.iarc.fr). EPIC recruited over half a million (520,000) people in ten European countries: Denmark, France, Germany, Greece, Italy, The Netherlands, Norway, Spain, Sweden and the United Kingdom. Recruitment was initiated in 1992, principally from the general population aged 20 years or over. Detailed information on diet and lifestyle was obtained by a questionnaire, and anthropometric measurements and blood samples were taken at recruitment. Blood aliquots from most donors are stored in liquid nitrogen at a centralised, international biobanking facility at the International Agency for Research on Cancer (IARC) for future analyses.

4. Why do we need biobanks?

Collections of human biological specimens are essential both for cancer research and clinical diagnosis. The development of high-performance molecular analysis platforms has resulted in that the prime bottleneck for translation of the advances in basic research to cancer control is not the molecular testing, but access to well characterised specimens with associated follow-up data.

The main advantage of biobanking is *not* merely that scientists do not need to collect samples again, when samples are already available. The main advantage of biobanking is that it is possible to obtain a very long longitudinal follow-up on health outcomes without having to wait. In other words, a translational research

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