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Trade is central to achieving the Sustainable Development Goals: a case-study of antimicrobial resistance

Accelerating action on the Sustainable Development Goals

The 17 Sustainable Development Goals (SDGs) adopted by 198 nations in September 2015, provide a transformative framework for global action across a wide range of areas. Health is an essential component across many goals, such as those relating to hunger, the environment, and education, and SDG3 focuses explicitly on the achievement of health and well-being for all [1]. Trade also is explicitly mentioned as part of specific targets relating to several of the SDGs. However, it is also a critical determinant of other Goals where it has not been referenced. This paper discusses the often overlooked centrality of trade as a determinant of health in the context of achieving the SDGs, through a case-study of antimicrobial resistance (AMR)[2]. Although not explicitly mentioned in the SDGs, AMR is undoubtedly threatens the sustainability of humanity and planet [3]. It is responsible for an estimated 700,000 deaths annually; forecast to be 10 million by 2050 [3].

Trade and health

The link between trade (agreements) and health (systems) has been well-documented over the past decade [4-8] and can be grouped into four areas as a descriptive framework to understand their interactions. First, health is affected by commodities traded. This may be commodities harmful to health, such as tobacco and alcohol [9, 10], or those which may be beneficial, such as fresh fruit and vegetables [11-13]. Second, the effects of trade agreements and the provisions set out within these. Here the initial focus was on access to medicines and intellectual property (and this connection is explicitly acknowledged in SDG Goal 3 Target 3B), mainly through the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) [14-16]. Over the past five years the focus has been increasingly on regional and bilateral trade agreements, often related to non-communicable diseases and their risk factors [17-20]. Third, the impact of trade in services [21], including the movement of health workers, telemedicine, medical tourism and foreign direct investment in health systems [22-24]. Finally, the wider determinants of trade on health, both positive and negative [25], including patterns of employment, urbanisation income and housing, with considerable evidence to suggest trade as determinant of health inequities [8, 26, 27].

Figure 1: Descriptive framework on trade and health
Trade and antimicrobial resistance

AMR has rapidly ascended the political agenda, and is now recognised as a major threat to health, prosperity and global health security [28]. Substantial funding – with estimates of 40 billion USD over the next ten years – is being sought to tackle AMR and the World Health Assembly endorsed a Global Action Plan on AMR in 2015 [28]. But meeting these challenges will not be straightforward. AMR is a ‘wicked problem’, involving a great number of stakeholders across animal, human and environmental spheres, often with conflicting interests and networks. [29].

Trade and AMR intersect in several ways. On a fundamental level trade (mobility) of people, animals and goods is connected to the spread of microbes, and in human-to-human transmission there is a clear association with travel routes and the emergence of AMR [5, 30]. Here we outline core areas where trade is critical to addressing the issue of AMR, highlighting key areas for action to achieve the SDGs and the 2030 agenda. We focus in particular on connection between trade and AMR in terms of commodities traded and possible impact through trade-related regulation and agreements. We reflect on the role of trade in services and impact on wider determinants.

Availability of antimicrobials

Trade of antimicrobials themselves impacts on their availability for human and animal consumption. Access to good quality antimicrobials is determined by intellectual property provisions set out as part of trade agreements – defining availability and price within a country– as well as regulations concerning safety and substandard medicines, relying on local action and enforcement. Part of the complexity of addressing AMR is balancing access to medicines against overconsumption of antimicrobials; at the global level there is consensus that we are probably consuming too many antimicrobials, but many of the worlds’ poorest still lack access to the essential medicines they need. This is in contrast to SDG3.8 “Achieving universal health coverage including access to safe, effective, quality and affordable essential medicines for all”. For example, more than a million children die each year of sepsis and untreated infection [31]. In poorer regions, the problems are less related to overconsumption of antimicrobials, and more to lack of access, failure to complete full courses, human use of drugs produced for animals, and circulation of substandard drugs. Therefore, efforts to address AMR have to acknowledge appropriate access is part of a wider global trading system which links incentives and profits from medicines to volume of sales. Simultaneously, intellectual property provisions are either insufficient or insufficiently implemented to ensure access for all those who require it. Here trade and the existing trade agreements, including TRIPS, have a central role to play. Indeed, this is reflected in one of
the targets linked to SDG3 – ‘the health goal’ – which states explicitly ‘...provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health, which affirms the right of developing countries to use to the full the provisions in the Agreement on Trade Related Aspects of Intellectual Property Rights regarding flexibilities to protect public health, and, in particular, provide access to medicines for all.’; i.e. it speaks directly to the need to make better use of flexibilities granted under TRIPS to increase access to medicines. Addressing AMR and maintaining drug effectiveness while increasing access will be a key challenge and require nuanced equity sensitive policy implementation. WHO’s recent reclassification of antimicrobials into access, watch, and reserve marks a step change in this direction [32].

Innovation

Trade and intellectual property protections affect development of new antimicrobials. The importance of trade and intellectual property provisions to health and the innovation of pharmaceuticals is explicitly set out in SDG Target 3B. It is acknowledged as a core aspect of the Global Strategy to Fight AMR, and affirmed by the Political Declaration resulting from the UN General Assembly Special Session on AMR in 2016. In this context, the Political Declaration, much liked the UK Governments’ Review of AMR, calls on governments to: ‘recognise the importance of delinking the cost of investment in research and development on AMR from the price and volume of sales so as to facilitate equitable and affordable access to new medicines, diagnostic tools, vaccines ...’.

This is important as some of the largest unmet needs in the research and development (R&D) of new antimicrobials are found in diseases such as tuberculosis (TB) which contribute substantially to the global AMR burden [33]. New drugs that would shorten the six-month TB treatment course would alleviate the huge burden on patients and health systems and help to reduce the emergence of approximately 480,000 new multi-drug resistant TB cases, which is at least partly related to poor adherence to the long treatment course [33]. However, R&D for TB treatment is not profitable enough to warrant sufficient investment from pharmaceutical companies. This is reflected in the huge funding gap for TB; less than one third of the $3.7 billion funding target for new drugs called for in the Stop TB Partnership’s Global Plan to Stop TB 2011-2015 was raised. Concerns extend to diagnostic tools, vaccines for disease prevention, and further AMR-related innovation in the widest sense. It is likely, for example, that healthcare facilities will require new types of furniture and tools with antibacterial surfaces and so forth. Such products may be an area of future innovation but need to be affordable by LMICs.
Trade also impacts on the availability of substandard ‘counterfeit’ antimicrobial medication. While it is hard to estimate this clandestine activity, trade in counterfeit medication itself is estimated to run into billions [34]. Availability of substandard antimicrobials is likely to undermine all attempts at public regulation of antimicrobials, such as oversubscribing, or the provision of antimicrobials through informal providers. Little is known about the impact of counterfeit trade in animal drugs [35]. However, here trade agreements and greater regulation through bodies such as the World Trade Organisation (WTO) offer solutions to this challenge.

Trade in food products that contain resistant bacteria

Trade in food products that contain resistant bacteria will further affect the spread of AMR. This provides opportunities for regulation and intervention. Food, animal and plant safety in trade is regulated globally through the WTO’s Sanitary and Phytosanitary (SPS) Agreement. It sets out basic standards of food safety based on science, while providing some room for countries to set and retain their own regulation. A recent analysis of interpretive nutrition labelling and trade discussions under WTO regulation found that these were often at odds and there was a risk that trade agreements may constrain public health regulation [36]. The most significant sector in terms of trade relating to AMR is in livestock, food animals and their feed, particularly in those animals that host resistant bacteria. Trade is likely to be a route for spreading resistance; at the same time where animals are tested for resistant strains as part of efforts to control the spread of AMR, the trade effects are likely to be immediate.

For example, the global trade in meat is significant: the United States Department of Agriculture predicted that global production of beef and veal would rise to 62 million tonnes in 2017, with global exports predicted to be 9.6 million tonnes. Export of broiler chicken meat was expected to be a record 11.2 million tonnes [37]. Drug-resistant Escherichia coli can live on beef carcasses even after 24 hours in a chiller and in minced beef that has been stored for up to eight days [38]. A study to estimate the prevalence of Methicillin-Resistant Staphylococcus Aureus (MRSA) in raw meat samples provided by retail traders in The Netherlands demonstrated that MRSA was present in many of the samples, ranging from 35.3% of the samples of turkey, to 2.2% of game samples [39]. While many LMICs export food products and animals, their capacity to monitor AMR through adequate surveillance may be limited by overall budget constraints [35, 40].

A further challenge here is that although many farmers are advised to vaccinate their animals, it is hard to enforce and to differentiate between livestock vaccinated or those infected. Vaccination is also not currently routine practice in all regions. Thus, strategies to
contain AMR at national levels through vaccination may then clash with global AMR control, and be to the detriment of farmers seeking to trade their animals across national borders.

Discussion

Our case study highlights the need to consider trade when seeking to address AMR and in achieving the SDGs. The relationship between trade and AMR in achieving the SDGs discussed here primarily falls into two aspects of trade and health: commodities traded and the possible impact of trade agreements (see Figure 2). Trade of AMs and of food, including livestock, falls into the category of ‘commodities traded’, while issues around innovation and regulation relate to ‘trade agreements’. Other areas of trade and health also affect AMR, even though these have been explored to a lesser extent. Trade in services, including medical tourism has been documented as contributing to the spread of resistant bacteria [41]. Equally increases in global trade and the resulting changing patterns of employment have resulted in intensive urbanisation and changes in farming [5], which in turn affect resistance in animals and its’ transmission. This also links closely to SDG 11 focused on urbanisation.

Figure 2: Trade and health framework for AMR

Given the close connection between food products, including food animals, and the spread of AMR, it seems likely that this may become subject of future trade discussions and dispute where individual countries may wish to introduce, for example, public health regulation which requires labelling of antibiotic usage for food, or restrict imports from specific countries. Similar public health regulations around interpretive nutrition labelling for food have led to trade discussions in the past, for example regulation surrounding fatty cuts of meat in Ghana [42], or the EU-US dispute on the use of growth-hormone in cattle [43]. It has yet to be established in AMR could be used as a rationale for a ‘public health emergency’ which allows for greater flexibility around IP regulation under WTO TRIPS, as highlighted in SDG3 [44],[43].

Regulation

This all underlines the need to ensure that trade agreements, and regulating bodies, such as the WTO and the World Intellectual Property Organisation (WIPO), consider AMR in the discussions on and adjudication of disputes on intellectual property protection. Standard setting bodies such as the Codex Alimentarius Commission and the OIE are central to the relationship between trade and AMR as WTO Members are obliged to base regulations on
relevant international standards. These standard-setting bodies are central to this intersection and will offer important avenues to address AMR and contribute to the SDGs through stronger regulations. Free-trade agreements could also play an important role because they typically liberalize trade in agriculture to a greater extent than WTO commitments and can include more specific obligations. This relates closely to SDG 16 (transparent institutions and participatory policy processes).

The role of civil society and think tanks

It is important to develop international regulation and work with national regulators now, to prevent pitching trade against public health advocates in relation to AMR [45, 46]. Civil society has played a very active role in highlighting the intersection between trade and health, ranging from the HIV access movement to the recent opposition to the TTIP Agreement between the EU and the US [47]. Civil society and think-tanks are crucial actors in responding to AMR. In Sweden, which has responded to AMR faster and earlier than other countries, public mobilisation and non-governmental organisations such as ReAct have been critical to placing the issue high on public and policy agenda [48]. Equally, recent protest by doctors and drug sellers in Punjab, Pakistan in response to stricter laws on substandard drugs highlight the importance of involving civil society actors from the outset and the need for greater public debate and civil society involvement on AMR.

Conclusion

The example of AMR demonstrates that accelerating action on health and the SDGs needs greater understanding of the impact of trade. The SDGs acknowledge the close linkages between trade and sustainable development, but these could be made more central. A first step is analysing where the intersections between health and trade lie. Here civil society, think tanks and universities have a critical role to play. Second, advances are needed in governance mechanisms to better facilitate collaboration between health and trade, both in terms of where health convenes, as well as where health needs to engage for a better governance for health [25]. Third, these challenges throw down the gauntlet to think-tanks and academic institutions to go beyond knowledge generation and dissemination. There is need to develop new ways of working on health and trade to tackle the big issues in sustainable development – such as the threat of AMR. The myriad of ways in which trade will affect sustainable development, as evident from this case-study of AMR, also hold lessons for sectors other than health. This includes lessons about the interlinkages between sectors and Goals, the importance of governance, and the need for strong and just institutions as well as inclusive processes.
We have read and understood BMJ policy on declaration of interests and that we have none.

JH had the idea for the paper and wrote the first draft, all other authors contributed subsequent drafts and reviewed the final version of the paper. All authors agreed the final version of the paper.

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### Figure 2

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<td>• Availability of AMs.</td>
<td>• Regulation of counterfeit medicines.</td>
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<tr>
<td>• Availability of food, including livestock which may contain resistant bacteria</td>
<td>• Innovation of new AMs.</td>
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<td>• Interpretive labelling of food.</td>
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<td>e.g. spread through human mobility</td>
<td>• Pattern of urbanisation and effect on livestock farming practices</td>
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