Trade as central to achieving the Sustainable Development Goals: a case-study of antimicrobial resistance (AMR)
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Accelerating action on the Sustainable Development Goals

The 17 Sustainable Development Goals (SDGs), adopted by 198 nations in September 2015, seek to provide a transformative framework for global action across a wide range of areas. Health is an essential component across many goals relating to hunger, the environment, nutrition, agriculture, sustainable production and consumption, and education, and SDG3 focuses explicitly on the achievement of health and well-being for all.[1] The SDGs also explicitly recognise the importance of collaboration across sectors and between partners (SDG17). They recognise the need to address inequities as a cross-cutting issue. Discussing the political origins of health inequity and the global market system the flows of goods (SDG10), people and ideas calls for a focus on governance arrangements, including for trade.[2] This paper, the first in a series, discusses the centrality of trade as a determinant of health in the context of achieving the SDGs, through focus on an in-depth case study of antimicrobial resistance (AMR). Trade offers a particularly interesting case for examining how to accelerate action on the SDGs as it highlights the networked nature of the goals, and the intersectoral partnerships required to achieve these. The paper is part of a project involving the BMJ, the Canadian Institutes for Development Research (IDRC) and the Graduate Institute in Geneva amongst others, to explore the role of think tanks and academic institutions in accelerating action on the SDGs.[1]

Trade and health

The link between trade (agreements) and health (systems) has been well-documented over the past decade.[3-7] Evidence of the effects of trade on health can be grouped into four areas. First, health effects relating to commodities traded. This may be commodities harmful to health, such as tobacco and alcohol,[8,9] or where trade has led to harmful overconsumption, as in the case of nutrition.[10-12] Second, the effects of trade agreements and the provisions set out within these. Here the initial focus was on access to medicines (SDG 3.8) and intellectual property, mainly through the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS).[13-15] Over the past 5 years the focus has been increasingly on the newer generation of regional and bilateral trade and investment agreements and the implications of investor protection and dispute resolution mechanisms for public health regulations. This has often been in relation to non-communicable diseases and their risk factors.[6,16-18] The most publicised examples here include the use of trade and investment agreements by the tobacco industry, specifically Philip Morris, to challenge
plain packaging of cigarettes in Australia and Uruguay under Investor-State Dispute Settlement (ISDS) mechanisms,[19] citing infringement of trademark protection.[20,21] Similarly nutrition guidance labelling, which is intended to guide the consumer towards a healthier diet and is a result of national policies has been raised as a ‘Technical Barrier to Trade’ under WTO regulation.[22] The principles of non-discrimination in trade agreements have in many instances meant that it is hard for national governments to limit availability of unhealthy foods – Samoa had to remove a 4 year ban on turkey tails under WTO non-discrimination rules.[23] Third, the impact of trade in services,[24] including the movement of health workers, telemedicine, medical tourism and foreign direct investment in health systems.[25-27] Here the evidence base is again diverse with some suggesting the potential for net positive effects,[27] while other researchers are highlighting negative impacts especially on health equity.[28] Finally, there is now an evidence base of how trade affects the wider determinants of health, including patterns of employment, income and housing, with considerable evidence to suggest trade as determinant of health inequities.[7,29,30] The greater attention to and evidence on the connection between trade and health has resulted in considerable civil society advocacy, which has been successful in many cases in changing the political process, including protests in Belgium against the proposed EU US trade deal TTIP.[31,32]

The linkages between trade and health are explicitly acknowledged in the SDGs, including in SDG3 where access to medicines SDG 3.8 and the TRIPS Agreement are specifically mentioned. The Goals moreover refer to trade as part of several goals for example. SDG17 – with a general acknowledgement of the importance of trade to prosperity. Table 1 here below sets out the intersection between trade, and between AMR across all SDGs.

**Trade and antimicrobial resistance**

Antimicrobial resistance (AMR) has rapidly ascended the political agenda in global health, now recognised as a major threat to health, prosperity and global health security [33]. Substantial funding – with estimates in the region of 40 billion USD over the next 10 years – is being sought to tackle AMR and the World Health Assembly endorsed a Global Action Plan on AMR in May 2015.[33] Despite this concern and political momentum behind AMR, addressing these challenges will be far from straightforward, as AMR could be described as the classic ‘wicked problem’, involving a great number of stakeholders, often with conflicting interests and networks and great importance as to how the issue is framed; in the case of AMR this has been mainly around the economic and potential security impacts.[34] These complexities are reflected in the core trade issues concerning AMR. They are amplified by the ‘One Health’ nature of AMR, requiring action across the animal and human health
spectrum.[35] Existing research has demonstrated the challenges in achieving policy change on OneHealth given this cross-sectoral nature.[35]

Trade and antimicrobial resistance intersect in several ways across a wide spectrum. On a fundamental level trade reflected in the mobility of people, animals and goods is connected to the spread of microbes, indeed in human-to-human transmission there is a clear association with travel routes and the emergence of resistance.[4,36] Here we outline core areas where trade is critical to addressing the issue of AMR, as a vignette of the wider role that trade plays in achieving the SDGs.

Availability and innovation

Trade of antimicrobials themselves impacts on their availability for human and animal consumption. Access to good quality appropriate antimicrobials is determined by intellectual property provisions set out as part of trade agreements – determining what is available within a country and at what price – as well as regulations concerning safety and counterfeit medicines, relaying on local action and enforcement. Part of the complexity of addressing AMR is balancing access to medicines against overconsumption of antimicrobials;[37] at the global level there is consensus that we are probably consuming too many antimicrobials, but many of the world’s poorest still lack access to the essential medicines they need. More than a million children for example die each year of sepsis and untreated infection.[38] In poor regions and populations, additional challenges are that full courses of antimicrobials are often not taken, there is use of drugs produced for animal use in humans, and there is demand for or limited regulation on counterfeit or substandard drugs. Therefore, all efforts to address AMR have to acknowledge this is part of a wider global trading system which links incentives and profits from medicines to volume of sales, while at the same time provisions for intellectual property are either insufficient or insufficiently implemented to ensure access for all those who require it. Here trade and the existing trade agreements, including foremost amongst these the TRIPS agreement, 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 for all.

Addressing AMR and maintaining drug effectiveness while increasing access to medicines will be a key challenge and require nuanced equity sensitive policy implementation.
Trade and the linked intellectual property protections also affect innovation in development of new antimicrobials. Innovation in new needs–based antimicrobials has been acknowledged as a core aspect of the Global Strategy to Fight AMR, and was 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 and other results to be gained through research and development’.

This is important as not only is there often lack of access to antimicrobials by the poorest, but equally some of the largest unmet needs in the research and development of new antimicrobials are found in diseases such as tuberculosis (TB) which contribute substantially to the global AMR burden.[39] Development of new drugs that would shorten the six-month TB treatment course would alleviate the huge burden on patients and health systems struggling to ensure adherence over such an extended period. It would also 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 course of treatment.[39] However, research and development for TB treatment is not profitable enough to warrant sufficient investment from pharmaceutical companies. This is reflected in the huge funding gap for TB; while the Stop TB Partnership’s Global Plan to Stop TB 2011-2015 called for an investment of $3.7 billion towards the development of new drugs, only $1.2 billion was invested leaving a shortfall of $2.4 billion in comparison to the targets. The concerns around IP extend to diagnostic tools, vaccines for infection prevention, and further AMR related innovation in the widest sense. It is likely for example that hospitals and health care facilities will require new types of furniture and tools with antibacterial surfaces and so forth, and such products are likely to be an area of innovation in the future. However, for these to be within reach of LMICs requires full use of the IP provisions set out under the TRIPS Agreement.

As indicated, trade also impacts on the availability of counterfeit antimicrobial medication. While this is much harder to estimate as it is a clandestine activity, trade in counterfeit medication itself is estimated to run into billions.[40] This poses a challenge as counterfeit availability of AMs is likely to undermine all attempts at public regulation of AMs, such as for example oversubscribing, or the provision of AMs through informal providers. Little is known about the impact of counterfeit trade in animal drugs.[41]

*Trade in food products that contain resistant bacteria*
Trade in processed 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 Sanitary and Phytosanitary (SPS) Agreement under the World Trade Organization (WTO). 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 the food labelling and trade disputes under WTO regulation found that these were often at odds and there was a risk for trade agreements to limit potential for public health regulation.[22] 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 carrying 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. The global trade in meat is huge: 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.[42]

Drug-resistant Escherichia coli can live on beef carcasses even after 24 h in a chiller and in minced beef that has been stored for up to 8 days.[43] A study to estimate the prevalence of methicillin-resistant Staphylococcus aureus 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.[44] While many LMICs export food products and animals, their capacity to monitor AMR through adequate surveillance may be limited by overall budget constraints.[41,45]

A further challenge here is that although many farmers are advised to vaccinate their animals, it is hard to enforce in many areas or 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

The importance of trade for AMR outlined here highlight the need to consider trade in the regulations seeking to address AMR at national, regional and global level. The intersection between trade and AMR provides a good example of the type of multi-level governance required to address AMR,[38] but equally of the need for better governance to achieve the SDGs. Equally, it underlines the need to ensure that trade agreements, and specifically trade
bodies, such as the World Trade Organisation (WTO) and the World Intellectual Property Organisation (WIPO), consider AMR in the management and adjudication of intellectual property regulation. These agencies are already actively considering the issue, as evidenced by a symposium organised by WTO, WIPO and WHO focusing on AMR. [46]

Given the close connection between food products, including food animals, antimicrobial resistance and the spread of AMR, it seems likely that this may become subject of future trade disputes where individual countries may wish to introduce, for example, public health regulation which requires nutrition guidance labelling of antibiotic usage for food, or restrict imports from specific countries on the basis of resistant strains. Similar public health regulations around nutrition labelling for food have led to trade disputes in the past, for example Chilean proposals to introduce mandatory food labelling in an effort to curb obesity in 2013, were raised at the WTO and later implemented in an amended version,[22] or the EU-US dispute on the use of growth-hormone in cattle.[47] On the other hand, Ghana has been able to implement public health regulation to restrict fat content in meat including imports through a carefully treaded path of focusing on fat content of meat rather than labelling or specific imports.[23] Indeed a recent analysis of nutrition labelling that has been raised at the WTO, suggested that there is considerable policy space to ensure labelling compliant with existing trade regulation.[22] While this suggests promise for governance arrangements it is worth highlighting that of course labelling for antibiotic use in food stuff has not yet been explored in practice.

Outbreaks, such as the swine flu in 2008, are used to support trade restrictions, and it has yet to be established in AMR could be used as a rationale for a ‘public health emergency’ which allows for such trade restrictions in current WTO rules.[47,48] 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.[49,50] Given the evident complexities in addressing AMR and trade and the essential role regulation, surveillance and its enforcement these need to considered by funders seeking to tackle these challenges. Addressing the intersections between trade and AMR set out here again suggests the central role of governance. This is to allow for regulation to required to stop the rise of AMR while allowing equitable access, but equally to develop trade and health governance mechanism that are nuanced enough to enable trade while allowing the protection of public health.

Conclusion
What the example of AMR demonstrates is that to accelerate action on health and the SDGs we need greater understanding and analysis of the impact of trade. It highlights the great interlinkages between different Goals and Targets, as set out in Table 1. A first step here will be to understand where the intersections between health and trade lie. Second, there needs to be advances in the governance mechanisms that can facilitate better collaboration between these, both in terms of where health convenes, as well as where health needs to engage for a better governance for health. Third, this will require not only new types of knowledge and analysis but new ways of working. These challenges throw down the gauntlet to think-tanks and academic institutions going beyond knowledge generation and dissemination, to innovate new ways of working on health and trade to tackle the big issues in global health – such as the threat of AMR – and to accelerate action on the SDGs and ensure health and well-being for humanity.

We declare we have no conflict of interest.

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Table 1: Sustainable Development Goals and Targets relevant to Trade and Antimicrobial Resistance

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<th>Sustainable Development Goal</th>
<th>Note: The lines in grey are Goals and Targets only relevant to AMR.</th>
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<td><strong>2: End hunger, achieve food security and improved nutrition and promote sustainable agriculture</strong></td>
<td>2b: Correct and prevent trade restrictions and distortions in world agricultural markets, including through the parallel elimination of all forms of agricultural export subsidies and all export measures with equivalent effect, in accordance with the mandate of the Doha Development Round</td>
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<td><strong>3: Ensure healthy lives and promote well-being for all at all ages</strong></td>
<td>3.1: By 2030, reduce the global maternal mortality ratio to less than 70 per 100,000 live births</td>
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<td>3.2: By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births</td>
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<td>3.3: By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases</td>
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<td>3.8: Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all</td>
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<td>3b: Support the research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect developing countries, 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</td>
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<td>3d: Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks</td>
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<td><strong>Goal 6: Ensure availability and sustainable management of water and sanitation for all</strong></td>
<td>6.2: By 2030, achieve access to adequate and equitable sanitation and hygiene for all and end open defecation, paying special attention to the needs of women and girls and those in vulnerable situations</td>
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<td><strong>Goal 8: Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all</strong></td>
<td>8a: Increase Aid for Trade support for developing countries, in particular least developed countries, including through the Enhanced Integrated Framework for Trade-Related Technical Assistance to Least Developed Countries</td>
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<td><strong>Goal 9: Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation</strong></td>
<td>9.5: Enhance scientific research, upgrade the technological capabilities of industrial sectors in all countries, in particular developing countries, including, by 2030, encouraging innovation and substantially increasing the number of research and development workers per 1 million people and public and private research and development spending</td>
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<td><strong>Goal 10: Reduce inequality within and among countries</strong></td>
<td>10a: Implement the principle of special and differential treatment for developing countries, in particular least developed countries, in accordance with</td>
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<td>Goal 12: Ensure sustainable consumption and production patterns</td>
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<td>12.6: Encourage companies, especially large and transnational companies, to adopt sustainable practices and to integrate sustainability information into their reporting cycle</td>
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<td>12a: Support developing countries to strengthen their scientific and technological capacity to move towards more sustainable patterns of consumption and production</td>
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<th>Goal 14: Conserve and sustainably use the oceans, seas and marine resources for sustainable development</th>
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<td>14.6: By 2020, prohibit certain forms of fisheries subsidies which contribute to overcapacity and overfishing, eliminate subsidies that contribute to illegal, unreported and unregulated fishing and refrain from introducing new such subsidies, recognizing that appropriate and effective special and differential treatment for developing and least developed countries should be an integral part of the World Trade Organization fisheries subsidies negotiation</td>
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<th>Goal 16: Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels</th>
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<td>16.7: Ensure responsive, inclusive, participatory and representative decision-making at all levels</td>
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<td>16.8: Broaden and strengthen the participation of developing countries in the institutions of global governance</td>
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<th>Goal 17: Strengthen the means of implementation and revitalize the global partnership for sustainable development</th>
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<td>17.6: Enhance North-South, South-South and triangular regional and international cooperation on and access to science, technology and innovation and enhance knowledge sharing on mutually agreed terms, including through improved coordination among existing mechanisms, in particular at the United Nations level, and through a global technology facilitation mechanism</td>
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<td>17.9: Enhance international support for implementing effective and targeted capacity-building in developing countries to support national plans to implement all the sustainable development goals, including through North-South, South-South and triangular cooperation</td>
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<td>17.10: Promote a universal, rules-based, open, non-discriminatory and equitable multilateral trading system under the World Trade Organization, including through the conclusion of negotiations under its Doha Development Agenda</td>
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<td>17.11: Significantly increase the exports of developing countries, in particular with a view to doubling the least developed countries’ share of global exports by 2020</td>
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<td>17.12: Realize timely implementation of duty-free and quota-free market access on a lasting basis for all least developed countries, consistent with World Trade Organization decisions, including by ensuring that preferential rules of origin applicable to imports from least developed countries are transparent and simple, and contribute to facilitating market access</td>
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<td>17.14: Enhance policy coherence for sustainable development</td>
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<td>17.15: Respect each country’s policy space and leadership to establish and implement policies for poverty eradication and sustainable development</td>
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<td>17.16: Enhance the global partnership for sustainable development, complemented by multi-stakeholder partnerships that mobilize and share knowledge, expertise, technology and financial resources, to support the achievement of the sustainable development goals in all countries, in particular developing countries</td>
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17.17: Encourage and promote effective public, public-private and civil society partnerships, building on the experience and resourcing strategies of partnerships.