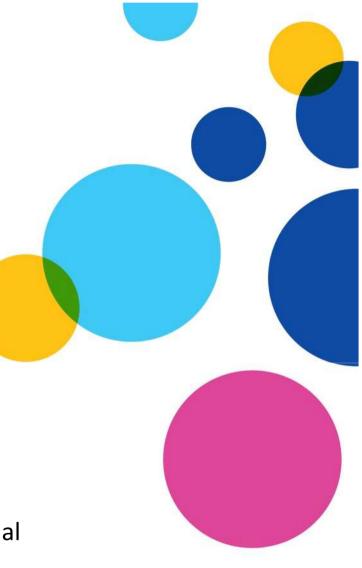
One Health Antimicrobial Stewardship – the challenge of implementation

Professor Karin Thursky Director, NHMRC National Centre for Antimicrobial Stewardship Peter Doherty Institute



stewardship

noun | stew·ard·ship | \'stü-ərd-ship, 'styü-; 'st(y)urd-\

Popularity: Top 1% of lookups

Examples: STEWARDSHIP in a sentence 🗸

Editor's note: Good STEWARDSHIP 🗸

Definition of STEWARDSHIP

- 1 : the office, duties, and obligations of a steward
- the conducting, supervising, or managing of something; *especially*: the careful and responsible management of something entrusted to one's care *stewardship* of natural resources

The scale of the problem

- Animal use:
 - ¾ of antimicrobial use is non human
 - Understand gross usage, but not where and how, and why..
- Human use:
 - General practice/ Community 80% of human use
 - 15% of all GP consultations end in antibiotic prescription
 - Commonest reason is URTI, >80% are viral
 - Aged care highest intensity of use in community
 - 10% of residents receiving antimicrobial at any time
 - Hospitals 40% prevalence of antibiotic use
 - 20-50% of use is inappropriate
 - Most common reason is 'prophylaxis'

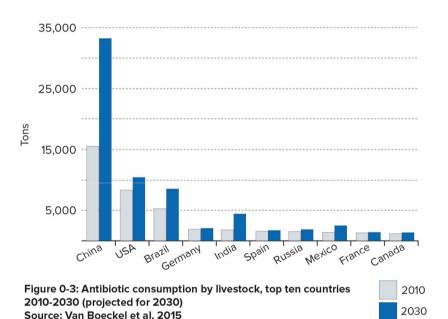




A new sense of urgency



- Identification of the MCR1 gene in pigs in China Jan 2015 (Lancet)
 - Conferred colistin resistance, plasmid
- 19 countries, animal and human isolates
- Calls for bans on colistin use in animals
- Calls for urgent action on AMR
- A new focus on a One Health approach





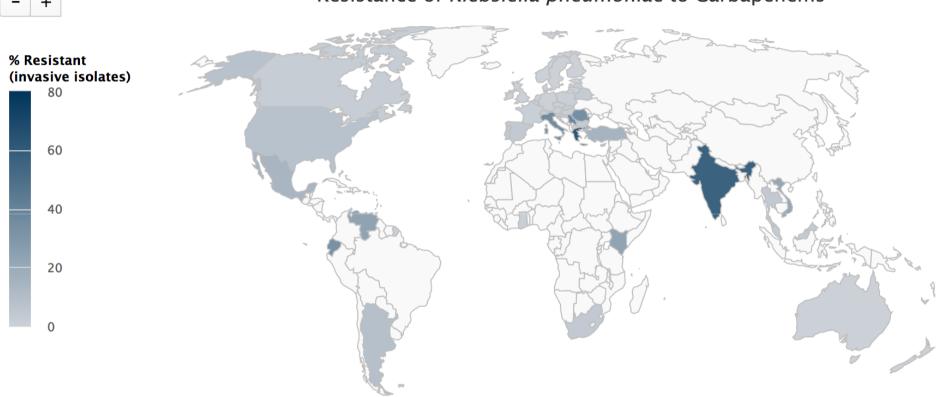
Antibiotic Resistance of Klebsiella pneumoniae F 昌 ÷ \sim 100 % Resistant (invasive isolates) 75 50 25 Australia India Malaysia South Africa United Kingdom **United States** Aminoglycosides Amoxicillin-clavulanate Carbapenems Cephalosporins (3rd gen) Fluoroquinolones Piperacillin-tazobactam Polymyxins

Center for Disease Dynamics, Economics & Policy (cddep.org)

2015 data, CDDEP

National Centre for Antimicrobial Stewardship





Resistance of *Klebsiella pneumoniae* to Carbapenems

Lots of missing data

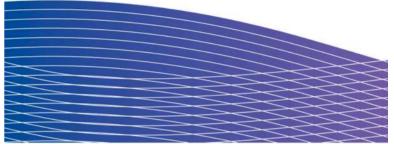
Validity of data (e.g only sickest patients get microbiology)

The O'Neill Report May 2016

Review on

Antimicrobial Resistance

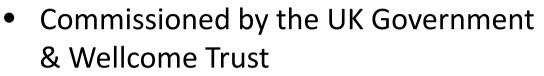




TACKLING DRUG-RESISTANT INFECTIONS GLOBALLY: FINAL REPORT AND RECOMMENDATIONS

THE REVIEW ON ANTIMICROBIAL RESISTANCE CHAIRED BY JIM O'NEILL

MAY 2016



- Report presented to G20, UN meetings
- 'Implementation ideas'
- A supra-national global organisation to set priorities for new diagnostics, vaccines, new drugs
- Market entry awards to pharma
- Accessibility to all nations

Stewardship –23 mentions.....but undefined

UN Draft Declaration on AMR (Sep 2016)

"Acknowledge that the resistance of bacterial, viral, parasitic and fungal microorganisms to antimicrobial medicines that were previously effective for treatment of infections is mainly due to:

- 1. The **inappropriate use** of antimicrobial medicines in the public health, animal, food, agriculture and aquaculture sectors
- 2. Lack of access to health services, including to diagnostics and laboratory capacity
- 3. And antimicrobial residues into soil, crops and water

Resistance to antibiotics, which are not like other medicines, is the greatest and most urgent global risk, requiring increased attention and coherence at the international, national and regional levels" Plan.....Global Interagency Group: WHO/UN and World Org for Animal Health (OIE)



S

After the UN declaration on AMR, what comes next?

Filed Under: Antimicrobial Stewardship Chris Dall | News Reporter | CIDRAP News | Sep 28, 2016 **f** Share **y** Tweet **in** LinkedIn **Sep** 28, 2016 **f** Share **y** Tweet **in** LinkedIn **set** Email

developing nations use antibiotics as a substitute for sanitation, hygiene, and medical care. Asking them to reduce antibiotic use essentially removes a critical tool from their healthcare arsenal.

This is where organizations like the World Health Organization (WHO), the Food and Agriculture Organization (FAO), and the World Organization for Animal Health (OIE) will play a significant role. But how these UN bodies will ensure every country is holding up its end of the bargain remains an open question.

The challenge of implementation

"Implementing this will not be easy, at all," said Gian Luca Burci, JD, former legal counsel for the WHO. The UN declaration calls for the creation of a body that will coordinate the efforts of the WHO, FAO, and OIE. But coordination will be a challenge, Burci explained, because those organizations represent different constituencies with different priorities.

The declaration has no set goals and is non-binding



K raises alarm on superbugs



EWS

lospital bugs kill lore than cars

NDREW NCCLL Scottisk Pattitical Reporter

YOUR COMPENTS

OTLAND'S filthy hospitals killed more peo t year than the nation's roads.

ures released yesterday show there were 248 the from C-diff infectiona, while MRSA bugs claim ther 48 lives.

1 total of 296 compares with 272 deaths on thanfs roads. Hospital bugs were also a contribuor in another 683 deaths. Labour's Jackie Baille 1. 'It is frightening to think it is more dangerous in hospital than on the roads.





'Next pandemic' could be man-made

CDC warns about growing threat of antibiotic resistance

DELA TODAS

Antibiotic resistance that turns ordinary disease-causing barteria into illnesses that cur't be controlled could bring about the "aext pandemic," Centers for Discase Control and Prevention Director Tom Frieden warned at a



Die Wendelugten Dinner

The Times-Pleagune ?

CDC's Tum Frinden appeared July 16 before an oversight subcommittee of

New rules to stro meat inspection

By Bertis Farmed

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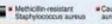
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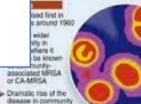
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Superbug ed for 60 percent of hospital int 19,000 deaths out of 94,000 inf





National AMR strategy plans **Greece: 2008** Denmark: 2010 France: 2011 UK: 2013 (updated implementation plan 2014) US, Spain: 2014 Norway, Germany: 2015 Australia: June 2015 Sweden: 2016 WHO Global Action Plan: 2015 The O'Neill Report: May 2016

UN Draft Report: Sep 2016

s://www.google.com.au/imgres?imgurl=http%3A%2F%2Fimg2-azcdn.newser.com%2Fsguare-image%2F10423-20110401030547%2Fsuperbug-shuts-dc

Australia's First National Strategy to address Antimicrobial Resistance



Objective One

Increase awareness and understanding of antimicrobial resistance, its implications and actions to combat it, through effective communication, education, and training

Implement effective antimicrobial stewardship...animal and human

settings to als

Develop nationally coordinated One Health surveillance of antimicrovial resistance and antimicrobial usage

Objective Four

Improve infection prevention and control measures across human health and animal care settings to help prevent infections and the spread of resistance

Objective Five

Agree a national research agenda and promote investment in the discovery and development of new products and approaches to prevent, detect and contain antimicrobial resistance

Objective Six

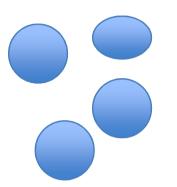
Strengthen international partnerships and collaboration on regional and global efforts to respond to antimicrobial resistance

Objective Seven

Establish and support clear governance arrangements at the local, jurisdictional, national and international levels to ensure leadership, engagement and accountability for actions to combat antimicrobial resistance



A reality check



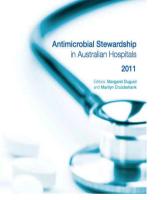
Pre 2008 Few leaders in AMS RMH – approval system

implemented 2005

> NAUSP Adult DDDs

Triggered formation of AMS working party with ACQSHC

2008



AMS Book 2011 Revised version 2018 to include community, indigenous, aged care etc.

Antimicrobial stewardship

Safe and appropriate antimicrobial prescribing is a strategic goal of the clinical governance system

This criterion will be achieved by: Actions required:

3.14 Developing, implementing and regularly reviewing the effectiveness of the antimicrobial stewardship system

 3.14.1 An antimicrobial stewardship program is in place
3.14.2 The clinical workforce prescribing antimicrobials have access to current endorsed therapeutic guidelines on antibiotic usage⁴⁵
3.14.3 Monitoring of antimicrobial usage and resistance is undertaken

3.14.4 Action is taken to improve the effectiveness of antimicrobial stewardship

Standalone accreditation criteria 2013 Update 2018

NAPS introduced 2013 Web portal 2014

Appropriateness & Guidelines concordance Adults and paeds Key partner for national AMR strategy 2015





AS

Structures and processes to support AMS in Australia (.....in hospitals)



- Australian Commission on Quality and Safety in HealthCare
 - National accreditation program includes AMS as a stand-alone criterion
 - National observation & medication chart (between the flag)
 - Implementation workbooks and toolkits
 - A national clinical care standard for AMS
- National guidelines for AB prescribing endorsed by accreditation (Therapeutic Guidelines)
- High quality Infection Prevention/Medical care
 - BUT....average hand hygiene compliance, especially doctors
- National Antimicrobial Prescribing Survey
- Tight regulation of drugs/quality
- Well established AMS models (approvals, post prescription review)
 - BUT issues in rural and regional sites
- Already low rates of gram negative resistance, MRSA declining
 - BUT.....high rates of VRE

2015...

Clinical Care Standards



Clinician Fact Sheet: Antimicrobial Stewardship

The goal of the Antimicrobial Stewardship Clinical Care Standard is to ensure that a patient with a bacterial infection receives optimal treatment with antibiotics. This means that patients are offered the right antibiotic to treat their condition, the right dose, the right route, at the right time and for the right duration. This should be based on accurate assessment and timely review as to lessen the risk of adverse effects and reduce the emergence of antibiotic resistance.

UNDER THIS CLINICAL CARE STANDARD

A patient with a life-threatening condition due to a suspected bacterial infection receives prompt antibiotic treatment without waiting for the results of investigations.

A patient with a suspected bacterial infection has samples taken for microbiology testing as clinically indicated, preferably before starting antibiotic treatment.

A patient with a suspected infection, and/or their carer, receives information on their health condition and treatment options in a format and language that they can understand.

When a patient is prescribed antibiotics, whether empirical or directed, this is done in accordance with the current version of the *Therapeutic Guidelines* (or local antibiotic formulary). This is also guided by the patient's clinical condition and/or the results of microbiology testing.

When a patient is prescribed antibiotics, information about when, how and for how long to take them, as well as potential side effects and a review plan, is discussed with the patient and/or their carer.

When a patient is prescribed antibiotics, the reason, drug name, dose, route of administration, intended duration and review plan is documented in the patient's health record.

A patient who is treated with broad-spectrum antibiotics has the treatment reviewed and, if indicated, switched to treatment with a narrow-spectrum antibiotic. This is guided by the patient's clinical condition and the results of microbiology tests.

National Centre for Antimicrobial Stewardship (NCAS)

The NCAS is a new NHMRC-funded Centre of Research Excellence that will investigate the evidence gaps in what is known about the relationships between antibiotic use in humans and animals and antibiotic resistance.

The NCAS represents the first One Health collaboration where researchers, scientists and clinicians working on antimicrobial resistance within the human world and the animal world have formally come together to investigate the same key research questions as they apply to livestock, veterinary care, community settings and hospitals general

NAPS National Antimicrobial Prescribing Survey

Welcome Caroline! | My



000000

Please select your module below

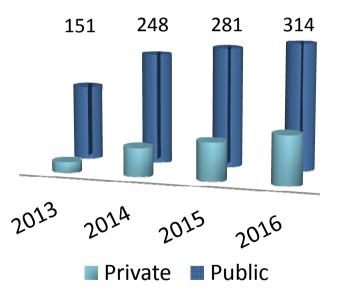


www.naps.org.au

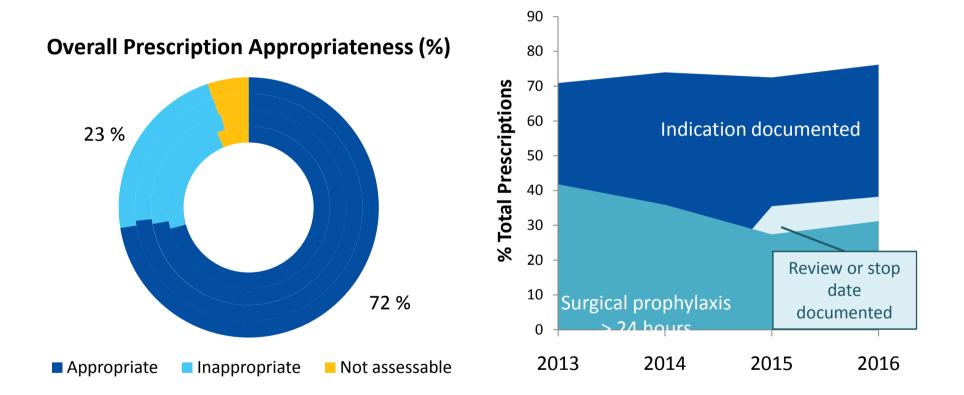
Participation

- Point prevalence survey
- All states and territories
- 33% of all public hospitals in Australia
 - 87% of principle referral hospitals
- 14% of all private hospitals in Australia
 - Annual participation is growing

Total Number of Participating Sites









Antimicrobial Use in Aged Care Homes in Australia



2016 AC-NAPS report

- 251 residential aged care facilities 1867 prescriptions
 - All states, private and public
- Data on infection prevalence and antimicrobial use
- Poor documentation
 - 22.1% did not have the indication documented
 - 49.9% did not have a review/stop date documented
- Most common indication= UTI: 17.9%
- 23.3% of antibiotics were prescribed for >6 months.
- For those antimicrobials <6 months (n=1372)
 - 32.4% for residents with no signs/ symptoms of infection

Require implementation support:

Africa, Americas, Eastern Mediterranean, Western

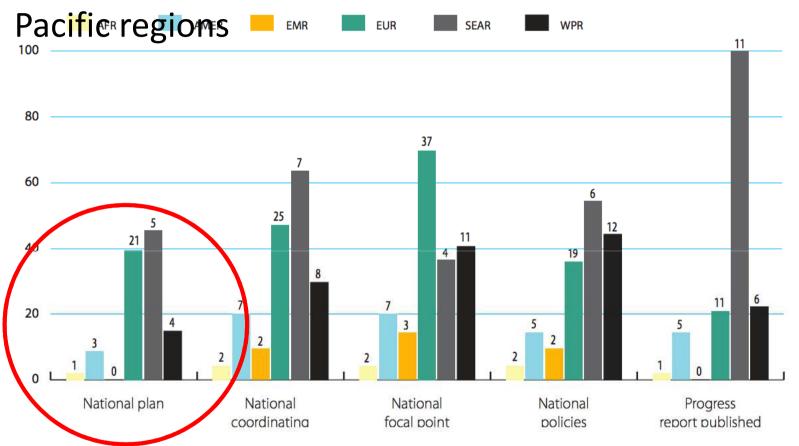


Figure 1.2 – Percentages of Member States that had a national plan for antimicrobial resistance, a coordinating mechanism, a focal point, a policy or a strategy and had prepared a report in the previous 5 years, by region (Note: numbers above the bars represent the numbers of participating Member States that answered "yes")

AFR, WHO African Region; AMER, WHO Region for the Americas; EMR, WHO Eastern Mediterranean Region; EUR, WHO European Region; SEAR, WHO South-East Asia Region; WPR, WHO Western Pacific Region

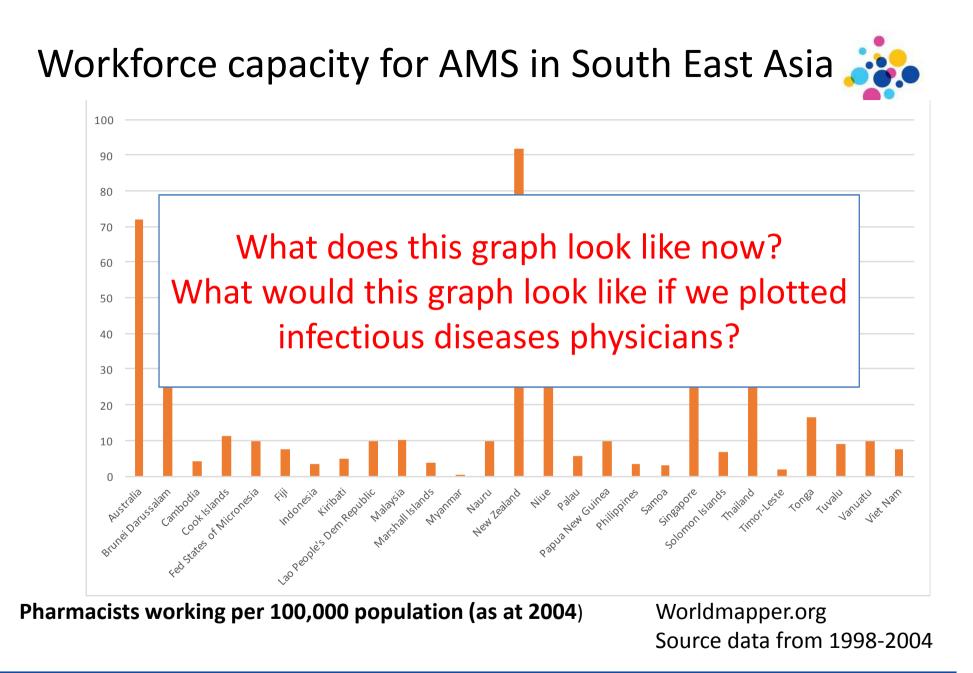
The Role of the WHO

N C A S

- AMS sits in Essential Medicines
- Lacks an implementation strategy (cannot be a one size fits all)

BUT

- AMS straddles Public Health, Quality and Safety, and Essential Medicines
- 3 separate governance arms
- Focus has been on usage surveillance & AMR surveillance
- Many national AMR strategies set targets for MRO rates. Is this the best outcome?
- Patient safety should be the priority (meaningful)



National Centre for Antimicrobial Stewardship

The Philippines as a case study





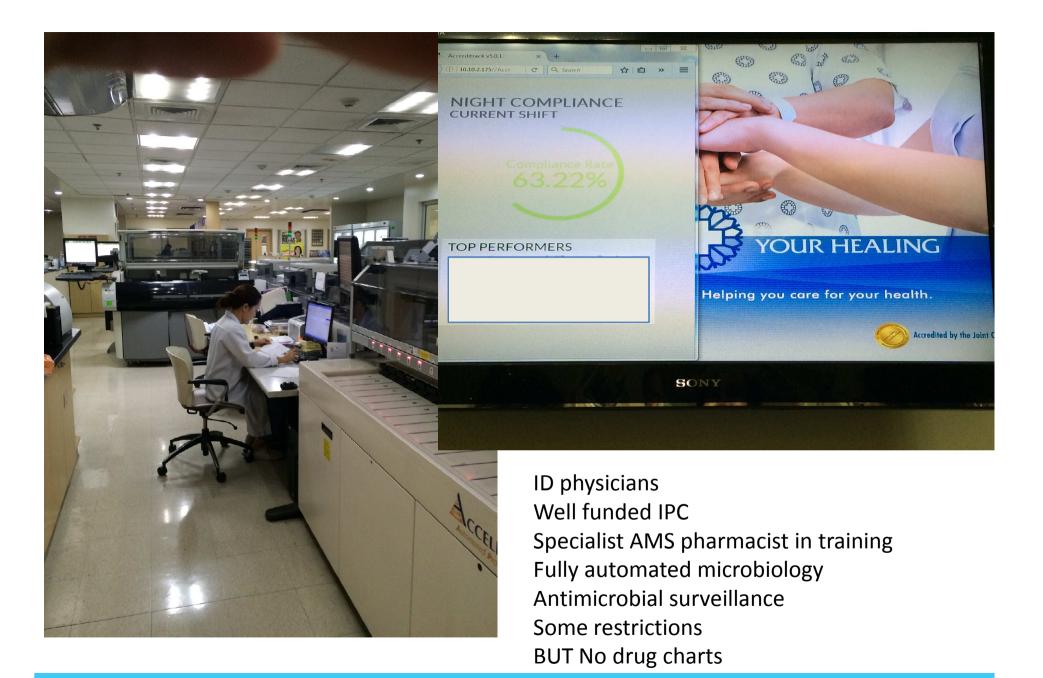


NCAS visit to WPRO May 2016 Site visits in Manila Purpose: Assess organisation readiness, identify gaps, and provide recommendations

The health care system

- Large private sector provides 30% pop and 70% of HCW
- Good links between private and public (supportive
- 4 levels of hospitals (only 20% level 3 or 4 with micro)
- Licensed hospitals *automatically* granted accreditation (being driven by universal health insurance)
- Inequity of access to health services/large out of pocket expenses
- National AMR policy 2015
- Administrative order for Includes AMS but funding only for IPC practioners 1: 100 beds

- Several AMS champions
- No dedicated funding for AMS
- No AMS training programs
- National guidelines being developed but no implementation plans
- AMR surveillance 24/1800 sites (undertakes credentialing activities) (ARSP)- WHONET
- National drug formulary- 6 antibiotics – tied to reimbursement but only for ARSP accredited hosp
- 3rd generation cephalosporins and FQ unrestricted
- No antimicrobial usage surveillance



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1500 bed university hospital AMS program in place (HEALS) **ID** expert Pharmacist Nurse to patient ratio 1:20 Poor IT infrastructure Only basic patient record systems A few clinical pharmacists Some clinical guidelines/ pathways (e.g Dengue, CAP) Microbiology reports hand delivered to wards once per day No real-time notification of +BC

Their national AMR strategy - goals



- Reduce by 30% CRE infections acquired during hospitalization
- Maintain the prevalence of ceftriaxone-resistant Neisseria gonorrhoeae to 0%
- Reduce by at least 30% overall MRSA bloodstream infections compared to rates in 2014
- Reduce by 30% MDR Pseudomonas spp infections acquired during hospitalization compared to estimates in 2014
- Reduce by 25% ciprofloxacin-resistant non-typhoidal salmonella infections compared to 2014

Is this the right focus? What about patient safety?

Our recommendations (short term)



Theme	Action item	Leading groups
Workforce	Appoint and provide dedicated funding to AMS champions and explore public-private collaboration for education and mentoring	DOH and WHO
Workforce	Clinical pharmacists should be recognised as an essential part of the AMS workforce, with dedicated government level funding provided	DOH
Guidelines	National guideline implementation should be discussed as a matter of urgency and an implementation plan developed	Guidelines Committee and AMS champions
Guidelines	Local hospital guidelines and clinical pathways should be reviewed and brought into line with national recommendations where possible	Hospital AMS/ID clinicians
Education	Develop specific AMS training package for clinical pharmacists, ICPs and clinicians that local hospitals can utilise (and modify as required depending on their local hospital context)	DOH, WHO and AMS champions
Documentation	Introduction of a standardised national medication chart whereby the medication order and administration are directly written onto the same document	DOH
Documentation	Improvements are made to ensure greater transparency and communication of patient alert information	DOH, Hospital executives
Documentation	Adaptation and implementation of clinical practice guidelines for the early recognition and management of sepsis should be a priority for all hospitals	Hospital AMS/ID clinicians
Restriction	Consider the addition of fluoquinolones and 3 rd and 4 th generation cephalosporins to hospital restriction lists	Hospital AMS/ID clinicians
Audit and review	Use of community dispensed antimicrobials should also be monitored, including an approval form if it is for a restricted antimicrobial	Hospital AMS/ID clinicians
Audit and review	Audit and feedback of antimicrobial prescribing quality should be undertaken, particularly for non-restricted antimicrobials	Hospital AMS/ID clinicians

Understanding AMS: Requires a mixed methods approach



- How are antibiotics being used?
 - Volume, indication, appropriate AND inappropriate use
- What are the drivers? Prescriber knowledge and attitudes
- What interventions fit workflow and are acceptable?
- What interventions are effective?
- What interventions are sustainable to change prescribing behaviour?

Can we ultimately change practice and policy?

The National Centre for AMS



A health services research centre

A One Health Approach Cross stream collaboration and facilitation Multi-institutional Human: Hospitals, Aged Care, General practice

Animal: Companion, Livestock

Royal Melbourne Hospital University of Melbourne NCAS **Doherty Institute** Monash University Other research groups

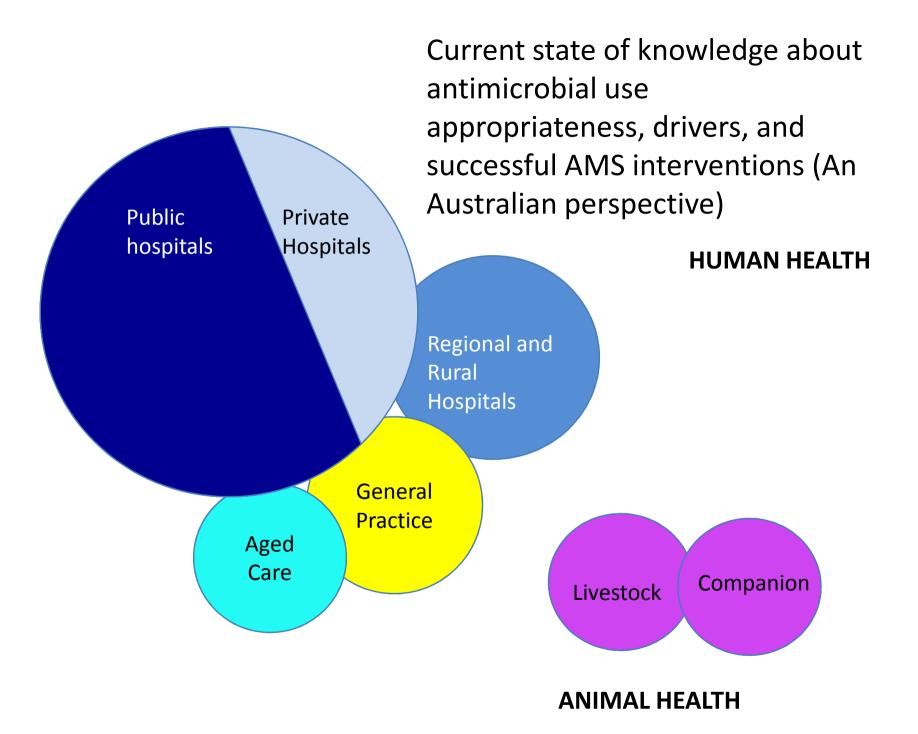
Policy role

National AMR Strategy AURA Program Partner (NAPS) **Commission AMS Advisory** Inter-jurisdictional networking

Activities

NAPS, ACNAPs, SNAPS, Vet NAPS Guidance (68 hospitals) **Educational Workshops** Mentorships Emerging regional role/ WHO





AMS implementation challenges in regional, rural and remote hospitals

Evaluation of NAPS data looking at patterns of prescribing and appropriateness in regional/rural/remote hospitals

- Inappropriate prescribing of antimicrobials for CAP, COPD and surgical prophylaxis higher
- >25% all orders for prosthetic joint infections, sepsis and endocarditis occurred in **non-major city hospitals**

Qualitative study (focus groups, purposive interviews)

Current models for AMS programs (barriers and facilitators)

Develop models for delivery of AMS

• E.g Telehealth, supportive prescribing roles nurses, pharmacists

The Role of the Nurse in AMS

1. Perceptions of the nursing role:

How do nurses perceive their role and influence in AMS ? How do members of the multidisciplinary team perceive the nurse role ? What are the barriers, enablers to support nursing involvement, participation?

What could nursing participation look like?

2. Knowledge and understanding:

What do nurses know and understand about AMR and AMS ?

3. Current situation:

Explore current models of AMS inclusive of nurses – what's in place, what's worked well, what's worked less well ?

4. Evaluation of models, intervention

What works where, for who, what circumstances



Antimicrobial Use

Differs dramatically:

- 1. B/w food animals and companion animals
- 2. Intensity of production
- 3. Vets versus farmers
- 4. B/w species



Investigating prescribing practices in animals



- Survey of surgical prophylaxis: Dogs and cats, horses, cattle
 - Low use of antimicrobials with high importance rating
 - Dogs and cats: Drugs and doses appropriate but administered after surgery in many instances & for prolonged durations
 - Horses & cattle: Drugs appropriate but doses variable and administered after surgery in many instances & for prolonged durations

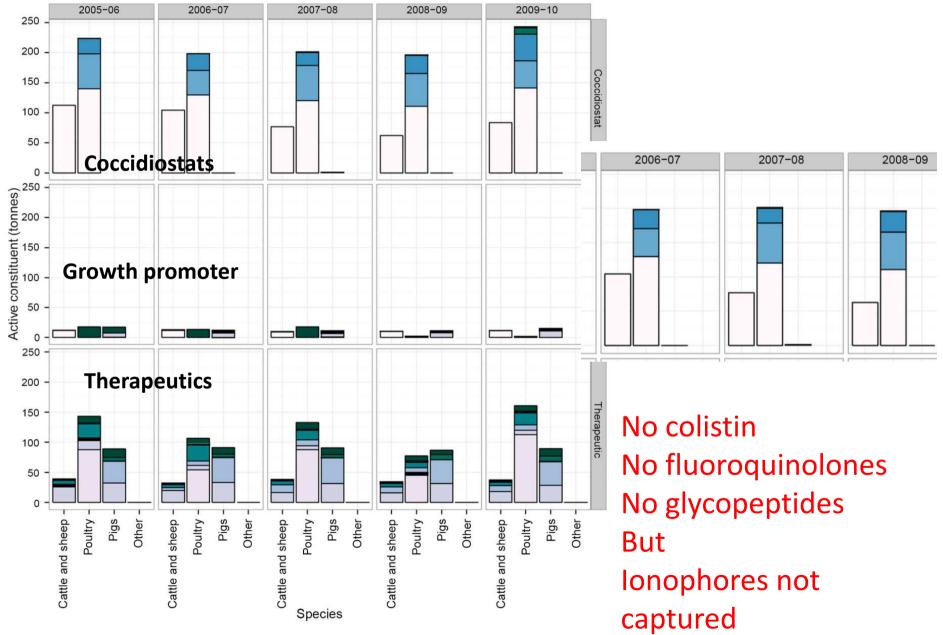
Hardefeldt, LY, Browning, GF, Thursky, K, Gilkerson, JR, Billman-Jacobe, H, Stevenson, MA, Bailey, KE. Antimicrobials used for surgical prophylaxis by companion animal veterinarians in Australia. Veterinary Microbiology 2017

AMS in Veterinary Medicine



- VET-NAPS: Species/Drug/Dose/Indication
- Mixed methods study
 - Online questionnaire, Focus group discussions
- Study population to cover diversity of veterinary practices
- Development of evidence based guidelines for surgical prophylaxis
- Trial of stewardship options
- External funding (Vic, Fed): training and educational materials

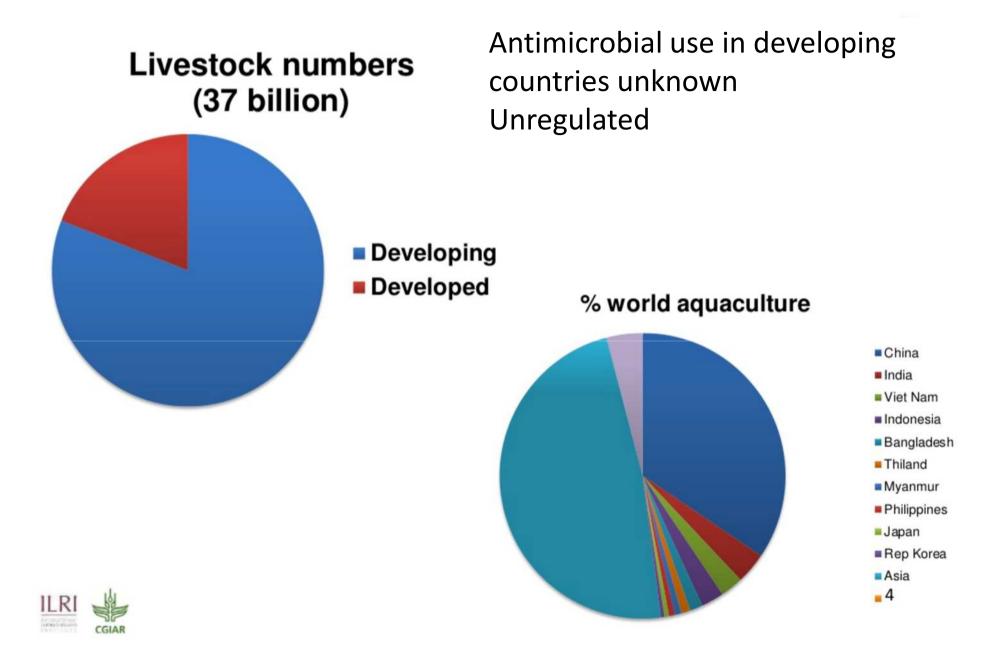
Australian Livestock Use Over Time



Livestock Stream



- Industry becoming engaged in this space
- Developing their own AMS programs (commercially sensitive)
- NCAS opportunity to develop audits and surveys, VETNAPS
- Pig industry and largest cattle/dairy group engaged
- Other key areas for AMS: Label recommendations and dosage/withdrawal time
- Poor knowledge about use over lifecycle & impact on AMR



National Centre for Antimicrobial Stewardship

"If we treat ducks for two days and they aren't cured we change to human drugs. We cocktail 10 tablets of this, 10 tablets of that and 20 tablets of this one. Altogether 200 tablets are mixed in 100 or 200 L of water for the ducks to drink. No one taught me, just my experiences."

Antibiotics: practice and opinions of Cambodian commercial farmers, animal feed retailers and veterinarians

Chhorvoin Om and Mary-Louise McLaws

Antimicrobial Resistance & Infection Control20165:42DOI: 10.1186/s13756-016-0147-y©The Author(s). 2016Received: 7 August 2016Accepted: 3 November 2016Published: 11 November 2016

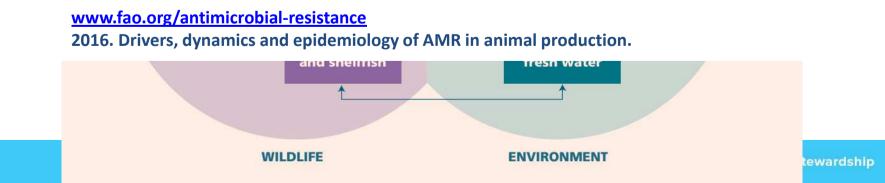
HUMANS



We do not understand

- Dynamics and interactions of genes and microbes within microbiota, and microbiomes, scales of microbial ecosystems
- 2. The impact of antimicrobial use on bacterial populations and the extent of resistance gene transfers between animal and human gut environments
- 3. The relationship of AMR in livestock, and incidence of resistant infections in humans

Need molecular sequencing, epigenetics, integrated surveillance between animals and humans



Appearance of β-lactam Resistance Genes in Agricultural Soils and Clinical Isolates over the 20th Century

David W. Graham¹, Charles W. Knapp², Bent T. Christensen³, Seánín McCluskey² & Jan Dolfing¹

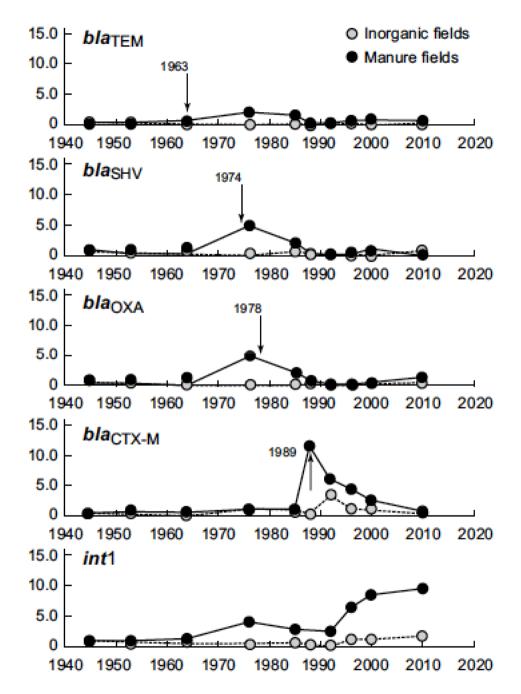
Sci Rep. 2016 Feb 16;6:21550



- ? Agricultural vs. medical use driving AMR
- VanX proto-resistance and multi-resistance genes detected in ~30,000-year old DNA from permafrost. (D'Costa, Nature 2011)
- Incr. AB use has mobilised AMR genes, accelerated bacterial AMR evolution in strains not previously intrinsically resistant
- Phenotypic detection of AMR is only observed when a strain is exposed to an antibiotic.
 - Often false presumption that AR acquisition is primarily driven by factors at the point of detection (e.g., a hospital)
 - Original acquisition of ARGs or mutations might occur elsewhere, including the natural environment.

Unique Study Opportunity

- Systematic soil archiving since 1923 in a facility in Denmark established to study the role of manure versus inorganic fertilisers
- V. Detailed soil and field management records.
- DNA harvested from 1923-2010
 - Broad spectrum β -lactamases (blaTEM and blaSHV)
 - Extended-spectrum (blaOXA and blaCTX-M) (ESBL), were chosen as "biomarkers" for the appearance of β -lactam resistance over time
 - Int1 (integrons) also analysed (represent mobile genetic elements and horizontal transfer of AR)



AR genes emerged in manure fertilised fields only

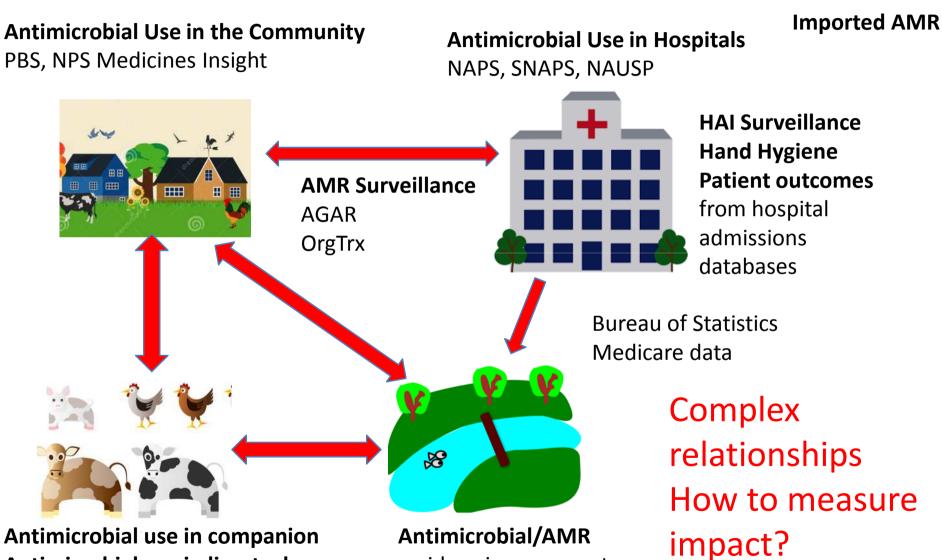
Rise correlated with introduction of antibiotics into agriculture in the 50's

Fall associated with banning of antibiotics for nontherapeutic use in the 90's

Dates correlate with the first published reports of BLAC resistance in humans

Lack of data linkages





Antimicrobial use in livestock **AMR Surveillance in animals**

residues in crops, water





Twitter: NCAS_Aus Website: <u>https://ncas-australia.org</u>

