The importance of research using personal information to scientific discovery and the reduction of the burden of disease

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In what will be its fifth consultation paper, the Bioethics Advisory Committee (BAC) will present its deliberation on the issues arising from the use of personal information in biomedical research. It is within this broad framework that I shall provide a perspective as both a practitioner of medicine and a scientific investigator.

Fundamentally, public interest in safeguarding privacy of personal information must be properly balanced with public interest in enabling biomedical research in ways that will advance the nation's health. It presents an important principle of "reciprocity": the notion that accepting benefit from past medical research, inherent in the use of medical services, carries some expectation of a willingness to participate in future research for the common good.

Undoubtedly, the BAC will propose recommendations as an endeavor to attain this balance, but my main concern is with the way in which these recommendations will be implemented. As with all processes that require judgment, implementation without an understanding of the operational complexities will often arrive at too simplistic decisions with negative consequences. Thus, this paper is prepared with a view to the future, and is directed at two concerns relating to the execution phase downstream.

The first concern is an emphasis on the division between clinical care and medical research. The distinction between continuous improvement of medical practice and academic research is fast disappearing. Both activities can be called investigative medicine in which systematic analysis and ultimately the publication of the results is expected. During the SARS crisis some sectors of the medical community sought to compartmentalize and separate clinical care and research. The argument was that at a time of crisis, we should not be wasting resource on academic questions. However, we quickly learned that when confronted with an unknown pathogen paralyzing the country, a research strategy was critically needed to uncover the root cause of the epidemic and to structure a science-based response. Moreover, publishing the results of our findings in academic journals not only disseminated the results globally, but also brought international prestige that included investor confidence so important to stabilize the economy. A great fear would be that, in the attempt to safeguard the privacy interest of individuals, a boundary will be drawn makes artificial distinctions between clinical practice improvement and research. I am concerned that differential restrictions

would be placed on one or the other under a misguided view that clinical practice is for the common good whereas biomedical research is not.

Biomedical research is conducted to benefit patients with disease and improve public health in general. Virtually every medical procedure today is the result of some form of clinical investigation. A simple example were the practicing physicians who noticed that in their medical practice, young men were hospitalised with undiagnosed fatal respiratory infections. They examined the medical records and found them to be all gay men. It was this simple form of physician effort that brought the world's attention to a new syndrome of Acquired Immunodeficiency Syndrome or AIDS.

Clinical studies test whether new approaches are better than old approaches. For over 60 years until the 1970s, the only treatment for breast cancer was the removal of the entire breast along with the overlying skin, the underlying muscles and all lymph nodes in the arm pit. It was a disfiguring operation that always resulted in swollen arms with limited mobility. Surgeons were sure this surgery was necessary to remove all possible deposits of cancer. Then, an academic surgeon, Bernie Fischer, challenged this dogma by conducting a large clinical trial to test whether less radical surgery would yield the same results as the drastic operation. This study involved patient volunteers. When it was first launched, he was criticized by the established surgical community for doing unethical experiments on cancer patients because many surgeons were sure that without extensive surgery, more cancers would return. Instead, Fischer's study conclusively showed that the less extensive surgery was just as good in treating the cancer as the disfiguring procedure and had far fewer long term complications. This study and others dramatically changed the entire way we treat breast cancer.

One branch of medicine (epidemiology) deals with the study of the causes, distribution, and control of disease in whole populations. Population research with volunteers has contributed significantly to how we manage common diseases. The Framingham Study in the United States started in 1948 followed 5,209 healthy volunteer subjects for 50 years to assess who would get heart disease and who would be spared. At the start of the study, everyone answered questions about their life style and gave blood for analysis. At the end of the study, the blood tests were correlated with the development of heart attacks. This study was one of the first to show that high cholesterol was a major risk factor for heart attack and led to the use of cholesterol lowering drugs to prevent cardiovascular disease. These drugs, in turn, all underwent clinical trials on patient volunteers to prove that they were effective in reducing cardiovascular events and had no serious side effects. Other conclusions from the Framingham Study were that smoking increased cardiovascular risk, and that specific forms of cholesterol were protective of heart disease. Every outcome from this academic research project became the basis for current medical practice in cardiovascular health.

Likewise, even Chinese herbal medicine today is the result of four thousand years of careful and systematic observation and experimentation. The professional knowledge of the individual practitioner is not simply reading a medical textbook but active observation, systematic note-taking, and even giving patients a new mixture of herbs never tried before. So accessing patient information is the first form of medical investigation, and one that is essential for doctors to adjust to new diseases and potentially new treatments.

How should the regulations and legislation be constructed? There should be only one set of guidelines for all forms of investigative medicine whether it is for the MINDEF, Ministry of Health (MOH), A-STAR, or for University research. Moreover, investigations from one sector should not be cordoned off from the other: e.g., University researchers should not be prohibited from using data acquired through an MOH public health project. The issues of proportionality and the caveats of community sensitivity over research questions enunciated in bioethical literature sufficiently cover most, if not all, contingencies. Singapore is simply too small to have such silos of investigative medicine. There is not enough expertise to service exclusively single silos. Even in more developed jurisdictions, the best research that leads to major public health changes come from deep collaborations across academic – government lines.

The second concern is that the distinctions between de-identification and anonymization (both are means to safeguard privacy) will be confused. De-identification is a process whereby information about a patient such as exposure to environmental agents, age, height, race, disease, and disease outcome is separated from information that can identify the individual (e.g., NRIC number, name, address – collectively called patient identifiers). Researchers can work with this information and derive important results. The key distinction is whether this dataset of an individual patient can ever be linked back to his identifying information? If such a link is destroyed and identifying the dataset is impossible, then the data is said to be anonymized. In some cases, that key that links that clinical data to the patient identifier is important. For example, if one wishes to understand how a single blood test could predict outcome ten years later (as the case of the Framingham Study), then such a link is an absolute necessity. Unreasonable demands that keep critical databases from interacting will severely limit the benefit of such research to the public. Luckily, current information technologies have encryption solutions to resolve these problems. Systems are available for a “trusted third party” to hold the key to linking personal identifiers with the personal information such that individual investigators can intermittently update their information without ever being able to access the personal identifiers (Figure 1). Such information security systems have already been in place and are highly functional. All of e-commerce and e-banking is completely based of the trust of the customers that important personal financial information is kept confidential, yet linked.

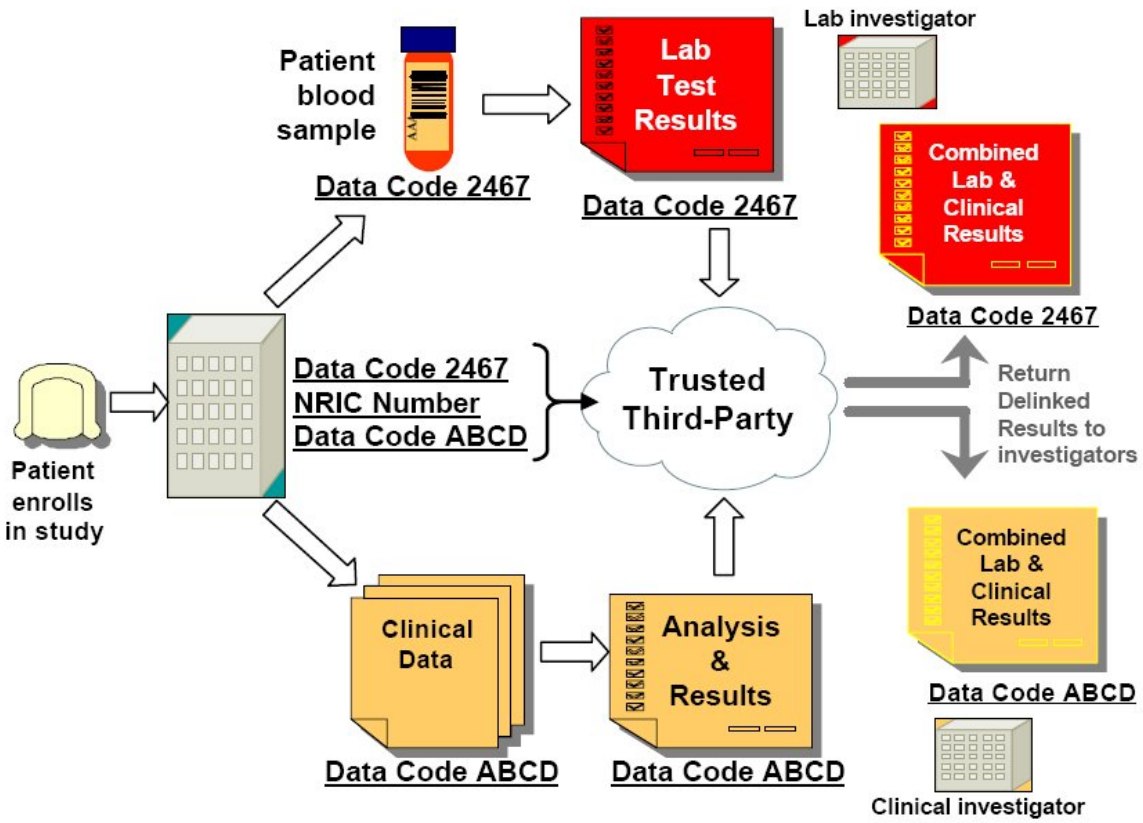

Figure 1. Flow of de-identified information using a Trusted Third Party framework

This discussion has far reaching importance. If proper structures for ethical access of information are in place, we can accelerate discoveries that can make a difference in the delivery of care, improve Singaporean public health, and create new knowledge valuable globally. Whereas a patient's participation in a clinical study may last only a few months, the value of his medical information increases with time. Thus, any requirement for fully rendering data anonymous, which forever cannot be linked to an individual's identifier should be considered with great deliberation. This is because the effort and cost in assembling the patient study and its analysis will be also forever lost.

In Singapore, we are embarking on a new way of conducting research and conceptualizing how we can reap the benefits of this research. Our great strength and advantage in this globalize world is our ability to integrate processes, institutions, and actions that leverages on our small size and high social trust. The proper execution of privacy safeguards in the use of personal information in biomedical research will bring dividends in better and more cost effective health care and put Singapore in the forefront of medical investigations.