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Review article

Towards integrated cross-sectoral surveillance of pathogens and antimicrobial resistance: Needs, approaches, and considerations for linking surveillance to action

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ABSTRACT

Pathogenic and antimicrobial-resistant (AMR) microorganisms are continually transmitted between human, animal, and environmental reservoirs, contributing to the high burden of infectious disease and driving the growing global AMR crisis. The sheer diversity of pathogens, AMR mechanisms, and transmission pathways connecting these reservoirs create the need for comprehensive cross-sectoral surveillance to effectively monitor risks. Current approaches are often siloed by discipline and sector, focusing independently on parts of the whole. Here we advocate that integrated surveillance approaches, developed through transdisciplinary cross-sector collaboration, are key to addressing the dual crises of infectious diseases and AMR. We first review the areas of need, challenges, and benefits of cross-sectoral surveillance, then summarise and evaluate the major detection methods already available to achieve this (culture, quantitative PCR, and metagenomic sequencing). Finally, we outline how cross-sectoral surveillance initiatives can be fostered at multiple scales of action, and present key considerations for implementation and the development of effective systems to manage and integrate this information for the benefit of multiple sectors. While methods and technologies are increasingly available and affordable for comprehensive pathogen and AMR surveillance across different reservoirs, it is imperative that systems are strengthened to effectively manage and integrate this information.

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1. Introduction

Human, animal, and environmental health are inherently interconnected, especially in the context of infectious diseases and antimicrobial resistance (AMR) (Fig. 1). These three sectors of health remain poorly integrated, however, given they are characterised by different incentives, have largely developed independently, and substantially differ in terms of governance and practice. The One Health framework provides an approach and philosophy to improve and safeguard equally the health of humans, animals, and the environment, and has recently formed the foundation of the World Health Organisation's *One health joint plan of action* (World Health Organisation, 2022). Integrated cross-sectoral surveillance driven by the One Health framework has the potential to mitigate the dual crises of infectious diseases and AMR (Gardy and Loman, 2018; Zinsstag et al., 2011), potentially addressing the urgent need for collaborative, multisectoral, and transdisciplinary approaches to health (World Health Organisation, 2022; Zinsstag et al., 2011). Implementation relies on two critical aspects to enable coordinated and tailored action across sectors: standardised and broad pathogen and AMR data across reservoirs, accompanied by shared systems for data contribution, use, and interpretation across multiple sectors of health.

Surveillance efforts have traditionally been focused on individual pathogens and sectors. From the human health perspective, the benefits of surveillance for individual pathogens are well-recognised, whether AMR nosocomial infections (Siegel et al., 2007; World Health Organisation, 2021), neglected tropical diseases (Hürlimann et al., 2011; Muleta et al., 2021; Tabah et al., 2016) or novel viruses (Ahmed et al., 2020; Bedford et al., 2020). Indeed, most emerging or re-emerging human infections over the last two decades have been vector-borne or zoonotic. The SARS-CoV-2 pandemic has highlighted the importance of combining genomic surveillance data from environmental sources such as wastewater with case notifications to detect potential hot spots of viral circulation, serve as an early warning for undetected 'cryptic' transmission, and activate appropriate public health responses (Daughton, 2020; Lahrich et al., 2021). Much potential exists to use similar cross-sectoral approaches for early detection and proactive management of other microbial threats to humans, animals, or the environment. This is especially critical in settings that require disentanglement and understanding of multiple pathogens and/or complex transmission pathways. However, several major barriers preclude the widespread adoption of cross-sectoral approaches. High cost and complex logistics are required to simultaneously monitor several sample types, especially with conventional approaches. A further challenge is the historically limited collaboration across human, animal, and environmental health sectors reflecting different incentives (including economic and social drivers), institutional, professional and scientific barriers, and divergent practices, for example the preference for direct pathogen monitoring in clinical settings (Platts-Mills et al., 2018; Rogawski McQuade et al., 2020) versus indicator monitoring in

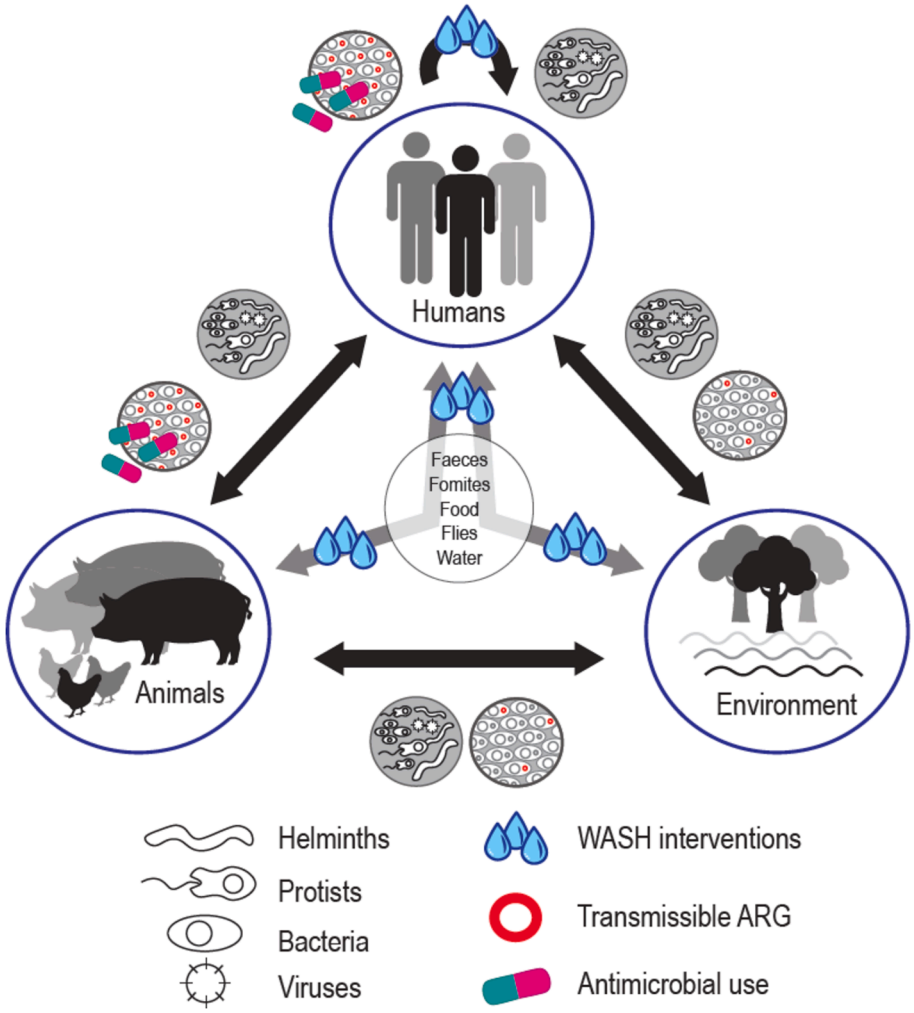

Fig. 1. Pathways of diverse pathogen and ARG transmission across different reservoirs. Transmission pathways can be interrupted at several points by improvements to water, sanitation and hygiene (WASH). Antimicrobial use in human and animal populations can contribute to the spread of antimicrobial resistance genes (ARGs) through these populations, and into the environment.

environmental settings (Goddard et al., 2020b; Holcomb et al., 2020). This siloed approach, i.e., discipline- and sector-specific pathogen surveillance, leads to limited understanding and prohibits effective management of human, animal, and environmental health.

We advocate moving towards cross-sectoral integrated surveillance: a system involving collaborative efforts between multiple health sectors (e.g. clinical, agricultural, veterinary, food safety, and wildlife health) to produce and disseminate information with the purpose of improving an aspect of human, animal or environmental health (Bordier et al., 2020; Hayman et al., 2023). Through this approach, it becomes possible to simultaneously identify and characterise pathogens and AMR affecting health, track their transmission across different reservoirs, vehicles and vectors, and to provide an evidentiary basis to help resolve the factors contributing to their persistence and transmission. Here we summarise the needs and challenges in which a cross-sectoral approach to surveillance would enable the development of more effective measures to reduce the impacts of infectious diseases and AMR. We highlight that, due to recent methodological innovations in molecular and genomic techniques, it is possible to develop informative, convenient, and affordable surveillance programs. We evaluate the currently available analytical techniques for pathogen and antimicrobial resistance gene (ARG) detection, and demonstrate their existing use in cross-sectoral surveillance research and programs. Finally, we outline how integrated surveillance initiatives can be fostered at multiple scales of implementation, and recommend key considerations that can cultivate an effective 'enabling environment' for catalysing, growing and maintaining such initiatives.

2. Why is there a need for cross-sectoral surveillance of pathogens and AMR?

There are many contexts in human, animal, and environmental health sectors where an integrated approach to surveillance that encompasses not only each of these sectors, but multiple pathogens, AMR determinants and transmission pathways, is critical to developing effective measures of control. Here, to demonstrate the importance of developing such approaches, we summarise the needs and challenges of three related core areas of human health facing these crises: enteric pathogens in informal settlements, ARG transmission across reservoirs, and AMR hospital-acquired infections (Table 1). These represent three critical and connected areas where cross-sectoral surveillance would be of greatest benefit now and in the immediate future. Informal settlements host 13 % of the world's population (1 billion people) and have been highlighted as hotspots for pathogen and AMR transmission (Nadimpalli et al., 2020). The density of people and animals in an environment compromised by inadequate water and sanitation management make informal settlements a priority area for improving global health through One Health approaches. This crisis encompasses the transmission of ARGs across reservoirs, which is exacerbated by climate change due to enhanced opportunities for zoonoses (The Lancet Infectious Diseases, 2023). This flows on to the risk of hospital-acquired AMR infections, with a predicted exponential increase in AMR-related deaths (O'Neill, 2014). While the principles of cross-sectoral surveillance also extend to various aspects of animal, plant, and ecosystem health, we do not extensively cover these here.

2.1. Enteric pathogens in informal settlements

Diarrhoeal diseases cause approximately 1.7 billion illnesses and 1.6 million deaths worldwide each year, with a disproportionate burden in children under five (L. Liu et al., 2016; Troeger et al., 2018; World Health Organisation, 2017). This is a significant human health issue in informal settlements: communities, often in low- and middle-income settings, where water, sanitation and hygiene (WASH) facilities and practices are absent or inadequate. The extensive connectivity between humans, animals, and the natural and built environment leads to transmission of enteropathogens between reservoirs and hosts via the faecal-oral route (French et al., 2021; Kotloff, 2017; Troeger et al., 2018; Wagner et al., 1958); a complex network of transmission pathways exist with many possible intermediates, including food, water, recreational

Table 1
Key surveillance needs, suggested detection techniques, and potential systems to reduce pathogens and AMR in different settings.

	Enteric disease in informal settlements	ARG transmission	Hospital-acquired AMR infections
Key problem	High childhood morbidity and mortality from enteric infections, including diarrhoea, due to inadequate water quality, hygiene, and sanitation (WASH)	Growing worldwide AMR due to widespread antimicrobial usage across all sectors, selecting for ARGs and transmission between organisms and reservoirs	Increasing morbidity and mortality from hospital-acquired pathogens, including those introduced during invasive procedures and surgery, and those with an environmental or animal source
Surveillance purpose	Inform next-generation WASH improvements by resolving pathogen abundance, diversity, and exposure pathways in informal settlements	Enhance antimicrobial stewardship and develop sustainable solutions by understanding global trends and mechanisms of AMR	Inform hospital disinfection and infection control procedures by resolving pathogen exposure pathways and evolution of AMR phenotypes
Organisms of concern	Enteropathogenic bacteria, viruses, protists, fungi, and helminths	Pathogenic and non-pathogenic bacteria, fungi, and protists carrying and transmitting ARGs	Pathogenic bacteria, fungi, and protists, as well as non-pathogenic carriers of ARGs
Major reservoirs/ sources	Human stool, animal stool, wastewater, drinking water, recreational and agricultural water, soils, food, fomites, flies, air	Humans, animals, plants, built environments, natural environments, food, fomites, air	Patients, staff, visitors, surgical equipment, medical devices, hospital surfaces, hospital water, food, air
Primary surveillance method	qPCR arrays to monitor levels of multiple pathogens using DNA extracted from major potential sources	Metagenomic profiling of global resistome using DNA extracted from major potential sources	Culture-based monitoring of prevalence, evolution, traits, and resistance profiles of key nosocomial pathogens
Supporting surveillance methods	Culture-based antimicrobial susceptibility testing and genomics recommended (routine surveillance and testing during acute illness) to study pathogen viability and evolution; metagenomic sequencing allows holistic insights and resistome profiling	Culture-based antimicrobial susceptibility testing and genomics recommended to confirm phenotypic resistance and study pathogen evolution	Metagenomics or qPCR arrays to profile wider pathogen levels/diversity and the resistome, which may not be captured by culture-based methods
Governance strategy	Local healthcare providers, officials responsible for municipal water and sanitation services, and government, integrated with bodies that set national and international standards and strategies	Local healthcare providers and government agencies, integrated with bodies that set national and international standards and strategies	Individual hospitals with oversight from local and national governments
Key stakeholders	Settlement residents, local and national government, medical / veterinary / agricultural / environment / food sectors, philanthropic organisations, intergovernmental organisations, media	General public, local and national government, medical / veterinary / agricultural / environment / food sectors, pharmaceutical companies, intergovernmental organisations, media	Hospital patients, clinicians, nurses, other hospital staff, local and national government, pharmaceutical companies, device manufacturers, general public, media

spaces, surfaces, and insect vectors, in addition to direct contact between hosts. Enteropathogen diversity presents challenges to the development of comprehensive detection methods (Goddard et al., 2020a; J. Liu et al., 2016c). Ten pathogens are responsible for most deaths from diarrhoeal disease in children under five years of age: the viruses rotavirus, adenovirus, and norovirus; the bacteria *Shigella* spp., *Vibrio cholerae*, *Campylobacter* spp., non-typhoidal *Salmonella enterica*, and enterotoxigenic and enteropathogenic *Escherichia coli* (ETEC and EPEC); and the protists *Cryptosporidium* spp. and *Entamoeba histolytica* (J. Liu et al., 2016c; Troeger et al., 2018). Animals serve as major reservoir for some of these pathogens (Zambrano et al., 2014), and animal exposure additionally contributes to parasitic infections (Certad et al., 2017) and the acquisition of AMR pathogens (Lewnard et al., 2020). Soil-transmitted helminths also contribute to chronic enteric infections, resulting in reduced quality of life, stunting, malnutrition, anaemia, and impaired development (Pullan et al., 2014). Detailed surveillance across both environmental and host reservoirs with an understanding of local disease context is therefore critical to facilitate optimal interventions (Prüss-Üstün et al., 2016).

An estimated 829,000 annual diarrhoeal deaths, of which 297,000 are children under five, are potentially preventable by improvements to water and sanitation management (Prüss-Ustün et al., 2019). To date, most approaches to reducing disease burden have primarily focused on improving access to WASH through household level interventions including point-of-use water filtration or chlorination, provision of latrines and soap, and increased hand-washing (Clasen et al., 2015; Freeman et al., 2017; Strunz et al., 2014; Wolf et al., 2014; Ziegelbauer et al., 2012). Mixed results from recent studies assessing the impact of these interventions suggest, however, that they are insufficient to reduce enteric disease in highly contaminated or densely populated areas such as urban informal settlements (Bauza et al., 2020; Rogawski McQuade et al., 2020). This highlights the need to more broadly reduce exposure to faecal contamination through transformational interventions that can impact enteropathogen transmission along multiple transmission pathways (Rogawski McQuade et al., 2020), for example as envisaged through the Revitalising Informal Settlements and their Environments (RISE) program (Brown et al., 2018; Leder et al., 2021). Despite this, integrated cross-sectoral surveillance and research in informal settlements and other settings has been restricted, largely due to constraints such as limited financial and human resources. Many existing research surveys target only a limited group of enteropathogens (Guzman-Otazo et al., 2019; O'Brien et al., 2017; Shrestha et al., 2017) or use general faecal indicators (e.g., *E. coli*) as a proxy for pathogen contamination (Julian, 2016; Suvajit Saha et al., 2019). In addition, many studies have focused on only one or two reservoirs (Bauza et al., 2020; Collinet-Adler et al., 2015; Fuhrmeister et al., 2019; Harb et al., 2019; Rogawski McQuade et al., 2020; Vasco et al., 2016), meaning literature is sparse on comprehensive pathogen detection in the wider environment, including zoonotic sources, soil, food, and fomites (Bauza et al., 2020; Fuhrmeister et al., 2019). Improved surveillance, where multiple pathogens are simultaneously monitored across multiple sources, would help resolve the dominant transmission pathways. Such approaches could also be used to both generate evidence both to inform and assess targeted interventions to reduce exposures.

2.2. Antimicrobial resistance gene (ARG) transmission across reservoirs

Currently, approximately 1.3 million deaths per year are attributable to AMR and this annual figure is predicted to rise to an alarming 10 million by 2050 (Murray et al., 2022; O'Neill, 2014). A complex network of genetic, epidemiological, and behavioural factors spanning clinical, veterinary, agricultural, food, wastewater, and environmental sectors all contribute to amplification and dissemination of ARGs (Dantas et al., 2008; Finley et al., 2013; Rizzo et al., 2013; Woolhouse et al., 2015; Zhu et al., 2019). The antimicrobial 'resistome' describes the diverse collection of ARGs and mobile genetic elements (acquired and intrinsic) present in a microbial community in pathogens and non-pathogens across different hosts and environments (Collignon and McEwen, 2019; Kim and Cha, 2021). Some environments have been labelled as 'hotspots' of ARG transmission, such as urban wastewater (Rizzo et al., 2013), intensive agriculture (Berendonk et al., 2015), and informal settlements (Nadimpalli et al., 2020), given the high density of human and animal bacterial inputs into the environment. Interrupting transmission in these hotspots may help to reduce the introduction and spread of ARGs in the environment. Current AMR surveillance systems in the context of public health are, however, largely centred around clinical isolates of human pathogens (World Health Organisation, 2021). Data on the resistome in environmental sources are scarce (Berendonk et al., 2015; Huijbers et al., 2015), and disentangling human-driven AMR from naturally occurring AMR is important for interpretation of risk, as even pristine ecosystems harbour diverse AMR determinants (Hwengwere et al., 2022). It's increasingly recognised that cross-sector surveillance and action are necessary to impact AMR, in turn ensuring long-term availability of effective antimicrobials. As a result, a One Health approach is now the cornerstone of several national AMR strategies (One Health Master Action Plan for Australia's National Antimicrobial Resistance Strategy – 2020 and beyond, 2021).

Transmission of ARGs across reservoirs has contributed to the increasing incidence of multidrug-resistant pathogens (Forsberg et al., 2012; Jiang et al., 2017). For example, carbapenem-resistant *Klebsiella pneumoniae* has been implicated as a key trafficker of ARGs from environmental bacteria to important pathogens (Wyres and Holt, 2018). This bacterium occupies a wide range of niches, including soils, waters, plants, and diverse animals including humans where it opportunistically causes infections (Wyres et al., 2020). It acquires and disseminates ARGs across the genus and to other pathogens, including *Salmonella*, *Enterobacter, Pseudomonas*, and *Acinetobacter* species (Evans et al., 2020; Martínez et al., 2014; Mathers et al., 2015; Villegas et al., 2007). *Clostridioides difficile,* recognised as an 'urgent threat' by the USA Centre for Disease Control (CDC, 2019), has also undergone global spread and persistence facilitated by widespread use of cephalosporins, clindamycin, and, more recently, fluoroquinolones (Gerding, 2004; Knight et al., 2019). Although long viewed as a hospital-associated infection, the last two decades have seen *C. difficile* infection become an emerging and significant problem in the community, with sources such as livestock and the environment playing a critical, yet still underappreciated, role in *C. difficile* transmission to humans (Knight and Riley, 2019). *C. difficile* is a One Health issue with well-documented impact on human health, underappreciated yet significant impact in animal health (particularly neonatal pigs), and massive spore contamination of the environment and agricultural byproducts, all driven by antimicrobial misuse (Lim et al., 2020). For both multidrug-resistant *K. pneumoniae* and *C. difficile,* a detailed mechanistic understanding of transmission pathways outside of the hospital setting and how these can be interrupted is lacking, in part due to a lack of integrated surveillance systems.

Yet the challenges of developing integrated AMR surveillance systems are significant and multifaceted. The thousands of known ARGs (Alcock et al., 2020), as well as the potential for the emergence of novel AMR mechanisms, requires comprehensive and dynamic genotypic surveillance, presenting a barrier to adoption of cross-sectoral approaches. Moreover, culture is needed to confirm AMR phenotypes, despite its labour- and time-intensiveness. Solely relying on molecular detection of ARGs is inadvisable due to the potential for non-functional genes or resistance resulting from more complicated mechanisms (e.g. (Nicolas-Chanoine et al., 2018; Tian et al., 2020; van Duin et al., 2020)). Additionally, accepted thresholds defining resistance and susceptibility to antibiotics are based on clinical relevance and are poorly defined in environmental contexts (Berendonk et al., 2015). Capturing the relevance of ARGs within the resistome is challenging without consolidated knowledge of antimicrobial use in humans, animals and plants. Despite these challenges, sensitive molecular techniques for resistome profiling and transmission, and their associated analytical tools, are increasingly

available and rapidly improving alongside growing representation and improved annotation of environmental resistomes in public databases (Berendonk et al., 2015; Collignon and McEwen, 2019; Huijbers et al., 2019; Kim and Cha, 2021). Continuing improvements support the cross-sectoral approach to curb the spread of AMR, facilitating work to close gaps in surveillance, and enable better resolution of where and how to act to control ARG transmission.

2.3. Healthcare-associated infections

Healthcare settings are important loci of AMR transmission, resulting from the influx of vulnerable patients and healthcare workers to and from the community with selective pressures for AMR such as the widespread use of antimicrobials and disinfectants (Ciusa et al., 2012; Magill et al., 2014; Polk et al., 2007). Hospitals and other healthcare-associated environments contain complex microbial communities that act as important reservoirs of pathogens that cause healthcare-associated infections (HAIs). The interchange of pathogens within such healthcare settings is reflected by the success of several community AMR pathogen lineages (e.g. *S. aureus* USA300 and *E. coli* ST131) (Banerjee et al., 2013; Uhlemann et al., 2014). Microbes rapidly colonise hospital environments, including newly constructed ones (Chng et al., 2020; Lax et al., 2017) and once established present significant risks of transmission to patients (Anderson et al., 2017; L. F. Chen et al., 2019; Chia et al., 2020). Several studies have noted the possibility of transfer of AMR pathogens from surfaces and inanimate objects, especially in rooms that were previously occupied by patients colonised by such pathogens (L. F. Chen et al., 2019; Freedberg et al., 2016). Any object that has contact with a patient may be a potential source of HAI pathogens, including both invasive (e.g. catheters, needles) and non-invasive (e.g. stethoscopes, sphygmomanometers) medical devices. This has led to increased efforts at strict sterilisation and cleaning protocols as part of regular infection prevention activities (National Health and Medical Research Council, 2019). Aqueous environments in hospitals such as hospital plumbing and sinks also serve as important reservoirs for HAI pathogen transmission (Kanamori et al., 2016; Kizny Gordon et al., 2017; Kotsanas et al., 2013; Weingarten et al., 2018). Genomic and metagenomic approaches have proved crucial for establishing these associations (Constantinides et al., 2020; R. C. Johnson et al., 2018; Roberts et al., 2020), and for providing meaningful public health interventions which improve patient outcomes (Gorrie et al., 2021).

While a One Health framework has not traditionally been applied to healthcare settings (Dalton et al., 2020), there are clear contributions from the environment, veterinary medicine, and agriculture to HAIs beyond healthcare settings themselves. One recent example of how animal husbandry has influenced HAIs is the emergence of *mcr-1*, a mobile gene conferring resistance to polymyxins (Y.-Y. Liu et al., 2016; Macesic et al., 2019). The polymyxins are a class of last-line treatments for Gram-negative infections in humans that have been extensively used in animal husbandry. The emergence of this form of resistance represents a significant threat to a precious component of our armamentarium for treating AMR Gram-negative infections and has led to a push to stop the use of these antimicrobials outside of human settings (Wang et al., 2020). From a horticultural perspective, there have been concerns about the widespread use of azole drugs. The azoles are antifungal agents that are used to prevent crops from being affected by moulds, but are the front-line drug class for the treatment of invasive fungal infections in humans, and one of only three available antifungal drug classes (with the echinocandins and amphotericins) for human treatment (Fisher et al., 2018). In Europe, emerging azole resistance in *Aspergillus fumigatus* has caused human infections, thus highlighting the importance of cross-sectoral approaches in addressing HAIs (Burks et al., 2021; Schoustra et al., 2019). The use of novel techniques such as genomics may also help disentangle the true contribution of animal health to HAIs (or indeed vice versa), as reflected in a recent study which illustrated that while similar ARGs were carried by human and animal isolates, the mobile genetic elements where they were located were different, thus refuting a possible link (Ludden et al., 2019).

Healthcare settings and HAIs are integral to any strategy for cross-sectoral surveillance. This surveillance occurs already through centralised reporting on phenotypic AMR from microbiology laboratories (for example in Australia, through the Australian Passive AMR Surveillance System, APAS) and recently there have been increasing public health efforts to integrate genomics into tracking pathogens causing HAIs (Lane et al., 2021; Peacock et al., 2018). The first challenge now is how these efforts can be applied at the individual hospital level, where there may be a multitude of potentially relevant sample types both from patients and from environmental screening. The second challenge lies in using surveillance approaches such as genomics and metagenomics across sectors: not only in research efforts, but as an integrated element of routine infection prevention activities.

3. How is cross-sectoral surveillance data generated? Techniques for pathogen and ARG detection across reservoirs

Recent methodological advances mean that cross-sectoral surveillance is increasingly possible. Integrated systems require methods that account for the diversity of pathogenic agents and their resistance traits, and are applicable to any source and sample type. Below, we evaluate the value of traditional culture-based approaches in integrated surveillance and expand on currently available molecular and genomic techniques that allow the simultaneous detection of a wide range of pathogens and ARGs across reservoirs (Fig. 2). There are advantages and limitations to each technique that should be used to guide decision making in research and large-scale surveillance efforts, with respect to resource constraints (Table 2). Further details and technical discussion about these techniques can be found in **Supplementary File 1**; we recommend adopting similar molecular and culture protocols irrespective of the sample type for cross-sectoral surveillance to be most effective. To enable strong surveillance and response platforms, ideally microbial data should be integrated with epidemiological data of humans and animals, ecological data, and antimicrobial usage and stewardship across sectors (Gardy and Loman, 2018; MacDougall and Polk, 2005).

3.1. Microbial culture: An avenue for in-depth genomic and phenotypic analyses

Growing an organism in pure culture is widely used to isolate bacterial pathogens and detect AMR. Bacteria can be identified through a series of selective and differential culture media that isolate or indicate one or a related group of pathogens (Humphries and Linscott, 2015): this requires some *a priori* knowledge to guide the choice of media. Alternatively, a general growth medium (such as blood agar or MacConkey agar) can be examined for colonies that resemble pathogenic species, which are then further defined by biochemical tests (for example, an API strip) (Humphries and Linscott, 2015). Antibiotic-supplemented agar plates can be used to selectively isolate AMR bacteria or confirm AMR phenotypes (Bard and Lee, 2018). The susceptibility of bacterial isolates can be determined through minimum inhibitory concentration (MIC), colony-forming unit (CFU), disk diffusion, or Etest assays (Jorgensen and Turnidge, 2015), though high-throughput mass spectrometry assays and antibiotic panels (i.e. antibiograms) are also increasingly used (Luna et al., 2007; Oviaño and Bou, 2018; Vrioni et al., 2018).

The major advantage of culture-based approaches for surveillance is that they confirm microbial viability and phenotypic AMR, which is especially useful where correlation between AMR genotypes and phenotypes is poor (Bouganim et al., 2020; Feldgarden et al., 2019; van Duin et al., 2020). Culture also provides an avenue to conduct deeper studies on individual isolates of interest, including whole-genome sequencing or various physiological, biochemical, or infection studies. Notably, phylogenomic analyses can inform understanding of

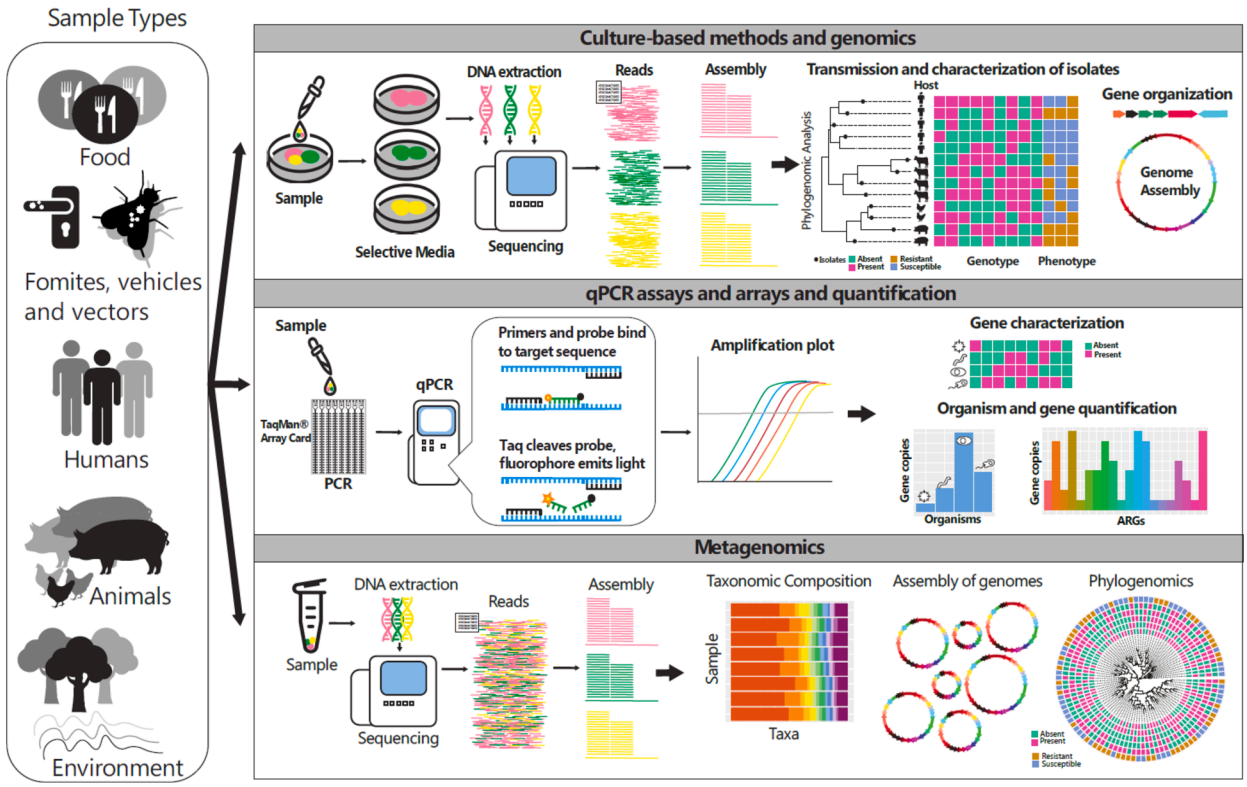

Fig. 2. Key techniques for monitoring pathogens and ARGs across different samples.

transmission dynamics between different sources. For example, population genomics has shed light on the diversification, ARG acquisition, and nosocomial spread of *Klebsiella* pathogens (David et al., 2019; Holt et al., 2015; Perlaza-Jiménez et al., 2020), as well as zoonotic transmission and AMR evolution in *C. difficile* (Knight et al., 2019; Knight and Riley, 2019). Cryogenic storage of isolates enables large-scale retrospective phenotypic and genomic studies (De Paoli, 2005). In the environmental and food sectors, surveillance is driven by public health regulations and the perceived relationship between key pathogens of human health concern (e.g. *Campylobacter, Salmonella*) and faecal indicator organisms, such as *E. coli* and *Enterococcus faecium*. Indicators have also been used to monitor AMR in different reservoirs (Harwood et al., 2000; Łuczkiewicz et al., 2010), and their use as a proxy for faecal contamination removes the need for *a priori* knowledge of which pathogens to attempt to cultivate. However, multiple studies have shown that faecal indicators weakly correlate with pathogen abundance and distribution, are increasingly present in animal and environmental reservoirs independent of faecal contamination (reported as 'naturalised'), and do not reflect the complex eco-evolutionary dynamics of individual pathogens or ARGs (Devane et al., 2020; Field and Samadpour, 2007; Harwood et al., 2005; Pickering et al., 2018): there remains a need to comprehensively evaluate the distribution and abundance of pathogens themselves.

Despite the advantages and the relatively low cost, training, and infrastructure required, culture is increasingly being superseded by molecular methods in many surveillance programs. Culture is typically inferior to PCR-based methods with respect to speed, safety, sensitivity (especially in environmental samples with low pathogen load), and especially scalability (Liu et al., 2014; Steensels et al., 2015). Furthermore, it can be challenging to distinguish between closely related organisms (Chattaway et al., 2017), or identify causative pathogens in mixed culture. Slow-growing, fastidious, or highly infectious pathogens may be difficult or dangerous to isolate, and for patients awaiting urgent treatment, rapid identification takes priority. Culture is rarely practical for monitoring multiple pathogens and is largely restricted to bacterial pathogens: pathogenic viruses, protists, helminths, and fungi are instead typically diagnosed via microscopy or ELISAs (enzyme-linked immunosorbent assays) (Madigan et al., 2012). Given these limitations for broad surveillance, culture-based approaches are most effectively applied to in-depth surveillance and investigation of specific pathogens of interest.

3.2. *qPCR assays and arrays: Best practice for broad and sensitive pathogen detection*

Molecular methods for pathogen detection overcome most of the limitations associated with culture. Diverse bacterial, viral, and eukaryotic pathogens of interest can be detected from a nucleic acid extract (DNA, RNA or both), regardless of the sample type that they were extracted from, through PCR-based amplification. Sensitive and specific quantitative PCR (qPCR) assays have been developed to quantify many pathogens of interest, as well as other gene targets such as ARGs. qPCR has demonstrated advantages in sensitivity compared to non-molecular techniques (Benjamin-Chung et al., 2020; Byrne and Robson, 2015; Lothigius et al., 2008), including for environmental samples and non-bacterial pathogens that are challenging to isolate (Clark et al., 2011; Ishii et al., 2013; Lappan et al., 2021), and offers higher-throughput screening than culture. It is amongst the fastest approaches for pathogen identification: for example, whereas the food-borne pathogen *Listeria monocytogenes* can take five days to culture, DNA extraction and quantification takes only hours (Alessandria et al., 2010).

Standard qPCR is well-suited for detecting single targets across multiple samples: these targets may be specific pathogens or ARGs, or broad indicators. Library-independent microbial source tracking (MST) utilises qPCR to identify gene targets indicative of the gut origin (human or animal) of faecal contamination. This offers a straightforward molecular approach that informs potential areas for management based on the faecal sources detected, and overcomes the source specificity limitations of culture-based faecal indicator analysis (Harwood et al., 2014). To simultaneously monitor several targets (e.g. a set of pathogens or

Table 2
Comparison of commonly used methods for pathogen detection and ARG profiling. Estimated costs are given in USD.

	Strengths	Limitations	Sensitivity/specificity	Costs and scalability	Equipment and expertise required
Culture	Isolates can be further characterised and biobanked. Confirms presence of viable pathogens and phenotypic AMR. Standard method requiring low cost, resources, and expertise.	Restricted primarily to bacteria and some protists (ELISAs often used for viruses, microscopy often used for protists and helminths). Inferior to molecular tests in terms of speed, sensitivity, specificity, and scalability. Risks associated with handling viable infectious organisms.	Low sensitivity. Requires live/intact pathogen at sufficient concentration to be observed. Low to medium specificity. Dependent on media specificity to distinguish from other organisms. Phenotypic or molecular tests are often required for reliable identification.	Low cost per sample, but depends on culture media/ tests required to identify pathogen. Low to moderate scalability. Cost and labour increases with additional samples and pathogens.	Moderate microbiology training required. Basic microbiology facilities, selective and differential media, and reagents required. Minimal computational analysis required.
Standard quantitative PCR (qPCR) and reverse transcriptase qPCR (RT-qPCR)	Can specifically and sensitively detect any pathogen (bacteria, virus, protist, helminth) or ARG of interest using appropriate primers and probes. Pathogen and ARG quantification possible with appropriate reference standards. Assays can be multiplexed (detection of multiple targets in one reaction).	Does not confirm pathogen viability, phenotypic resistance, or other genotypic/phenotypic traits. Extensive manual handling and high costs with large numbers of samples and/or pathogens. Multiplexed assays require careful optimisation with more than two assays per reaction.	High sensitivity. Theoretical detection limit is approximately 3 gene copies per reaction (Ståhlberg and Kubista, 2014). High specificity. SYBR Green will detect non-specific amplification, but TaqMan primers and probes are very specific.	Low cost per sample (approximately $2.10 for one target). Small increase in cost and labour with additional samples, large increase for additional pathogen or ARG targets. Moderate scalability. Large sample numbers are scalable with robotics.	Moderate molecular biology training required. Requires molecular biology facilities and reagents, including real-time thermal cycler with a high upfront cost. Minimal computational analysis required.
Quantitative (RT)-PCR arrays (e.g. TaqMan array cards)	Multiple targets may be simultaneously screened (e. g. 47 with standard TaqMan array cards). Can target any pathogen (bacteria, virus, protist, helminth) or ARG with appropriate primers and probes. Semi-quantitative to quantitative with appropriate reference standards. Simple and fast (~2–3 h) to prepare and run from extracted nucleic acids. Minimal pipetting errors.	Does not confirm pathogen viability, phenotypic resistance, or other genotypic/phenotypic traits. Lower sensitivity than standard qPCR (Harvey et al., 2016; Kodani et al., 2011; Liu et al., 2014) in exchange for higher pathogen throughput. Inflexibility: assays require optimisation to perform under universal conditions on the card.	Medium to high sensitivity. Lower than qPCR, likely due to smaller reaction volume and universal reaction conditions being slightly suboptimal for each target. High specificity. Well-designed TaqMan primer and probe sequences are very specific.	Moderate cost per sample (approx. $60 for TaqMan array cards) but cost-effective for up to 47 targets (approx. $1.28 per sample per target). Moderate to high scalability. Low labour cost, but arrays must be run one-by-one (standard TaqMan array cards allow eight samples to be run per card).	Moderate molecular biology training is required. Requires molecular biology facilities and reagents, including real-time thermal cycler and adapters (e.g. array card block) with a high upfront cost. Minimal computational analysis required.
Shotgun metagenomics	Comprehensive and largely unbiased information on the composition, diversity and potential functions of entire community, including bacteria, eukaryotes, and DNA viruses. Comprehensive method for resistome profiling. Reconstruction of whole genes and genomes is possible.	Limited to DNA-based organisms. Compositional data only (non-quantitative) without the use of spike-ins or microbial load data. Most communities are dominated by bacteria. High sequencing depth and additional analysis may be required for extensive viral and eukaryotic characterisation.	Medium to high sensitivity. High sequence depth required to capture full community, but most organisms at least partially sequenced. Less sensitive for eukaryotes, depending on their abundance. High specificity. Pathogen- or strain-specific genes can be detected. Genomes can be assembled with high sequencing depth.	High cost per sample (approx. $200 per sample). Extensive bioinformatics resources required for analysis of sequencing data; increases moderately with sample number. Low scalability. Cost is prohibitive and computational resources may be limiting.	Advanced bioinformatics training and moderate molecular biology training required. Very high upfront cost required for sequencing, but can be outsourced. Molecular biology equipment, library preparation reagents, and sequencing reagents also required. Extensive computational analysis and supercomputing resources are required.

ARGs), standard qPCR reactions can be multiplexed, where multiple primer sets are added to the same tube or well with different fluorescent markers, allowing detection of several targets from the same nucleic acid sample (Skerniškytė et al., 2016; Vondrakova et al., 2014). For larger numbers of targets, various qPCR array systems have been developed in which customised or fixed primer and probe combinations are arrayed on plates, microfluidic cards, or chips in lyophilised form (Heaney et al., 2015; Quan et al., 2018; Zhu et al., 2020), enabling broad and simultaneous screening for a panel of gene targets within a sample. For example, the customisable TaqMan Array Card (TAC) technology has been used to detect causative agents of diarrhoea (J. Liu et al., 2016a; Liu et al., 2014, 2013), pneumonia (Kodani et al., 2011; Weinberg et al., 2013), and meningitis (Zhao et al., 2019), among other infections (J. Liu et al., 2016b). Quantitative enteropathogen data from TACs have been integral to the landmark MAL-ED (Malnutrition and Enteric Disease Study) (Platts-Mills et al., 2018; Rogawski et al., 2018) and GEMS (Global Enteric Multicenter Study) (J. Liu et al., 2016c) cohort studies. Recent work has also shown that TAC enables sensitive and accurate monitoring of pathogens across most sample types (Baker et al., 2018; Lappan et al., 2021; Tsai et al., 2019), including food (Tsai et al., 2019) and domestic animal faeces (Baker et al., 2018), making it an attractive option for surveillance across reservoirs. There are also

recent developments in qPCR arrays hosting hundreds of ARG targets (Banu et al., 2017; Hurst et al., 2019; Jouhten et al., 2016; Pholwat et al., 2019, 2017), and qPCR microchip systems that run thousands of nanolitre-volume reactions simultaneously, albeit with reduced sensitivity compared to standard qPCR, which have also successfully been applied across One Health reservoirs (Grembi et al., 2020; Wang et al., 2014; Zhu et al., 2013).

qPCR array technologies offer benefits compared to single-target standard qPCR, but factors such as the universal, non-customisable PCR conditions under which to run an array can complicate pathogen quantification, and the cost per sample can be high (with cost-effectiveness achieved by the large number of targets that can be simultaneously detected). Thus, qPCR arrays are best suited for purposes where several targets need to be simultaneously monitored, whereas standard qPCR remains the best and most sensitive approach for quantifying few targets across multiple samples. While these approaches enable comprehensive surveillance, qPCR by itself lacks the ability to distinguish viable pathogens, confirm phenotypic resistance to antimicrobials, or enable further study of the detected organisms. Further technical discussion on qPCR-based surveillance can be found in **Supplementary File 1**. It is nonetheless a powerful technique with significant advantages in sensitivity, specificity, and efficiency over culture-based approaches. There are opportunities within qPCR-based surveillance for comprehensive detection across reservoirs, with great utility in cross-sectoral applications to increase the resolution of pathogen and AMR transmission pathways and evaluate the effectiveness of public health interventions.

3.3. *Metagenomic sequencing: Holistic insights into microbial composition, capabilities and resistance*

Metagenomics involves the sequencing and analysis of the total DNA of a sample, providing a comprehensive and detailed view of the composition and capabilities of the microbial community without the need for known targets. Metagenomic sequencing has proven useful for both clinical and environmental applications (Chiu and Miller, 2019; Ko et al., 2022; Tringe and Rubin, 2005), including for pathogen detection (Dilthey et al., 2019; Fresia et al., 2019; Lindner and Renard, 2013; Mohiuddin et al., 2017; Naccache et al., 2014; Yang et al., 2016), and has enabled the ongoing microbiome revolution. Quince et al. (2017) provide a comprehensive overview of how to conduct a shotgun metagenomics study and what information this can provide (Quince et al., 2017). Metagenomics is unparalleled in terms of target range: it can capture genomic information from bacteria, DNA viruses (Gregory et al., 2019; Ren et al., 2017; Roux et al., 2015), RNA viruses (using metatranscriptomics (Batovska et al., 2019; Shi et al., 2017)), and eukaryotes. As a result, these technologies have been used to simultaneously detect over a hundred pathogens in sewage treatment plants (Li et al., 2015) and trace pathogen strains across different reservoirs (Zolfo et al., 2018). This can be done without prior knowledge and can implicate surprising or novel aetiological agents (Greninger et al., 2015a, 2015c; Phan et al., 2014; Senjuti Saha et al., 2019; Thoendel et al., 2017; Wilson et al., 2014), or inform their likely sources in an alternative whole-community approach to microbial source tracking, without the limitations of selecting appropriate indicator organisms (Knights et al., 2011).

In addition to short-read DNA sequencing, where total DNA is sheared into small fragments, there have been significant recent developments in long-read sequencing technologies (e.g. Oxford Nanopore). These technologies firstly carry several logistical advantages including portable USB-sized instruments (e.g. MinION), cheap instrument cost and the ability to do small run sizes. From a technical perspective, they are capable of reliably generating long reads (e.g. >50 kb), which are particularly well suited to *de novo* genome assembly (Lu et al., 2016), and also facilitate full-length amplicon sequencing approaches for species-level identification. There have been substantial improvements in accuracy rates with the newest (R10.4.1) flow cell technologies and basecalling models: error rates have decreased from $\sim$ 10 % to $<$ 1 % (Hall et al., 2024). Furthermore, the technologies are capable of real-time result generation with minimal computational requirements. Adaptive sampling takes advantage of these capabilities by enabling selection of molecules for sequencing based on real-time assessment (Martin et al., 2022). This for example allows selection of pathogen reads for sequencing, while rejecting human reads. While there is promising potential to use portable sequencers such as MinIONs to address some critical surveillance gaps (Charalampous et al., 2019; Greninger et al., 2015b; Quick et al., 2016), reagent costs, supply chains, and data processing requirements needed to support the continued use of such systems represent a significant remaining barrier to their widespread uptake as part of low-cost sequencing solutions within low- and middle-income countries (LMICs) (Marais et al., 2023).

A major benefit of metagenomics is the deep information unavailable through other means. Metagenomics can reveal functional traits of pathogens and other community members including toxin production, metabolism, motility, and substrate transport. Importantly, it can provide a community-wide, strain-resolved perspective on the resistome across host and environmental reservoirs (Lax et al., 2017; Mahnert et al., 2019; Pal et al., 2016); for example, metagenomic evidence has demonstrated interconnected microbiomes and resistomes across human stool, animal stool, and built and natural environments, supporting the role of inadequate sanitation in the transmission of both enteric pathogens and AMR (H. Chen et al., 2019; Fresia et al., 2019; Pehrsson et al., 2016). There are also broader questions that can be addressed with metagenomics: for example, understanding pathogen ecology, including the pathogen traits, environmental factors, and interspecies interactions that determine the growth and survival of pathogens in hosts and environments. By contrast, both culture and qPCR are limited to the low to moderate number of pathogens that are specifically targeted. However, the sensitivity for pathogen detection can vary with sequencing depth and community complexity. Comparative studies in human stool have reported higher sensitivity with metagenomics for bacteria compared to protists and helminths (Forbes et al., 2017; Loman et al., 2013; Schneeberger et al., 2016; van Boheemen et al., 2020; Zhou et al., 2016). The presence of host DNA, for example in many human-, animal-, and food-associated microbiomes, can also greatly dampen signals: high sequencing depth and host DNA depletion, if necessary, are recommended (Fischer et al., 2014; Hasan et al., 2016; Heravi et al., 2020). Metagenome-assembled genomes are typically inferior to pure culture genomes due to their potential incompleteness, contamination, and heterogeneity (Bowers et al., 2017), and hence are less robust for detailed profiling, but enable the discovery of previously uncharacterised species: this is also increasingly being alleviated by long-read technologies.

Overall, metagenomics is better suited for in-depth studies rather than routine surveillance. With common budget constraints, metagenomics ultimately trades shallow information on large numbers of samples, such as that provided by standard qPCR, for deep information on fewer samples. For the sole purpose of pathogen detection, metagenomics has significant advantages but is currently too resource-intensive to be competitive in practical instances in many countries. Metagenomics requires advanced laboratory and computational expertise, sequencing facilities, and high-performance computing, and despite great improvement in recent years, retains a high cost per sample (Greninger, 2018). This will be especially prohibitive in low-resource settings that typically suffer the greatest infectious disease burdens, with a turnaround time that additionally inhibits urgent clinical applications. However, as these technologies continue to develop, especially in the realm of real-time long-read sequencing, it is likely they will become more affordable and accessible and may represent the future of cross-sectoral surveillance.

3.4. Selecting or combining methods to accommodate contextual needs and resource constraints

The major methods for pathogen and AMR surveillance have individual strengths and weaknesses (Table 2). They vary in their target range, specificity, sensitivity, scalability, flexibility, turnaround time, and information provided. For example, while culture-based methods are ideally suited for profiling pathogen evolution, viability, and resistance, these approaches are poorly suited for monitoring the broad range of pathogens (especially viruses, protists, and helminths) of public health concern. qPCR arrays can quantitatively assess multiple diverse pathogens and ARGs across a broad range of samples, but do not provide phenotypic or genomic information. Although metagenomic approaches are best practice for community and resistome profiling, they do not provide phenotypic information and are expensive and resource intensive. Ultimately no single approach exists to meet all surveillance needs and instead methods must be selected that best suit the needs of a given surveillance program amid resource constraints (Box 1). For example, qPCR arrays are more suited if the priority is to measure levels of a broad range of targets across reservoirs, whereas culture-based approaches are more suited to an in-depth analysis of the evolution, traits, and transmission of a given pathogen. The best information can be gained by combining multiple methods. For example, to understand variations in AMR, side-by-side metagenomic profiling of the resistome can be combined with culture-based resistance tests for one or more key pathogens. When paired, these methods confirm AMR genotypes and phenotypes and can indicate when phenotypes are not reflected by known ARGs. In the context of patients requiring urgent treatment, however, pathogen detection should be targeted and rapid. Thus, different objectives for surveillance and priorities across sectors dictate different combinations of approaches.

Resource constraints are also a major factor in determining the scope and methods of a surveillance approach. The methods vary in the amount of training and equipment required, as well as their costs on both a 'per sample' and 'per target' basis (Table 2). Metagenomics is becoming routine in well-resourced settings, such as major hospitals, but is typically prohibitive in resource-poor settings such as informal settlements in LMICs given the expensive equipment, 'per sample' costs, and extensive expertise required. qPCR-based and culture-based approaches can, however, also be prohibitive at the scale often required to understand major trends and resolve transmission pathways. Hence our argument here (Section 4) that sustainable finance and capacity building (especially in LMICs) are essential elements of any surveillance effort for cross-sectoral surveillance operations to be scalable.

4. Considerations for building fit-for-purpose cross-sectoral surveillance systems

While significant progress has been made with aligning scientific methods to facilitate cross-sectoral research, including in a One Health context, this does not guarantee its scaling-up and material success in improving health in practical settings. Recent analysis and perspectives on existing and future One Health surveillance systems outline a critical need for integration of expertise and data across sectors (Bordier et al., 2020; Hayman et al., 2023), yet several critical challenges constrain efforts to establish and institutionalise cross-sectoral surveillance systems (Bordier et al., 2020; Filter et al., 2021; Hayman et al., 2023; I. Johnson et al., 2018). These challenges include (i) disciplinary, institutional and regulatory silos; (ii) differing incentives and priorities of relevant sectors and stakeholders to engage; (iii) unsupportive funding structures (siloed, short project-based financing timeframes); (iv) a gap between academic and non-academic stakeholders (i.e. governments, communities, industry); (v) limited capacity, especially in marginalised communities and LMICs; and (vi) implementation gaps between science or best evidence and real-world action, as well as discrepant motivators for change. Overcoming those challenges to build One Health surveillance systems will require new models of collaboration and investment at a range of scales (French et al., 2020; Hayman et al., 2023). There is no universal approach for all locales to follow. A tailored approach is needed to build local human and institutional capacity, expand collaboration across disciplines and silos, and demonstrate value for money over time, especially in resource-constrained settings. The focus should be on fit-for-purpose strategies aligned with specific needs, priorities, and investment potential, rather than pursuing exhaustive surveillance from the outset (Box 2).

Such fit-for-purpose approaches can be seen in the increasing number of integrated surveillance efforts that are finding novel ways to overcome these challenges at a range of scales and level of ambition (Aenishaenslin et al., 2021; Bordier et al., 2020). The scope, complexity, and governance structure of such efforts varies: ranging from time-bound focused projects and more ambitious programs catalysed by researchers (e.g. RISE (Brown et al., 2018)), to national, regional and global surveillance efforts directed by governments and multilaterals (e.g. Global Antimicrobial Resistance and Use Surveillance System (GLASS)) (Table 3). These examples illustrate the benefit of a step-by-step approach that is tailored to their local context and capabilities. They are strategic in their approach by including pathogens/areas of most relevance and those with potential to have the greatest impact. Implementation is sequenced to grow these platforms over time as more resources and capacity is built and new partners are added. Importantly, they involve transdisciplinary approaches with partnerships beyond academia, for example with communities, industry, non-profit organisations, and governments (Hadorn et al., 2008; Jahn et al., 2012; Pohl,

Box 1
Recommendations for integrated surveillance techniques:

1. Surveillance should be carried out across samples from all potential reservoirs and vehicles (including human clinical samples, soil, water, food, domestic or farm animals) to better understand the distribution of pathogens and ARGs.
2. Culture-based techniques should be used to confirm pathogen viability and AMR phenotypes and allow in-depth phylogenomics of isolates of interest. Areas of concern can be flagged by patterns in molecular surveillance data.
3. qPCR arrays are ideal for broad pathogen detection across a range of sample types. If the number of relevant pathogens is small, standard qPCR may be applied for better sensitivity and accuracy. Otherwise, broad array panels provide better pathogen coverage.
4. Metagenomics is ideal for broad resistome profiling across multiple environmental sources, as well as deeper studies of pathogen ecology including characterisation of emerging or novel pathogens. This enables important research avenues, but remains expensive and intensive for routine surveillance. Areas of concern may be followed up with culture-based techniques.
5. For molecular techniques, the best available extraction and sample preparation methods for each sample type should be used to maximise recovery of the organisms present. Subsequently, the nucleic acid extracts should be treated as uniformly as possible for pathogen and ARG detection to avoid biases introduced by variable methods.

Box 2
Eight considerations for cultivating fit-for-purpose ongoing surveillance initiatives:

1. *Step-by-step approaches:* Adopt an incremental approach to build local human and institutional capacity, expand collaboration across disciplines and silos, and provide evidence of value for money to grow and expand surveillance efforts over time and geographic scales.
2. *Build broad partnerships:* Adopt a transdisciplinary approach that involves partnerships beyond academia, with communities, industry, non-profit organisations, and governments. Allow sufficient time for partnerships to grow, evolve, and mature.
3. *Invest in dialogical governance:* Set up and maintain a collaborative, inclusive governance system, to oversee and provide direction to the surveillance platform.
4. *Just and ethical transboundary science:* Build surveillance and translation on local knowledge, capacity and approaches to co-design and co-implement, resisting a neo-colonial approach to transboundary scientific collaborations, and advancing toward self-sufficient science implementation in LMICs.
5. *Nurture T-shaped researchers:* Recruit and train team members that have deep, specialised disciplinary expertise as well as broad transdisciplinary capability to operate across disciplines, in a matrix structure, and with non-academic stakeholders.
6. *Include the social sciences:* Integration of social science of human-animal-environmental interactions into surveillance systems. Incorporating human and animal behaviours into context-specific models is crucial to understanding pathways of transmission.
7. *Make data interoperable and shareable:* Develop a secure central database, set standards for data collection and quality (including the import of information from existing databases), and ensure data is appropriately and easily shared across sectors.
8. *Use data for decision-making:* Develop capacity and systems for regular data analysis so that emerging microbial risks are recognised, interpreted and flagged for public health intervention.

2005). As such, many take a local co-design and co-production approach to result in novel insights and better uptake of surveillance information, and therefore deliver a greater impact (Whittaker et al., 2021). Regardless of the scale and level of ambition of One Health surveillance efforts we identify five key considerations to foster the development of such initiatives: (1) effective stakeholder engagement; (2) explicit governance structures; (3) continual capacity building; (4) sustainable finance; and (5) data management for translational action.

4.1. Stakeholder engagement and partnerships

Development of effective integrated cross-sectoral surveillance for pathogens and AMR depends on effective engagement with a wide range of stakeholders (Bordier et al., 2020; I. Johnson et al., 2018). Depending on the goals of the surveillance program, it will be typically necessary to engage multiple sectors and disciplines, including potentially within government agencies, research organizations, NGOs, the private sector, and the patients or communities that surveillance is designed to serve. Effective engagement involves building trust, clarifying priorities for data collection and action, and overcoming disincentives for participation. To facilitate stakeholder engagement, an explicit operational strategy and engagement model are recommended, outlining how stakeholders will participate (whether direct, indirect, or symbolic), how they will collaborate across sectors and disciplines, how progress will be coordinated and evaluated, and how information/data will be shared and translated into action (Goodman and Sanders Thompson, 2017). Where surveillance requires extensive community engagement, for example as in the case of the RISE program focused on revitalising informal settlements (Leder et al., 2021), we recommend the ethical implications of integrated surveillance to participating communities be at the centre of such a stakeholder engagement model, including considerations around informed consent, histories of past research within those communities, community priorities, privacy, and balancing current and future burdens placed on communities with potential benefits of such surveillance (Lebel and McLean, 2018; Minkler, 2004). Cooperation between related surveillance programs, for example the national AMR surveillance programs of different countries, is also critical.

4.2. Governance and collaboration

The broad and diverse range of partnerships with stakeholders requires careful consideration of the collaborative governance and management arrangements for a surveillance platform. Effective governance arrangements need to be established and maintained to build support, track progress against actionable targets, generate financing, ensure inclusive decision-making, and evaluate whether the surveillance platform is meeting the needs of those it seeks to serve (Brown et al., 2019). While existing governance and organisational structures of hospitals, governments, and multilaterals can be adapted for this purpose, alternative strategies may be necessary for poorly resourced settings such as informal settlements, where community-led initiatives can play a pivotal role. For example, delivery of RISE (Brown et al., 2018) is facilitated by a trio of governance entities – a facilitating board, a scientific advisory panel, and an end-users advisory panel – each focusing on specific aspects namely institutional governance, research integrity, and community engagement. Ultimately, the form, mandate and interactions of the governance structure will depend on the level of ambition, scope and priorities and geographic context of the respective surveillance platforms, as outlined in Table 3. Common to all is the value of bidirectional communications, dialogue and agenda-setting to overcome problems of top-down governance and management and avoid exclusion of some population groups (Hollaender et al., 2008; Pohl, 2005). Such a transdisciplinary approach can help break down the barriers to effective scientific collaboration between academic, government, industry, and community groups.

4.3. Capacity building

Human and institutional capacity building should be a core component of cross-sectoral surveillance platforms, not an ‘optional extra’. Sufficient time, effort, and financial support is required to develop necessary expertise, laboratory infrastructure, and computational resources and data systems for effective surveillance programs (Table 2). While capacity building is essential for all initiatives, it is especially important in LMICs that are disproportionately burdened by pathogens and AMR; historically they have been under-resourced by the international scientific community and too often treated as sites for data collection, through ‘helicopter’ research from high-income countries (Haelewaters et al., 2021), rather than locally-embedded, ethical, and equitable scientific collaborations. For example, the RISE program has established and resourced in-country laboratories to perform TAC-based pathogen surveillance (Lappan et al., 2021), run by national staff who have been extensively trained in all aspects from sample collection to data analysis to project management. Capacity building should be a continuous and iterative process, extending beyond technical training to encompass higher-level engagement and mutual learning, while

Table 3
Examples of cross-sectoral surveillance systems at a range of scales.

Scale and level of ambition	Example	Notable features
Global surveillance systems	Global Antimicrobial Resistance and Use Surveillance System (GLASS) (https://www.who.int/initiatives/glass)	• Global collaborative effort run by World Health Organisation (WHO) to standardise AMR surveillance • Three levels: Routine, focused, and surveys/studies • Implementation at headquarters, regional and country offices • Provides support to capacity building and laboratory strengthening in LMICs
	Global Initiative on Sharing Avian Influenza Data (https://gisaid.org/)	• Global database designed for rapid sharing of influenza and COVID-19 genomic data • Data is open to users that agree to uphold etiquette and usage guidelines • Governed by executive, scientific and database experts
Multi-country surveillance systems	European Antimicrobial Resistance Surveillance Network (EARS-Net) (https://www.ecdc.europa.eu/en/about-us/networks/disease-networks-and-laboratory-networks/ears-net-data)	• Publicly funded system for AMR surveillance, administered by ECDC • Database exclusively covers invasive isolates from clinical laboratories • Provides reporting protocol for data submission and annual reports for public interpretation
	Regional Disease Surveillance Systems Enhancement (REDISSE) Project (https://projects.worldbank.org/en/projects-operations/project-detail/P159040)	• Series of disease surveillance projects with 16 participating countries in West Africa • Strengthening surveillance and response systems, particularly for Ebola • Training program to deliver masters-level to students in the region • Funding from the World Bank and other partners to integrate and modernise surveillance systems and build laboratory capacity
National surveillance systems	Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) (https://www.canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars.html)	• Canadian surveillance system covering enteric bacteria in humans, animals and retail meat • Different surveillance components use unified methodology • Information is used to support policies and measures
	UK Human Animal Infections and Risk Surveillance Group (HAIRS) (https://www.gov.uk/government/collections/human-animal-infections-and-risk-surveillance-group-hairs)	• UK surveillance system aimed at identifying hazards and assessing emerging zoonotic pathogens • Releases pathogen-specific reports detailing risks to UK population • Cross-sectoral with membership from several government agencies
Research programs (3–7 years, broader scientific focus with targeted outcomes such as public health interventions)	Revitalising Informal Settlements and their Environments (RISE) (Leder et al., 2021)	• Randomised controlled trial developing and assessing novel water and sanitation infrastructure in LMICs • International transdisciplinary research team including local community involvement • Measuring human, animal and environmental outcomes • Building capacity in LMIC laboratories
	Watershed Interventions for Systems Health in Fiji (WISH-Fiji) (McFarlane et al., 2019)	• Collaborative program designing interventions to reduce water-related disease • Local community and government involvement, strong focus on capacity building
Research projects (1–3 years, narrow scientific focus and number of stakeholders)	Social Microbes Study, Baker et al. (2018)	• Characterised environmental pathogen distribution in relation to human and domestic animal sanitation conditions • Used TaqMan Array Card to profile prevalence and abundance of multiple pathogens in environment
	Bacterial colonisation and succession in a newly opened hospital, Lax et al. (2017)	• Examined bacterial dynamics in a newly opened hospital • One year of surveillance across surfaces, patients and staff • Metagenomics enabled concurrent pathogen and AMR tracking over time and space

mobilising social science and communication methodologies. Importantly, capacity building is not just the one-way transfer of knowledge, resources, and skills; it also involves valuing and incorporating local knowledge, including Indigenous knowledge, and promoting co-designing of surveillance platforms to circumvent neo-colonial approaches (Standing and Taylor, 2007). Cross-sectoral surveillance programs can particularly benefit from 'T-shaped researchers' capable of breaking the siloed status quo (Brown et al., 2015); in this framework, collaborators will develop the deep, specialised disciplinary expertise (e.g. in technical pathogen detection and analysis), as well as broad transdisciplinary capability to operate across disciplines, sectors, and with non-academic stakeholders. Capacity building also provides numerous wider economic and social benefits (Australian Centre for International Agricultural Research, 2022).

4.4. Sustainable finance

Investment is needed into surveillance programs at a scale commensurate with the scope and ambition to convene interested partners and catalyse collaboration. While public funds are increasingly allocated to pathogen and AMR surveillance, it is important that the scale of the investment is sufficient to ensure that the data gathered is useful for developing interventions. For example, delivery of national One Health action plans for AMR depends on extensive, balanced government investment across all implicated sectors. Even at the narrower scale of individual hospitals, a significant budget is needed not only to identify, but understand and thereby interrupt transmission of AMR pathogens from environmental sources. Securing reasonable investment requires explicit assessment of the cost benefits of One Health approaches, with detailed One Health economics frameworks already being developed (Häsler et al., 2021). Targeted financing may be sufficient to catalyse surveillance efforts in under-resourced settings, for example, informal settlements. As Table 3 shows, seed funding or project-based funding can establish important foundations to test partnerships, build credibility, and refine a more ambitious strategy (Adler et al., 2009). Longer-term funding is essential for scaling up surveillance infrastructure and operations, with funding from multiple parties (i.e. consortia funding) often optimal given the ambitious, ongoing, transdisciplinary, and cross-sectoral operations required. The RISE program exemplifies successful blended finance mechanisms, pooling resources from diverse sectors to match ambitious goals. While the volume of finance is important, it is also important to ensure equitable decision-making and control over resources, especially in the context of LMICs (Bruno Stöckli et al., 2018). Regardless of what financial strategy is pursued, securing and maintaining sustainable finance is likely to be an ongoing issue, not 'set and forget', which reinforces the importance of agile leadership and management, strong governance systems, and diverse partnerships across multiple sectors.

4.5. Data management

An integrated cross-sectoral surveillance system requires the integration of a large ever-growing amount of data that is created by, contributed to, and analysed by different sectors, including clinical, veterinary, agricultural, and environmental groups within research, industry, or government bodies. There are several examples of cross-

sectoral surveillance systems currently in use (Bordier et al., 2020), from which inspiration may be drawn. Data must be created, stored, managed, interpreted, and disseminated in a standardised way that is easy to integrate across these sectors. The application of FAIR (findable, accessible interoperable, reusable) principles is essential. Data from each sector, including pathogen and ARG surveys, disease notifications, and antimicrobial usage data, can either be input into large integrated databases or shared through interoperable separate systems (Gardy and Loman, 2018). Secure data storage and management platforms are vital that maintain data security, individual patient privacy, and associated protections, while enabling knowledge discovery and actionable insights (Gardy and Loman, 2018). Outputs should include frequent semi-automated reports that compile summary data from all sectors and allow deeper analysis of spatiotemporal trends. For example, for the RISE program, monthly reports are automatically generated on the levels of 35 pathogens across human, animal, and environmental samples. The production of such reports, in addition to more nuanced use of the data by researchers, can be used to highlight major or emerging pathogens and ARGs, including when and where they are prevalent, to stimulate and accelerate action for targeted corrective interventions. Datasets should be seamlessly linked or shared with appropriate stakeholders, for example governmental bodies responsible for public health responses, to enable timely interventions in response to emerging microbial threats. Regular stakeholder forums would also help to interpret data and analyses in light of the policy agenda and galvanise new action.

5. Conclusions

The dual crises of infectious diseases and AMR are underpinned by the connection between humans, animals, and their shared environment: they are One Health issues. If the United Nations Sustainable Development Goals are to be achieved, these dual crises require urgent attention through an integrated cross-sectoral approach. Increasing public and governmental awareness of the gravity of infectious disease and AMR threats is a key step towards the commitment to fund broad surveillance initiatives. As investments are made, they need to be aimed at interventions and restorative actions. Documenting the situation is insufficient – a practicable program to stop the spread of pathogens and reverse the evolution of AMR is required. The methodological and conceptual advances highlighted throughout this review show that more unified and comprehensive approaches to pathogen and AMR detection are now possible, delivering the foundational surveillance needs for such a program. However, operationalising these methods to deliver fit-for-purpose surveillance and intervention efforts presents multiple challenges. Transdisciplinary partnerships are essential to achieve improved surveillance programs and policy outcomes. Recognising the importance of integrated cross-sectoral surveillance can lead to increased collaboration and to practicable, globally coordinated approaches to improve human and planetary health.

CRediT authorship contribution statement

Rachael Lappan: Writing – review & editing, Writing – original draft, Visualization, Conceptualization. **Steven L. Chown:** Writing – review & editing, Funding acquisition. **Matthew French:** Writing – review & editing, Writing – original draft. **Laura Perlaza-Jiménez:** Writing – review & editing, Visualization. **Nenad Macesic:** Writing – review & editing, Writing – original draft. **Mark Davis:** Writing – review & editing. **Rebekah Brown:** Writing – review & editing. **Allen Cheng:** Writing – review & editing. **Thomas Clasen:** Writing – review & editing, Funding acquisition. **Lindus Conlan:** Writing – review & editing. **Frederick Goddard:** Writing – review & editing. **Rebekah Henry:** Writing – review & editing. **Daniel R. Knight:** Writing – review & editing. **Fuyi Li:** Writing – review & editing. **Stephen Luby:** Writing – review & editing, Funding acquisition. **Dena Lyras:** Writing – review & editing. **Gaofeng Ni:** Writing – review & editing. **Scott A. Rice:** Writing – review & editing. **Francesca Short:** Writing – review & editing. **Jiangning Song:** Writing – review & editing. **Andrea Whittaker:** Writing – review & editing. **Karin Leder:** Writing – review & editing, Funding acquisition. **Trevor Lithgow:** Writing – review & editing, Writing – original draft. **Chris Greening:** Writing – review & editing, Writing – original draft, Conceptualization.

Declaration of competing interest

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Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary material

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