Three I's and the Future of Medicine

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Professor Gordon Arthur Ransome was a legend in his time and truly an iconic figure in the history of Singapore medicine. I never had the good fortune of working for Professor Ransome. However, even as a medical student, I remember my Professors speaking with awe and affection about his clinical prowess, his compassion for patients and his devotion to teaching. He also set very high standards – I was told his nickname was "kosong" as he was inclined to give "zero" marks to students who performed poorly in the clinical examinations.

It is a special privilege to deliver this prestigious Gordon Arthur Ransome Oration. I thank the Master and Council of the Academy of Medicine, Singapore, for this exceptional honour.

The Burden of Disease

Professor Ransome practised medicine for 33 years before his retirement in 1971. If we look at a snap shot of Singapore at the mid-point of his career around 1955, infectious diseases and tuberculosis were the dominant causes of mortality, accounting for nearly a third of all deaths (Fig. 1).

This has completely changed. In 2004, cancer and cardiovascular diseases were the main causes of death. However, mortality figures alone do not tell the whole story. To better understand the total burden of disease, one also needs to take into account the impact of severe disability arising from disease. The disability-adjusted life year (DALY) is a measure commonly used for this purpose.[1] DALY combines premature mortality (years of life lost to premature death) and ill health (years of life lived with a disability, weighted by the severity of the disability) to reflect disease burden.

An analysis using this methodology[2] showed that in Singapore in 2004, cardiovascular diseases (mainly ischaemic heart disease and stroke) and cancer were the 2 leading causes contributing to the burden of disease, accounting for 38% of the total DALYs (Fig. 2). These were followed by mental disorders (which include anxiety, depression and schizophrenia), diabetes and neurological disorders, that accounted for another 33% of the total DALYs. It is noteworthy that 5 sets of medical conditions alone account for more than 70% of total DALYs.

We should expect these medical conditions to become even more dominant in the future because of Singapore's rapidly ageing population. This is because the burden of diseases such as cardiovascular diseases, cancer and neurological disorders rises exponentially in progressively older age groups (Fig. 3).

Reducing Years Lost to Premature Death and Disability

This situation is not unique to Singapore, but similarly affects many countries across the world. Against the backdrop of the high and rapidly rising burden of chronic disease, the challenge and promise of modern medicine is to increase the years of healthy life for our patients and the general population, in a cost-effective manner. In other words, to reduce the years lost through ill-health and disability, and premature death (Fig. 4).

To do this requires us to achieve a combination of the following:

i) Prevent or delay disease onset;
ii) Prevent or reduce complications and reduce disease severity and duration;
iii) Improve survival;
iv) Improve functional recovery.

The main thrust of my lecture today is that given the immensity of these challenges, it seems likely that incremental improvements to the healthcare system alone will not be sufficient. Instead, the central question is this: can we make quantum-leap changes that substantially reduce years lost to premature death and disability, and in a cost-effective way? I believe we can, and that we can endeavour to do this through approaches encapsulated by three *I*'s.

Singapore already has a very good first-world health system. While we should continue to learn and adapt best practices from around the world, Singapore has also reached the stage where we need to develop our own "leap-frogging" approaches that deliver best outcomes, cost-effectively. We can do this through *integration* and *innovation*, which are empowered by research, particularly research which is carried out locally in Singapore.

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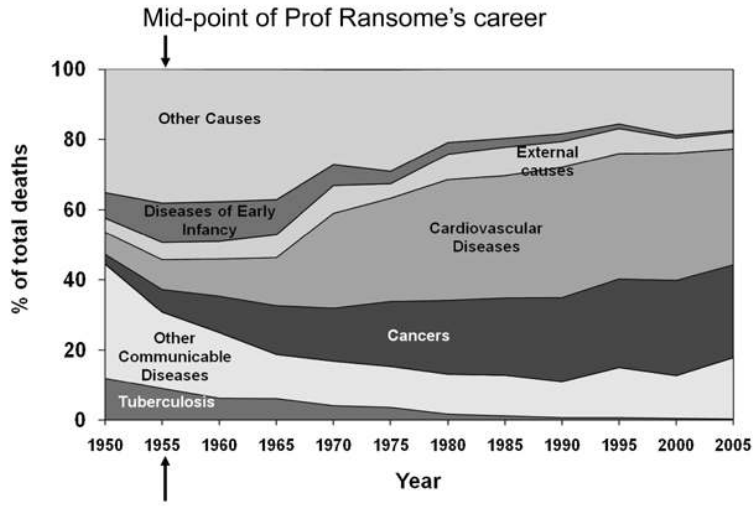

Fig. 1. Major causes of death in Singapore.

Source: Epidemiology & Disease Control Division, Ministry of Health.

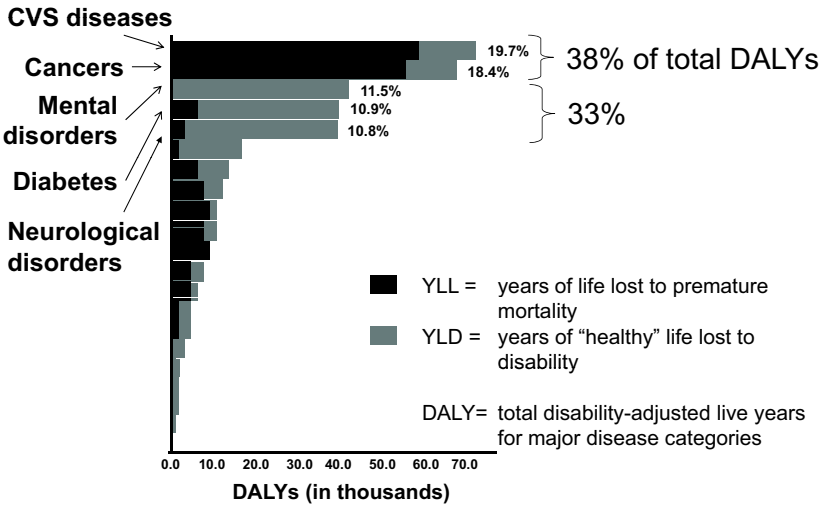

Fig. 2. Five leading causes of burden of disease in Singapore, 2004.

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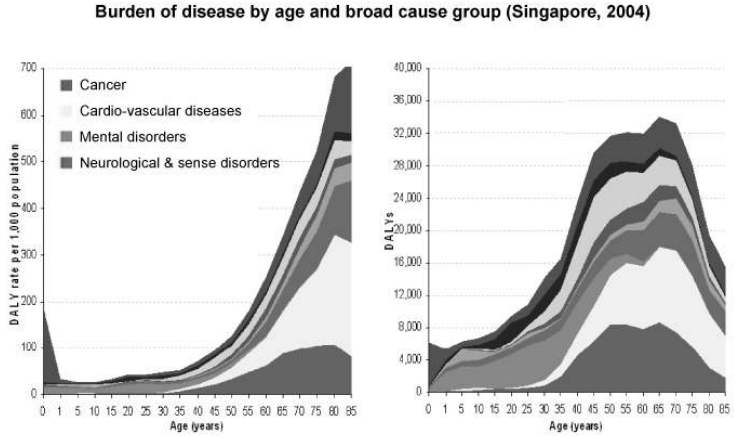

Fig. 3. Burden of disease rises rapidly with age.

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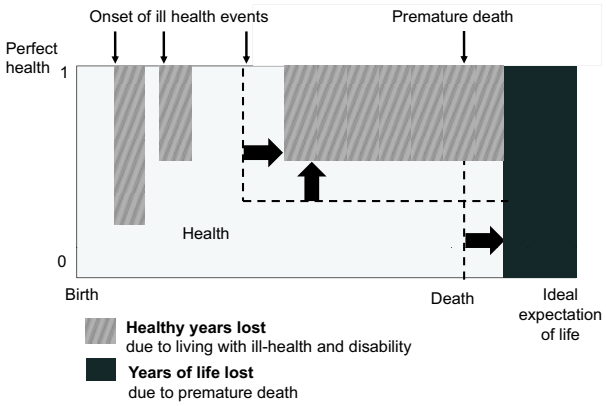

Fig. 4. The challenge and promise of modern medicine. Reducing years lost to premature death & to disability.

Allow me to first set the context by outlining the key developments in biomedical science research, and in public health in Singapore over the past 10 years.

Biomedical Science Research in Singapore

Biomedical Sciences (BMS) research has grown dramatically in Singapore over the past 10 years, since the government decided to invest in developing the sector in the year 2000.

In Phase One of the BMS initiative, from 2000 to 2005, impressive progress was made in increasing the critical mass and pipeline of talented researchers, strengthening BMS intellectual capital as reflected in the rapid rise in high impact research publications, developing state-of-the-art research infrastructure particularly in Biopolis, growing the industry R&D base, as well as expanding the BMS sector's contribution to Singapore's economy. For example, BMS manufacturing output increased from S$6 billion in the year 2000 to S$18 billion in 2005 and S$24 billion in 2007.

For Phase Two of the BMS Initiative, from 2006-2010, the primary focus is on building up the Translational and Clinical Research (TCR) capability in Singapore. The rationale is that TCR is the most critical rate limiting step in the translation of basic science discoveries into useful applications. A strong TCR capability would enable basic science discoveries, in Singapore and elsewhere, to be developed in an effective and timely manner into new diagnostic tools and therapeutic agents. If we succeed in this, it would become a key driver for better healthcare for Singaporeans while developing advances in medical care that would help Singapore maintain its position as a regional medical hub. At the same time, it would contribute to economic growth through the commercialisation of indigenous intellectual property and by attracting and anchoring pharmaceutical, biotech and medical device companies in Singapore.

Over the past 3 years, many initiatives and programmes have been launched to develop TCR in Singapore. The most important thrust has been to grow the critical mass of TCR talent, particularly physician-scientists, by creating career tracks, training programmes and a supportive environment and infrastructure. A crucial element of this strategy was the establishment of academic medical centres in the Outram and Kent Ridge campuses respectively, that will drive cutting edge and cost-effective clinical care, high impact research and quality education, by creating synergies between these 3 missions. Within the academic medical centres, a specific investment is being made to develop strong investigational medicine capabilities to facilitate the design and conduct of Proof-of-Concept and early phase clinical trials in man.

To bring the best basic science and clinical research groups in Singapore together,[5] TCR Flagship programmes were successfully launched. Each Flagship programme spans all the way from basic science through translational research to clinical application, and leverages on the greatest complementary strengths in Biopolis, universities and hospitals and national disease centres. The aim is for these programmes to be highly competitive for the quality of science, as well as for taking through basic science discoveries to application in efficient and effective ways. These programmes would also provide useful platforms for collaboration with research institutions and industry.

In order to extend the impact into the general community, several initiatives have also been launched to enhance health services and public health research.

Existing Programmes to Control Chronic Diseases

Singapore has a strong track record in improving population health. Specific health promotion programmes in schools and in the workplace, as well as national health education campaigns, have been linked with robust integrated screening programmes for obesity, diabetes, hypertension and hypercholesterolaemia and national screening programmes for breast and cervical cancer. The Ministry of Health also oversees a Chronic Disease Management Programme that helps to ensure consistent, high quality care for patients detected to have chronic diseases.

These efforts appear to be bearing some fruit. The most recent National Health Survey carried out in 2004, suggested that the prevalence of diabetes and hypercholesterolaemia in the adult population may be starting to trend down (Table 1).

Transforming Medical Approaches to High Burden Chronic Diseases Through Integration and Innovation

This is very encouraging, but these efforts while important, will probably not be enough to achieve the required reduction in years lost to premature death and disability. We need larger, quantum-leap changes in our healthcare system.

Table 1. Prevalence of Diabetes, Hypertension, Hypercholesterolaemia, Obesity and Smoking in Singaporeans Aged 18 to 69 Years[3]

	1992 (%)	1998 (%)	2004 (%)
Diabetes	8.6	9.0	8.2
Hypertension	22.2	27.3	24.9
Total cholesterol >6.2 mmol/L	19.4	25.4	18.7
Obesity (BMI ≥30)	5.1	6.0	6.9
Smoking ≥1 cigarette/day	18.3	15.0	12.6

I would like to suggest 3 strategies which I believe can transform the medical approaches to high burden chronic disease through integration and innovation.

Strategy #1: Leverage on the TCR Flagship Programmes as Major Change-drivers

The first TCR Flagship programme award in 2007, to the Singapore Gastric Cancer Consortium, serves as a good illustration of this strategy.

Gastric cancer is one of the top 5 cancers in men in Singapore. Prognosis of gastric cancer is poor because patients usually present late with advanced disease.

The Singapore Gastric Cancer Consortium brings together the best expertise available in Singapore, combining the clinical strength of 4 public hospitals (National University Hospital, Singapore General Hospital, Changi General Hospital, and Tan Tock Seng Hospital) with scientific expertise in the National University of Singapore, the National Cancer Centre of Singapore, and A*STAR research institutes (Genome Institute of Singapore, Institute of Molecular and Cell Biology). Each of the groups involved in gastric cancer research were doing very good work, but each by itself was unlikely to have the breadth and depth of multidisciplinary expertise required to seriously address a complex and difficult clinical and public health challenge such as gastric cancer. The Consortium serves a critical role of bringing all these different groups together to work synergistically at a scale that can make a substantial impact.

The Consortium is organised around 4 research themes, namely early detection, biological understanding, molecular epidemiology and improving treatment. Taking early detection as an example, prior health services research by the NUS group had indicated that screening of Chinese men for gastric cancer was cost-effective, particularly if they were positive for *Helicobacter pylori*.[4] The Consortium's high risk cohort study has to date detected 10 cases of very early gastric cancer after 1629 surveillance patient-years. The early results from the Consortium suggest that for subjects with 3 or more risk-factors, screening yields are significant, with one cancer being detected for every 91 tests done (personal communication — Yeoh KG). Notably, for the 10 patients with very early gastric cancers detected in this study, the tumours could be excised endoscopically leading to cure.

The work of the Consortium has the potential to completely transform the detection and care for gastric cancer. Genetic and biomarker studies can enhance stratification of subjects for screening to further increase detection rates, as well as of gastric cancers so as to optimise treatment regimes. A parallel study seeks to ascertain if confocal endomicroscopy can improve the detection of early, submucosal gastric cancer. The better understanding of the biology of gastric cancer also paves the way for clinical trials with novel treatments, which hopefully would lead to improved outcomes.

Strategy #2: Creating New Clinical Care Models

Integration and innovation can also be applied to create new clinical care models that significantly improve outcomes, more cost-effectively. I would like to illustrate this strategy with the example of psychoses.

Psychoses contribute significantly to the burden of disease. In the past, a major problem was late diagnosis, with patients diagnosed after a mean delay of 2.6 years (median 1 year). This resulted in substantial morbidity, a higher degree of disability, and a high need for hospitalisation both acute and long term.[5] In 2001, the Early Psychosis Intervention Programme (EPIP) was funded by the Ministry of Health.[6] The programme established extensive links with general practitioners, counselors in higher education institutions, police, and the Armed Forces, creating a network which identified potential cases of pyschosis early. These cases are referred for evaluation to dedicated clinics run by the Institute of Medical Health (IMH). Patients diagnosed to have early psychosis benefit from clinical intervention and treatment initially in IMH. When stabilised, the patients are referred back to general practitioners as part of a shared care programme.

The outcomes have been impressive. The time to diagnosis of psychosis was reduced from a median of 1 year to 4 months. Early therapy has resulted in much better clinical responses and reduced treatment default rates. This is reflected, for example in the fact that suicide rates fell sharply, employment rates doubled, and re-admission to hospital rates, average lengths of stay and chronic hospitalisation went down substantially.[7]

In 2008, the Institute of Mental Health in partnership with Duke-NUS Graduate Medical School, Genome Institute of Singapore, National University of Singapore, and others, won a TCR Flagship programme award. This research is likely to yield important information on key genetic, biological, cognitive and social risk factors which should further improve the early detection of those at high risk of developing psychosis.

These 2 examples, the Singapore Gastric Cancer Consortium and the Early Psychosis Intervention

Programme highlight a number of important points. The first is that Focus is critical. A relatively small number of conditions cause most of burden of disease, and the systematic application of a focused approach undergirded by strong research can result in transformative changes to care and outcomes.

The second is the importance of Integration, to bring together the best groups across Singapore, across clinical sectors, between basic science, clinical research and clinical communities.

The third is that Innovation also requires the creation of appropriate funding models and "rules" that promote and support the widespread partnerships necessary for success.

Strategy #3: Position to be a key site in Asia for new drug and medical device development for diseases important in Asian populations

Ultimately, the most profound impact is created by discoveries that completely change the paradigm of the disease. The discovery by Marshall and Robin that most stomach ulcers are caused by infection with *Helicobacter pylori*, revolutionised treatment and allowed stomach ulcers to be cured by antibiotics.

While such truly transformational work is difficult to achieve, many useful advances in clinical care can be made by making the translation of indigenous scientific discoveries into clinical applications, better, faster and cheaper. This is certainly a major goal for Singapore's Biomedical Sciences Initiative.

In parallel, Singapore aspires to become a preferred site in Asia for the validation and development of new diagnostic tests and treatments for key diseases in Asian populations. To achieve this, a critical factor is the presence of thought-leaders and deep expertise in the biology of specific conditions. A good example is the recent agreement established between Astra Zeneca and 2 key centres in Singapore, namely the National Cancer Centre and the National University Health System. The strong expertise in hepatocellular carcinoma in Singapore made it attractive for Astra Zeneca to work with investigators here to design and carry out studies on a number of promising drug candidates as well as to test 6 novel compounds in a mouse model.

The Last "I"

The title of my presentation today is "Three I's and the future of medicine". ***I**ntegration* and ***I**nnovation* are critical, but the most important "I" is ***I**ndividuals* – talented individuals and leaders with the vision and passion to create real and positive change.

The true legacy of Professor Ransome was not just in the patients he had helped and the clinical services that he had developed, but in the leaders that he helped nurture. This photograph (Fig. 5) of his farewell gathering is instructive. With Professor Ransome, we see a remarkable group of individuals who later shaped and created the Singapore medicine we know and admire today – Dr Andrew Chew, the late Professor Seah Cheng Siang, Professor Khoo Oon Teik, Professor Lim Pin and Dr Kwa Soon Bee.

Fig. 5. A farewell gathering held for Sir Gordon Arthur Ransome.
Standing (L-R): Dr Andrew Chew, Professor Seah Cheng Siang (late), Professor Khoo Oon Teik, and Professor Lim Pin
Seated (L-R): Professor Gordon Ransome and Dr Kwa Soon Bee

Their outstanding work, in turn, has been taken up and brought to greater heights by successive generations of influential leaders. This year's National Medical Excellence Awards recognise 5 such individuals – Professor John Wong, Professor Low Poh Sim, Professor Chew Chong Lin, Professor Ng Han Siong and Professor Michael Chee. In the audience today, we have many others who are making a remarkable impact in clinical service, research and education.

It is because of the strength of this leadership and our ability to integrate and coordinate, that I view the future with great optimism despite the daunting challenges ahead. I am convinced that the three I's – *Individuals, Integration, Innovation* – will take Singapore medicine, biomedical research and education, to new heights of excellence for the benefit of our patients, of Singapore and of the wider global community.

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