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Public Health in an Age of Genomics

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FOREWORD

This report presents the findings of a research project to investigate the drivers and criteria shaping the application of genomic biotechnology to health in different national settings, and the barriers to implementation nationally and internationally. The research was conducted under a joint project of the OECD Working Party on Biotechnology and the UK-based ESRC Genomics Network, on “Personalised Medicine and Global Public Health”.

A case study approach was adopted for the project, the survey work being undertaken over the summer of 2012. The case studies focused specifically on the application of genomics to stratified medicine – i.e. the use of genomic and other information to identify those sections of the population that are likely to respond particularly well or badly to a given medical intervention – and to infectious disease control in each country. The findings are based on the active participation in the survey of seven self-selected countries, including both OECD member and non-member countries (Finland, Israel, Luxembourg, Mexico, the United Kingdom, China and South Africa).

The report outlines a number of potentially important patterns that are seen to emerge when the country case studies are set alongside one another and viewed in transnational perspective. The data, albeit based on limited evidence from a small sample of countries, suggest a significant divergence in the way that different countries are tending to adopt genomics for public health, which may have important implications for thinking about how genomic science and technology might best be employed in the interests of global public health.

The Committee for Scientific and Technological Policy (CSTP) agreed to the declassification of this report in May 2013. The report is published under the responsibility of the Secretary-General of the OECD.

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EXECUTIVE SUMMARY

This report presents the findings of a small research project, jointly conducted by OECD and the UK-based ESRC Genomics Network, to investigate the drivers and criteria shaping the application of genomic biotechnology to health in different national settings, and the barriers to implementation nationally and internationally.

The research was conducted over the summer of 2012 in seven self-selected countries, including both OECD member and non-member countries, and focused specifically on the application of genomics to stratified medicine – i.e. the use of genomic and other information to identify those sections of the population that are likely to respond particularly well or badly to a given medical intervention – and to infectious disease control in each country. A case study approach was adopted, with the aim of capturing the different ways in which genomic science and technology are being pursued for public health purposes in each of the different national settings. Rather than attempt to impose, *a priori*, a strictly comparative approach on this small and potentially unrepresentative sample, transnational patterns were identified inductively from the case studies in the course of data analysis.

The report outlines a number of potentially important patterns that are seen to emerge when the country case studies are set alongside one another and viewed in transnational perspective:

- While the application of genomics for the development of stratified medicine remains predominantly a research field, with relatively few actual examples of successful implementation to show to date, the use of genomics more broadly for infectious disease control is already yielding significant public health benefits, both in terms of the ability to diagnose and track the movement of infectious disease outbreaks and in terms of the ability to enhance and accelerate the production of effective vaccines.
- There appear to be significant differences of priority between higher income countries, which have already completed the epidemiological transition, and which are motivated primarily by the promise of stratified medicine as a means of addressing their growing burden of chronic disease, and lower and middle income countries, which tend to concentrate more heavily on efforts to control the infectious diseases that still beset them.
- It is generally agreed that international collaboration in both research and implementation is essential if the full potential of genomics for infectious disease control both nationally and globally is to be realised. By contrast the development of stratified medicine tends to be seen as primarily a national issue, with international initiatives in this area directed towards fostering an appropriate regulatory and economic environment supportive of national innovation.
- Consequently, richer countries, with their tendency to prioritise stratified medicine, are less dependent on, and less inclined to seek, international collaboration than low and middle income countries with their greater stress on genomics for infectious disease control.

- The benefits of stratified medicine are likely in many cases to be realised within more or less local genetic populations, and so will be felt chiefly on a national or regional basis. By contrast, infectious diseases pose potentially global threats, and the benefits of genomics for infectious disease control may therefore be felt on a global as well as a local scale.
- So far as the development of genomics for public health is concerned, it thus appears that the kind of work most likely to be of global benefit is being prioritised chiefly in low and middle income countries, which possess only limited resources to pursue such work, and which face other heavy demands on such resources as they do possess. Meanwhile, richer countries appear more inclined to invest in lines of genomic research and development that orient them chiefly towards domestic matters, and that provide less incentive to collaborate internationally in research and implementation.

It must be stressed that these findings, based as they are on limited evidence from a small sample of participating countries, are necessarily tentative and provisional. Also, the findings represent only a snapshot of a rapidly developing field, as of summer 2012. The situation in many of the participating countries will almost certainly have moved on by the time this report is published. Bearing in mind these caveats, however, the data nonetheless suggest a significant divergence in the way that different countries are tending to adopt genomics for public health, which may have important implications for thinking about how genomic science and technology might best be employed in the interests of global public health.

PUBLIC HEALTH IN AN AGE OF GENOMICS

Introduction

The pursuit of public health is an important economic, scientific and social endeavour for all countries. Governments recognise the links between health, economic productivity and national prosperity and have long had an interest in developing policies and programmes to improve the health of their citizens.

The way governments conceive of public health has evolved over time, and continues to evolve in the context of different national and international factors. Social and technological developments have led to changes in patterns of health and illness domestically and globally. In the richest economies, increasing standards of living and improvements in preventive and curative medicine have led to a massive decline in the incidence of infectious disease, and to an equally dramatic increase in the morbidity and mortality due to chronic disease. In some emerging economies and developing countries, the continuing burden of infectious disease has been compounded by the rising problem of chronic disease attributable to socioeconomic changes, including the introduction of western-style diets. Meanwhile, greater mobility has increased the spread of infectious diseases across oceans and facilitated global pandemics such as influenza and SARS that threaten developed as well as developing countries.

At the same time, knowledge of the causes, prevention and treatment of both infectious and chronic disease has expanded rapidly, with profound consequences for the organisation and effectiveness of public health policy and practice. Now, we find ourselves in the midst of yet another transformation in biomedical science. The first decades of the current century may well be remembered for the advances occurring in genomics and in associated areas of science and technology. These advances promise new understandings of disease and more effective ways of tackling ill health. Under the right conditions, they have the potential to transform innovation in biomedicine and healthcare. They may also be changing the ways in which countries conceive of and seek to practice public health.

These developments are of immediate interest to the OECD, and especially its Working Party on Biotechnology. The 2009 OECD report on *The Bioeconomy to 2030: designing a policy agenda* argued that growth of the bioeconomy has the potential to create economic and social benefits for OECD and non-OECD countries in the next generation. The report identified health and the delivery of healthcare as key factors in the bioeconomy, and identified a number of ways in which the application of biotechnology is expected to improve health outcomes. In order to inform policy in this area the OECD needs to understand the drivers and criteria shaping the application of biotechnology to health in different national settings, and the barriers to implementation nationally and internationally. Consequently, as a first step towards generating such understanding and as part of its Programme of Work and Budget 2011-2012, the Working Party on Biotechnology decided to undertake a research project on Public Health in an Age of Genomics, jointly conducted by the OECD and the ESRC Genomics Network. This report outlines the project and its findings.

Methodology

Initial discussion of the overall aims and methods of the project, involving representatives of the ESRC Genomics Network and the OECD Secretariat took place between December 2011 and January 2012. At this point, two key methodological decisions were taken.

First, it was agreed that, in view of the limited resources available to conduct the necessary research, it would be difficult to design and undertake a systematic comparative survey of genomics for public health in different countries. In addition, given the lack of existing knowledge about how the role of genomics for public health is understood in different countries, it was decided that it would potentially be counter-productive to determine in advance the dimensions along which such a comparison might best be conducted. Consequently, it was agreed that the project should adopt a case study approach, looking at a number of OECD member and non-member countries to determine how genomic science and technology are being pursued for public health purposes in different national settings. Data collection should therefore proceed through circulation of questionnaires employing a series of open-ended questions allowing respondents to present their views on the drivers and criteria shaping application of genomics to public health and the barriers to implementation that they faced in their respective national settings. Data analysis would then proceed inductively, to build up a picture of how each country was responding to these drivers and barriers in light of its particular socioeconomic circumstances, and to identify, if possible, international patterns of opportunity and constraint of relevance to OECD policy.

Secondly, in view of resource limitations, it was agreed that responsibility for data collection should be devolved to the participating countries. In order to understand how genomics is being adopted for public health purposes in different socioeconomic settings, the project would aim to include a range of countries including OECD members, countries that are not members of OECD but are represented on the Working Party on Biotechnology, and others. Countries would be invited to participate by the OECD secretariat, and data collection in each country would be managed by a country co-ordinator, who would be a member of the OECD Working Party on Biotechnology or, where the country was not represented on the Working Party, an expert identified by the OECD secretariat. Each country co-ordinator would be responsible for identifying six to twelve potential respondents in their own country, who would be individuals well placed to comment on national strategies for promoting genomics for public health. The country co-ordinators would distribute the standard questionnaire to their selected respondents, collect and collate the responses, and forward them to social science researchers at the ESRC Genomics Network for analysis and write-up.

Invitations were issued to a number of countries in March 2012. Initially nine countries agreed to participate, but subsequently two countries pulled out on grounds of lack of resources at a time of global economic down-turn. The seven remaining countries were Finland, Israel, Luxembourg, Mexico, United Kingdom, China and South Africa. In April 2012, the respective country co-ordinators, along with four social science researchers from the ESRC Genomics Network, formed a project steering committee, supported by members of the OECD secretariat. A full list of the steering committee members is provided in Appendix A.

Meanwhile, a draft of the questionnaire was piloted with respondents from the United Kingdom, and the results presented to a meeting of the steering committee in June 2012. In the light of these results, the steering committee refined the questionnaire to focus on two specific and contrasting areas of genomics for public health that were considered particularly salient to the aims of the study. The first area specified in the questionnaire was stratified medicine, which is the use of genomic and other information to identify those sections of the population that are likely to respond particularly well or badly to a given medical intervention, and to target those interventions accordingly. The second area specified was the use of

genomics for infectious disease control through improved understanding of pathogens and their hosts, and through the use of genomic biotechnology to develop vaccines and other interventions. A copy of the final version of the questionnaire is provided in Appendix B. The questionnaires, along with a number of supporting and explanatory documents, were distributed to respondents by the country co-ordinators in July 2012, and all responses were collated and returned for analysis to the social science researchers at the ESRC Genomics Network by the end of August 2012.

Unsurprisingly, since the country co-ordinators were asking for voluntary contributions from busy professionals, the number of responses varied from country to country, with some countries failing to meet the hoped-for target of a minimum of six responses, while the amount of detail provided by respondents also varied. Moreover, it was recognised from the beginning that, given the limited scale and scope of the study and the nature of the methodology adopted, caution would need to be exercised when interpreting the results. The participating countries were self-selected and small in number, while the inductive case study methodology meant that we could not expect, *a priori*, that we would be able to generalise from one country to another. Within each country, moreover, the respondents were recruited through the country co-ordinators' personal networks, so cannot be assumed to represent an unbiased or definitive view of the situation in that country. Given these constraints, however, it was hoped that the data collected would be sufficiently rich not only to provide a snapshot of the state of genomics for public health in each country, but also to allow some suggestive patterns to emerge when all the countries are seen together.

A summary report of the key findings was presented to the OECD Global Forum on The Evolving Promise of the Life Sciences in Paris, 12 November 2012 and the full report was prepared for submission to OECD in December 2012. The findings are outlined in the remainder of this report. First the findings from each of the country case studies are presented individually, with the aim of representing the rather different ways in which each of the participating countries is experiencing and responding to the various drivers and barriers that confront the application of genomics for public health. The next section outlines what is seen as a number of potentially important patterns that emerge when the country case studies are set alongside one another and viewed in transnational perspective. Finally some general if tentative conclusions are given about the rather different priorities that drive the application of genomics for public health in more and less developed countries.

FINDINGS FROM THE COUNTRY CASE STUDIES

Finland

Stratified medicine

It would seem, from the responses received, that there is a high level of satisfaction in Finland with initiatives to promote research into stratified medicine. Respondents wrote favourably of strong national co-ordination of research infrastructure, including strategic funding for research, the development of effective IT systems within the health care sector, and considerable interest and investment in biobank and biomarker research. In part, this builds on an established tradition of public health research into risk factors for chronic disease: three respondents commented on the 40-year prospective cohort study of risk factors for chronic disease being undertaken by the National Institute for Health and Welfare, including collection of DNA samples for genotyping and eventual sequencing, with a view to linking genomic information with long-term health data. Another noted that the Finnish Institute for Molecular Medicine (FIMM) currently hosts the country's first cancer biobank, while further biobank infrastructure is being implemented for disease- and population-based tissue and collections. Six respondents expressed strong hopes for the new national law on biobanking, which is expected to come into force early 2013, and one identified the growing biobank network centred on FIMM as a major success of national initiatives for stratified medicine. Respondents expressed a hope that such work would be further extended, including establishing additional population and patient biobanks and initiating a project for a first-generation Finnish genome reference database.

Respondents also indicated a strong national commitment to clinical and translational as well as basic research in Finland, with investment in infrastructure, organisation and funding for personnel. FIMM, in particular, was seen as undertaking translational research aimed at producing new treatments for cancer. Collaborative translational research networks were seen to extend beyond FIMM to connect with academia, industry and clinical facilities, including hospital-based molecular diagnostic services where novel genetic tests are being developed from molecular genetics research findings, and in some cases from second-generation sequencing technology used to analyse patient samples. Respondents attributed considerable success to research in this area, including the identification of biomarkers used in diagnosing and screening for hereditary cancers, improved cancer diagnostic services, novel and effective cancer treatments and other improvements in cancer care, as well as increased understanding of genetic risk factors for cardiovascular disease. Here too, respondents saw opportunities to extend this work further to include other tumour types and to participate more fully in national and European cancer networks.

Respondents were more cautious when considering the extent to which such research had influenced medical practice and ultimately public health. Three respondents commented that it was too early to observe significant success in terms of improving public health, though two of the three noted that the results of biomarker discovery were "very promising", particularly in relation to cancer screening and diagnostics. A fourth respondent observed that the main success of work in this area had been "to demonstrate, with a limited patient group, the feasibility and possibilities of personalised care". There was some doubt about whether enough is being done to implement such possibilities in practice, however. In

response to the question “What policy initiatives and actions have been taken in your country to implement stratified medicine?” most respondents cited significant basic and translational research initiatives. By contrast, three respondents from the fields of healthcare provision, public health research and public health policy, declared that they did not know of any such initiatives – by which it appears to mean that they knew of no initiatives concerned with implementing stratified medicine, as distinct from research. Two of these respondents added that some research initiatives are at least partly conducted with a view to eventual implementation, but evidently see this as secondary to the main research orientation.

Our respondents identified three different kinds of drivers for work on stratified medicine in Finland. One cluster of perceived drivers – identified especially by respondents working in public health policy and health research – focused on expectations that stratified medicine would deliver significant efficiencies in the cost and effectiveness of health care through targeted delivery of “personalised medicine” and avoidance of adverse drug reactions. Three of our respondents noted that this was particularly important in a context of rising health care costs and an ageing population, while one respondent noted that Finland possessed an “optimal size of population to implement stratified medicine cost-effectively”.

The second cluster of perceived drivers, emphasised mainly by respondents who are involved in research, focused on research interest and opportunities. Three respondents, all from research laboratories, cited new technological developments including advances in sequencing technology, automation and bioinformatics. Two respondents stressed the importance of new technologies, and more importantly the data they generate, for clinical research including stratified clinical trials; while two other respondents emphasised the peculiarly favourable opportunities for stratified medicine research in Finland, due particularly to the availability of comprehensive health records including patient and demographic registers. The third cluster of perceived drivers, mentioned by three respondents, focused on commercial interest and anticipated business opportunities, with one respondent going so far as to suggest that stratified medicine research should include “Steps to boost demand in addition to supply side stories”.

In considering barriers to the development of stratified medicine in Finland, respondents showed little dissatisfaction with basic research capacity or strategy, although four respondents pointed to a lack of bioinformatic personnel and infrastructure. The main focus of concern, however, was with perceived difficulties in the articulation of basic research with clinical research and implementation. Three respondents pointed to a lack of funding for proof-of-concept research and for implementation; while a further three noted that funding for implementation was generally considered to be the responsibility of the commercial sector, but was inhibited by the poor return on stratified diagnostics and by an unfavourable reimbursement system for stratified treatments. One respondent also suggested that the absence of an indigenous pharmaceutical industry is a barrier to implementation. To overcome such barriers, respondents proposed a variety of solutions including additional investment in translational research and infrastructure, efforts to improve the participation of hospitals in clinical studies, and financial incentives to encourage diagnostics companies to work with the pharmaceuticals industry to develop companion diagnostics.

A number of respondents also identified regulatory barriers to the development of stratified medicine in Finland, including the slow pace of drug approval procedures, restrictions on off-label use of drugs for research purposes, and difficulties in demonstrating treatment effects in small patient populations. Solutions to such problems were chiefly seen to lie at the international level. In particular, respondents called for improved collaboration between Finnish national authorities and the European Medicines Agency (EMA), particularly around regulation of new diagnostics, and through involvement in the EMA Innovative Medicines Task Force. Two respondents mentioned intellectual property issues as important, with one calling for the maintenance of a strong European patent regime, and another for more complementary and parallel IP systems between countries and continents. Another suggested that common international legislation on biobanking would help to facilitate developments in Finland.

Apart from regulatory matters, however, Finnish respondents did not on the whole see any need for new international initiatives to promote stratified medicine in their own country. At the level of research, a number of respondents noted that Finland is already involved in a range of international biomedical research collaborations and networks, with effective means of sharing infrastructure, samples and data. While such collaborations might be strengthened, they did not pose a major barrier to continuing development. Indeed, when attention turned from research to implementation of stratified medicine, the responses became positively anti-internationalist, with three respondents urging that appropriate initiatives for implementation should be focused at the national rather than an international level: “Predominantly this is a matter for each country itself”, as one respondent put it.

That did not mean that our respondents were uninterested in what was happening in other countries. In fact, eight out of the thirteen Finnish respondents referred in one way or another to a need for examples of successful implementation from other countries. However, it appears that they saw such examples, not primarily as models to be implemented in Finland, but rather as a means of persuading Finnish decision makers that stratified medicine was worth supporting and promoting. Respondents were concerned that there was a lack of awareness among politicians, health care professionals and the public about the benefits that might be expected to follow from implementing stratified medicine. Consequently, they called for efforts to identify and disseminate “public success stories” and “concrete examples” from other countries which would “strengthen the view of the overall picture and benefits” of stratified medicine in general. Such examples were not restricted to instances of effective medical innovation; one respondent also called for examples of successful administrative and business models, while another pointed to the United Kingdom life science strategy as an example of a successful initiative. In effect, our respondents saw international comparison as providing ideas and impetus for the implementation of stratified medicine in Finland, while seeking to avoid international interference in domestic control over just how such implementation should be achieved.

Infectious disease control

In contrast to their generally very full responses to the questions on stratified medicine, it was striking just how little most of our Finnish respondents had to say when asked about genomics and infectious disease control. Infectious disease control evidently does not figure prominently in the consciousness of the majority of those who responded to our questionnaire. Asked about policy initiatives and actions to implement genomics for infectious disease control in Finland, three respondents stated that they were not aware of such initiatives, while two observed that while there were no specific initiatives in this area, some relevant provisions are included in other activities such as the National Institute for Health and Welfare. Only three respondents – one from a government clinical laboratory and two from health research – provided any more than the most cursory answers to the remaining questions.

It is unclear whether this represents a realistic picture of the extent of efforts to promote genomics for infectious disease control in Finland, or is simply a consequence of the way that our sample of respondents was recruited. Insofar as efforts are being made to implement genomics for infectious disease control, however, it appears that they are driven by a combination of epidemiological concerns to improve the ease, speed and accuracy of identification of infectious agents on the one hand, and clinical concerns to improve efficacy and reduce the costs of treatment through stratification and targeting on the other. Two respondents noted some success in fulfilling the first of those aims, notably through the statistical database of the National Infectious Diseases Register and through the introduction of new screening technologies for microbial diagnostics. Perceived barriers to implementation included a shortage of trained bioinformaticians, lack of incentives for healthcare personnel to engage in infectious disease work, and slowness in validating clinical tests; while proposed solutions included improved financial and policy support, as well as better international sharing of samples and data, international research collaboration, and active participation in the European Union Innovative Medicines Initiative.

Israel

Stratified medicine

Questionnaire responses from Israel indicated significant levels of activity around stratified medicine across the country's universities and major hospitals. Policy initiatives to support this work include a national institutional review board specialising in "genomic medicine", which deals with ethical approval for all biomedical investigations in this area, from collection of human samples for sequence analysis samples to development and testing of innovative genetic therapies. The National Laboratory for the Genetics of Israeli Populations maintains a biobank of DNA samples from healthy volunteers, while initial efforts are underway elsewhere to collect genomic data on diseases. It appears from respondents' comments that interest in stratified medicine in Israel are not confined to the use of genomic information; respondents referred, for instance, to developments in gastrointestinal internal imaging and to the development of the anti-tumour drug Doxil, use of which is more usually stratified according to clinical rather than genomic criteria. Consequently, it would appear that the adoption of genomics for stratified medicine may still be at a relatively early stage of development.

The main drivers that our respondents identified for work in this area are researcher interest and commercial interest: the questionnaire responses indicated that there are many start-up companies working in this area, as well as projects undertaken by the large Israel-based generic pharmaceutical company TEVA. The principle barrier to development of stratified medicine in Israel, as indicated by questionnaire responses, appears to be scarcity of funding for research and development. In particular, translational research funding is not provided by the Israeli Ministry of Health, and instead is left to industry to support and promote. Respondents suggested that international initiatives could be helpful in surmounting this barrier, for instance if the European Research Council were to provide programmatic funding for translational medicine. Israeli researchers would also benefit from international exchange of ideas and expertise. Additionally, respondents noted that work in this area was delayed by slow approval procedures for phase I clinical trials.

Infectious disease control

Respondents were somewhat more positive in their comments about efforts to promote the use of genomics for infectious disease control. Notably, the Israeli Ministry of Health has recently set up a national advisory committee to undertake a technology needs assessment and options appraisal for the application of genomic technologies, including next-generation sequencing, to advance public health initiatives efforts in the area of infectious diseases. A strategic plan for capacity building, focusing on implementation of NGS platforms and human resource development, is now pending approval. Use is already made of low-throughput sequencing technologies for sequence-based microbial typing and other purposes, while a number of national projects are under way to build on NGS technologies in the fields of healthcare-associated infections, antibiotic resistance, food safety and environmental health.

The main driver for activities in this area was a strong sense that existing and novel genomic technologies are of major value for characterising new and emerging pathogens; for improving epidemiological investigation, mapping and prediction, from local outbreaks to global disease spread; and for relating environmental contamination to clinical infection. The main barrier to further development in this area was seen to be a lack of bioinformatic capacity in the public health sector, including both a shortage of trained bioinformaticians and limited IT infrastructures to support bioinformatics pipelines for public health. Respondents also identified a shortage of dedicated funding for genomic research in public health as a barrier. Insofar as respondents thought that international initiatives would help to promote the development of genomics for infectious disease control in Israel, they saw such benefits arising particularly

from collaborative research and public health networks dedicated to next-generation sequencing and global initiatives for sharing of genomic information.

Luxembourg

Stratified medicine

According to our respondents, the period since 2008 has seen significant public investment in stratified medicine research and development in Luxembourg. This includes the creation, in collaboration with leading United States institutions, of three major programmes aimed at development of molecular diagnostics: the Integrated BioBank of Luxembourg, the Luxembourg Centre for Systems Biomedicine, and a pilot programme to find and validate biomarkers for use in disease management and therapeutic follow-up in lung cancer. In 2010 these and a number of other research programmes were brought together to create the Personalized Medicine Consortium to co-ordinate and support research in the areas of cancer, type 2 diabetes and Parkinson's disease. Respondents also mentioned that commercial development in the area of molecular diagnostics is also promoted through the Luxembourg BioHealth Cluster.

While respondents were enthusiastic about these initiatives, they were careful not to make excessive claims about their impact on public health, with four of the five respondents suggesting that it was too early to draw conclusions in this respect. However, two respondents pointed to promising results from the lung cancer programme, which indicated that genomic analysis of tumours was likely to prove beneficial in guiding therapy; while one observed that a personalised medicine approach was already being implemented in a number of areas including treatment of HIV and prescription of anticoagulants and tamoxifen.

Much of the work in this area is driven, according to our respondents, by a desire to promote innovation in healthcare, to modernise and transform the Luxembourg healthcare system, and to make Luxembourg “a leader in adopting new advances in personalised medicine”. The benefits that respondents expected to accrue from such work include improved safety and efficacy through genomic stratification, leading to reduction in healthcare costs, with the expectation that innovation in healthcare should ultimately be cost-neutral. In addition, one respondent suggested that work in stratified medicine was driven by political expectations that leadership in healthcare innovation would help to bring with it national economic development and growth. Other drivers mentioned by respondents included the role of researchers, the availability of new biobanking and genome screening technologies, and the political power of patient organisations.

Respondents were notably restrained in identifying barriers to the development and implementation of stratified medicine for public health in Luxembourg. Of the checklist options provided in the questionnaire, three of the five respondents ticked “availability of trained personnel”, and two ticked “availability of implementation funding”, “organisation and structures of healthcare provision” and “perceived relevance to local needs”. No respondents ticked “availability of research funding”, “market access/incentives for pharmaceutical and medical technology manufacturer”, “intellectual property regimes” or “ethical concerns”. Asked to provide further information, one respondent commented only that the question about barriers was “not applicable”, while another indicated that barriers to the development and implementation of stratified medicine had been “much alleviated” since the establishment of the Personalised Medicine Consortium two years previously.

However, in responding to other, more open questions on the questionnaire, a number of respondents did go on to identify other barriers, particularly to translation and implementation of research findings into stratified healthcare. Factors mentioned by our respondents included the small size of the country, which limited patient recruitment; a lack of support for clinician scientists, including the absence of a medical

university in Luxembourg; the lack of a mechanism to fund and implement pilot studies of novel innovations in real healthcare settings; the fact that pathology is organised on a national rather than a local level, which makes it difficult to pilot diagnostic innovations; and the lack of an accurate electronic health record system. Two respondents noted that there was no agency within the Ministry of Health with responsibility to champion the introduction of personalised healthcare; and two suggested that research and development are hindered by personal data protection regulations and ethical procedures. Interestingly, one respondent commented that “consumer satisfaction with [the] existing healthcare system means that there is little demand from patients or healthcare providers for change”. Finally, one respondent cautioned against placing “too much emphasis on genomics”; while the advancement of stratified medicine “will necessarily involve genomic medicine... other personalised strategies will have more impact than genomics”.

Suggestions for how to overcome these barriers also focused primarily on how best to achieve translation and implementation of stratified medicine into healthcare, including calls for the creation of a national working group of stakeholders and for funding of pilot projects. Respondents also saw international networking and collaboration, particularly through the European Union, as important. It is notable, in this regard that no mention was made of collaboration in basic research, where Luxembourg is already well integrated into international networks. Rather, collaboration was seen as important primarily as a way of advancing translational work and implementation. As one respondent put it: “International collaboration is always relevant as the country *per se* is too small to evaluate the impact of such approaches.” Respondents accordingly called for enhanced opportunities for international partnerships with clinician-investigators, exchange of best practices, and opportunities to consult with international experts in regulatory affairs.

Infectious disease control

This generally positive assessment of what Luxembourg is doing to promote stratified medicine contrasted quite markedly with respondents’ views about initiatives to promote genomics for infectious disease control. Like their Finnish counterparts, the majority of Luxembourg respondents showed a striking lack of knowledge of work in this area, with four of the five respondents saying they were unaware of any relevant policy initiatives, while the fifth did not answer any of the questions in this section of the questionnaire. One respondent did note that genomic research into retroviruses is on-going at the *Centre de Recherche Publique de la Santé*, but added that further work is needed to bring this to a point where it can be piloted clinically. Only one respondent offered any insight into this situation, observing that the main barrier to promoting genomics for infectious disease control in Luxembourg is the fact that responsibility for controlling infectious disease in the Grand Duchy rests exclusively with the *Laboratoire National de Santé*; it would appear that, in this instance at least, institutional separation of infectious disease control from other elements of the healthcare and biomedical research system may seriously impede innovation in this area. Two respondents suggested that international collaboration might help to overcome such barriers, but offered no specific recommendations for how to achieve this.

Mexico

Stratified medicine

Turning now to Mexico, our respondents noted a number of basic research initiatives under way in the field of stratified medicine. These include the National Institute of Genomic Medicine, established in 2004, where high-throughput technology has been adopted to support research on-going in laboratories around the country, as well as programmes supported by the Foundation Carlos Slim for Health and the Mexican Association of Medical Schools. Key successes have been the sequencing of the Mexican Genome, as well as basic research into the genomics of the Mexican population, resulting in a major biobank containing

diverse human genetic material. Researchers have also produced valuable findings regarding genomic aspects of diabetes, high blood pressure and some types of cancer.

As in other countries, rather less has been achieved in terms of translating and implementing these research findings into medical practice. One respondent mentioned that there has been some success in rolling out detection of breast cancer genes, while another observed that there is optimism regarding the development of potential new drugs. However, three of the seven respondents indicated that it is as yet too early to talk of successful implementation of stratified medicine, while one stated that “actually the stratified medicine is unknown for many health care personnel in Mexico”. Another respondent suggested that the main achievement of the government to date has been the establishment of regulation to govern clinical innovation and implementation, rather than any success in implementation itself.

Regarding the drivers behind the efforts to develop stratified medicine in Mexico, two of our respondents identified research interest, including the creation of the National Institute of Genomic Medicine, as the most important factors. Three referred to expectations that innovations in stratified medicine will bring health benefits, and ultimately economic benefits, by making possible earlier diagnosis, better prediction, improved control of drug response and more effective treatment, particularly for diseases such as diabetes and renal failure that impose significant strain on the Mexican health system. One respondent also mentioned the role of private pharmaceutical manufacturers as a driver for stratification of diagnosis and treatment.

Respondents also identified a wide range of barriers to development of stratified medicine for public health in Mexico, with at least two respondents ticking each of the items on the questionnaire checklist of potential barriers. The leading candidates, however, were “availability of research funding” and “availability of implementation funding”, each ticked by six of the seven respondents and “availability of trained personnel”, ticked by five respondents. “Organisation and structures of healthcare provision”, “lack of bioinformatics or other infrastructure”, “national/international regulatory regimes” and “market access/incentives for pharmaceutical and medical technology manufacturers” each received four ticks. In answer to the more open-ended questions, one respondent noted that Mexico’s small biomedical research community, though highly skilled, tended to focus on basic research and was poorly connected to medical applications; while another suggested that the Mexican research system is rather conservative and hence inhospitable to innovative younger researchers and interdisciplinary initiatives. Translation and implementation, meanwhile, was seen by a number of respondents as particularly problematic, not least because of the under-development and inaccessibility of the basic health services.

Respondents accordingly made a wide range of recommendations for initiatives that would help to overcome these barriers. While some focused primarily on promoting specific research programmes, for instance into variation in drug response among Mexico’s different genetic populations, most were more concerned with the need to build an effective national research and innovation system, ranging from support for basic research technology platforms such as the creation of a national network of biobanks, through promotion of commercial involvement in stratified medicine development and closer engagement with medical research and training, to health system modernisation, legislative reform and the promotion of effective governance and commercialisation structures to facilitate innovation. International collaboration in research and implementation was mentioned by six of the seven respondents as a means of improving access to technology and expertise, creating opportunities for commercialisation, and consolidation of domestic research and development capacity. The need for international assistance to address a lack of bioinformatic resources and expertise was mentioned by two respondents, while better integration into international markets and encouragement of domestic entrepreneurial initiative were also seen as desirable.

Lack of awareness and appreciation of the potential benefits of stratified medicine on the part of politicians, medical professionals and the public was also mentioned as a barrier by a number of respondents, who called for efforts to raise awareness among decision makers by supporting demonstration projects in stratified medicine. International collaboration was seen as valuable here too, not least because politicians listen to the recommendations of international organisations, while examples of successful implementation from other countries could be persuasive.

Infectious disease control

Mexican respondents also had much to say about the use of genomics for infectious disease control. Serious efforts are clearly being made to harness genomics for infectious disease control in Mexico, with respondents highlighting research being conducted under the auspices of the National Institute of Genomic Medicine, as well as the more applied epidemiological investigations and surveillance work undertaken by the National Institute of Epidemiological Diagnosis and Referral (INDRE). Acquisition of new sequencing technologies was seen by respondents as an important development in this respect. Four of our seven respondents wrote of the Mexican success, in collaboration with international partners, in quickly sequencing, characterising and developing vaccines for the H1N1 influenza in 2009; while two respondents indicated that similar strategies were being pursued with respect to other pathogens, including antibiotic-resistant *Mycobacterium tuberculosis* and a local drug-resistant form of *Salmonella typhimurium*.

Respondents identified two key sets of drivers for these activities. First, mentioned by three of the seven respondents, is the continuing public health burden of infectious diseases in Mexico, including both local epidemic diseases and the threat of global pandemics. Secondly, Mexico's growing technical capacity in research and disease surveillance, combined with access to new and more effective genomic technologies for identifying and characterising infectious agents, was seen by three respondents as a major driver for public health research and development. Nonetheless, continuing development in this area was seen to face a number of barriers and challenges, as identified in responses to the checklist of possible barriers, with six out of seven respondents ticking "availability of research funding", five ticking "availability of implementation funding", and four ticking each of "perceived relevance to local needs" and "availability of trained personnel".

Asked to elaborate on these barriers and the best ways of overcoming them, respondents identified three general clusters of issues. First, respondents noted a lack of capacity within the existing research system; while Mexico possesses a core of well-trained researchers and physicians, the group is small and needs to be expanded and developed through additional funding and new training opportunities. Respondents also called for more strategic direction of research funding, particularly to focus on diseases of national importance, including Chagas disease and leprosy; while one respondent called for a national biobank network to cover the range of relevant pathogens, including viruses, bacteria and other parasitic diseases, as well as arthropod vectors. Collaboration between research centres, including basic, clinical and applied microbiological research institutions, should also be encouraged. Respondents felt that international co-operation could help to address all these issues, particularly through improved international networking and expansion of training opportunities, as well as through access to international funding sources and collaborative research initiatives.

Secondly, respondents noted significant difficulties with translating and implementing research findings into public health practice. Two respondents proposed organisational remedies, one calling for efforts to promote closer collaboration between research groups in public health and in basic and clinic microbiology, and another proposing the organisation of a network of medical schools to promote teaching and research around new social responses to disease. One respondent commented that research funding and reward structures tend to privilege basic over more practically-oriented research; another stated that neither

government nor the private sector currently funds translational or applied research; while a third suggested that the private sector is insufficiently well organised in Mexico to offer systematic funding for translational research, with problems of market access discouraging international companies from investing in the country. In addition, two respondents observed that there are significant barriers to collaboration between public and private sector institutions, due in particular to inadequacies in the existing framework of intellectual property regulation, which undermine incentives for public-sector researchers to seek co-funding from private sector organisations. On the whole, respondents saw these as primarily domestic issues, which did not require international action. Indeed, one respondent observed that, at the level of disease surveillance, Mexico is already sufficiently well connected to relevant international networks through the National Institute of Epidemiological Diagnosis and Referral, which collaborates with the international United States-based Laboratory Response Network for infectious diseases.

Finally, five of the seven respondents commented in one way or another on what they saw as a lack of awareness and appreciation among policy makers, medical practitioners and the public regarding the benefits of genomic science and technology for infectious disease control. Educational initiatives, public engagement and lobbying of decision makers were all advocated as ways of redressing this deficit. One respondent suggested that efforts should be made to disseminate examples of how genomics has contributed to the fight against infectious disease, while another observed that the Mexican response to the H1N1 pandemic of 2009 had helped to generate new interest in this area of work. Unlike in the case of stratified medicine, however, respondents did not call for any international initiatives to raise consciousness, with the exception of one, from a public health policy background, who suggested that a World Health Organisation declaration on the effective use of genomics for infectious disease control would be valuable.

United Kingdom

Stratified medicine

Turning finally to the United Kingdom, it was evident that respondents had a sense of the United Kingdom as among the world's leading countries in the development of genomic medicine including stratified medicine. On the basic research side, respondents mentioned the considerable investment in the United Kingdom Biobank, as well as the research under way at the Wellcome Trust Sanger Institute, through which the United Kingdom also participates in key international projects including the 1000 Genomes Project and the International Cancer Genome Consortium. Respondents also observed that the UK government has actively promoted translational research and a strategic orientation towards implementing stratified medicine, for instance with the 2003 White Paper *Our inheritance, our future: realising the potential of genetics in the National Health Service (NHS)*, the creation of the Health Innovation Challenge Fund and the Stratified Medicine innovation Platform, and the 2012 report *Building on our inheritance: Genomic technology in healthcare* published by the independent cross-government Human Genomics Strategy Group. The National Institute of Clinical Excellence was also mentioned as facilitating implementation of stratified medicine through the inclusion of companion diagnostics in evidence-based pharmaceutical guidelines. Despite such initiatives, respondents noted that applications of genomics for stratified medicine delivery remain somewhat limited at present. However, they did mention some important innovations, notably in the field of cancer therapeutics, while national audits show an increase in the provision of novel drugs requiring companion diagnostics.

The major drivers for the development of stratified medicine identified by our respondents were the United Kingdom's aging population and rising burden of chronic diseases, and the need to address lifestyle and environmental determinants of ill health. Stratified medicine was seen as helping to address these problems by transforming understanding of the role of genetic variation in disease and enabling more accurate disease classification, diagnosis and targeting of drugs and other interventions. Stratified medicine

was expected to deliver improvements in health and efficiencies in healthcare by contributing to the re-organisation and targeting of public health resources including population-based prevention programmes and health service provision.

In terms of barriers, respondents did not regard basic research funding as a major barrier, though some concern was expressed that this should be maintained through the present economic crisis, particularly to support major cohort studies, which were seen as making an important contribution to international efforts to develop understanding of the role of genetic variation in disease. Further development of informatics platforms was also seen as essential to preserve and interpret the increasingly large volume of complex genomic data and to enable the use of those data by researchers, clinicians and the wider public. Respondents were less sanguine about the lack of funding for translational research and implementation, which they argued needs to be significantly increased. In addition, they suggested that there is an increasingly urgent need to expand and augment existing programmes to prepare the NHS for the delivery of stratified medicine through strategic service development, training of genetics specialists, and increased knowledge of genomics among healthcare professionals more generally. Primarily, however, respondents' concerns focused on domestic barriers and responses, and they had less to say about the need for international action to promote the development of stratified medicine. Only one respondent noted that the development of stratified medicine depends on studies conducted across large population cohorts, and argued that more should be done to enable researchers in different locations to share data and link datasets. The same respondent also noted that international harmonisation of policy and practice between countries is needed, while allowing for differences in domestic laws and taking account of differing social contexts.

Infectious disease control

In the United Kingdom the Health Protection Agency (HPA) is responsible for monitoring and tracking infectious diseases and developing processes and policies for control, intervention and prevention. Respondents noted that the HPA works closely with academic partners to advance the use of genomics in a number of high-profile research programmes, including research into pathogens using whole-genome sequencing at the Wellcome Trust Sanger Centre and other centres in the United Kingdom. Such collaborative work also has direct public health applications, and respondents cited a number of examples, including the use of whole-genome sequencing to elucidate the origin and cause of an outbreak of a novel strain of *E.coli* in Germany in 2011, and improvements in contact tracing and screening of communities who may have been exposed to tuberculosis. The HPA is actively developing a strategy for investment and implementation of genomics in relation to a number of key priority infections, as well as creating frameworks for implementation and developing exemplars of effective cross-agency working.

Respondents also noted that there is substantial genomic research under way in the United Kingdom into the causative agents of diseases of particular relevance to low and middle income countries. The Sanger Centre, in particular, is involved in various international as well as large national projects, for example jointly leading a project funded by the Bill and Melinda Gates Foundation to evaluate the effects of vaccination in pneumococcal strains from across the world. The Sanger Centre is also involved in the international Malaria Genomic Epidemiology Network, which seeks to understand how genome variation in human, mosquito and *Plasmodium* populations affects the biology and epidemiology of malaria, and to use this knowledge to develop improved tools for controlling the disease.

According to our respondents, the factors driving the development of genomics for infectious disease control included the growth of antibiotic resistance among infectious agents and the resurgence of hospital-acquired infections. The new technical possibilities provided by genomic technologies, including the increasing availability and affordability of whole-genome sequencing, were also identified as powerful drivers in this regard. In particular, respondents mentioned the unprecedented power of whole genome sequencing to distinguish different strains of disease agents, which is already transforming surveillance and

tracking of disease outbreaks and shedding light on the evolution and spread of antibiotic resistance, as well as the expectation that new genomic technologies offer new and more efficient methods for developing vaccines against a wide range of infectious agents.

Respondents also identified a number of barriers to further developments of genomics for infectious disease control. One significant barrier was seen to be the availability of implementation funding. Funding has been directed through the HPA towards a number of exemplary initiatives, and steps are being taken by the Health Innovation Challenge Fund (HICF) to target translational research in this area. But informants noted a reluctance to invest on a large scale in technological platforms that they fear might rapidly be superseded, and suggested that this is hindering the diffusion of technologies such as whole genome sequencing from major academic centres into mainstream public health laboratory practice. Shortage of trained personnel was also identified as a significant barrier, particularly in the areas of sequencing, bioinformatics and the ability to extract practically meaningful information from large amounts of analysed data. Respondents accordingly called for the creation and implementation of a coherent strategy for establishing appropriate IT and data handling infrastructure, training and retention of core staff to support that infrastructure, and commitment across academic and public health bodies to make effective use of it. This should include a concerted effort to establish and make accessible historical archives of phenotypic and genomic data and associated information.

Internationally, respondents noted that effective characterisation of the agents responsible for epidemic and pandemic outbreaks often requires accumulation of a critical mass of data not just on a national but on a global scale, which in turn requires both national and global funding and collaboration. However, it is notable that respondents spoke, in effect, from a position of perceived leadership in the promotion of international collaboration. Thus one respondent observed that the development of international disease surveillance networks depends on all partners having access to the same technologies, which inevitably limits development to the pace of the slowest members. For another, the problem was chiefly one of economic under-development: “There undoubtedly needs to be a continued focus on ensuring the technologies of genomics are applied to diseases which primarily affect the world’s poor, and continued investment in public-private partnerships and other mechanisms to ensure that resulting health applications can be developed and delivered to those where traditional economic drivers don’t exist.” Respondents from the United Kingdom evidently felt a sense both of frustration and of responsibility in confronting the barriers that global inequality pose for the development of genomics for infectious disease control.

China

Stratified medicine

It was clear from the responses to our questionnaire that research into human population genomics and the identification of health risk genes has grown enormously in China over the past decade or so. In particular, respondents mention the National Infrastructure for Chinese Genetic Resources (NICGR), which since its launch in July 2003 has seen the establishment of twenty-seven biobanks and databases comprising normal subjects, sub-optimally healthy subjects, and patients with a range of major chronic diseases. A number of respondents also referred to other initiatives being pursued by the Ministry of Science and Technology and National Natural Sciences Foundation, including the Centre for Bioinformatics at Peking University. Though such initiatives are still largely confined to basic research, this growth in R&D capacity was itself seen by a number of our respondents as a major success in efforts to promote stratified medicine in China, and evident pride was taken in the rate at which light is being thrown on genetic and epigenetic risk factors in a variety of diseases.

Our respondents had less to say about initiatives to translate and implement stratified medicine into practice, though mention was made of developments in tumour diagnosis and treatment, and of the rolling-out of new-born and (in some urban centres) prenatal genetic screening for a range of conditions. On the manufacturing side, respondents referred to China's efforts to promote industrialisation of genome-based medical technologies, especially through the National Engineering Research Centre for Biochips in Shanghai; while two respondents observed that Merck Serono had opened a research centre in Beijing in 2011, signalling the growing involvement of multi-national pharmaceutical companies in pursuit of stratified medicine in China.

Asked about the drivers for the development of stratified medicine in China, our respondents focused overwhelmingly on anticipated health benefits. However, their view of those benefits was strikingly individualised, with the majority (seven out of eleven) of our respondents referring to expectations that stratified or "personalised" medicine would bring improvements to the care of individuals through enhanced medical safety and efficacy, while only one respondent suggested that benefits would also be seen at the population level, with stratified medicine contributing to the "pursuit [of] a more healthy nation". One respondent mentioned "The increasing demand of the people [for] health" as a key driver, while another suggested that stratified medicine would contribute to a market approach to medicine by creating "positive net economic value for the drug developer".

Given the rapid growth in the technical capacity for research in human genomics in China, particularly the expansion of biobanking facilities, it is perhaps surprising that our Chinese respondents scarcely mentioned advances in science and technology as a driver for stratified medicine, with only two respondents seeing this as a relevant factor. Interestingly, two respondents alluded to cultural factors that might also be driving the science and implementation of stratified medicine, one linking the growth of human genetic biobanks with efforts "to protect the genetic resources of our country", and another noting that stratified medicine is consistent with the attention to the constitutional type, health status, age and gender of patients that is central to traditional Chinese medicine.

Asked to select from a range of potential barriers to the development of stratified medicine in China, most respondents ticked several of the available options. "Availability of research funding" and "Availability of trained personnel" headed the list, with ten out of eleven respondents ticking the first, and eight out of eleven ticking the second; "National/international regulatory regimes" and "organisation and structures of healthcare provision" came next, with six and five ticks respectively. Of these factors, responses to the more open-ended questions suggested that, despite the rapid advances of recent years, lack of research capacity was foremost in the minds of our Chinese respondents. Six called for more concerted programmes of research into genomics and health in China, including measures to improve professional and academic development in this field. One respondent also emphasised the need to extend research initiatives from existing centres of excellence to include other parts of the country, with training and mentoring networks and measures to promote the kinds of "standard design, technical methods, work protocols for research" that would facilitate co-ordination and data-sharing between different centres.

Support for research also dominated respondents' views of what kind of international action could help to promote the development of stratified medicine in China. Ten out of eleven respondents called for some combination of international research funding, research collaboration, and research training, with six of these stressing a need for assistance in training scientific and technical personnel – reinforcing the view that Chinese respondents were primarily concerned with the need to develop the national research capacity. In addition, one respondent called for international collaboration in collecting and analysing samples from common cancers, and another wrote of a need to "Encourage foreign medicine enterprises into China".

It was notable that, in contrast to their emphasis on the need for greater basic research capacity, Chinese respondents said very little about a need for translational research or implementation of stratified

medicine, with only two making any reference to the need to translate work on genetic risk factors into new diagnostics or treatment pathways. Two respondents also identified a need to expand provision of personal medical services and improve the general standard of training of healthcare professionals if stratified medicine was to be implemented effectively. Finally, a single respondent (from a public health policy background) identified a need to build relevant industrial capacity in China, meaning not just biotechnology in the narrow sense of the word, but also allied developments in information technology and research instrumentation. The same respondent also called for improved intellectual property regulation to protect Chinese patents, but was the only one to do so; despite several respondents selecting “National/international regulatory regimes” from the checklist of possible barriers, no-one else elaborated on what kind of regulation they had in mind.

Infectious disease control

In response to questions about the development of genomics for infectious disease control, Chinese respondents reported a wide range of activities around the genomics of infectious agents. At the more basic end of the research spectrum, these included mapping and data-basing the genomes of various pathogens, studies of microbial evolution and genomic function, and research into pathogen-host interactions and pathogenicity. Much of this work is evidently undertaken with a view to translation and practical application, including the development of new diagnostics, epidemiological surveillance and prediction, the targeting of treatment and the development of vaccines; and respondents recounted a number of practical success stories. Seven respondents wrote of China’s success in developing recombinant vaccines for diseases as diverse as hepatitis B, H1N1 influenza and, at a more developmental stage, HIV; while Chinese efforts to characterise and chart the evolution of the SARS outbreak in 2003 were mentioned by three respondents. These activities appear to be spread over a number of research and development centres, but respondents noted that work on pathogen characterisation and surveillance is supported and co-ordinated by the Ministry of Science and Technology and Ministry of Public Health, while one respondent singled out the foundation, in 2005, of the National Institute of Diagnostics and Vaccine Development at Xiamen University as an important step in building China’s research and development capacity in this area.

Infectious disease, including both endemic and emerging infections, was plainly seen by our respondents as representing an urgent and perhaps increasing public health challenge in China; one respondent even suggested that transmission of infections had been exacerbated in recent years by high rates of migration from rural to urban centres. Concern to address the problems of infectious disease was frequently cited as a key driver for genomic research and innovation in this area. This was reinforced, moreover, by international initiatives, with one respondent referring specifically to the impetus that WHO’s Expanded Programme on Immunisation had given to vaccine development efforts within China. Seven researchers also identified advances in relevant science and technology, including bioinformatics, microbial functional genomics and high-throughput gene detection techniques as important drivers, while one respondent mentioned the growth of networked laboratory surveillance of disease outbreaks.

Respondents’ views of the barriers to development of genomics for infectious disease control largely mirrored their views on stratified medicine, with “Availability of research funding” and “Availability of trained personnel” again heading the list of options ticked from the checklist. Responses to the open questions also indicated that research capacity was a crucial limiting factor. As with stratified medicine, most respondents did not distinguish between basic research and translational or implementation work, though two did comment on the need for more translation of research findings into practice. More pressing, it seems, was a sense that developments in genomic science and practice remain concentrated in major urban centres, with two respondents commenting on the difficulties of extending the scientific capacity for infectious disease control from key centres to the rest of the country. For one of these respondents, the issue was primarily one of uneven economic development across urban and rural centres. For the other,

however, investment in “innovative, cost-effective approaches that are compatible with the existing health-care system in both urban and rural areas – e.g. rapid diagnostic tests that can be used widely”, backed up by further training of personnel and support for scientific infrastructure, offered a means of addressing this problem.

As with stratified medicine, respondents saw international collaboration as a valuable means of helping to build China’s indigenous research capacity, both by providing training opportunities and by providing access to new research technologies and methodologies – though one respondent cautioned that it was necessary “to adapt cutting-edge technologies to the realities of our country’s laboratories”. But it is worth noting that Chinese respondents also saw the benefits of collaboration around infectious disease control as flowing in both directions – not just into China, but outwards to the rest of the world. Thus two respondents pointed out that infectious disease control is not merely a national concern but has international and global implications, and that consequently, as one respondent put it, “an integrated global approach is necessary to understand transmission and evolution of infectious disease agents”. International co-operation and exchange would thus benefit not just China, but would contribute to the work of infectious disease control in an international context.

South Africa

Stratified medicine

It was noted above that respondents from some countries – notably Finland and Luxembourg – had much to say about the development of genomics for stratified medicine, but little about infectious disease control. In the case of South Africa, this pattern was reversed. South African responses to the sections of the questionnaire that asked about stratified medicine were very brief compared to those relating to control of infectious diseases. Moreover, insofar as South African respondents answered questions about stratified medicine, they referred solely to initiatives aimed at the characterisation, diagnosis and treatment of infectious conditions, in particular sexually transmitted infections. No mention was made by our respondents of any other area of stratified medicine development. Consequently, we conclude that, at least as seen by our respondents, medical genomics in South Africa is devoted more or less exclusively to work on infectious disease control, and we accordingly discuss it under that heading alone.

Infectious disease control

At a national level, respondents noted that the development of medical genomics in South Africa has been facilitated by the adoption of a national strategic road map for health and biotechnology, and more generally by policy documents including the National Strategic Plan and the Innovation Plan of the Department of Science and Technology. Additionally, the Biotechnology Advisory Committee has recommended the creation of several Regional Innovation Centres to facilitate the development of new biotechnology platforms. Respondents also discussed a number of institutional initiatives in which genomic science and technology were being employed to assist specifically in the identification and tracking of infectious disease agents. Sexually transmitted infections figured prominently in the responses, particularly the work of the HIV/STI Centre of the National Institute of Communicable Diseases (NICD), which uses genotyping technologies to map HIV infection within South Africa and in some neighbouring countries. This includes conducting HIV surveillance for the National Department of Health and the South African National Blood Transfusion Services, and tracking the development and transmission of drug resistant forms of HIV. The HIV/STI Centre also employs sequencing technologies to contribute to the development of vaccines against HIV, and studies host genetic markers associated with protection from HIV-1 infection or with attenuated or more rapid HIV-1 disease progression. Elsewhere in South Africa, molecular diagnostics are used to study the epidemiology of gonorrhoea, particularly multi-drug-resistant strains of the disease.

Respondents also pointed to important work on other infectious diseases besides STIs. The NICD's Centre for Respiratory Diseases and Meningitis employs a range of molecular technologies to assist in the surveillance of a number of diseases, including influenza and influenza-like illnesses (ILI) as well as several other vaccine-preventable pathogens, and makes an important contribution to national vaccine planning and decision-making. Similarly, a third NICD institute, the Centre for Emerging and Zoonotic Diseases conducts laboratory diagnosis of a range of notifiable and newly emerging pathogens, contributes to the development of new diagnostic platforms to aid research and surveillance and facilitate on-site diagnosis in remote areas, and employs sequencing and cloning technologies aimed at production of recombinant antigens and development of vaccines. Finally, another important area of infectious disease control undertaken at other centres in South Africa involves using genomic technologies for rapid identification of insecticide resistance in malaria vectors, which has contributed to the control of a major malaria epidemic in the region. Respondents also indicated that South African researchers in these areas are well connected internationally, and contribute to a number of international initiatives devoted to infectious disease control, including data-basing of HIV genotypes and collaborating with international partners in the field of enteric pathogens.

Considering the drivers for this work, respondents stressed the need to reduce the burden of infectious diseases in South Africa, particularly among the least privileged, through more effective health interventions and improved response to disease outbreaks. Respondents noted that genomics had the potential to deliver such improvements in a number of ways: through greater speed and convenience and increased discrimination of diagnostic testing; through better tracking of the spread of emerging and drug-resistant pathogens; and through new and more efficient means of vaccine development and production. Respondents also identified a number of barriers facing the development of genomics for infectious disease control in South Africa. First, there is limited availability of funding for both basic and implementation research, which depends chiefly on soft grant monies. Among other things, the preponderance of short-term funding makes it difficult to retain well-trained scientists – particularly bioinformaticians – both for research and development and for institutions delivering diagnostic and surveillance services. Respondents accordingly argued that sustained investment was necessary in order to establish sustainable career paths, achieve a critical mass of scientific expertise and maintain the necessary research and development capacity, not just in major centres but also in local institutions.

The cost of purchasing and maintaining the necessary technology platforms was also identified as a significant barrier. Genome sequencing platforms, for instance, were mentioned as prohibitively expensive for all but a handful of central institutions – a situation that was seen to militate against decentralised information sharing and collaboration between local public health agencies and actors. Respondents therefore called for a reduction in the price of molecular diagnostic technologies, and suggested that South Africa could benefit from improved relationships and perhaps collaboration with genomic apparatus manufacturers. Here too, fixed-term grant funding was seen as compounding the problem, since the lifespan of equipment often exceeds grant-funding periods.

Finally, respondents noted that the adoption of genomics for infectious disease control was limited by the absorptive capacity of the South African health services, which struggle to meet the many demands they face; in this context, expensive genomic innovations are rarely seen as a high priority. This problem is particularly marked in the case of STIs, identification and management of which is chiefly organised around the low-cost route of syndromic management, which eschews expensive diagnostics in favour of broad-based treatment of symptomatic cases; as a result, there is little incentive for diagnostic technology manufacturers to invest in South Africa, and little translation of genomic research findings into clinical practice.

Respondents suggested that international collaboration could assist greatly in overcoming all these barriers, by providing access to medium and long-term funds, facilitating technology transfer into the

country, creating opportunities for sharing expertise and skills, and training up new generations of South African scientists. In addition, respondents proposed that international collaboration could also play a valuable educative role. It was suggested that the insecure funding situation for genomic research and implementation can be attributed to a lack of awareness among public health agencies and policy makers, who are inclined to perceive genomics as a basic research field, and hence of limited significance for public health. Respondents accordingly called for better scientific education of health bureaucrats, with a view to raising health-related science funding in South Africa to more adequate levels. International agencies were seen as potentially contributing to such efforts by demonstrating to policy makers and health care professionals how genomic technologies can assist in the work of infectious disease control. In particular, it was suggested that the World Health Organisation could usefully explain to policy makers the importance of systematic diagnostic sampling and surveillance of STIs. At the same time, South African respondents were aware that the state of genomics for infectious disease control in their own country is considerably more advanced than in many neighbouring countries, and that South Africa consequently has something of a responsibility to help to promote public health developments elsewhere in Africa. International collaboration in the development and use of genomic science and technology was therefore seen as particularly crucial for strengthening intra-continental networks of public health diagnosis and surveillance.

ANALYSIS OF COUNTRY CASE STUDIES: TRANSNATIONAL PERSPECTIVES

As noted when the methodology for this study was discussed, caution needs to be taken in drawing any general conclusions, given the nature of the sample and the methods of data collection. However, a number of interesting patterns begin to emerge from the findings, which may warrant further research and analysis. These patterns are drawn out in this final section of our report.

Stratified medicine

All of the countries that participated in the study reported a significant commitment to the development of stratified medicine, with the partial exception of South Africa, where discussion of stratified medicine was entirely concerned with prevention and treatment of infectious diseases; accordingly South Africa is solely discussed in the context of infectious disease control (below), and the present discussion on stratified medicine is confined to the remaining six countries.

The picture of stratified medicine that emerged from our study was of a primarily research-led field, driven at least in part by the dramatic new possibilities that come with rapid developments in genomic technology, including the increasing availability of new high-throughput sequencing technologies, the growth of biobanks, and the development of new bioinformatic capabilities to interrogate the resulting mass of genomic data. In some countries, notably China and Mexico, this research interest appears to be coloured in addition by a perception of the genetic distinctiveness of national populations and a desire to characterise and conserve national genomic resources. More generally, our respondents saw such research as driven by a widespread expectation that developments in stratified medicine would lead to significant improvements in healthcare through better targeting of interventions and avoidance of adverse drug reactions. Just how these anticipated benefits were framed differed somewhat from country to country, however: in countries like Finland, Luxembourg and the United Kingdom, with well-established healthcare systems and ageing populations, increased efficiency and savings in the cost-effectiveness of healthcare delivery figured prominently among the expected outcomes; whereas in China and Mexico, the focus was primarily on the benefits to individual patients. Respondents also occasionally listed commercial interests among the drivers of stratified medicine. Only in Finland and Israel did this appear to be a prominent concern, however; while one Chinese respondent anticipated rather different benefits in the form of a move towards introducing elements of a market economy into healthcare.

However, respondents were generally aware that the benefits of stratified medicine still exist, largely in the realm of expectation rather than delivery. Thus, while respondents were able to cite occasional examples of successful stratification of medical interventions – haematological cancers in Finland and lung cancer in Luxembourg, for instance – these were predominantly local examples, both geographically and in terms of being confined to a few, quite specific conditions; while the general view among respondents was that it was still too early to look for significant improvements in healthcare attributable to stratified medicine.

The research-led and largely promissory character of stratified medicine also informed the way that respondents thought about barriers and solutions to the development of stratified medicine for public

health. In countries with less-developed national science establishments, lack of research capacity was seen as the predominant barrier to the development of stratified medicine. Availability of research funding and especially availability of trained personnel – particularly in bioinformatics – emerged clearly as major concerns in China and Mexico, and respondents from these countries cited the need to develop training opportunities, foster inward technology transfer, and build research infrastructure among the most important measures to promote stratified medicine. International assistance and collaboration were seen as particularly important in helping to overcome such barriers and to foster domestic research capacity. By contrast, for more science-intensive countries – particularly Finland, Israel, Luxembourg and the United Kingdom – concern about research capacity figured much less prominently. Insofar as a shortage of trained personnel was seen to represent a barrier to research development in these countries, it was almost entirely in the field of bioinformatics, which is currently undergoing a period of very rapid development.

In the more science-intensive countries, on the other hand, the main barrier to development of stratified medicine was seen to lie in the lack of effective translation of basic research into clinical benefits. In some countries, notably Finland, Luxembourg and the United Kingdom, efforts are already being made to address this problem through earmarked funding and other measures to promote translation and implementation – though respondents from all three countries suggested that allocation of translational research funding still falls short of what they would wish. Elsewhere, there was a strong sense that matters of translation and implementation remain seriously under-represented in policy and in the allocation of research and development funds. Respondents from Finland and Israel stated that in their countries, funding of translational and implementation research is seen to be a responsibility primarily of the commercial sector; while in Mexico, biomedical science policy focuses mainly on basic research, and neglect of translation is seen in the context of a need to build an effective national system of innovation more generally.

In China and Mexico, under-development of the health services was also seen as a significant barrier to translation and implementation of stratified medicine. In the European countries, the challenge was rather to reorganise and reorient the existing health services in ways that would facilitate the introduction of stratified medicine: in the United Kingdom, this was seen in terms of wholesale re-education of National Health Service staff; Luxembourg respondents focused on the need to reorganise pathology services nationwide; and a Finnish respondent stated that the system of reimbursement of medical services tended to discourage the introduction of new genomic diagnostics in that country. Ironically, one Luxembourg respondent added that the high level of consumer satisfaction with existing health services actually tended to reduce the demand for further innovation in personalised healthcare.

These differing national contexts also revealed the ways that respondents thought that international action could be of value in helping to implement stratified medicine on a national basis. The United Kingdom, in keeping with its status as an international leader in translational research, looked for cross-national collaboration in building large patient cohorts for research purposes, and called for harmonisation of policy and practice around implementation. Israel favoured European funding initiatives to promote and integrate translational medicine research across the European Economic Area. Finland called for regulatory harmonisation – although four respondents stated that implementation was primarily a local rather than an international matter. In the case of China, issues of international collaboration around implementation of stratified medicine were scarcely mentioned by our respondents, apart from one who noted a need to encourage foreign companies into the country. In all four countries, it is notable that international initiatives to facilitate the implementation of stratified medicine were conceived chiefly in terms of promoting research or creating favourable regulatory or economic environments, and not in relation to the practical or organisational aspects of stratified medicine. Implementation, it seems, is seen as an overwhelmingly local matter.

In large part, this appears to be because implementation depends heavily upon health service organisation, funding and management, all of which are administered on a mainly national level, and which differ considerably from one country to another. It can be surmised that this national orientation is informed, at least in part, by the fact that the science of stratified medicine is to a considerable extent organised around knowledge of particular national and regional genetic populations and sub-populations, as is apparent from the emphasis on national biobanks as the preferred way of generating the genomic knowledge base for stratification of healthcare interventions. But whatever the reasons, a key finding of the study is that international initiatives are seen to be largely irrelevant to the task of implementing stratified medicine. At most, such initiatives may be important in helping to foster favourable regulatory and economic environments in which countries can pursue their own interests in stratified medicine, and perhaps in providing evidence that the promise of stratified medicine can in fact be realised, albeit usually on a local basis.

It should be added that Luxembourg proved to be something of an exception in this respect; there, international collaboration was seen as crucial for effective implementation, primarily because Luxembourg is a small country with too small a population in which to trial medical innovations. The only other country that called for significant international collaboration around implementation of stratified medicine was Mexico; but in this case, the focus was primarily on building a functioning national innovation system more generally, including better integration into international markets and better opportunities for commercialisation, rather than on how to implement stratified medicine in practice.

It was also noted by some respondents – particularly from Finland, Mexico and, to a lesser extent, Luxembourg – that the development and implementation of stratified medicine was being hindered by a lack of understanding and appreciation on the part of politicians and decision makers of the benefits that stratified medicine may bring to personal health care and public health. The promissory message of stratified medicine, it was implied, is not being heard by many of those responsible for taking decisions about where to allocate resources for public health. Respondents suggested that this problem could best be addressed by efforts to raise awareness among policy makers, and especially by disseminating and publicising examples and demonstrations of successful innovation in stratified medicine. Here too, international initiatives were seen as potentially helpful, since examples of successful implementation were often to be found in other countries rather than at home, necessitating effective international collation and communication of exemplary case studies. Such initiatives might be especially effective, according to a respondent from Mexico, if undertaken by respected international organisations, which are more likely to be heeded by politicians.

Infectious disease control

Turning now to the use of genomics for infectious disease control, the first thing to note is that where stratified medicine was seen as a field of as yet largely unfulfilled promise, respondents from all the countries studied agreed that application of genomics to the work of infectious disease control is already yielding significant public health benefits. This includes the delivery of new, more discriminating and increasingly convenient tools for characterising, diagnosing and tracing infectious agents and disease outbreaks. And it includes powerful new techniques for designing and producing vaccines with which to combat those diseases. However, while everyone agreed on the value and utility of research and development in this area, the countries studied effectively fell into three distinct groups in terms of the level priority they gave to such work, at least insofar as represented by the views of the respondents.

Looking first at Finland and Luxembourg, the majority of respondents from these countries were able to provide only very limited information about policies and practices to promote genomics for infectious disease control. That is not to say that such policies and practices are not in place in Finland and Luxembourg; on the contrary, respondents mentioned relevant work under way at the Finnish National

Institute for Health and Welfare and at the *Laboratoire National de Santé* in Luxembourg. However, it does suggest that, in these countries, initiatives to promote genomics for infectious disease control are pursued rather separately from work on stratified medicine and other aspects of medical genomics, and that those concerned with stratified medicine have only limited knowledge of work on infectious disease control. One Luxembourg respondent went so far as to suggest that this separation of functions actually hinders the advancement of genomics for infectious disease control in that country.

The Finnish and Luxembourg responses contrast with the very high level of awareness of the use of genomics in infectious disease control shown by respondents from China, Israel, Mexico and South Africa. In this second group of countries, infectious diseases are evidently given much greater prominence both in national public health policy and in genomic research and development. Indeed, in the case of South Africa, it appears from the responses received that medical genomics is oriented almost exclusively to the elucidation and control of infectious disease, with little interest in the kinds of chronic disease studies favoured by proponents of stratified medicine in the other countries that were looked at.

Finally, the United Kingdom appears to represent in effect a third position in the study, falling somewhere between the other two groups of countries. In the United Kingdom, as in Finland and Luxembourg, efforts to combat infectious diseases are the responsibility of a separate government body, the Health Protection Agency (HPA). But the HPA maintains strong collaborative links with academic researchers on the one hand and personal healthcare providers on the other. Consequently, not only is a considerable amount of work being done to develop genomics for infectious disease control, but also those informants who are not themselves directly involved in such work nonetheless appear to have a fairly high level of awareness of what kind of work is under way.

These differences in emphasis and awareness plainly relate to the very different problems that infectious diseases pose to the participating countries. Israel, Mexico, China and South Africa are all countries which continue to struggle under a serious burden of infectious disease, both endemic and epidemic. Consequently, it is not surprising that infectious disease control should be seen within these countries as a priority for medical research and development. By contrast, in Finland, Luxembourg and the United Kingdom, infectious diseases are generally far less burdensome, epidemiologically and economically, than chronic diseases such as cardiovascular disease, diabetes and cancer. Consequently, in these countries, infectious disease control is less central to public health policy than in countries that have not yet completed the epidemiological transition; while the focus of genomics for infectious disease control, as understood by our respondents, is rather narrower, concentrating primarily on efforts to identify, trace and contain new strains of antibiotic-resistant pathogens and nosocomial infections.

That said, work in genomics for infectious disease control is evidently not determined solely by domestic priorities. Respondents from Mexico and China, in particular, also reported that their countries devote considerable resources to emerging diseases of global as much as national significance, particularly influenza and SARS. While the reasons for this were not explained, we might hypothesise that it is due in part to the greater vulnerability of these countries' populations to infection in general – but also, perhaps, to the fact that these countries are more conscious of the potentially devastating effects of a global pandemic than those with less recent memories of high mortality from epidemic disease. In the United Kingdom, meanwhile, a substantial amount of research and development work is also devoted to infectious diseases such as malaria, which primarily affect poorer countries. In this case, it would appear that such efforts may be attributed to a sense of global leadership in the development of genomic medicine more generally, and to engagement with the global philanthropic efforts of organisations such as the Bill and Melinda Gates Foundation.

In many respects, the barriers that respondents regarded as impeding the development of genomics for infectious disease control mirrored those they identified in the case of stratified medicine, as did their

views on how to overcome those barriers. Thus respondents from Mexico, China and South Africa all indicated that a lack of research capacity is a crucial limiting factor in the field of infectious disease control as in the field of stratified medicine, while Israeli respondents complained of a shortage of research funding. All four countries also agreed that international collaboration in research and assistance in providing training opportunities will be vital if these deficiencies are to be addressed effectively. By contrast, respondents from Finland, Luxembourg and the United Kingdom were less concerned about research capacity (though they shared with the other countries a general worry that a shortage of trained bioinformaticians is hindering developments in this area), and placed less stress on international action to meet this need – again, mirroring their views on stratified medicine.

In one important respect, however, respondents' views on the role of international initiatives in relation to genomics for infectious disease control diverged quite markedly from their views on stratified medicine. In the case of stratified medicine, respondents generally saw implementation as primarily a national matter, with the role of international action confined, on the whole, to establishing an appropriate regulatory and economic environment for development. In the case of genomics for infectious disease control, by contrast, there was a striking uniformity of opinion across the different countries that international collaboration and co-ordination is essential, not just to create a suitable environment for innovation, but also for the work of implementation itself. In particular, respondents from Finland, Mexico, United Kingdom, China and South Africa all commented on the need to share biological samples and data if genomics is to be effectively employed in efforts to control infectious diseases. Though respondents did not make the point explicitly, it seems reasonable to attribute this internationalist perspective to an appreciation that infectious diseases are themselves in many cases international phenomena, unconfined by national boundaries and often capable of moving rapidly from one population to another; consequently, the science and practice of infectious disease control must in turn be pursued on an international scale. As a respondent from China observed, the corollary of this is that the benefits of effective infectious disease control will likewise not be confined to specific countries, but will be experienced internationally and globally.

CONCLUSIONS

Based on this overview of how different countries are applying genomics to public health in the rather different fields of stratified medicine and infectious disease control (see also the Annex), some more general possible conclusions can be drawn from the evidence of the case studies.

First, the applications of genomics for the development of stratified medicine and for infectious disease control have so far reached rather different stages of development. Stratified medicine is still predominantly a research field, sustained in large part by expectations that it will ultimately lead to significant benefits both in terms of population health and economies in terms of efficiency of healthcare provision, but with relatively few actual examples of successful implementation to show. In comparison, the use of genomics for infectious disease control is already yielding significant public health benefits, both in terms of the ability to diagnose and track the movement of infectious disease outbreaks and in terms of the ability to enhance and accelerate the production of effective vaccines.

Secondly, stratified medicine and the use of genomics for infectious disease control appear to be associated with rather different orientations towards international collaboration, particularly when it comes to implementing new medical interventions. In the field of infectious disease control, it is generally agreed that international collaboration is essential to understand the nature, evolution and movement of pathogens both locally and on an international scale. In the field of stratified medicine, by contrast, most countries agree that implementation is primarily a national issue, and that international initiatives should be confined to fostering an appropriate regulatory and economic environment for innovation.

Thirdly, there are significant differences in the degree of emphasis that different countries place on stratified medicine and infectious disease control. Richer countries, which have already completed the epidemiological transition, tend to concentrate primarily on the promissory field of stratified medicine, in the hope of addressing the growing burden of chronic disease. Accordingly, insofar as this work is reaching the stage of translation and implementation, these countries tend to eschew international collaboration and to concentrate primarily on their own domestic concerns. Low and middle income countries, by contrast, tend to concentrate more heavily on efforts to control the infectious diseases that still beset them. In consequence, they find themselves heavily dependent up international collaboration, not only for assistance in building their own domestic research and development capacity, but also because, even where they possess such capacity, the work of applying genomics to the control of infectious diseases necessitates a high degree of collaboration between countries.

There thus appears to be something of a divergence in the way that different countries are developing the new science and technology of genomics for the purposes of improving public health. Without obviously setting out to do so, it appears that richer countries are inclined to invest in lines of scientific and technical development, focused on stratified medicine, that tend to orient them chiefly towards domestic matters, and even towards something of an isolationist stance on matters of public health policy and practice. Meanwhile, countries with less in the way of financial and scientific resources find themselves

undertaking the kind of work on infectious diseases that not only depends heavily on collaboration with other countries, but that is also more likely to benefit the global community as a whole. Plainly, we are talking here about general tendencies, not hard-and-fast distinctions. To an extent, moreover, this divergence is mitigated by philanthropic concern at the health problems faced by low and middle income countries. Nonetheless, it would appear that countries with more pressing health and development needs and less in the way of resources to address those needs find themselves having to undertake precisely the kind of public health work that both requires and entails a greater level of global citizenship than their richer neighbours.

As said, these are tentative conclusions, emerging from a very preliminary exploration of the use of genomics for public health in different countries. They will require substantially more research if they are to be validated with anything like the rigour they deserve. However, if true, they have profound implications for policy in the field of global public health. That poorer countries should bear the main burden of addressing issues of international concern while richer countries orient their activities primarily towards their own social and economic interests is plainly an injustice, albeit an unintended one. Others will hopefully address themselves to determining whether or not this is actually the case, and if so, to taking appropriate action.

ANNEX: SUMMARY OF KEY FINDINGS BY COUNTRY

Country	Stratified medicine	Infectious disease control
Finland	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Strong co-ordination of research infrastructure - Strong commitment to clinical and translational as well as basic research - Research into risk factors for chronic disease - growing commitment to biobanking and utilisation of genetic information in society <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Too early to say - Promising work on cancer screening and diagnostics <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Expectation of efficiencies in the cost and effectiveness of health care - Research interests and opportunities - Commercial interest and anticipated business opportunities <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Difficulty articulating basic research with clinical research and implementation → more investment in translational research - Poor incentives for commercial investment → provide financial incentives - Slow pace of drug approval procedures, restrictions on off-label use of drugs → enhance collaboration with European Medicines Agency - Intellectual property issues → strengthen and harmonise IP regimes 	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Most respondents unaware of such initiatives <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Improved epidemiology through National Infectious Diseases Register - Introduction of new screening technologies for microbial diagnostics <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Improve the efficiency of identifying infectious agents - Improve the efficiency of treatment through stratification and targeting <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Lack of bioinformaticians, more suitably trained personnel needed in this area - Lack of incentives for infectious disease work → improved financial and policy support - Slowness in validating clinical tests → active participation in the European Union Innovative Medicines Initiative <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - International research collaboration - Better international sharing of samples and data

	<p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Research: already well networked - Implementation: “a matter for each country itself”, but share examples of successful implementation from other countries 	
Israel	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Significant levels of activity, but still at a relatively early stage of development - Single national institutional review board for “genomic medicine” - Biobank of DNA samples from healthy volunteers, plus initial efforts to collect genomic data on diseases <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Researcher interest - Commercial interest <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Scarcity of funding for research and development, especially translational research - Slow approval procedures for phase I clinical trials <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - European Research Council funding for translational medicine - International exchange of ideas and expertise 	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - National advisory committee to undertake technology needs assessment and options appraisal for relevant genomic technologies - National projects to implement next-generation sequencing technologies for healthcare-associated infections, antibiotic resistance, food safety and environmental health - Strategic plan for capacity building pending approval <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Improved characterisation of emerging pathogens - Improved prediction of local and global disease outbreaks - Improvement in relating environmental contamination to clinical infection <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Lack of bioinformatic capacity including shortage of trained bioinformaticians and limited IT infrastructures - Shortage of funding for genomic research in public health <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Participation in collaborative research and public health networks dedicated to next-generation sequencing - Global initiatives for sharing of genomic information

<p>Luxembourg</p>	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Significant public investment in research and development - Major research programmes aimed at development of molecular diagnostics - Commercial development of molecular diagnostics <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Too early to say - Promising results in management and follow-up of lung cancer <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Desire to promote innovation in healthcare and make Luxembourg a leader in personalised medicine - Expectation of improved safety and efficacy and reduced healthcare costs - Expectation of national economic development and growth - New biobanking and genome screening technologies - Researcher interest - Patient organisations <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Mostly in relation to translation into practice - No dedicated agency within the Ministry of Health → create a national working group of stakeholders - Lack of funding for implementation research → provide funding for pilot projects - Lack of clinical research facilities and support for clinician scientists 	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Most respondents unaware of such initiatives - Research into retroviruses <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Not discussed <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Not discussed <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Separation of infectious disease control from other elements of the healthcare and biomedical research system may impede innovation <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Improved integration of infectious disease control with other areas of healthcare and biomedical research
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	<ul style="list-style-type: none"> - Small patient populations for clinical research - Lack of an accurate electronic health record system - Excessive data protection and ethical procedures - Lack of consumer demand <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Basic research: already well networked - International networking and collaboration around clinical research, translation and implementation, particularly through the European Union - International partnerships with clinician-investigators - Exchange of best practices - Consultation around regulatory affairs. 	
Mexico	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Basic research into genomic aspects of diabetes, high blood pressure and cancer - Establishment of National Institute of Genomic Medicine - Basic research into the genomics of the Mexican population - Sequencing of the Mexican Genome, biobanking - Regulation to govern clinical innovation and implementation <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Too early to say - Detection of breast cancer genes - Optimism regarding the development of new drugs <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Researcher interest - Expectations of health and economic benefits 	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Basic research under the National Institute of Genomic Medicine - Applied epidemiological and surveillance work at National Institute of Epidemiological Diagnosis and Referral (INDRE), including new sequencing technologies - Success, in collaboration with international partners, in sequencing, characterising and developing vaccines for H1N1 influenza <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Promising efforts to control antibiotic-resistant pathogens <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Public health burden of infectious disease, including both local epidemic diseases and the threat of global pandemics - Growing technical capacity in research and disease

	<p>from improved disease control, particular diabetes and renal failure</p> <ul style="list-style-type: none"> - Private pharmaceutical manufacturers <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Shortage of research funding and conservative research system → support basic research platforms - Shortage of implementation funding, and tendency of researchers to focus on basic research - Shortage of trained personnel → improve training opportunities - Under-development of basic health services hinders translation and implementation → pursue health system modernisation - Lack of bioinformatics infrastructure - Need for more effective governance structures - Lack of market incentives for pharmaceutical and medical technology manufacturers → promote commercial involvement in R&D - Lack of awareness of potential benefits among politicians, medical professionals → raise awareness by supporting demonstration projects <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Improve access to technology and expertise, especially in bioinformatics - Create opportunities for commercialisation, improve integration into international markets and encourage domestic entrepreneurial initiative - Raise awareness among decision makers through examples of successful implementation 	<p>surveillance, characterisation and control</p> <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Shortage of research funding → target research funding more strategically - Lack of perceived relevance to local needs → focus on diseases of national importance including parasitic diseases and arthropod vectors - Shortage of trained personnel → create research training opportunities, organise a network of medical schools to promote teaching and research including social responses to disease - Shortage of translation and implementation funding and privileging of basic over more practically-oriented research → encourage closer collaboration between basic, clinical and applied research institutions - Weakness of the private sector, lack of market incentives including inadequate IP regulation - Lack of awareness among policy makers, medical practitioners and the public → promote educational initiatives, public engagement and lobbying of decision makers and disseminate examples of successful interventions <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Mexico is already well connected to relevant international disease surveillance and control networks - Improve international networking in basic research, improve access to international funding sources and collaborative research initiatives - Create research training opportunities
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<p>United Kingdom</p>	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Very strong basic research base - Commitment to translational research and implementation including National Health Service initiatives - Inclusion of companion diagnostics in evidence-based pharmaceutical guidelines. <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Limited at present - Important innovations in cancer therapeutics - Increasing provision of novel drugs requiring companion diagnostics <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Aging population and rising burden of chronic diseases - Expectation of improvements in health and efficiencies in healthcare - Expectation that R&D leadership will generate inward investment and economic growth <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Lack of funding for translational research and implementation → needs to be increased - Need to prepare the NHS for the delivery of stratified medicine → strategic service development, training of genetics specialists, and increased knowledge of genomics among healthcare professionals in general <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Basic research: already well networked - Translation and implementation: barriers are primarily domestic 	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Substantial research into disease agents, including those of relevance to low and middle income countries - Strong leadership in infectious disease monitoring and control through Health Protection Agency, including implementation frameworks and exemplars of effective cross-agency working - Good integration of pathogen research with infectious disease monitoring and control <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Significant improvements in characterising and tracing novel pathogens, contact tracing and community screening <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Growth of antibiotic resistance resurgence of hospital-acquired infections - Rapidly increasing power of genomic technologies to characterise and distinguish disease agents - Expectation of more efficient methods for developing vaccines <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Reluctance to mainstream expensive but possibly short-lived technologies such as whole genome sequencing into public health laboratory practice - Shortage of trained personnel in the areas of sequencing, bioinformatics and data mining → establish a coherent IT infrastructure and training strategy - Make better use of historical archives of phenotypic and genomic data and associated information
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	<ul style="list-style-type: none"> - Promote collaboration in studies of large population cohorts by sharing data - Harmonise regulatory and research policy and practice 	<p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Global collaboration and funding to accumulate data for effective characterisation of the agents of epidemic and pandemic outbreaks disease - Address inequalities in access to up-to-date technologies to assist in global efforts against diseases affecting the world's poor - Promote investment in public-private partnerships and other mechanisms where traditional economic drivers are inadequate
China	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Basic research: considerable growth over the past decade of research into human population genomics and genetic and epigenetic risk factors in disease - Significant growth in capacity, including biobanks and databases established through the National Infrastructure for Chinese Genetic Resources (NICGR) - Efforts to promote industrialisation of genome-based medical technologies including biochips - Growing involvement of multi-national pharmaceutical companies in R&D <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Limited: some developments in tumour diagnosis and treatment, and in new-born and prenatal genetic screening <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Anticipated health benefits, primarily to individuals - Growing popular demand for health - Potential to introduce elements of market economy into health care - Desire to protect national genetic resources - Compatibility with traditional Chinese medicine 	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Basic research: substantial efforts including mapping and data-basing of pathogen genomes, studies of microbial evolution and genomic function, research into pathogen-host interactions and pathogenicity - Central government support and coordination of pathogen characterisation, epidemiological surveillance and prediction, including emerging diseases such as SARS - Central government support for development of new diagnostics, targeted treatment and vaccines <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Development of new vaccines including for hepatitis B and H1N1 influenza <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - High public health burden of endemic and emerging infections - International initiatives, including WHO's Expanded Programme on Immunisation - Advances in science and technology including bioinformatics, microbial functional genomics and high-throughput gene detection techniques

	<p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Shortage of research funding → systematic measures to promote research - Availability of trained personnel → improve professional and academic development of researchers - Concentration of research in existing centres of excellence → need for measures to facilitate collaboration, co-ordination and data sharing with other centres - Limited awareness of translation and implementation research - Uneven development of personal medical services - Weak intellectual property regime <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Improve access to international research funding, collaboration and training - Improve access to international collaboration in collecting and analysing samples from common cancers - Encourage foreign medicine enterprises into China 	<p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Availability of research funding - Availability of trained personnel - Need to improve translation of research findings into practice - Concentration of high-technology diagnostic and other resources in major urban centres → develop cost-effective technologies for use in resource-poor settings, build infrastructure and train more personnel <p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Improve access to international research funding, collaboration and training - Improve access to new research technologies and methodologies - Contribute to international and global efforts to understand the evolution and transmission of pathogens and control infectious diseases
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<p>South Africa</p>	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Respondents referred solely to initiatives aimed at the characterisation, diagnosis and treatment of infectious conditions 	<p><i>Initiatives and successes:</i></p> <ul style="list-style-type: none"> - Strategic planning for health including genomic R&D - Plans for a Technical Innovation Agency to facilitate development of new biotechnology platforms - Identification, mapping and tracking of: HIV infection including drug resistant strains; gonorrhoea including multi-drug-resistant strains; influenza and influenza-like illness; and insecticide-resistant malaria vectors - R&D into vaccines against a range of diseases including HIV - Development of new diagnostic platforms to aid research and facilitate on-site diagnosis in remote areas <p><i>Impact on medicine and public health:</i></p> <ul style="list-style-type: none"> - Improved surveillance and tracking of infectious diseases - Improved control of malaria outbreaks <p><i>Main drivers:</i></p> <ul style="list-style-type: none"> - Heavy public health burden of infectious diseases - Expectation of more effective health interventions and improved response to disease outbreaks <p><i>Barriers and solutions:</i></p> <ul style="list-style-type: none"> - Limited availability of funding for both basic and implementation research - Limited funds for expensive technological platforms → need to reduce prices, favourable relationships with manufacturers - Dependence on short-term grant funding militates against retaining well-trained scientists and practitioners → need for sustained investment to build a critical mass of expertise - Limited absorptive capacity in the health services – cheaper methods of disease management take precedence over expensive genomic measures, e.g. in the case of STIs
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		<p><i>Potential areas for international action:</i></p> <ul style="list-style-type: none"> - Researchers already well connected to international initiatives for infectious disease control, including in the areas of HIV and enteric pathogens - Improve access to medium and long-term funds - Facilitate technology transfer into the country - Create opportunities for sharing expertise and skills and training scientists - Improve awareness among public health agencies and policy makers of the successes of genomics for infectious disease control – international organisations such as WHO can be particularly effective in this regard - South Africa well placed to provide leadership in building and strengthening intra-continental networks of public health diagnosis and surveillance
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APPENDIX A: STEERING GROUP MEMBERS

Dr. Mark BALE (Interim Director of Health Science & Bioethics, Department of Health, United Kingdom)

Prof. David CASTLE (Chair of Innovation in the Life Sciences, University of Edinburgh, United Kingdom)

Prof. Adam HEDGECOE (Associate Director, Cesagen, University of Cardiff, United Kingdom)

Prof. Avi ISRAELI (Director General, Ministry of Health, Israel)

Prof. Gerardo JIMENEZ-SANCHEZ (Professor of Genomic Medicine, National University Autonomous of Mexico, and Chair, Working Party on Biotechnology, OECD)

Dr. Susan KELLY (Senior Research Fellow, Egenis, University of Exeter, United Kingdom)

Dr. Françoise MEISCH (Project Officer, Life Sciences Sector Development, Luxinnovation, the National Agency for Innovation and Research, Luxembourg)

Dr. Moleleki NTSANE (Senior Specialist - Policy Investigation, National Advisory Council on Innovation, Department of Science and Technology, South Africa)

Dr. Kimmo PITKÄNEN (Head of Development, Institute for Molecular Medicine, University of Helsinki, Finland)

Prof. WANG Wei (Dean of the School of Public Health and Family Medicine, Capital Medical University, Beijing, China)

Dr. Steve STURDY (Deputy Director, ESRC Genomics Policy and Research Forum, University of Edinburgh, United Kingdom)

Dr. Rachael RITCHIE (OECD Secretariat)

APPENDIX B: QUESTIONNAIRE FOR THE OECD-EGN PROJECT

PUBLIC HEALTH IN AN AGE OF GENOMICS

The OECD in conjunction with the ESRC Genomics Network (EGN) is undertaking case studies looking at the impact of genomics on public health in selected countries. The results of this work will help OECD to prioritise its initiatives in global public health.

The Country Coordinator for your country has identified you (or someone delegated by you) to complete this questionnaire to aid them in collecting information for this project. **Please return this document to your Country Coordinator within two weeks of receipt.**

For additional information, please contact:

Dr. Jim Philp, Policy Analyst at the OECD Tel: + 33 1 45 24 91 43, Email: James.Philp@oecd.org or

Dr. Steve Sturdy, Deputy Director ESCR Genomics Forum Tel: +44 (0)131 651 4741, Email: s.sturdy@ed.ac.uk

Please read the accompanying information sheet before completing this questionnaire. Please be as specific and complete as possible when responding.

Where useful, PLEASE PROVIDE OR MAKE REFERENCE TO POLICY DOCUMENTS OR OTHER SOURCES that support your responses.

SECTION 1: BACKGROUND INFORMATION

1. Please identify the country from which you are responding:_____
2. Please identify the sector and field in which you work (check all that apply):
Sector:
 Government Private Sector Non-governmental (other)_____

Field:
 Public health policy Technology policy Healthcare provider/commissioner
 Regulatory affairs Pharmaceutical/devices industry DNA sequencing/biobanking
 Research laboratory Clinical/public health laboratory services
 (other)_____
3. Please acknowledge that you have read the accompanying information sheet and are consenting to participate in the ‘Public Health in the Age of Genomics’ project (check box):
 I have read the accompanying information sheet and am consenting to participate in the ‘Public Health in the Age of Genomics’ project.

SECTION 2: STRATIFIED MEDICINE

The value of genomic technologies and tools like biomarkers to improve prevention, diagnosis and treatment of disease is well established. Many countries have recognised this fact and are integrating stratified medicine into delivery of public health.

In this part of the questionnaire, we are interested in how countries seek to promote and *deliver* stratified medicine, including:

- biobanks and other research into genetic risk factors, population characteristics etc.
- development and implementation of new diagnostics
- identification and management of child and adult genomic risk
- disease stratification and treatment pathways

4. What policy initiatives and actions have been taken in your country to implement stratified medicine?

5. What are the main drivers for development of stratified medicine?

6. What have been the major successes of these initiatives in terms of improving public health?

7. What social, economic and cultural factors have limited your country's ability to implement stratified medicine? [tick all that apply]

- | | |
|---|--|
| <input type="checkbox"/> perceived relevance to local needs? | <input type="checkbox"/> market access/incentives for pharmaceutical and medical technology manufacturers? |
| <input type="checkbox"/> availability of research funding? | <input type="checkbox"/> intellectual property regimes? |
| <input type="checkbox"/> availability of implementation funding? | <input type="checkbox"/> lack of bioinformatics or other infrastructure? |
| <input type="checkbox"/> availability of trained personnel? | <input type="checkbox"/> ethical concerns? |
| <input type="checkbox"/> organisation and structures of healthcare provision? | <input type="checkbox"/> other? (please specify) _____ |
| <input type="checkbox"/> national/international regulatory regimes? | |

Please provide examples to illustrate your answer(s) to question 7.

8. What steps do you think need to be taken to overcome such barriers?

9. What forms of international collaboration and action would help to promote the development and adoption of stratified medicine in your country?

10. What initiatives would you hope to undertake in future?

SECTION 3: INFECTIOUS DISEASE CONTROL

Genomic technologies such as genome sequencing provide powerful new tools to improve characterisation, tracking and surveillance of infectious agents. Infectious disease control is a fundamental part of many national public health programmes but is also increasingly pursued in ways that transcend national boundaries.

In this part of the questionnaire, we are interested in how countries seek to employ genomic technologies to promote and *deliver* infectious disease control including:

- Infectious disease epidemiology
- Monitoring and tracking emerging diseases
- Environmental pathogen monitoring (e.g. cholera, *E.coli*)
- Vaccine development

11. What policy initiatives and actions have been taken in your country to implement genomics for infectious disease control?

12. What are the main drivers for implementation of genomics for infectious disease control?

13. What have been the major successes of these initiatives in terms of improving public health?

14. What social, economic and cultural factors have limited your country's ability to implement genomics for infectious disease control – for instance: [tick all that apply]

- | | |
|--|--|
| <input type="checkbox"/> perceived relevance to local needs? | <input type="checkbox"/> market access/incentives for pharmaceutical and medical technology manufacturers? |
| <input type="checkbox"/> availability of research funding? | <input type="checkbox"/> intellectual property regimes? |
| <input type="checkbox"/> availability of implementation funding? | <input type="checkbox"/> ethical concerns? |
| <input type="checkbox"/> availability of trained personnel? | <input type="checkbox"/> other? (please specify) _____ |
| <input type="checkbox"/> organisation of healthcare provision? | |
| <input type="checkbox"/> national/international regulation? | |

Please provide examples to illustrate your answer(s) to question 14.

15. What steps do you think need to be taken to overcome such barriers?

16. What forms of international collaboration and action would help to promote the development of genomics for infectious disease control in your country and internationally?

17. What initiatives would you hope to undertake in future?

Thank you for completing the questionnaire!

[Please return this document to your Country Co-ordinator within two weeks of receipt]