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# HAI AP News

Penang, Malaysia

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HAI AP Est. 1981

Health Action International (HAI) was formally founded in Geneva in 1981 and coordinated from Penang by Action for Rational Use of Drugs in Asia (ARDA)<sup>1</sup>. In 1995 Health Action International Asia Pacific (HAI AP) was formed as a collaborative network in the Asia Pacific Region to increase access to essential medicines and improve their rational use through research excellence and evidence-based advocacy. HAI AP is committed to strive for health for all now. HAI AP News is the organ of Health Action International – Asia Pacific and presents the happenings in the regional campaigns for more rational and fairer health policies and carries material in support of participants' activities

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## **Message from the Chair**

This issue of HAIAP news celebrates 'World Health Day', 7 April 2018, with the theme: Universal health coverage: for everyone, everywhere. The slogan is 'Health for All'.

Why? The '**Right to Health and Health for All**' should always be at the forefront guiding efforts.

Although many things have challenged us over the years, especially last year when we lost our dearest coordinator, HAIAP will still keep on working to strive for health for all.

We will continue as an independent network, working to increase access to essential medicines and improve their rational use through research excellence, evidence-based policy advocacy, and through strengthening the capacity and involvement of civil society in government decision making.

It is crucial in this world that non-governmental organisations continue their efforts as social monitors of the work of both government and international organisations.

We will continue to work for affordable access to essential and life saving medicines and diagnostics and their rational use. We encourage countries in the Asia Pacific region to use all the flexibilities in TRIPs that are legally available to them such as *Compulsory Licensing* and *Government Use* and to withstand pressure **not** to do so that is exerted by Pharmaceutical Corporations.

Antimicrobial resistance (AMR) is a challenge for all of us and we look forward to getting news of our partners specific or unique challenges and the innovative activities they have launched to counter the threat of AMR.

We encourage partners to share any news about their activities for circulation in the HAIAP News and the website and so we can learn from each other.

Niyada Kiatying Angsulee Chair, HAIAP Governing Council

<sup>1</sup> Full details: <https://tinyurl.com/y8pftlxy> Page 2.

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## World Health Day - April 7, 2018

### **Universal Health Coverage**

In this 70th anniversary year since the Alma Ata Declaration in 1978, WHO is calling on world leaders to live up to the pledges they made when they agreed the Sustainable Development Goals in 2015, and commit to concrete steps to advance #HealthForAll. The focus this year is on **Universal Health Coverage**. This means ensuring that everyone, everywhere can access essential quality health services without facing financial hardship.

- Universal health coverage is about ensuring all people can get quality health services, where and when they need them, without suffering financial hardship.
- No one should have to choose between good health and other life necessities.
- UHC is key to people's and nations' health and well-being.
- UHC is feasible. Some countries have made great progress. Their challenge is to maintain coverage to meet people's expectations.
- All countries will approach UHC in different ways: there is no one size fits all. But every country can do something to advance UHC.
- Making health services truly universal requires a shift from designing health systems around diseases and institutions towards health services designed around and for people.

#### **What UHC is not**

- UHC does not mean free coverage for all possible health interventions, regardless of the cost, as no country can provide all services free of charge on a sustainable basis.
- UHC is not only about ensuring a minimum package of health services, but it is about ensuring a progressive expansion of coverage of health services and financial protection as more resources become available.
- UHC is not only about medical treatment for individuals, but also includes services for whole populations such as public health campaigns – for example controlling the breeding grounds of mosquitoes that carry viruses that can cause disease.
- UHC is not just about health care and financing the health system of a country. It encompasses all components of the health system: systems and healthcare providers that deliver health services to people, health facilities and communications networks, health technologies, information systems,

quality assurance mechanisms and governance and legislation.

Some countries have already made significant progress towards universal health coverage. But half the world's population is still unable to obtain the health services they need. If countries are to achieve the SDG target, one billion more people need to benefit from UHC by 2023.

Gonoshasthaya Kendra (GK) in Bangladesh aims to improve the quality of life, and particularly the health of the rural masses in an expanding region, by ensuring affordable and accessible health care.

***At the same time GK is providing medical services in 12 Rohingya refugee camps in south-east coastal districts of Bangladesh.***

<http://www.gonoshasthayakendra.com/>

***News from GK: new dialysis centre for all who need it in Dhaka, Bangladesh***

*From Dr Zafrullah Chowdhury*

The GK Dialysis Centre was opened on 13 May 2017 with the capacity to serve 400 patients a day. Haemodialysis uses a machine to replace the function of the kidneys to filter blood to remove waste products and water from the blood.

The GK Dialysis Centre is equipped with 85 of the best of German manufactured dialysis units and 15 Japanese made units. It is the single largest dialysis facility in the country.



The Centre was set up to provide affordable dialysis for poor patients. The charges vary according to economic status of the patient. We planned to provide free dialysis for up to 25 ultra-poor patients per day, and for 300 poor patients at BDT 1100 per session, and another +/- 100 middle class patients at BDT 1500 per session. We had hoped some rich patients will also avail of our services at BDT3,000 per session. As per our calculation the actual cost per session is BDT 1,700 per session. We are hoping to have sufficient rich patients to meet the deficit of approximately BDT 80,500 per day.

However, at present we are serving only 200 plus patients daily. The charges have been revised downwards so the ultra-poor continue to get free services, the poor pay BDT800, lower middle class BDT 1100, middle class BDT1500, upper middle class BDT 2500 and the rich BDT3000. [The current conversion rate is BDT81 for USD1]. The revisions were made to accommodate a larger number of poor patients coming from outside Dhaka city having spent a substantial amount on transport and having someone to escort them. We have observed that if a patient can afford to undergo haemodialysis three times a week for 3 months, they can go back to work and travel without escorts to the dialysis centre.

Bangladeshi NGOS, industrialists, business houses and a host of individuals have contributed to the setting up of the Dialysis Centre. Dr Yunus's Grameen Social Business has extended an interest free loan to meet the deficit.

### **Dr Zafrullah Chowdhury responded to questions from D+C/E+Z in February this year**

*D+C Development and Cooperation (D+C/E+Z) is a German organisation that produces a website that is up-dated daily. Through that medium they discuss international development affairs and explore how they relate to other fields of policy-making, such as security, peace, trade, business and environmental protection.*

<https://www.dandc.eu/en/article/dialysis-saves-lives-people-who-suffer-kidney-failure-it-very-expensive> 23/2/2018

#### **What are the reasons for kidney failure?**

Diabetes can cause kidney failure, and so can hypertension, skin diseases during infancy, kidney infections, frequent change of antibiotics; and chemicals in food and agriculture and kidney toxic medicines. Heavy use of painkillers is another reason. Kidneys are small, fist-sized organs that purify blood. If kidneys fail, the person concerned needs dialysis, a treatment that requires big machines. The treatment is simple and life-saving, but it is expensive and time consuming. Every week, a patient needs three sessions of four hours.

#### **How many people in Bangladesh need dialysis?**

About one million people do, and every year, an additional 50,000 new patients need dialysis. Many cannot afford the treatment however. Private health-care providers charge 3,000 to 8,000 Taka per session. That is roughly the equivalent of \$30 to \$80. Dialysis has to be supplemented with a haemoglobin enhancer which costs 1,800 Taka per week. Blood examinations every three months cost approximately another 3,000 Taka. Families struggle to make those payments. They end up selling assets like land or a house, but run out of money eventually and the patients drop out of the treatment scheme – which is their death sentence. In Bangladesh,

families are on their own because we do not have a government-run national health service that covers everyone as is the case in Taiwan, Iran or Britain, for example.

Global institutions like the World Health Organisation and the World Bank are paying too little attention to health economics. I think European donor governments should promote, at the global level, the kind of governmental health care that works so well in their own countries. The challenge is twofold. Services must not only become available, but affordable too. The free market does not deliver that. To cover everyone, solidarity is more important than competition. And in regard to non-communicable diseases, we must consider that availability and affordability are both long-term issues. If you are diabetic or suffer from hypertension, you must take your pills every day for the rest of your life. It is not like taking an antibiotic for a few days. People who depend on dialysis need a session every other day. Making that happen is a huge challenge.

#### **What is GK's contribution?**

We have set up a new dialysis centre at our hospital in central Dhaka. We have the capacity to handle 400 patients per day in four shifts. Presently we are treating on average 215 patients per day. Some of them travel from afar, up to 400 kilometres, for this purpose. We charge less than 50% of the market price. Our rates range from 800 Taka to 3,000 Taka. We cross-subsidise services for the poor. Our own costs are about 2,000 Taka, and we hope the centre will break even in three years.

Dr Zafrullah continued: We actually treat 25 patients who are destitute entirely free of charge. But you are correct, of course, GK cannot solve all of our country's health-care problems. We do our best, setting examples of what can – and must – be done. And we are decentralising our services and will soon open two smaller dialysis centres in Sylhet and Rangpur. Moreover, we want to expand the existing centre in Dhaka.

#### **How can GK afford such major investments?**

No foreign donors are involved so far. We got support from local business people and philanthropists. I also got a discount from the German manufacturer that makes the best dialysis machines. Things could and should be easier, however. In Bangladesh, you pay one per cent tax when you import industrial machines, but the rate is at least 31% for medical equipment. Moreover, philanthropic donations are not tax-deductible. We face many challenges. That said, we always welcome donations including from Germany or other rich nations, if people there want to support us.

## World Health Day in the Philippines:

### *Philippines response to the introduction of Dengvaxia®* From Delen de la Paz



In preparation for World Health Day a demonstration was held on April 5 calling on the World Health Organization to admit accountability over the *Dengvaxia*® fiasco. In a press release from the Health Alliance for Democracy (HEAD), together with the ILPS Health Commission and the People's Health Movement, Dr Joseph Carabeo, HEAD Secretary General stated: 'The World Health Organization is privy to the unfinished clinical trial of *Dengvaxia*®. It has allowed transnational corporations (TNCs) like Sanofi to hold its reins and impose medical interventions based on commercial considerations.' He continued 'Two members of WHO's Strategic Advisory Group of Experts (SAGE) on Immunization have links with Sanofi. This is the same group within WHO that recommended the use of *Dengvaxia*® in March 2016,' .... 'Corporate interests may have well permeated into the ranks of WHO to push for profit over health.' ..'To make matters worse, the WHO is now the foremost proponent of Universal Health Coverage'. Presence of conflict of interest in policy making is matter of concern.

### **Dengue Vaccine *Dengvaxia*® and associated risks.<sup>2</sup>**

Dengue fever is caused by any one of four different virus strains that are spread by the bite of infected mosquito (the female *Aedes aegypti*). When people have been infected by one sort of virus and they recover, they will be immune to that virus only. Unfortunately they can still be infected by the other three sorts of viruses. An infection with a second type of virus may cause a more severe disease.

*Dengvaxia*®, a quadravalent vaccine produced by Sanofi-Pasteur received first marketing authorizations in



late 2015 and was made available in several Asian and Latin American countries including the Philippines.

Even in 2015 the importance of understanding potential factors other than age that may be associated with the increased relative risk of hospitalization and of severe dengue was highlighted.<sup>3</sup>

By 2017 it had been recognised that there were severe issues of safety associated with *Dengvaxia*®. It had been noted that the excess cases of hospitalised dengue (in the age group 2-5 years) could be related to sero-status. Among sero-negative individuals, the response following infection after vaccination may act as a second infection, which has typically been associated with a higher risk of serious disease. Individuals seropositive at the time of first vaccination had a durable protection against severe dengue and hospitalization during the entire 5-year period of observation. The risk of severe dengue in vaccinated sero-positive persons is the lowest (less than 1 per 1,000 seropositive persons vaccinated).

Further findings showed that the vaccine could be harmful in **sero-negative** children whatever their age and the higher risk in younger children is simply the result of a lower prevalence of prior infection.

***Given concerns regarding antibody dependent enhanced (ADE) dengue disease, the analysis of pre-specified subgroup for vaccination should have been on the basis of sero-status rather than age.***

Immunization began in the Philippines in April 2016 and the Global Advisory Committee on Vaccine Safety GACVS was presented with the program's early post-market surveillance experience in June 2016. In the areas in the Philippines where *Dengvaxia*® was introduced (mainly through school programmes), the sero-prevalence was estimated to be at least 85%. For every 1,000 sero-negative persons vaccinated, there was an increase of about 5 cases of hospitalized dengue and 2 cases of severe dengue.

<sup>2</sup> [http://www.who.int/vaccine\\_safety/committee/GACVS-StatementonDengvaxia-CYD-TDV/en/](http://www.who.int/vaccine_safety/committee/GACVS-StatementonDengvaxia-CYD-TDV/en/)

[http://www.who.int/immunization/diseases/dengue/q\\_and\\_a\\_dengue\\_vaccine\\_dengvaxia\\_use/en/](http://www.who.int/immunization/diseases/dengue/q_and_a_dengue_vaccine_dengvaxia_use/en/)

<sup>3</sup> <https://academic.oup.com/jid/article/214/12/1793/2632615>  
Critique of World Health Organization Recommendation of a Dengue Vaccine. Scott B. Halstead

WHO acknowledges that until a full review has been conducted vaccination must only be recommended in individuals with a documented past dengue infection, either by a diagnostic test or by a documented medical history of past dengue illness. Research is underway to develop an affordable rapid diagnostic test that can be used at the time of vaccination.

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## 4<sup>th</sup> People's Health Assembly - Bangladesh 15-19 November 2018

The People's Health Movement marks the 40<sup>th</sup> anniversary of the landmark Primary Health Care Declaration of Alma Ata in 1978 with a return to Bangladesh for the 4<sup>th</sup> People's Health Assembly (PHA4). The event will take place from 15 to 19 November 2018 in Savar, (near Dhaka) Bangladesh, 18 years after the first People's Health Assembly was held there.

In the context of escalating threats to health worldwide and the shift away from Primary Health Care, the Assembly will bring together civil society organizations and networks, social movements, those from academia and other stakeholders from around the globe to share experiences, for mutual learning and to develop joint strategising to fight back against neoliberal approaches to health.

PHM organized the first PHA in Savar, Bangladesh in December 2000 and more than 1400 people from 75 countries attended. Participants developed and endorsed the People's Charter for Health, PHM's founding document. The second Assembly was held in Cuenca, Ecuador in July 2005 and attended by 1492 people from 92 countries. The third Assembly was held in Cape Town (South Africa) in July 2012 and attended by about 1000 people from over 90 countries.

The objectives of this Assembly and associated activities include:

- To evaluate and critically analyze current processes and policies having an impact on health and healthcare at global, regional and local levels;
- To collectively review PHM's organization and programming and to provide a renewed mandate for the years to come;
- To enhance the capacity of civil society health activists to engage with and intervene in the policy making process, to monitor and drive policy implementation and to ensure accountability in the functioning of health systems;
- To foster and support constructive dialogue, planning and mobilization around health and the broader social determinants of health,

- To launch renewed sustainable structures and dynamics, both within and outside the health sector, that will continue to drive coordinated action to secure universal and equitable access to health and health care.

The PHA4 will focus on four main themes or 'thematic axes' of PHA-4 that PHM will continue to develop over the next several months:

- The political and economic landscape of development and health
- Social and physical environments that destroy or promote health
- Strengthening health systems to make them just, accountable, comprehensive, integrated and networked
- Organizing and mobilizing yet again for Health for All.

For more information please visit

<http://www.phmovement.org/en/node/10805> or contact [globalsecretariat@phmovement.org](mailto:globalsecretariat@phmovement.org)

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## World TB Day – March 24

Each year World TB Day is commemorated on March 24 to raise public awareness about the devastating health, social and economic consequences of tuberculosis (TB) and to step up efforts to end the global TB epidemic. The date marks the day in 1882 when Dr Robert Koch announced that he had discovered the bacterium that causes TB, which opened the way towards diagnosing and curing this disease.

Despite significant progress over the last decades, TB continues to be the top infectious killer worldwide, claiming over 4 500 lives a day. The emergence of multidrug-resistant TB (MDR-TB) poses a major health security threat and could risk gains made in the fight against TB.

The theme of [World TB Day 2018](#) – '**Wanted: Leaders for a TB-free world**'- focused on building commitment to end TB, not only at the political level with Heads of State and Ministers of Health, but at all levels from Mayors, Governors, parliamentarians and community leaders, to people affected with TB, civil society advocates, health workers, doctors or nurses, NGOs and other partners. All can be leaders of efforts to end TB in their own work or terrain.

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### ***TB in India***

*Elimination of tuberculosis by 2025: India's PM  
Mr Narendra Modi*

Launching the TB Free India Campaign at 'Delhi End TB Summit', on March 13, 2018, PM Narendra Modi said his government is implementing a national strategic plan to end tuberculosis by 2025. He said:

'The global target for eliminating TB is 2030, but I announce that the target for India to eliminate TB is 2025, five years before the global target. TB mainly affects the poorest of the poor and every step taken towards the elimination of this disease is a step towards improving the lives of the poor.'

Since state governments play an important role in this, Modi said he has personally written to the state governments to join government's efforts to eliminate TB,

strengthening the spirit of cooperative federalism.

PM Modi said that 'if we end TB in India, the world will have a better chance of ending it globally as India carries the world's greatest burden of TB. If we make a village in India TB free, then a city and then another, we will achieve the target of ending TB in India.' He stressed that all forces must come together to fight this battle - the private and public sectors and the civil society - all must join hand to overcome TB.



#### Drug-resistant TB

- Anti-TB drug resistance is a major public health problem that threatens progress made in TB care and control worldwide.
- Drug-resistant tuberculosis is a form of TB caused by bacteria that do not respond to, at least, isoniazid and rifampicin, the two most powerful, first-line (or standard) anti-TB drugs.
- The primary cause of drug-resistant TB is poor case management, nonadherence to the prescribed regimen, a poor national programme, or some combination of these three. Inappropriate or incorrect use of anti-TB drugs, or use of poor quality medicines, can all cause drug resistance.
- Today, treatment for drug-resistant TB can take up to two years, is extremely complex and expensive and leads to horrible side effects such as vomiting, deafness, blindness, psychological depression and fatigue.
- A few drugs are reserved for use when standard treatments fail to cure patients.
- About 480,000 people developed drug-resistant TB in the world in 2014.
- About 190,000 drug-resistant TB deaths are estimated to have occurred in 2014.

WHO's Director General Dr Tedros Adhanom Ghebreyesus said WHO will stand by India, and by every country that decides TB has no place in its future.

#### TB in India's livestock

India's National Antimicrobial Resistance Action Plan acknowledges

'the burden of AMR in livestock and food animals has been poorly documented in India. Aside from sporadic, small, localized studies, evidence that can be extrapolated to the national level is lacking. Given that there are few regulations against the use of antibiotics for non-therapeutic purposes in India, the emergence of AMR from antibiotic overuse in the animal sector is likely to be an unmeasured burden in India...'

In a Study of zoonotic TB in districts of Karnataka state Dabade et al (2017)<sup>4</sup> discuss the close association of cattle and buffaloes with farmers and their family members in rural India. The animals are sheltered under the same roof where the family members sleep, cook and eat. This close proximity of humans to cattle/buffaloes exposes farmers and family members to tuberculosis (TB), especially if they are vulnerable (eg malnourished children along with adults, diabetics, people with HIV and AIDS, people with addiction to alcohol, or smokers). Their study examines the spread of TB from animals to humans and its public health significance.

They tested 203 animals and 12 were positive. These 12 tuberculin-positive animals were associated with households consisting of 77 individuals and of these individuals five TB cases were found of which two had been treated and cured, one was on treatment for active TB, and two were fresh cases.



<sup>4</sup> Gopal Dabade, Ashok Kale, B R Athani, Venkatesh Sankri, S L Pawar, S N Megeri. A study on zoonotic tuberculosis in selected rural areas of Bagalkot and Belgaum districts of Karnataka state. *Clin Tuberc Other Mycobact Dis* 9 (2017) 30–35.

The authors recommendations covered the need for more studies and collaboration with WHO together with involvement of the Ministry of Agriculture and other ministries along with the Health Ministry, the farming community, meat sellers, veterinary graduates, medical graduates and the milk industry.

They concluded that there is evidence that the struggle against TB in India needs to take into account the very nature of TB as a zoonotic disease. A more holistic view is necessary in order to address TB from a public health angle. There is an urgent need to introduce a strict surveillance strategy to reduce and finally eradicate TB. This cross sectional study with limited resources highlights the need for further research in this neglected area. This issue is the most important outcome as there are many areas that this study could not examine because of lack of technological inputs and resources. The authors note that though isolation or culling of tuberculin positive cattle is the ideal solution, other restrictions such as on-the-spot inspection of butchers shops by trained veterinarians or consideration of tuberculin-testing as an eligibility criterion for banks loans may contribute to controlling zoonotic TB.

### **Can India, with the highest burden of TB, be free of it by 2030?**

*In the Deccan Herald, March 24 2018, Dr Gopal Dabade President, Drug Action Forum, Karnataka, explains:*

The medicines to treat tuberculosis, like streptomycin, became available in 1944, five years after the tuberculin test did. So, it is obvious that the tuberculin test became a useful and powerful tool in many developed countries to detect, isolate and thus prevent suffering and death from tuberculosis.

According to WHO, 'Globally, 1.7 billion people are estimated to be infected with *M. tuberculosis* and, in 2016, 1.7 million people died from TB, including 400,000 among people infected with HIV'.

India has the highest burden of TB. The WHO's TB statistics for India for 2016 give an estimated incidence of 2.79 million TB cases in the country. That is 2.79 million people newly contracted the disease in just that year.

'These numbers and facts from the pages of history are a wake-up call for action to achieve the stated goal of 'TB-free' status by 2030. Is India ready?'

### **The Stop TB program says:**

Integrated health systems are essential for ending TB. Fragmentation and isolation of TB programmes within country health systems must end, as must the separation of programs aimed at tackling different forms of TB and



co-infections with specific diseases. Instead, TB interventions should be integrated to the greatest extent possible with HIV and AIDS and maternal and child health programs, and made part of the efforts to deliver primary health care in the context of universal health coverage. Efforts to tackle TB should also include zoonotic TB, embracing the **One Health** approach that recognizes that the health of humans is connected to the health of animals and the environment. There is an urgent need to increase the human resources available to end TB, and to improve the collection and analysis of data to better inform and correct programming.

[www.stoptb.org](http://www.stoptb.org)

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## **Access to Hepatitis C treatment**

### **Australia: Observations on the launch of new drugs for hepatitis C**

*Marianne Martinello Postdoctoral research fellow Infectious diseases physician, Behzad Hajarizadeh Lecturer, Gregory J Dore Head Infectious diseases Physician.*

*Source Australian Prescriber Volume 41 : Number 1 : February 2018. Full text free online at [nps.org.au/australianprescriber](http://nps.org.au/australianprescriber)*

Morbidity and mortality from hepatitis C virus infection have been increasing in Australia. This is partly due to the low uptake of treatment with interferon. The development of highly effective direct-acting antiviral therapy and the listing of these drugs on the Pharmaceutical Benefits Scheme (PBS) in March 2016 has revolutionised the clinical management of hepatitis C in Australia.

In 2015, an estimated 227,300 Australians were living with chronic hepatitis C. However, while the vast majority (82%) had been diagnosed, only a small proportion had ever received treatment (22%) and even fewer had been cured (14%). There was a persistently low uptake of treatment (1% per year).

Australia is currently unique in providing unrestricted government-subsidised direct-acting antiviral therapy to all adults living with chronic hepatitis C virus infection. 'Access for all' was achieved through strong advocacy, robust data, bipartisan political support and established partnerships between government, clinical, academic and community organisations. In the first 10 months of PBS listing (March–December 2016), an estimated 32,400 Australians started treatment.

Some key features of the PBS listing have enabled the rapid uptake of treatment. First, unlike most other countries, there are no restrictions based on the stage of an individual's liver disease or drug and alcohol use. This situation permits direct-acting antiviral uptake across the entire infected population. Encouragingly, significant (direct-acting antiviral) uptake has been reported among marginalised populations, including people who inject drugs and people living with HIV.

Second, access to treatment has been enhanced with a wide range of health professionals (including authorised nurse practitioners and GPs) able to prescribe, with dispensing through public hospital and community pharmacies.

The substantial uptake of therapy in the first 10 months after PBS listing has established a basis for the elimination of hepatitis C in Australia. Evaluating the progress towards elimination will require monitoring treatment uptake, adherence, adverse effects and outcomes, particularly among populations at high risk of transmission. There will also need to be monitoring of hepatitis C virus prevalence and incidence (both primary infection and reinfection) and monitoring of the impact of therapy on hepatitis C virus-related morbidity and mortality on the Australian population. One of the keys to hepatitis C elimination in Australia will be a sustained high uptake of direct-acting antiviral treatment with equitable access to therapy.

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## **Malaysia: access to Hepatitis C treatment through TRIPS flexibilities**

### **Malaysia's decision to resort to compulsory licensing for sofosbuvir was legally and morally sound**

*Letter: Dr. T Jayabalan, Professor Dr Mohamed Azmi Hassali, and Mr. T Rajamoorthy responded to the report by Mr. Azrul Mohd Khalib, the Chief Executive of the Galen Centre for Health and Social Policy, Malaysia concerning Malaysia's access to Hepatitis C treatment in March this year.*

*[The authors explain the use of the TRIPS flexibilities very clearly. BS, Ed.]*

We read with great interest the recent report that, according to Mr Azrul Mohd Khalib, the Chief Executive of the Galen Centre for Health and Social Policy, Malaysia has suffered a significant drop in the sixth annual US Chamber International Intellectual Property (IP) Index as a direct result of its decision last year to implement a government-use license to produce a generic version of a patented hepatitis C drug.

Mr Azrul contends that instead of resorting to such compulsory licensing, the authorities should have availed themselves of the alternative of voluntary licensing.

We cannot endorse this view as it ignores some inconvenient truths about the limitations of voluntary licensing. A free market mechanism, voluntary licensing will not encourage research and innovation as its primary concern is profitability. It will definitely not lead to a significant lowering of costs of medicines and better medical care as the Galen Institute mistakenly believes.

Hepatitis C is an infectious disease caused by the hepatitis C virus (HCV) that spreads through blood contacts such as blood transfusion, needle sharing, and

so on. The high incidence of this disease in our country is extremely worrying. It is estimated by the Ministry of Health (MOH) that there are approximately 500,000 patients in Malaysia who are infected with hepatitis C and every year an estimated 2,000 new cases are reported.

To make matters worse, the cost of treatment for hepatitis C was exorbitant until the compulsory licence was issued, which made it less accessible to needy patients. In July 2017, *The Star* newspaper carried a front-page story highlighting the plight of about 500,000 Malaysians suffering from hepatitis C, with only a handful able to afford the full course of treatment with a drug called sofosbuvir, which may cost up to RM300,000.

Sofosbuvir is a direct-acting antiviral (DAA) agent and used with a second DAA can cure about 95% of cases. As a result, the Cabinet in September 2017 approved the import of the generic version of this drug under the 'Rights of Government' under the Patents Act 1983 by exploiting the patented invention of sofosbuvir tablet 400mg.

The import right has been given to Malaysian pharmaceutical company Pharmaniaga Logistics Sdn Bhd and the supplier is Egyptian pharmaceutical company Pharco Pharmaceuticals (Pharco). Pharco has agreed to supply the hepatitis C treatment regimen (sofosbuvir and daclatasvir) for US\$300 in the public sector in Malaysia. The procurement of the 400mg sofosbuvir tablet is in accordance with the current government procurement procedures. The implementation of the Rights of Government for the 400mg sofosbuvir tablet is for use in government facilities only (MOH and Armed Forces hospitals), whereby at initial phase it will only be offered at 18 Ministry of Health (MOH) hospitals. The selection criteria for patients that will receive the treatment will follow the clinical guideline set by the MOH. This decision was made in the best interest of the patients, and to improve hepatitis C treatment access in order to protect public health. It is hoped that the implementation of the Rights of Government will enable more hepatitis C patients to receive treatment and at the same time reduce the cost of treating complications arising from the disease.

### **Use of the Rights of Government clause**

Malaysia is the first country to initiate such a move for the hepatitis C drug. The decision was made after the MOH's efforts at price negotiations with the patent holder proved unsuccessful. The last time Malaysia initiated the Rights of Government was in 2003 for some antiretroviral drugs (treatment for HIV infection).

Through the implementation of the Rights of Government, the cost of treatment will be much lower and more patients can be treated. At the same time,



access to treatment can be improved to achieve the Sustainable Development Goals (SDG) target set by the United Nations and targets of the World Health Organisation's Global Health Sector Strategy on Viral Hepatitis 2016-2020 to eliminate viral hepatitis as a major public health threat by 2030. The target is to reduce new viral hepatitis infections by 90% and reduce deaths due to viral hepatitis by 65%, focusing mainly on hepatitis B and hepatitis C, both of which can cause chronic liver disease including cirrhosis and liver cancer.

### **Voluntary licensing**

Voluntary licensing arrangements between a patent holder and another party may afford opportunities for significant cost containment. As with negotiated discounts, the benefits of voluntary licensing arrangements depend crucially on the terms of the licence.

Patent holders may, at their discretion, license to other parties, on an exclusive or non-exclusive basis, the right to manufacture, import, and/or distribute a pharmaceutical product. Depending on the terms of the licence, the licensee may act entirely or effectively as an agent of the patent holder; or the licensee may be free to set the terms of sale and distribution within a prescribed market or markets, contingent on payment of a royalty. Either option, or arrangements in between, may allow for substantial price reductions.

However, a voluntary licence may set price ranges or include other terms that maintain prices at or near the same level as those offered by the patent holder. Alternatively, the terms may limit how many patients or which categories of patients are eligible to benefit from the lower prices provided by the licensee. Voluntary licensing arrangements, which are at the discretion of the patent holder, are usually made for strategic reasons (eg entry into a particular market) rather than as price gestures and they may not entail any price reduction at all.

### **Compulsory licensing**

When a product is patented, competitive bidding is not a viable option to reduce prices because, unless a patent is made ineffective, there is no competition. Compulsory licences may be an important cost-containment measure in such a situation. The granting of such licences creates competition by one or more compulsory licensees, which in turn may force prices down. At the same time, the patent holder (and/or any voluntary licensees) can continue with commercial exploitation of the patent, and will receive compensation (generally in the form of a royalty) from the compulsory licensee/s.

Article 31 of the World Trade Organisation (WTO)'s Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) expressly allows the granting of

compulsory licences.<sup>5</sup> The Agreement contains no limits on the grounds under which such licences can be granted. The right of WTO member states, including Malaysia, to determine such grounds has been confirmed by the Doha Declaration on the TRIPS Agreement and Public Health (November 2001). Article 31 makes particular, but not exhaustive, reference to cases of national emergency or extreme urgency, dependency of patents, licences for governmental non-commercial use, and licences to remedy anti-competitive practices. National laws can, however, provide for the granting of compulsory licences whenever the title holder refuses to grant a voluntary licence 'on reasonable commercial terms' (Article 31 (b)) and for other reasons, such as public health or broad public interest considerations. The Agreement permits compulsory licences to authorise licensees to exercise any of the rights conferred by a patent, including production or importation.

Compulsory licences and government use provisions have been extensively used in developed countries, such as Canada and the USA, to address various public interests through the creation of competitive sources of supply.

It cannot be overemphasized that Malaysia's decision to resort to compulsory licensing for sofosbuvir was legally and morally sound. The decision was taken only after price negotiations failed to yield satisfactory results. No voluntary licence was offered to Malaysia before the government decided to exercise the Rights of Government provision. It is patently clear that the attempt to project voluntary licensing as an alternative, coupled with the US Chamber International Intellectual Property (IP) Index as a sword of Damocles, are all designed to pressurize developing countries and dissuade them from resorting to compulsory licensing.

The human cost of buckling under the pressure of big pharmaceutical corporations is best illustrated by the case of South Africa. That country is among those with the highest numbers of HIV and AIDS patients in the world. Although the situation was critical, the South African government was not prepared to override the patent on antiretroviral drugs (ARVs) which could have stemmed the epidemic. Hence while the incidence of HIV and AIDS started going down everywhere else with the introduction of ARVs in 1996, in South Africa, the figures began to dip only from 2007. The fear of antagonizing the drug companies had resulted in countless needless deaths.

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<sup>5</sup> Correa C. *Integrating Public Health Concerns into Patent Legislation in Developing Countries*. Geneva, South Centre, 2000, p. 93-94.

To conclude, the right to health is a fundamental human right and compulsory licensing is a particular right under patent law that is reaffirmed in the WTO TRIPS Agreement. We should not barter away either of these.

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## The Pharmaceutical Industry in Contemporary Capitalism

This article is adapted by Joel Lexchin from *Health Care under the Knife: Moving Beyond Capitalism for Our Health*, edited by Howard Waitzkin,

The pharmaceutical industry has remained near or at the top of the list for profitability for many decades. The myth is that its profits come from producing and selling the many therapeutic advances that industry research has generated, but the reality is far different. In the first place, after tax deductions only about 1.3 percent of the money that the industry spends actually goes into basic research, the type of research that leads to new medications. Second, most of the new medicines that come from the pharmaceutical corporations offer little to nothing in the way of new therapeutic options. For the decade 2005 to 2014, among 1,032 new drugs and new uses for old drugs introduced into the French market, for example, only sixty-six offered a significant advantage, whereas more than half were rated as 'nothing new,' and 177 were judged 'unacceptable' because they came with serious safety issues and no benefits.

The industry also justifies its high level of profits with the claim that drug development is inherently risky. Were drug development such a risky proposition, then one would expect that from time to time the fortunes of corporations would vary. As Stanley Finkelstein, a physician, and Peter Temin, an economist, both based at the Massachusetts Institute of Technology, point out, 'No matter how many times industry analysts warn that a patent expiration is going to make this or that company vanish, it hasn't happened.'

To maintain its attractiveness to the financial community, the pharmaceutical industry has developed several strategies. With the blockbuster model of development drying up, corporations have shifted to a 'nichebuster' model whereby corporations target small therapeutic markets with drugs that they can sell for hundreds of thousands of dollars per year per patient. In this sense, the challenges experienced by the pharmaceutical industry resemble those of others that operate in a

capitalist economy. Key to the industry's survival is its ability to extend the period during which it has a monopoly on the sale of products, and that translates into stronger intellectual property rights, both in the developed world and in the developing countries that represent the emerging sites of growth.

The full article is here <https://monthlyreview.org/2018/03/01/the-pharmaceutical-industry-in-contemporary-capitalism/>

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## TPP Update

The Trans Pacific Partnership Agreement rose from the dead and in March was signed in Chile by 11 countries: Chile, Peru, Mexico, Canada, Japan, Vietnam, Malaysia, Brunei, Singapore, Australia and New Zealand.

The developing countries generally dislike many aspects, especially procurement, state owned enterprises and Intellectual Property (IP) clauses, as these intrude into their domestic arena and seriously restrict what policies they can retain or introduce. But they reluctantly accepted them, in exchange for more exports to the other TPP countries.

Of the over 1,000 original provisions 22 provisions have been 'suspended', rather than removed. If the US rejoins, it is likely the eleven countries will lift the suspended provisions and it would become the old TPP again. The suspensions are mainly in the IP chapter. The US insisted on many of the extreme clauses but many others were unhappy about them.

In any case the Agreement must be ratified by national governments before it comes into effect. Activists in many countries including Australia and New Zealand are lobbying politicians to reject the Agreement.

For details on the history of this Agreement see:

[http://www.haiasiapacific.org/?page\\_id=526](http://www.haiasiapacific.org/?page_id=526)

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## Feature: Factors that get in the way of appropriate use of antimicrobial medicines in humans:

### Examination of studies of antimicrobial knowledge and use compared with accepted principles

Prepared by Beverley Snell from acknowledged sources

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#### Summary

The Therapeutic Guidelines<sup>6</sup> principles of good antimicrobial prescribing, the *Australian Commission on Safety and Quality in Health Care (ACSQHC)* recommendations provide good standards against which to measure prescribing of antibiotics.

Studies of antimicrobial prescribing and consumer knowledge about antimicrobials from Lao PDR, Cambodia, Philippines, Taiwan, Malaysia, India, Sri Lanka, Thailand, Oman, Australia, Pakistan, China, Solomon Islands and Fiji are examined to identify issues that contribute to suboptimal or appropriate prescribing and use of antimicrobials in humans compared with the accepted principles.

Factors contributing to sub-optimal understanding and use include absence of regulatory control of prescribing, sale and distribution of antimicrobials; absence of regulatory control of health practitioners; absence of political will; financing structures that depend on funds from the sale of expensive medicines; private practices that profit from the sales of medicines; absence of well functioning Medicines and Therapeutic Committees; prescribers' lack of knowledge of the appropriate treatments for specific organisms and of antimicrobial therapy in general; prescribers' perceptions of community expectations; community attitudes and expectations; absence of laboratory diagnostic tests to guide prescribing and inefficient laboratory practices; poor stock management to ensure reliable supplies of the right antimicrobial medicines, laboratory reagents, infection prevention and control consumables and absence of records across the whole system.

Australia was shown to be one country having all factors in place to enable best use of antimicrobials and independent not-for-profit bodies are in place to facilitate improvement of prescribing and use of antimicrobial medicines. But in Australia there is still much room for improvement.

#### Principles to guide best use of antimicrobial medicines

*Therapeutic Guidelines Australia*<sup>7</sup> has provided a comprehensive guide to good antimicrobial prescribing in humans as part of Therapeutic Guidelines Antibiotic - Version 15, 2014.

1. clarification of the indication for antimicrobial therapy
2. consideration of appropriate microbiological assessment and, if indicated, collection of specimens *before* the first dose of antimicrobial
3. selection of an antimicrobial for the specified indication that is consistent with appropriate clinical guideline

recommendations: consider the required spectrum of activity, potential adverse effects, drug interactions and cost, as well as patient factors such as history of antimicrobial hypersensitivity, recent antimicrobial use, and pregnancy and breastfeeding (*This point highlights the need for up to date standard treatment guidelines which are based on laboratory surveillance specific for the setting. The guidelines determine the next two points*)

4. selection of the appropriate dose, frequency and route; consider the severity and site of infection, as well as pharmacokinetic and pharmacodynamic parameters that influence dosage regimens
5. prescribing for the appropriate duration; consider specifying a review or stop date.

In addition:

Clearly document all antimicrobial therapy in the patient's medical records and/or medication chart. Documentation should include the indication and the intended duration of therapy before further review or cessation.

When an antimicrobial is prescribed, provide information about the indication and the intended plan for antimicrobial therapy and the potential adverse effects to the patient or the patient's carer.

In Australia the **Australian Commission on Safety and Quality in Health Care (ACSQHC)** recommends **five essential strategies** and other activities for effective antimicrobial stewardship which are arguably relevant to most national settings:

- implementing clinical guidelines that are consistent with the latest version of *Therapeutic Guidelines: Antibiotic* and that incorporate local microbiology and antimicrobial susceptibility patterns
- establishing formulary restriction and approval systems
- ensuring laboratories use selective reporting of susceptibility results consistent with hospital or health service antimicrobial treatment guidelines
- reviewing antimicrobial prescribing, with intervention and direct feedback to the prescriber.
- monitoring performance of antimicrobial prescribing and auditing antimicrobial use

Notably, in all the above principles, there is no mention of the need for a national regulatory framework.

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<sup>6</sup> <https://www.tg.org.au>

## Community Perceptions

Many studies have demonstrated that knowledge and perceptions of patients / community members are inaccurate, but do those perceptions have an impact on actual use?

In **Fiji** knowledge about antibiotics was assessed in a nationally representative study sample of 5000 Fijian community participants (Mataika and Yim, 2015). Education was highly correlated with knowledge of antibiotics with those having completed lower levels of education stating less knowledge of what antibiotics were. The terms amoxicillin or penicillin were more known and recognised than the term antibiotics. Large numbers of participants still used antibiotics for viral infections such as colds or flu. Antibiotics were used to treat headache, dengue, asthma, pregnancy and pain. Antibiotics were sometimes obtained without prescriptions from retail pharmacies (illegally) and they were frequently shared among family and friends. Despite knowing what antibiotics are, 67.1% of the surveyed population did not know what antimicrobial resistance was. A separate Fijian study asking doctors why they prescribe antibiotics when they are not necessarily appropriate showed that doctors perceived patient pressure as a reason (Pickmere et al, 2015). However there are no Fijian studies that show that physicians **are** significantly influenced by patient pressure.

Studies in other country settings show that community / patient perceptions and expectations do have an impact on antibiotic use both through prescriptions from authorised prescribers and also obtained from other sources. Lao PDR studies have indicated that patient perceptions **do** have a serious impact on AB use.

Along with studies in other Mekong countries that show very wide use of antibiotics in the community before physicians are consulted, a report of studies in **Lao PDR** (Khennavong et al 2011) of pre-treatment in Vientiane patients described antibiotic activity detected in urine samples pre-consultation with a doctor. In Vientiane, children had a higher frequency of estimated antibiotic pre-treatment than adults (60.0% versus 46.5%). Antibiotics are widely available without prescription at private pharmacies in Laos and dispensing of a single dose or an incomplete course is widespread.

Although Laos appeared at the time to have lower levels of antibiotic resistance in comparison to adjacent countries, (Phetsouvanh et al, 2006) extended-spectrum  $\beta$ -lactamase-positive *E. coli* and *Klebsiella pneumoniae* clinical isolates were present in Vientiane, (Stoesser et al, 2009). The high frequency of antibiotic use in the community, as revealed by urinary antibiotic activity, may cause worsening drug resistance (Stoesser et al, 2009).

In **Cambodia** 775 children of median age 4.6 years were investigated during the 2 days prior to attending an outpatient department. Urine samples were taken from all of them (with consent). For these outpatients, 7.3% of caregivers reported giving a known and named antibiotic and 37.8% children were given one or more unknown medications. However, the results of the urine tests showed antibiotic activity in 31.7 % of samples (against the 7.3% claimed by the caregivers). In addition, 16.3% (40/246) of urine samples that showed antibiotic activity did so against the MRSA or *S. typhi* isolates (Katherine et al. 2015). The most common source for obtaining medications was a private pharmacy followed by other health centres and sources such as relatives, mobile 'nurses' or charities.

A similar study was undertaken in the **Philippines**. Urine samples were taken for a bioassay to detect antibiotic activity. A total of 164 patients were found positive for antibiotic activity. Beta lactam antibiotics were reported by caregivers to have been most commonly given. Among bioassay positive patients, dengue 55%, was the most frequent diagnosis, followed by other viral infections, including measles, rubella, and mumps. The authors assert that unnecessary antibiotic use for febrile illnesses before hospital consultation is common in the low-income, highly populated urban community in Manila. Education targeting this group should be implemented to reduce unnecessary antibiotic use.

**Taiwan:** A Taiwanese paper introduces another dimension that is suggested to affect the use of antibiotics. It is submitted that an antibiotic prescription is a tangible measurement of *quality* (Bennett et al, 2015). Patients are interested in quality (as they perceive it) so there is competition between prescribers to deliver quality and so encourage patients to consult their practices. Ho ([2005], p. 246) argues that the intensive use of antibiotics also reflects cultural norms: 'The patient's primary purpose in seeing a doctor is to get a prescription. In the Chinese conception, every illness requires some sort of medicine. The idea that some diseases do not require medicine is unacceptable.'

A study in **Malaysia** (Ai Ling Oh et al, 2011), conducted in the out patient department of a hospital pharmacy in Penang found nearly 55% of the respondents had a moderate level of knowledge about antibiotics and their role. Although nearly 60% were aware of antibiotic resistance in relation to overuse of antibiotics, 38% still believed that taking antibiotics when having cold symptoms could help them to recover faster, and 47.3% expected antibiotics to be prescribed for common cold symptoms.

The findings exemplified in these few studies highlight the importance of *Improving awareness and*

*understanding of antimicrobial resistance through effective communication, education and training.*

They also highlight the need for regulatory control of the prescribing and dispensing of antibiotics.

### **Factors that Influence prescribing by medical staff and other providers**

In New Delhi, **India**, Kotwani and Holloway (2011), conducted exit interviews between December 2007 and November 2008 with patients after their attendance at private retail pharmacies, public sector facilities and private clinics to determine what prescriptions they had been given. A total of 33,132 patients were interviewed.

39% of the patients attending private retail pharmacies and public facilities and 43% of patients visiting private clinics were prescribed at least one antibiotic. Consumption patterns of antibiotics were similar at private retail pharmacies and private clinics where fluoroquinolones, cephalosporins, and extended spectrum penicillins were the three most commonly prescribed groups of antibiotics. At public facilities, there was a more even use of all the major antibiotic groups including penicillins, fluoroquinolones, macrolides, cephalosporins, tetracyclines, and cotrimoxazole. Newer members from each class of antibiotics were prescribed. In this study, diagnoses were not requested.

A number of other studies in India by Kotwani, Holloway, et al show the same prescribing patterns for diarrhoea, respiratory infections and others, with the excessive use of fluoroquinolones and cephalosporins. (Kotwani et al 2012; Kotwani and Holloway 2014)

In Ujjain in central India (Hutchinson-Kern, 2015) selected households were surveyed to explore the relationship between health-seeking behaviour determinants (pre-disposing, treatment-related and illness-related factors) and outcomes of both antibiotic use in general and fluoroquinolone/third-generation cephalosporin use in particular. Informal healthcare providers (IP) were consulted for 58% of episodes and of these 47.4% prescribed an antibiotic, 34.4% specifically a fluoroquinolone and/or a third-generation cephalosporin.

Kanungo et al (2015) found that health-seeking behavior in India is influenced by factors including accessibility, acceptability and costs of healthcare. In the Hutchinson-Kern study 90% of those seeking care outside the home chose an IP - respondents in her study were within 15 minutes travel of an IP. She also concluded that diagnostic tests were almost completely absent.

According to Kotwani et al (2012) 'Important factors identified for antibiotic prescriptions by prescribers in India were diagnostic uncertainty, perceived demand and expectation from the patients, practice sustainability

and financial considerations, influence from medical representatives and inadequate knowledge.'

A study in **Sri Lanka** of 50 patients with acute respiratory tract infections, and five physicians (Tillekeratne, 2017) in the OPD of a large tertiary hospital was undertaken to assess Sri Lankan patients and physicians attitudes towards ARTI diagnosis and treatment. Most patients expected to receive medication prescriptions at their visit, but not specifically an antibiotic prescription. However, more than 70% of patients did receive antibiotic prescriptions. Interviews with physicians revealed that they incorrectly perceived that patients desired antibiotic capsules and cited patient demand as an important cause of antibiotic overuse. They also indicated that the high patient load and fear of bacterial super-infection drove antibiotic overuse.

In **Australia** the Aged Care National Antimicrobial Prescribing Survey (acNAPS) was undertaken in 2016<sup>8</sup>. A total of 251 Aged Care facilities (mostly inner regional Victoria and State Government operated) participated and 13,447 residents were interviewed.

Respiratory tract (34.5%), skin or soft tissue (29.3%) and urinary tract (14.8%) infections were the three most common indications for prescribing antimicrobials. Cephalexin (21.7%) was the most commonly prescribed antimicrobial. About one third (32.4%) of the antimicrobials were prescribed for residents with no signs and/or symptoms of infection in the one week prior to the antimicrobial study date.<sup>9</sup>

Other findings from the study were:

#### **Prolonged duration of antimicrobial prescriptions:**

The antimicrobial start date was greater than six months prior to the survey date for 23.3% of prescriptions and administration was continued.

**Widespread use of topical antimicrobials:** About one quarter of antimicrobial prescriptions were for topical use.

#### **Incomplete documentation of key prescribing elements:**

The antimicrobial start date was unknown for 3.2% prescriptions and the indication for antimicrobial use was not documented in 22.1% of cases. And the review or stop date was not documented in 50% of prescriptions.

Key issues that can promote antimicrobial resistance (AMR) were identified in the Aged Care facilities including **poor infection control practices and**

<sup>8</sup> acNAPS is a collaborative project between the National Centre for Antimicrobial Stewardship (NCAS), the Guidance Group, Victorian Healthcare Associated Infection Surveillance System (VICNISS) Coordinating Centre and the participating ACHs. It is supported by funding from the Australian Commission on Safety and Quality in Health Care (the Commission) under the Antimicrobial Use and Resistance in Australian (AURA) project.

<sup>9</sup> [http://www.infectioncontrolct.org/uploads/2/6/2/4/26245608/nh-hac\\_mcgreercriteriarevcomp\\_2012.pdf](http://www.infectioncontrolct.org/uploads/2/6/2/4/26245608/nh-hac_mcgreercriteriarevcomp_2012.pdf)

**excessive and inappropriate antimicrobial use** which have contributed to AMR being serious worldwide threat to public health. It is not surprising that Aged Care facilities are included in Australia's National AMR Plan.

In **Thailand** a study was conducted to evaluate the impact of education together with an antibiotic-control program on antibiotic-prescribing practices, antibiotic consumption, antimicrobial resistance, and cost of antibiotics in a tertiary care hospital in Thailand (Apisarnthanarak et al 2006). Local hospital antibiotic guidelines developed from existing published guidelines were used to measure the appropriateness of antibiotic use. A study was conducted of one year before and one year after the educational interventions that were based on principles of good antibiotic use and the recommendations in the hospital antibiotic guideline.

After the intervention there was a 24% reduction in antibiotic prescriptions and the incidence of inappropriate prescribing was reduced from 42% to 20%. A sustained reduction in use was observed with significant reduction in third generation cephalosporins. However, rates of use of cefazolin and fluoroquinolones increased. There were no significant changes for other antibiotic classes. Significant reductions in the incidence of infections due to methicillin-resistant *Staphylococcus aureus*, *Escherichia coli*, extended-spectrum  $\beta$ -lactamase-producing *Klebsiella pneumoniae* and third-generation cephalosporin-resistant *Acinetobacter baumannii* were also observed.

The researchers concluded that education and an antibiotic-control program constituted an effective and cost-saving strategy to optimize antibiotic use in a tertiary care center in Thailand.

The 2011 Thai National Drug Policy on the rational use of medicines, which comprises national strategies for the containment of antimicrobial resistance, as well as other policy movements offer an opportunity to consolidate *Antibiotic Smart Use*.

The *Antibiotics Smart Use* (ASU) program started in 2007 in Thailand as an innovative way to promote the rational use of antibiotics by strengthening human resources, improving health facility infrastructure, and empowering communities in a setting with limited resources and difficulty translating rational use of medicines from theory into practice. The project targeted three conditions not requiring antibiotic treatment: upper respiratory infections, especially the common cold with sore throat, acute diarrhoea and simple wounds. For these conditions ASU attempted to reduce unnecessary use of antibiotics. For more about the Smart Use program see

<https://www.reactgroup.org/toolbox/rational-use/examples-from-the-field/antibiotics-smart-use-thailand/>

**Policies**, despite not being law, reflect a strong commitment to support the rational use of medicines in Thailand – but can long term commitment be maintained? The team recognizes that strong political commitment is a crucial element for success. The Thai health system is structurally conducive to the overuse of antibiotics<sup>7</sup> because it allows physicians to dispense drugs, pharmacists to prescribe them and patients to medicate themselves. A strong Regulatory framework must be in place, and enforced and accompanied by bottom-up approaches (eg community empowerment) along with tools such as treatment guidelines and surveillance mechanisms with strong laboratory support and effective infection prevention and control.

In **Oman**, Al Maliky et al (2017) conducted a study to evaluate antibiotic prescribing in the Sultan Qaboos University Hospital (SQUH) by measuring the overall compliance with the local antibiotic prescribing guidelines. Analyses were performed using descriptive statistics and main outcome measures were antibiotic prescribing compliance with the local guidelines as well as with the overall Restricted Antibiotic Policy adherence at the hospital.

They found that compliance with local guidelines was suboptimal at 63% and of 211 restricted antibiotics prescribed, the overall adherence to Restricted Antibiotic Policy was inadequate at 46%. The majority of the antibiotics prescribed were broad spectrum at 90%, penicillins 31% and cephalosporins at 17%. It was concluded that the study has provided valuable baseline details of antibiotic prescribing patterns in SQUH.

It was concluded that additional studies would be required to address the reasons behind the non-compliance with local guidelines.

**Pakistan:** Atif et al (2017) in Pakistan investigated the prescribing patterns and utilization of antimicrobials in ten selected wards at Bahawal Victoria Hospital (BVH), Bahawalpur, Punjab, Pakistan.

They used a descriptive cross-sectional study using the World Health Organization (WHO) indicators for antimicrobial use<sup>10</sup>. Data from 1,000 prescription records were collected for the six months January to June 2016.

For the hospital indicators, a formulary list or essential medicines list was available, but standard treatment guidelines (STGs) for infectious diseases were not. For the prescribing indicators, the percentage of hospitalisations with antimicrobial(s) prescribed was 82.3%. Drug sensitivity testing was almost non-existent, with only 0.24% prescription records having drug

<sup>10</sup> World Health Organization. How to investigate antimicrobial use in hospitals: selected indicators. 2012. <http://apps.who.int/medicinedocs/documents/s21031en/s21031en.pdf>.

sensitivity tests. Ceftriaxone (39.6%), metronidazole (23.4%) and cefotaxime (23.1%) were the top most frequently prescribed antimicrobials.

In the absence of STGs for infectious diseases in Pakistan, prescribers do not have a standard to follow and they can prescribe antimicrobials freely, and it is difficult to measure whether antimicrobial prescribing is rational or not in the absence of a standard to measure against. Besides the availability of STGs, it is essential that the key recommended antimicrobials should be available all the time at hospitals.

**Solomon Islands:** The development and launch in 2015 of Antibiotic Guidelines in the **Solomon Islands** (*Solomon Islands Antibiotic Guidelines (SIAG)*) was a collaborative effort involving all clinical departments at the National Referral Hospital (NRH) and was led by local doctors.

Hutchinson-Kern et al (2016) conducted a study to assess the impact of the guidelines and whether introduction of guidelines is enough to change clinical practice. Doctors were surveyed before and after the implementation of the SIAG to assess its impact on prescribers' knowledge of rational antibiotic prescribing and antibiotic treatment for common indications. It was intended that the results would inform the design and implementation of more effective antimicrobial stewardship interventions for Solomon Islands.

All doctors, from intern to consultant, working at NRH were invited to participate. All prescribers had been given a copy of the SIAG at the launch of the guidelines in June 2015.

The survey was by administration of a pretested questionnaire covering:

1. Attitudes: confidence in prescribing in various scenarios; sources of information used to find information on antibiotic prescribing; attitudes about current and potential interventions to improve antimicrobial stewardship
2. General knowledge: questions to assess knowledge about antimicrobial resistance and rational prescribing of antibiotics
3. Specific knowledge: antibiotic treatment for common indications; antibiotic choice, dose, route and duration classified as 'correct' or 'incorrect' according to the new SIAG.

Data collection points were baseline, 2 months and 6 months after the launch of the guidelines. Participation was voluntary and results anonymous. No prior warning for the surveys was given.

Additional interventions were two continuing medical education sessions for all prescribers, two medical intern education sessions, posters promoting the SIAG and

highlighting dose changes, and ward treatment chart audits.

General knowledge did not change significantly over the study period but there was improvement in specific knowledge of antibiotic prescribing demonstrating that doctors were becoming familiar with the new SIAG. That was reflected in an antibiotic point prevalence study carried out at NRH during the same period.

The guidelines had introduced a number of significant dosing changes to commonly prescribed antibiotics. The survey demonstrated that prescribers continue to require support concerning changes. For example, at 6 months all respondents with the correct antibiotic for CAP in children used the old dosing.

Confidence in prescribing in different scenarios was high at both baseline and 6 months but this was not reflected by accuracy in responses to specific treatment questions particularly for serious but common infections such as severe community acquired pneumonia in adults.

The survey team acknowledged that practice change requires ongoing support and education. A national Antimicrobial Stewardship Committee was planned to provide oversight and input into the ongoing antimicrobial stewardship program.

In **China** research by Zhang and Harvey (2006) adapted Australian best-practice guidelines on the prophylactic use of antibiotics in surgery to a Beijing teaching hospital in 2002-2003. The guidelines were adapted in collaboration with local Chinese experts and their introduction was accompanied by educational interventions.

Antibiotics prescribed for surgical prophylaxis in 60 consecutive patients undergoing clean or clean-contaminated surgery (120 total) were compared with guideline recommendations in three phases; a pre-intervention period from June to August, 2002, an intervention period from June to August 2003 and post-intervention period from September to November 2003. During the intervention phase, feedback about prescriptions not in accord with the guideline was discussed with around 25 prescribers every two weeks.

While agreement was reached on the principles of antibiotic surgical prophylaxis there was no consensus on detail. Second and third generation cephalosporin antibiotics still predominated in both low-risk clean and clean-contaminated operations. The timing of prophylaxis was correct in virtually all patients and the duration of prophylaxis was less than 24 hours in 96% of patients undergoing clean surgery compared to only 62% of patients undergoing clean contaminated surgery.

The intervention had produced no improvement in the duration of prophylaxis nor the overuse and inappropriate choice of unnecessary broad-spectrum

and expensive drugs. Interviews and focus groups revealed an important explanation for the latter problem – that the Chinese government policy expected hospitals to support themselves so there was a vested interest in prescribing high profit medicines. It was concluded that improving antibiotic use in China would require hospital funding reform, more authoritative best-practice guidelines, and hospital authorities embracing quality improvement.

In **Fiji** a study of colistin use in major hospitals was undertaken (Pickmere et al, 2016). It had been noticed that the use of colistin had escalated alarmingly. Colistin is an expensive 'last-resort' broad-spectrum antibacterial agent, that is used to treat multi-resistant *Acinetobacter baumannii* (an opportunistic organism that often causes nosocomial infections) and certain other *spp*. Therefore, colistin use and misuse raises the potential for the development of significant bacterial resistance with profound clinical impact on the Fijian healthcare system.

The study was to determine the extent of the intravenous use of colistin and the rationale and reasons for its use during the time it had been available in Fiji. During the study period, records of treatment were sought and analysed for patients who had been treated with colistin. Information from physicians was gathered about their use of colistin. Records of treatments were gathered (with great difficulty) from pharmacy and patient files. Microbiology and Infectious Diseases teams were interviewed; cost issues were explored and resistance patterns of organisms were examined.

This study produced a range of significant findings:

**Patient records:** Comprehensive patient records are not routinely maintained and retrievable so drug use evaluation studies (DUEs) cannot be undertaken, diagnoses statistics cannot be maintained and quantities of medicines needed for treating those disease/conditions cannot be estimated.

**Stock-outs:** There are stock-outs of medicines in the wards, infection control consumables and equipment, laboratory supplies. Stock-outs of first-line antimicrobial drugs can lead to the prescription of restricted antimicrobials because the recommended antibiotics are not available.

**Patient Treatment:** Many of the patients treated with colistin were suffering from infections that warranted prompt treatment with colistin - inadequate infection prevention and control (IPC) (supposedly due to inadequate supplies) fostered the development of nosocomial MDR organisms. There had been a recent outbreak of *Acinetobacter baumannii* in the main referral hospital.

There is suboptimal understanding among prescribers of the use of protocols and standard treatment guidelines

and these documents are not always readily available so a detailed guideline for the use of colistin is needed. The third edition of the Antibiotic Guidelines was published in 2011 almost five years before. Revision of that edition was urgently needed.

**Laboratory services:** the laboratory is short staffed and capacity needs to be strengthened. Records of laboratory tests are not kept meaning there is no way to study resistance patterns.

**Infection prevention and control:** Infection prevention and control (IPC) is very poor, supposedly due to staff shortages and stock-outs of consumables needed for IPC.

**Cost implications:** The cost of purchasing colistin urgently by air from Australia (due to stockouts) for treating infected patients is unnecessarily high.

**Antimicrobial Stewardship** is urgently needed in all three hospitals to monitor all aspects of infection control, laboratory services and antimicrobial use according to STGs and protocols.

To address the identified issues it was recommended that quantification of medicines and other stock needs must be based on comprehensive patient records of treatment according to STGs. A reliable supply of stock of all medicines must be maintained so first-line antibiotics are always available when needed. IPC supplies must be guaranteed so meticulous IPC is in place throughout the hospitals and laboratory supplies must be guaranteed to facilitate efficient and prompt delivery of laboratory results. Microbiology services must be strengthened and accurate records maintained.

Up-to-date Standard Treatment Guidelines (STGs) and revised medicines-use protocols must be in the possession of all prescribers; and prescribers should be involved in their preparation. Protocols and guidelines must facilitate prompt initiation of treatment where necessary to overcome delays that can be caused through waiting for laboratory results or signatures.

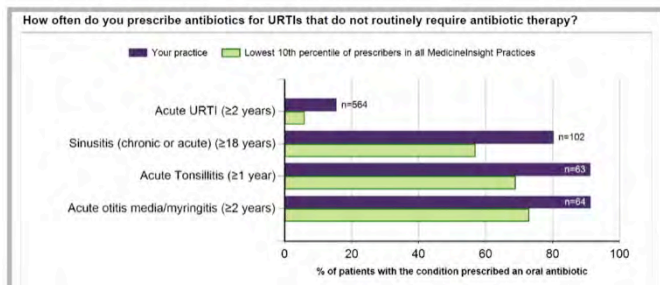
More cost-effective procurement of colistin from good quality generic manufacturers should be explored.

An Antimicrobial Stewardship team must be developed in all hospitals as a priority and resistance patterns of organisms should be studied routinely so prompt responses can be implemented when needed.

**Australia:** In an attempt to reduce inappropriate use of antibiotics for URTIs, and, in particular, to modify patient misconceptions about the effectiveness of antibiotics for URTIs, Wutzke et al 2006 and Australia's National Prescribing Service Ltd (NPS) have undertaken a comprehensive, multi-strategic program for health professionals and the community. Interventions targeted health professionals including prescribers at all levels. The evaluation used multiple methods and data sources



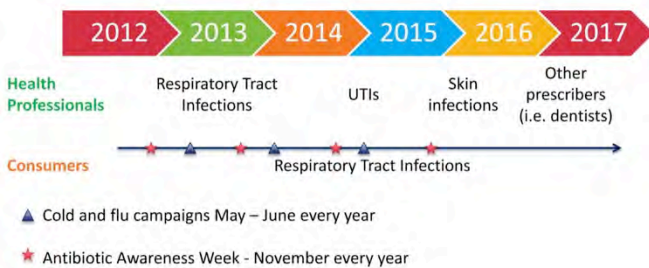
to measure process, impact and outcomes. Prescribers were provided with feedback rating their prescribing against their peers at the district and regional levels.



Consistent with intervention messages, the integrated nationwide prescriber and consumer program has been associated with modest but consistent positive changes in consumer awareness, beliefs, attitudes and behaviour about the appropriate use of antibiotics for URTIs together with a national decline in total antibiotic prescriptions dispensed in the community (from 23.08 million prescriptions in 1998–99 to 21.44 million in 2001–02) and, specifically, by a decline in use among the nine antibiotics commonly used for URTI.

After the rollout of the first health professional educational program it was concluded that *The NPS Common Colds Community Campaign*, in synergy with interventions for health professionals, communicated clear, consistent, positive and persuasive messages via multifaceted media and strong branding repeated over 5 years. A further 5 year campaign directed at the community and health professionals was conducted between 2012 and 2017 (NPS 2017). Analysis of that campaign is currently being undertaken.

## PROGRAM TIMELINE



## Discussion

Studies presented here demonstrate clearly the need for education of community people and health professionals as a basis for improving the understanding and use of antimicrobial medicines and controlling the development of AMR. Clear principles of appropriate antimicrobial prescribing are available and the WHO AMR Plan

template includes wide ranging strategies to support improved understanding and use of antimicrobials.

A strong regulatory framework is needed with sale and distribution of antibiotics on prescription only and restricted to authorised health professionals. The law needs to be enforced with penalties for non-compliance.

Political support and leadership are very important. Clear lines of authority need to be in place so there can be no misunderstanding about how decisions are made or confusion about who may authorise activities. The WHO AMR Plan template emphasises the importance of governance. As in other areas the support of key opinion leaders is very helpful and guidance from a well-functioning Medicines and Therapeutics Committee is very valuable.

It has been demonstrated that standard treatment guidelines must be in place but they alone do not have a sustainable impact on prescribing. Ownership of the guidelines is important and involving users in their preparation can assist ownership. Promotion of the guidelines needs to be supported by other ongoing interventions; and the guidelines must be kept updated by regular review. It has been shown that the impact of promotional messages ‘wears off’.

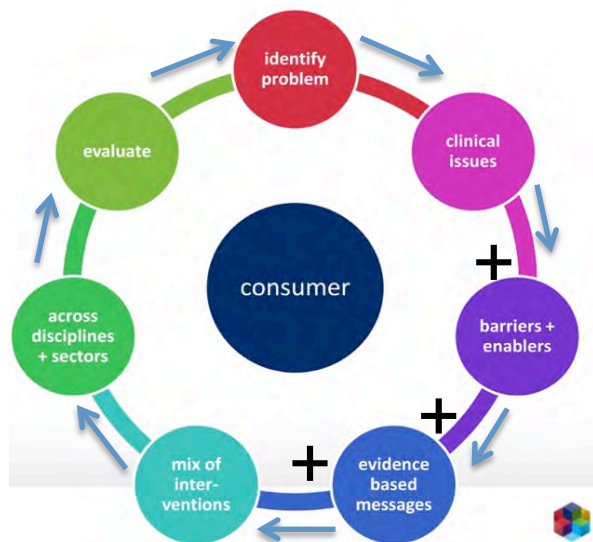
Even with political will, appropriate legal framework, sound governance and clear standard up-to-date specific treatment guidelines against which to measure use, improved use of antimicrobials cannot occur when other structures such as financial incentives for prescribing expensive medicines are part of the system for funding health services.

These studies also identify other factors that have an impact on the prescribing and use of antimicrobials. For example, other important factors that contribute to the inappropriate prescribing. For example as well as appropriate regulatory environment, financial environment and cultural environment there must be appropriate stock management. Comprehensive records of prescriptions, including diagnoses must be kept as must all laboratory and microbiology records. Without records there can be no monitoring and evaluation and no surveillance. Without records there can be no Antimicrobial Stewardship.

Good antibiotic prescribing depends on more than just compliance with the principles of good antibiotic prescribing. Structures such as efficient laboratory services for diagnosis and surveillance together with effective infection prevention and control need to be in place to enable compliance with the principles articulated by therapeutic guidelines.

Where studies have been undertaken and have identified issues that obstruct appropriate use of antimicrobial medicines, recommendations to address

the identified issues must be implemented promptly, the impact of the intervention measured promptly and evaluated; and further recommendations made and implemented. The process is a continuing cycle. The NPS program is a good example of this process (Dartnell and Heaney, 2017). Improved practices are more likely when there is a cyclic process as exemplified in the Australian NPS program.



Australia provides an example where all the elements needed for sustaining a good program for control of antimicrobial resistance in humans are in place:

- **Legislative framework:** with enforced regulations and penalties for non-compliance
- **Continuing Professional Development (CPD)** is mandatory for maintaining annual registration ]
- **Prescribing is controlled ]**
- **Major hospital policies are directed by therapeutic committees**
- **Authoritative up-to-date Treatment Guidelines** are available and widely used.
- **Independent ongoing professional education** is available
- **Records of all antibiotic prescriptions** are available through the PBS.
- **Laboratory services** are advanced.
- **Surveillance** is established and functioning.
- **Infection Control is efficient** and strictly enforced by regular audit.

**Does that mean that prescribing and use of antimicrobial medicines in Australia is perfect? Absolutely not!**

There is significant sub-optimal prescribing and use and plenty of room for improvement. Doctors still feel multiple pressures to prescribe antibiotics when they may not be necessary (Dartnell and Heaney, 2017). They cite patient expectations, time pressure, diagnostic

uncertainty, medical liability. They still believe their individual prescribing doesn't make a difference in view of other antibiotic use – hospitals, vets, agriculture. However Australia is fortunate to have an environment that makes improvement possible.

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