CNA Commentary

Small country, large research trials - what Singapore can learn from Denmark

Local research trials are important in getting data relevant to Singapore's health priorities and people, says NUS Professor of Bioethics Jerry Menikoff.

By Jerry Menikoff

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SINGAPORE: With the flu season upon us, especially as Singapore travelers pack their bags in anticipation of overseas holidays, can getting an email with the right message convince someone to get an influenza vaccine?

Researchers in Denmark set out to answer that question in 2022, with the ambitious goal of enrolling almost every Danish citizen aged 65 years or older in the Nudge-Flu clinical trial. They ended up doing just that - with almost 1 million participants – in a trial that was conducted quickly and at very low cost.

The research team attributed that not only to the use of a mandatory governmental electronic letter system, but also to the fact that Denmark – with its relatively small population and high levels of trust in the government - has several electronic databases that maintain various types of information about its citizens that can be accessed efficiently, safely and at minimal cost.

What might be the relevance of all of this to the people of Singapore? Clinical trials generally require large numbers of participants, and that puts smaller countries at a disadvantage when they join international trials with little to no say in how they are designed. This could mean potentially missing out on country- or culture-specific nuances.

It doesn't have to be this way, as the Denmark researchers have shown. Yes, smaller countries must work harder to overcome their disadvantage - but that smallness can become an advantage, enabling some steps to be taken that would be hard to do in much larger nations.

SMALL COUNTRIES CAN RUN LARGE CLINICAL TRIALS

One other aspect of the Danish study helped achieve the high enrolment rate. What was being done to the participants did not require their informed consent.

The seniors were randomly assigned to receive either a version of a message encouraging them to get the flu vaccine, or no message at all. They were merely given information to help them make a decision.

In a more usual clinical trial, where health and healthcare are affected in an important way (such as which medication they will receive), a person is not enrolled unless they have agreed to participate. It is a much more difficult and expensive trial to conduct, due to the time and effort of obtaining the consent.

The Denmark team has already moved on to show that their framework can work for even those types of more demanding trials. They are now conducting a trial testing whether a higher dose of flu vaccine is better than the standard dose that is used in Denmark for many older individuals.

To do this, the researchers determined they needed to ask 800,000 people to participate, with at least 200,000 of them agreeing to enrol. These numbers were smaller than those for the Nudge-Flu trial, but they are still stunningly large in the world of clinical trials and for a country whose entire population is under 6 million people.

A smaller pilot was successfully conducted with 12,000 people, which suggests they would indeed be able to complete the larger, full-size study, which is on track to be completed in 2024.

SINGAPORE'S CONDUCIVE ENVIRONMENT

The Danish researchers proved that a small country can successfully conduct huge trials on public health issues such as flu vaccination.

Like Denmark, Singapore has several characteristics that could be conducive for running different types of large-scale trials. Singapore has infrastructure in place for collection and sharing of medical information. It has a world-class community of top researchers who want to be doing even more cutting-edge research.

And there is a strong level of trust in the government. The 2023 Edelman Trust Barometer found that the government remains the institution most trusted by people in Singapore, ahead of the media, business and non-governmental organisations.

A centralised email system and country-wide databases could be used to efficiently identify possible research participants.

And obtaining informed consent – often the costliest and most labour-intensive step in a clinical trial – could be done electronically, using those systems. In the wake of the pandemic, there has been a growing recognition that remote consent is perfectly ethical and not inferior to in-person consent.

MYOPIA AND OTHER HEALTH PROBLEMS OF SPECIAL CONCERN

Conducting more home-grown clinical trials has been accurately described as a "win-win for patients and the economy". The companies conducting the trials will be creating new jobs, and if the trials lead to the development of new products, the manufacture of those products in Singapore can synergistically create even more jobs.

Among other things, such local research activity creates the opportunity for trials that will directly advance priorities in Singapore.

Healthier SG is the national initiative to make people healthier by preventing the development of chronic diseases, instead of having to treat them. But changing behaviour is always challenging, so information from Singapore-designed trials can be vital in attaining those goals.

Similarly, trials can be designed to tackle specific health problems of special concern in Singapore, but which are of less priority elsewhere. Singapore has been described as the "myopia capital of the world", where the condition is "increasing the risk of irreversible blindness in millions of people" and generating annual health care costs of more than US$700 million every year.

Solutions to a problem of this scope will likely require a better understanding of the causes and possible preventive measures. To what extent does providing secondary school children with laptops or tablets worsen the development of myopia, and is that nonetheless a trade-off worth making due to the educational benefits? How should the mix of cultures in Singapore shape anti-myopia measures?

These are Singapore-specific questions, and Singapore-specific research is needed to provide the most meaningful answers.

As we move on from the COVID-19 pandemic, we shouldn't forget that substantial factors in Singapore's successful campaign against the virus were the various ways in which local research – regarding how the virus spread, and how to treat it and prevent it – was rapidly conducted, with the results being used to create policy interventions.

Among many examples, Singapore researchers created and tested a first-in-the-world COVID-19 serology test; and multiple Singapore hospitals partnered with the United States National Institutes of Health in testing remdesivir as a treatment, which also played a role in obtaining access to COVID-19 treatments for patients in Singapore. That is a Singapore success story well worth repeating.

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