AMR Impact Report

Estimating the real human health impacts of AMR in Australia – a report coauthored by MTPConnect and CSIRO

Executive summary

Antimicrobial resistance (AMR) represents one of the greatest threats to human health in the 21st century, causing an estimated 1.27 million deaths in 2019 and a projected 10 million deaths per year by 2050. Accurate and timely estimates of the impact of AMR – particularly in relation to morbidity and mortality – are essential to the effective implementation and evaluation of AMR mitigation strategies, to the efficient allocation of resources, and to investment in solutions.

The objectives of this report are twofold. First, we survey what is currently known about the AMR mortality burden in Australia. According to a widely-cited report from the OECD, published in 2018, 290 people die each year in Australia due to AMR. However, the underlying methodology is not described in sufficient detail to enable evaluation of the estimate. Moreover, estimates we have derived from other published data – including the Global Burden of Disease study, the Australian Group on Antimicrobial Resistance, and a recent data linkage initiative in Queensland – are 2.4 to 18 times higher than that reported by the OECD. These estimates also come with important caveats.

Our second, objective, therefore, is to evaluate potential options for improving data collection and linkage in Australia that will enable accurate, longitudinal estimates of the AMR mortality burden and increase the effectiveness of this country's responses to the global challenge of AMR.

1 Measuring the impact of AMR on mortality

1.1 Why measure AMR-related mortality?

The phenomenon of antimicrobial resistance (AMR) represents one of the most significant threats to human, animal, and environmental health in the 21st century. According to research from the Global Burden of Disease program, an estimated 1.27 million people died because of AMR in 2019 (Murray et al. 2022). An earlier report from the UK Government and Wellcome Trust (O'Neill 2016) estimated that 700,000 deaths were attributable to AMR in 2014 and projected up to 10 million deaths annually by 2050 if no action were taken to combat AMR.

Accurate estimates of the AMR burden are required for informed policy-making and setting of intervention priorities. They are also essential to guide the development, implementation, and evaluation of AMR action plans, strategies, standards, and guidelines, and to inform investment decisions regarding new diagnostics, antimicrobials and vaccines (Hay et al. 2018; Limmathurotsakul et al. 2019; Van Der Meer et al. 2014).

While there have been a number of global studies of the AMR burden in terms of mortality, morbidity, and economic consequences, little is currently known about the impact of AMR in Australia. To date, the only published estimate for the annual AMR-related mortality in Australia comes from a two-page 2018 report[1] from The Organisation for Economic Co-operation and Development (OECD). The report estimated that a total of 290 people die each year in Australia due to infections from eight drug-resistant bacteria (OECD 2018). However, as discussed below, the approach by which this figure was calculated remains unclear and so the accuracy of the estimate is difficult to judge.

Our aim in this report, therefore, is to facilitate discussion of data-driven strategies that might be adopted within Australia to better measure and monitor the impact of AMR. This report represents a call to action for greater collaboration and coordination and less duplication of efforts.

The report's focus is on AMR-related mortality as the most definitive and easily measured outcome of resistant infections. In the following sections, we provide a brief overview of the methodology of calculating AMR burden, discussing three broad approaches, their limitations, and challenges. We consider the OECD estimate for AMR-related mortality in Australia and three further estimates derived (with many caveats) from data reported by the Global Burden of Disease initiative (Murray et al. 2022), the Australian Group of Antimicrobial Resistance (AGAR), and a project that focuses on AMR in Queensland. We conclude with discussion of various options for expanding data collection to provide more comprehensive and representative coverage of AMR-related mortality across the country, assisting Australia's monitoring of the burden of AMR and our ability to address this significant global challenge.

1.2 Approaches to estimating AMR-related mortality

Broadly speaking, there are three main approaches to calculating AMR-related mortality rates (for comprehensive discussion of conceptual and methodological issues, see De Kraker & Lipsitch, 2021; Dunachie et al. 2020; Limmathurotsakul et al. 2019).

[1] https://www.oecd.org/australia/Stemming-the-Superbug-Tide-in-Australia.pdf

1.2.1 Underlying cause of death

Death certificates in Australia and overseas typically report the cause of death. Counting deaths caused by AMR from death certificates has the advantages of being easily understood, allowing combination and comparison of international data, and avoiding double-counting of deaths (Dunachie et al. 2020). However, there are a number of factors that make this impractical.

First, Australia currently uses the International Classification of Diseases (ICD)-10 classification system for cause of death, which does not have specific codes for antibiotic-resistant bacterial infections. The 11th revision of the ICD, which came into effect internationally in 2022[2], includes a wider range of codes to describe AMR infection, but is still undergoing field testing, refinements, and validation in Australia[3].

Second, regardless of which ICD edition is in operation, there are more fundamental problems with using death certificates to estimate AMR-related mortality. Authors of deaths certificates can only document what they know. Without a pathology test result, it is not possible to categorise an infection-related death as AMR-associated.

Finally, even if authors have the relevant infection-related information, they are required to make a subjective judgement, reducing the often complex and multifactorial cause of death to a single cause. This is likely to lead to undercounting of AMR-related deaths. For example, an AMR infection leading to sepsis may not be recorded as the cause of death if the patient was admitted to hospital with an underlying medical condition such as heart disease or diabetes (Dunachie et al. 2020; Limmathurotsakul et al. 2019).

1.2.2 All-cause mortality

All-cause mortality avoids the problem of attributing a single main cause of death by counting any deaths within a certain period from the date of first positive bacterial culture for patients (e.g., in-hospital, 7-day, 30-day, or 90-day mortality). This approach is inclusive and comprehensive but inevitably includes deaths caused or contributed by other underlying and intermediate causes. In other words, it records the number of people who died *with* an AMR-related infection, not necessarily that they died *because* of the infection.

While deaths can be categorised according to the type of infection and presence of resistant pathogens, a more sophisticated control or matching approach is required to attribute causality to AMR infection.

1.2.3 Counterfactual modelling

The counterfactual approach compares all-cause mortality with an alternative scenario in which the person does not have an AMR infection (see Figure 1). In the case of AMR, modelling can rely on two potential counterfactuals:

- **Susceptible infection:** the AMR infection is replaced by a strain of the same bacteria that is susceptible to the relevant antimicrobial.
- **Uninfected:** the patient is not infected at all.

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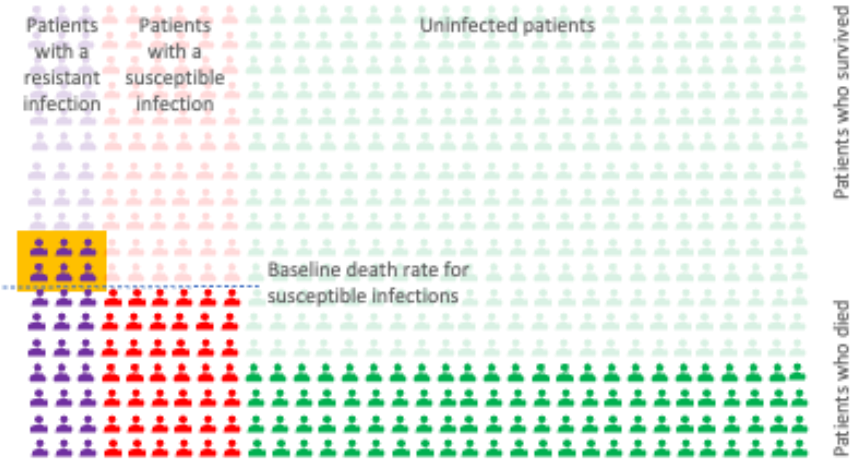
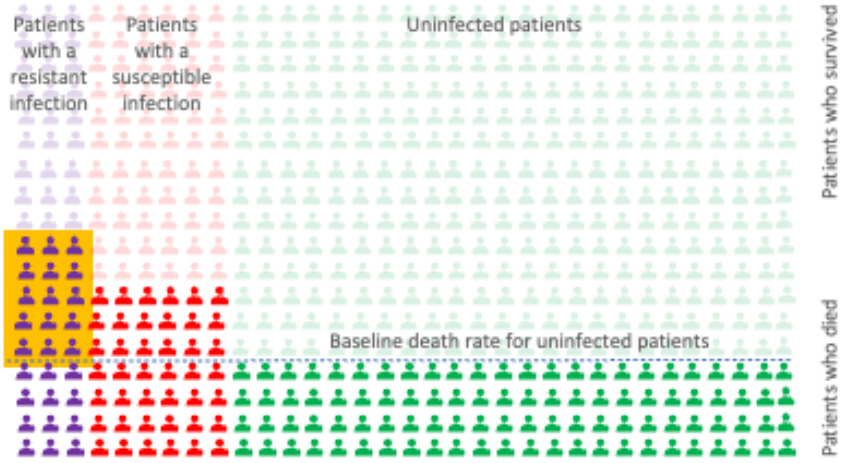
[2] https://www.who.int/news/item/11-02-2022-icd-11-2022-release

[3] International Classification of Diseases revision, AIHW. https://www.aihw.gov.au/about-us/international-collaboration/australian-collaborating-centre-for-who/icd-11

All cause mortality is the number of patients in a population who had an AMR infection when they died. Not all of these patients necessarily died *because* they had an AMR infection



Susceptible infection counterfactual: Deaths *caused by* AMR are commonly estimated by contrasting the death rates for patients with resistant and susceptible strains of the same pathogen.



No infection counterfactual: In some circumstances, it may be more appropriate to contrast death rates with AMR infection to a baseline of death rates for uninfected patients from the same population.

Figure 1: Measures of AMR-related mortality

A systematic review of 286 studies estimating the burden of resistant bacteria (Pezzani et al. 2021) found that the majority (53%) employed a susceptible infection counterfactual. Just 4% adopted the no-infection counterfactual, and 2% considered both counterfactuals. The remainder did not include any comparison.

However, the most appropriate counterfactual depends on the context (De Kraker & Lipsitch, 2021). A susceptible-infection counterfactual makes most sense when resistant and susceptible strains are in competition and so removal or reduction of the AMR infection is expected to result in an increase in susceptible infections (or vice versa) rather than a change in the overall burden of the pathogen. There is some evidence for competition between resistant and non-resistant strains of *Streptococcus pneumoniae* (e.g., Croucher et al., 2011), but for other bacterial pathogens, the available evidence suggests that resistant strains are in addition to rather than replacing susceptible strains. In such cases, the no-infection counterfactual may be more appropriate (De Kraker & Lipsitch, 2021).

The two counterfactuals can also provide insights into the potential effect of different interventions (De Kraker & Lipsitch, 2021). Where interventions target resistance specifically (e.g., antimicrobial monitoring and reporting, appropriate use of antibiotics, introduction of a new antibiotic) the susceptible infection counterfactual is relevant. But where an intervention also reduces susceptible infections (e.g., vaccinations, improved sanitation), the no-infection counterfactual is more appropriate.

Given these considerations, estimating the relative risk of death from drug-resistant infection relative to both counterfactuals would provide credible limits for the true burden of resistance (Dunachie et al. 2020; Murray et al. 2022).

A major challenge for the counterfactual approach is that it relies on high quality, granular datasets (Dunachie et al. 2020). These include at a minimum:

- Incidence of infections with that organism
- Prevalence of AMR in that organism
- Mortality rate of patients with drug-resistant infections
- Mortality rate of comparison group of patients (patients with no infection or patients with susceptible infection).

Estimation of the AMR-burden also relies on the assumptions within the model and (whichever counterfactual approach is taken) and the methods for selecting patients in the comparison group(s).

2 Estimating Australia's AMR-related mortality from existing data

As noted above, the only published estimate of AMR-related mortality in Australia comes from a brief report from the OECD. However, a recent publication from the Global Burden of Disease program provides AMR mortality estimates for the broader geographical region of Australasia[4]. Meanwhile, data from the Australian Group of Antimicrobial Resistance (AGAR) and a data linkage initiative in Queensland can be extrapolated to provide estimates for the country as a whole.

2.1 The OECD report: Stemming The Superbug Tide

In 2018, the OECD published a report focusing on the global economic benefits of efforts to tackle AMR (OECD, 2018). Accompanying this report, the OECD also released a two-page document focused on Australia. According to this document, "an average of 290 persons die each year in Australia due to infections from eight resistant bacteria." This translates to 1.17 deaths per 100,000 in Australia – considerably lower than the OECD average of 4.72. The OECD document concluded that "A broad policy package combining stewardship programmes, enhanced environmental hygiene, mass media campaigns, and rapid diagnostic testing could avert 180 deaths and save 15 million dollars per year in Australia."

The underlying data, models, and analyses which led to the 1.17 estimate are difficult to interpret. The original OECD (2018) report states that "Estimates of the number of incident cases for Australia… were provided by the projection model in Chapter 3. Other input data to model the health impact of infections (e.g. the increased risk of death for resistant infections) and their impact on use of health care services, including case fatality, length of stay associated with the development of an infection were extracted from extensive reviews of the literature conducted by the ECDC [European Centre for Disease Prevention and Control]" (p. 113).

The projection model as we understand it uses resistance proportions for eight bacteria in its calculations, with model outputs including the annual number of cases and incidence rate, the number of attributable deaths and attributable mortality rate. However, it is unclear what counterfactual was used or how the rates for Australia were derived from the global model as there is no option for including Australian based rates into the general burden of disease model used.

2.2 Global burden of bacterial antimicrobial resistance in 2019

The *Global burden of bacterial antimicrobial resistance in 2019* report, published in The Lancet in early 2022 (Murray et al. 2022), notes that Australasia has the lowest AMR burden of all geographical regions.

[4] The widely cited "O'Neill report" (O'Neill 2016) did not provide AMR-related mortality estimates for individual countries. The report was informed by commissioned analyses from KPMG (2014), which grouped countries by geographical region and from RAND (Taylor et al. 2014), which grouped countries by economic status. However, neither KPMG nor RAND reported current AMR-related mortality, focusing instead on projections for AMR-related mortality to 2050 under a range of different scenarios.

The reported analyses looked at AMR-related deaths relative to two counterfactuals[5]. Compared to susceptible-infections, there were an estimated 6.5 deaths (4.3–9.4) per 100,000 population, attributable to bacterial AMR in Australasia. Based on the 2019 population of Australia, this equates to 1,648 (1,090 – 2,384) total deaths. Relative to a no-infection counterfactual, there were an estimated 20.8 deaths (18·8–39·9) per 100,000 population, associated with bacterial AMR or 5,276 (4768-10120) total deaths in Australia.

The major limitation of this report (at least for current purposes) is that estimates are only provided at the level of geographical regions. As well as Australia[6], the Australasia region includes data from Fiji, Kiribati, Marshall Islands, Micronesia, Nauru, Palau, Papua New Guinea, Samoa, Solomon Islands, and New Zealand. These countries have wide variation in exposure to AMR as well as demography and epidemiology, health service response, and comprehensiveness of data collection. As such, it is unclear to what extent the Australasia estimates are representative of Australia.

2.3 The Australian Group on Antimicrobial Resistance (AGAR)

AGAR is part of the Antimicrobial Use and Resistance in Australia (AURA) Surveillance System which coordinates a number of surveillance programs including APAS (Australian Passive AMR Surveillance System) and NAPS (National Antimicrobial Prescribing Survey). However, AGAR is the only surveillance program within AURA that enriches pathology data with clinical outcomes.

AGAR brings together three surveillance programs examining blood culture isolates only:

- AESOP: Australian Enterococcal Sepsis Outcome Program
- ASSOP: Australian Staphylococcal Sepsis Outcome Program
- GNSOP: Gram negative Sepsis Outcome Program (comprising Enterobacterales, Pseudomonas aeruginosa, and Acinetobacter spp.)

Data are currently collected by 30 laboratories servicing 49 institutions across Australia. These include four private institutions and 11 regional or district hospitals from north-west Western Australia. Contributing laboratories provide minimum inhibitory concentration data and demographic data on isolates from all episodes of sepsis continuously. This approach aligns with the approach taken by the European targeted resistance surveillance system EARS-Net.

A subset of those hospitals also provide all-cause mortality data, determined for 7 and 30 days after a positive blood culture. This data can be requested as line-listed by age, sex and hospital, although they are limited for other variables and can be incomplete for all sites. The data AGAR requires is collected by the participating institution's scientist (laboratory data) and clinician (patient data) by accessing the institution's information systems. Outcomes are recorded as either: (a) died; (b) survived; or (c) no information about survival. To avoid interpretive bias, no attempt is made to assign attributable mortality.

Table 1 shows AGAR-sourced all-cause mortality estimates for four AMR hospital-associated pathogens in 2019. The total of 209 deaths (total of community and hospital onset)

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[5] The Lancet paper uses a different terminology to ours (and to technical discussion papers cited above). Mortality rates derived from a susceptible-infection counterfactual are referred to as "AMR-attributable deaths", whereas rates derived from a no-infection counterfactual are referred to as "AMR-associated deaths".

[6] Australian sources data included in the analysis are derived from AGAR, AURA, Australian Gonococcal Surveillance Programme (AGSP), HOTspots (northern Australia); WHO Western Pacific Region Gonococcal Antimicrobial Surveillance Programme (microbiology only).

comes from 27 hospitals with a combined 20,000 beds, representing 29.3% of all such beds in Australia[7]. Scaling this up, we can approximate the 30-day AMR all-cause mortality across all Australian hospitals to be 713.

Table 1: 30-day all-cause mortality for resistant and susceptible strains of 4 key pathogens in 27 Australian hospitals. Source: 2019 AGAR data from AURA 2021 report.

Resistant strains				Susceptible strains			
	Community onset	Hospital onset	Total		Community onset	Hospital onset	Total
ESBL *E. coli*	37	27	64	non-ESBL *E. coli*	216	69	285
ESBL *K. pneumoniae*	7	10	17	non-ESBL *K. pneumoniae*	66	30	96
Vancomycin-resistant *E. faecium*	8	56	64	Vancomycin-susceptible *E. faecium*	25	45	70
MRSA	44	20	64	MSSA	228	54	282
	96	113	209		535	198	733

More sophisticated extrapolations from AGAR data to a national estimate are also possible. For example, using AGAR mortality data stratified by age group and gender, one could estimate AMR mortality for each non-AGAR hospital based on their age- and gender-stratified patient numbers, available from the National Integrated Health Services Information (NIHSI[8]) Analysis Asset. Mortality estimates for each non-AGAR hospital could also be based on the most geographically similar AGAR hospital rather than the average of all AGAR hospitals.

These extrapolations to the national level rely on the assumption that the AGAR hospitals providing mortality data are representative of all Australian hospitals in terms of patient demographics, outcomes, and bacterium profile and resistance. AGAR does cover all States and Territories in Australia. However, due to the level and resource availability from the participating laboratories, the AGAR data are biased towards tertiary care hospitals in major capital city hospitals.

2.4 Queensland data linkage project

Researchers in Queensland (including Teresa Wozniak, co-author of this report) have adopted a computational data linkage approach using patient-level data to study the impact of AMR on mortality, morbidity, and healthcare costs. The project links Queensland Department of Health Pathology data to the Queensland Hospital Admitted Patients Data Collection for 134 Queensland hospitals including metropolitan, regional, and rural facilities.

[7] https://www.aihw.gov.au/reports/hospitals/hospital-resources-2017-18-ahs/data

[8] The National Integrated Health Services Information (NHSI) Analysis Asset is a federal Department of Health data store that covers approximately 89% of the Australian population. It contains data from public hospital admissions, emergency services, the Medical Benefits Schedule, the Pharmaceutical Benefits Scheme and the National Death Index.

In the first study from this group (Lee et al., 2021), the researchers identified 20,390 patients with hospital-associated bloodstream, urinary tract, or respiratory tract infection due to five key pathogens (*Enterococcus spp., E. coli, K. pneumoniae, P. aeruginosa,* and *S. aureus*). Relative to uninfected controls, death rates were higher for patients with all blood stream infections as well as those with *E. faecium* urinary tract infections and *P. aeruginosa* respiratory tract infections. However, analyses showed no significant difference in the risk of dying between patients with resistant versus susceptible infections.

A second study using the same linked datasets (Wozniak et al., 2022) focused on infections identified within 48 hours of hospital admission, which are assumed to have been acquired in the community prior to admission. Analyses showed that patients with drug-resistant *Enterobacterales* bloodstream infections or *P. aeruginosa* urinary tract infections were more likely to die in hospital than those with the drug-sensitive counterpart.

In analyses that are currently undergoing peer review (and so should not be cited), the group have used simulation modelling to extrapolate the Queensland data to the national in-patient population. Using a no infection counterfactual, they estimate that in 2020 in Australia, there were 1,031 deaths (95% Uncertainty Interval 294 - 2,615) from the five resistant hospital-associated infections. These premature deaths resulted in $439 million (95% UI $137 million, $1.18 billion) in annual costs due to loss of quality-adjusted life years. The major concern is whether data from Queensland hospitals are representative of other states. Confounding factors may include differences in geography, exposure to different pathogens and the balance of rural to metropolitan populations where the risk of AMR infection is unequal (see e.g., Bowen et al., 2019).

It is also important to note that, like AGAR, the Queensland data linkage initiative relies entirely on hospital data. It will, therefore, miss AMR-related deaths if the patient is discharged but dies shortly thereafter. It will also miss cases that are never admitted to hospital (i.e., the infection is acquired in the community and the patient dies before they reach hospital). The extent of this missing data is difficult to estimate. However, it may be more common in certain settings such as aged care or rural and remote communities, many of which can fall outside of surveillance reach (Wozniak et al. 2021).

2.5 Summary

Of the many ways in which the impact of AMR could be measured, one might expect the effect on mortality to be the most straightforward to estimate. In this report, we have identified or derived four estimates of annual AMR-related deaths in Australia (see Table 2). The differences between the numbers and the underlying methodologies demonstrate the challenges of arriving at even this AMR metric.

The estimate of 290 deaths per year from the OECD is by some distance the lowest. Unfortunately, the methods and assumptions are not described in sufficient detail to evaluate the validity of the estimate or explain the significant discrepancies with estimates derived from other data sources.

That being said, our other three estimates also have significant limitations. The Global Burden of Disease project gives us the largest estimates – 1,648 or 5,276 depending on whether a susceptible infection or a no infection counterfactual is used as a comparison. Notably, this study included a much broader range of antibiotic-bacteria combinations. It also includes Australia within a broader Australasia region alongside countries with less developed healthcare systems and potentially greater exposure to AMR. Given the interconnectedness of our region, it is in Australia's national interest to understand how AMR

impacts our neighbours. However, for current purposes, the AMR-mortality rate for Australasia is likely to overestimate the burden in Australia.

The AGAR program provides coverage of all Australian states and territories. However, its resource-intensive data enhancement to collect mortality data, means that smaller regional hospitals may be under-represented. A more fundamental limitation is that AGAR only reports all-cause mortality, so the annual estimate includes patients who died with an AMR infection but not necessarily because of resistance.

We would argue, therefore, that the best current estimate of deaths due to AMR in Australia is the 1,031 derived from the Queensland AMR data linkage project. Given that this estimate is based on a no infection counterfactual, one might expect it to be lower than the all-cause mortality derived from AGAR data. It is worth noting that the uncertainty around all of these estimates is large. However, there are a number of important differences in the data collected that might explain this apparent discrepancy. In particular, where AGAR focuses exclusively on sepsis (i.e., bloodstream infections), the Queensland study also counted mortality from urinary and respiratory infections. Moreover, the Queensland study included *Pseudomonas aeruginosa* infections in addition to the four infection types covered by AGAR. Pseudomonas lung infections are responsible for a relatively large number of deaths, potentially accounting for the discrepancy between the two estimates.

Table 2: Annual AMR-related mortality estimates for Australia

Source of original data	Date of collection	Antibiotic bacterium pairs	Scope of reported data	Approach	Australia estimate
OECD, 2018	2017	8	Australia estimate.	Counterfactual (but unclear what the counterfactual is)	290
Global Burden of Disease, Murray et al. 2022	2019	88 with 9 core pairs	Australasia estimate scaled to Australian population	Counterfactual (relative to susceptible infection)	1,648
				Counterfactual (relative to no infection)	5,276
AGAR data, AURA 2021	2018-19	4	27 tertiary hospitals across Australia extrapolated to the Australian hospital population.	All-cause mortality	713
Wozniak et al (2022)	2016	5	Queensland estimates of risk of mortality from Lee et al (2020) extrapolated to the Australian hospital population	Counterfactual (relative to no infection)	1,031 (95% Uncertainty Interval 294 - 2,615)

3 Improving data collection for the estimation of AMR-related mortality in Australia

Calculating the burden of AMR requires high quality microbiology data that is representative of both the AMR pathogens and the human population under surveillance. Critically, this microbiology data must be linked to clinical outcomes.

Our survey of Australian AMR-related mortality estimates has highlighted the limitations of currently available data. New approaches are required to systematically acquire datasets of sufficient breadth and quality to support the accurate assessment of AMR burden and changes in this burden over time (cf. Limmathurotsakul et al. 2019, OECD 2018). Here we consider the feasibility and usefulness of potential changes to data collection that might allow better longitudinal tracking of AMR-related deaths.

3.1 Addition of AMR information to death certificates

The forthcoming update from ICD-10 to ICD-11 in Australia provides an opportunity to amend coding standards and practices to better capture data on AMR infections in death certificates. As argued above, recording AMR as the singular cause of death is both subjective and impractical.

A different approach has been adopted in England and Wales, where the Department of Health and Social Care has mandated that all deaths linked to Methicillin--resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* be recorded as text on the certificate without necessarily specifying it as the cause of death. All such cases are noted as "involving AMR infection" in the UK Office for National Statistics reports (Office for National Statistics 2012, 2014, 2017). In effect, this provides all-cause rather than single-cause mortality data for these two resistant pathogens.

In order to provide a comprehensive measure of AMR-related mortality, such a mandate would need to expand to a broader range of priority pathogens. The approach also relies on medical staff having routine access to pathology data (including resistance status) and recording the infection on the certificate, and clinical coders being able to categorise those responses according to resistant pathogens and infection type. As a result, AMR infections are still likely to be undercounted.

Given these considerations, it seems unlikely that adding AMR information to death certificates can provide an accurate estimate of AMR-related mortality.

3.2 Expansion of AGAR's data enhancement program

In section 2, we discussed AGAR's data enrichment initiative which provides data on AMR-related mortality, in addition to pathology data. AGAR's ongoing nature means that it could, in principle, enable longitudinal tracking of AMR-related mortality and other health impact statistics at a national level.

Regional and rural hospitals were initially under-represented in AGAR. However, since 2018, AGAR has included regional hospitals in north-west WA with mortality data reported since 2021. Given the growing evidence of AMR hotspots in regional and remote Australia (Wozniak et al. 2021), further expansion of AGAR to include a broader range of regional hospitals across different states and territories would certainly be welcome. The challenge, however, is that the manual nature of collecting mortality data by AGAR does not easily scale. Any expansion would necessitate significant resources (i.e., personnel) to enrich the pathology data with patient outcomes via manual interrogation of hospital records.

A more fundamental issue is that, while AGAR data are provided for resistant and susceptible strains of key pathogens, these are not controlled in any way. The data can be stratified by age, gender, and hospital. However, counterfactual modelling requires patient-level data for matching and, due to ethics constraints, patient-level data cannot be utilised for this purpose. AGAR is clearly a useful and important resource for many purposes including estimation of all-cause mortality. However, if the aim is to estimate the impact of AMR on mortality based on counterfactuals, then the currently available AGAR data are unable to achieve this.

3.3 Upscaling of data linkage initiatives

An alternative and potentially more effective use of resources may involve expansion of the Queensland computational data linkage initiative to other states and territories. The initiative already has good coverage of regional hospitals and is designed for counterfactual modelling that can attribute deaths to AMR. Expansion of the initiative would not require new data collection. Instead, resources would be needed to set up new data linkages in other jurisdictions and conduct analyses using published methodologies (Lee et al., 2021) .

One possible approach to data linkage at the national level would be to build upon existing national patient data infrastructure such as the NIHSI Analysis Asset, an initiative of the Australian Institute of Health and Welfare (AIHW) and Commonwealth Department of Health and state and territory health authorities. De-identified data in the NIHSI Analysis Asset covers admitted patient care services (in public and private hospitals where available), emergency department services and outpatient services in public hospitals for all participating states and territories. It also includes data from Medicare Benefits Schedule, Pharmaceutical Benefits Scheme, Repatriation Pharmaceutical Benefits Scheme, Residential Aged Care, and National Deaths Index. AIHW Ethics Committee–approved purposes for the NIHSI Analysis Asset include “policies and programs designed to reduce the incidence and severity of disease and injury.” Analyses of AMR infection, treatment, and outcomes would therefore be suitable use of the data set.

Currently, the NIHSI Analysis Asset does not include pathology data. However, expansion to include pathology data (specifically microbiology data) would enable more extensive analyses of mortality than have been possible to date, such as 7 and 30 day mortality using the National Deaths Index data. It would also facilitate analysis of morbidity and healthcare costs associated with AMR and would address gaps in the current AGAR and Queensland approaches described above, particularly in relation to AMR detection outside of the hospital system (i.e., in primary care and aged care).

Linking to pathology data would be challenging with a complex mix of public and private pathology providers that differs not only at the state level but between Local Health Districts (LHDs) within the same state. Given also the jurisdictional differences in type of data collected and privacy legislation that may affect data linkage, a patchwork approach may be needed – at least initially – with different methodologies in each state or territory.

3.4 Conclusion

In the face of an escalating global AMR crisis, there is a clear and urgent need to improve data collection and integration that would enable accurate longitudinal estimation of Australia’s AMR burden. However, initiatives that might appear straightforward solutions – such as changing the way in which AMR is recorded on death certificates or expanding the ongoing AGAR data enrichment program – not only face significant implementation challenges but would at best provide “all-cause mortality” data.

Instead, we suggest, resources should be focused on data linkage projects that bring together pathology data with demographic and health outcomes at the level of individual patients. These data would enable a more accurate estimation of the number of deaths that are *due to* AMR (as opposed to counting all the people who died and had an AMR infection). Here and in Section 2 we have discussed a data linkage project in Queensland that demonstrates the feasibility and value of such an approach.

Ideally, a national data linkage program would build on national-level data infrastructure such as the NIHSI Analysis Asset. However, given the jurisdictional differences in legislation and the complexities of pathology provision between and within states and territories, a more piecemeal or patchwork approach may be necessary – at least in the short to medium term. Determining the optimal approach to data linkage within other states and territories is beyond the scope of this report but should, we suggest, be a priority for organizations concerned with addressing the impact of AMR. Researchers at the University of Technology Sydney, University of Wollongong, and CSIRO are currently exploring the value of linked data to inform and monitor AMR in the Illawarra region of NSW, but we are not aware of similar initiatives elsewhere in Australia.

In concluding, it is important to acknowledge the purposely limited scope of this report. First, our focus has been on bacterial resistance to antibiotics. Each of the four morbidity estimates reviewed in section 2 considered a limited number of "priority" bacterial pathogens and drug-bug combinations. However, drug resistant fungi such as *Candida auris* are increasingly recognised as a major public health problem with a higher death rate than resistant bacteria. Future initiatives should therefore consider patient mortality due to a broader range of drug-resistant microbes.

Second, we have focused on mortality as the ultimate and most tractable impact of AMR on human health. However, even when patients survive resistant infections, there is a significant morbidity and economic burden[9]. In order to provide cost-effective strategies to address AMR, data linkage initiatives and analyses should be designed to measure the impact of AMR, not only on patient outcomes, but also on the patient's journey through the healthcare system.

[9] In a recent economic report (Outbreak Consortium, 2020), researchers at the University of Technology Sydney estimated that urinary tract infections (UTIs) will cost the Australian health service $1.1 billion by 2030 if resistance of UTI infections to first-line antibiotics remains unchanged at around 21%. If resistance rates increase to 50%, that figure rises to $1.6 billion, primarily due to increased hospitalization of patients who would otherwise be treated successfully by their community GPs.

References

Bowen AC, Daveson K, Anderson L, Tong SY.An urgent need for antimicrobial stewardship in Indigenous rural and remote primary health care. Medical Journal of Australia. 2019; 211: 9-11.e1.

Croucher NJ, Harris SR, Fraser C, et al. Rapid pneumococcal evolution in response to clinical interventions. *Science.* 2011; 331(6016):430–434.

de Kraker ME, Lipsitch M. Burden of antimicrobial resistance: compared to what?. Epidemiologic reviews. 2021;43(1):53-64. https://doi.org/10.1093/epirev/mxab001

Dunachie SJ, Day NP, Dolecek C. The challenges of estimating the human global burden of disease of antimicrobial resistant bacteria. Current Opinion in Microbiology. 2020 Oct 1;57:95-101. https://doi.org/10.1016/j.mib.2020.09.013

Hay SI, Rao PC, Dolecek C, Day NP, Stergachis A, Lopez AD, Murray CJ. Measuring and mapping the global burden of antimicrobial resistance. BMC medicine. 2018 Dec;16(1):1-3. https://doi.org/10.1186/s12916-018-1073-z

KPMG L. The global economic impact of anti-microbial resistance. Kpmg Llp. 2014 Dec.

Lee XJ, Stewardson AJ, Worth LJ, Graves N, Wozniak TM. Attributable Length of Stay, Mortality Risk, and Costs of Bacterial Health Care–Associated Infections in Australia: A Retrospective Case-cohort Study. Clinical Infectious Diseases. 2021 May 15;72(10):e506-14. https://doi.org/10.1093/cid/ciaa1228

Limmathurotsakul D, Dunachie S, Fukuda K, Feasey NA, Okeke IN, Holmes AH, Moore CE, Dolecek C, van Doorn HR, Shetty N, Lopez AD. Improving the estimation of the global burden of antimicrobial resistant infections. The Lancet Infectious Diseases. 2019 Nov 1;19(11):e392-8. https://doi.org/10.1016/S1473-3099(19)30276-2

Murray CJ, Ikuta KS, Sharara F, Swetschinski L, Aguilar GR, Gray A, Han C, Bisignano C, Rao P, Wool E, Johnson SC. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet. 2022 Jan 19. https://doi.org/10.1016/S0140-6736(21)02724-0

OECD (2018), Stemming the Superbug Tide: Just A Few Dollars More, OECD Health Policy Studies, OECD Publishing, Paris, https://doi.org/10.1787/9789264307599-en

Office for National Statistics, Deaths involving MRSA: England and Wales: 2007 to 2011.

https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsinvolvingmrsaenglandandwales/2012-08-22 (2012),

Office for National Statistics, Deaths involving MRSA: England and Wales.

https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathsinvolvingmrsaenglandandwales (2014)

Office for National Statistics. Deaths involving *Clostridium difficile.* https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathsinvolvingclostridiumdifficilereferencetables (2017)

O'Neill J. AMR Review. Tackling Drug-Resistant Infections Globally: Final report and recommendations. 2016. https://amr-review.org

OUTBREAK Consortium (2020). A One Health Antimicrobial Resistance Economic Perspective. UTS. https://outbreakproject.com.au/antimicrobial-resistance-publications/utis-economic-report/

Pezzani MD, Tornimbene B, Pessoa-Silva C, de Kraker M, Rizzardo S, Salerno ND, Harbarth S, Tacconelli E. Methodological quality of studies evaluating the burden of drug-resistant infections in humans due to the WHO Global Antimicrobial Resistance Surveillance System target bacteria. Clinical Microbiology and Infection. 2021 May 1;27(5):687-96. https://doi.org/10.1016/j.cmi.2021.01.004

Taylor J, Hafner M, Yerushalmi E, Smith R, Bellasio J, Vardavas R, Bienkowska-Gibbs T, Rubin J. Estimating the economic costs of antimicrobial resistance. Model and Results (RAND Corporation, Cambridge, UK). 2014. https://www.rand.org/pubs/research_reports/RR911.html

Van Der Meer JW, Fears R, Davies DS, Ter Meulen V. Antimicrobial innovation: combining commitment, creativity and coherence. Nature Reviews Drug Discovery. 2014 Oct;13(10):709-10. https://doi.org/10.1038/nrd4448

Wang H, Paulson KR, Pease SA, Watson S, Comfort H, Zheng P, Aravkin AY, Bisignano C, Barber RM, Alam T, Fuller JE. Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21. The Lancet. 2022 Mar 10. https://doi.org/10.1016/S0140-6736(21)02796-3

Wozniak TM, Smith-Vaughan H, Andrews R. Convergence of surveillance blind spots with antimicrobial resistance hotspots. Australian and New Zealand Journal of Public Health. 2021 Dec 1;45(6):541-2. https://doi.org/10.1111/1753-6405.13165

Wozniak TM, Dyda A, Lee X. The increased length of hospital stay and mortality associated with community-associated infections in Australia. InOpen Forum Infectious Diseases 2022 Mar 17. https://doi.org/10.1093/ofid/ofac133