

# The proposed Drug Resistance Index (DRI) is not a good measure of antibiotic effectiveness in relation to drug resistance

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The issue of antimicrobial resistance for humankind does not need any introduction anymore. It is a widely recognised global health threat, that has sparked increasing attention, as acknowledged at the World Health Assembly at its 68th meeting in May 2015, and at the General Assembly of the United Nations (UNGA) in September 2016.<sup>1,2</sup> The World Health Assembly adopted a Global Action Plan on Antimicrobial Resistance that was endorsed by the UNGA. The plan formulates five key objectives; we draw attention to two of these. In its first objective, the Global Action Plan calls for improving ‘awareness and understanding of antimicrobial resistance through effective communication, education and training’. The fourth objective aims at ‘optimising the use of antimicrobial medicines in human and animal health’.

In their recent publication, Klein and coworkers state, in line with the first objective of the plan, that it is important to communicate trends in antibiotic resistance to a broad audience, and that this should be done in a clear and unambiguous way.<sup>3</sup> To this purpose, they propose to use a Drug Resistance Index (DRI), as a measure of antibiotic effectiveness in relation to drug resistance. The DRI was described in a previous article by Laxminarayan and Klugman.<sup>4</sup> It was developed as an easy to use tool to aid politicians and health authorities in getting an estimate of a country’s availability of effective antibiotics to treat the most common or severe bacterial infections in that given country. By combining, in a single metric, the use of various antibiotic groups and the resistance proportions of several pathogens, the aim is to improve and simplify communication about the

## Summary box

- ▶ The Drug Resistance Index (DRI) is proposed as measure of antibiotic effectiveness in a given country, by combining, in a single metric the use of various antibiotic groups and the resistance proportions of several pathogens.
- ▶ The DRI is a complicated measure that gives results that cannot be understood by common knowledge and logic.
- ▶ The DRI conveys a wrong message. A low DRI is meant to represent good antibiotic efficacy, but a low DRI may be the result of unnecessary, excessive use of too broad-spectrum antibiotics.
- ▶ Restrictive use of antibiotics is one of the cornerstones in the fight against antimicrobial resistance, therefore the DRI, whose interpretation may promote the opposite, should not be used.

effectiveness and consequences of antibiotic therapy. A low DRI is meant to indicate a high effectiveness of antibiotic therapy and a high DRI the opposite.

Unfortunately, a closer look at the DRI shows that combining different data in a single metric provides unclear and ambiguous information. The lack of inherent logic of this metric will more likely confuse than clarify. The intricacies of the DRI are three-fold. First, this metric is calculated by dividing two proportions: the proportion of use of each antibiotic is divided by the proportion of resistance to that antibiotic. Second, it combines total antibiotic use, which, for the large majority, mostly occurs in the community, with resistance proportions in pathogens that are mostly responsible for infections in hospitals and other healthcare settings.

The DRI is thus created with data from two different care sectors with different



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characteristics of patients, pathogens and antibiotic use. Such data should not be combined in one single index. In addition, for many countries, the reliability of the proportions used in the equation is questionable, since both antibiotic use, and resistance data often are rather raw estimates. In many countries, antibiotic resistance proportions are based on an extrapolation from very low numbers of clinical isolates, mirroring an often very sporadic or selective sampling procedure in hospitals. Third, it combines aggregated data of use of all antibiotics with aggregated resistance rates of different pathogens. Not every antibiotic is useful for every pathogen, and some are more important than others. In one country, increasing resistance to amoxicillin-clavulanic acid may be considered important, while in another of no consequence. Combining data in the way proposed may appear impressive but will not really add clarity.

A few examples of DRIs from Klein *et al* illustrate these problems.<sup>3</sup> The USA has a lower DRI than, for example, the Netherlands or Australia. This does not reflect the well-known low antibiotic resistance proportions (as reported by the European Antimicrobial Resistance Surveillance Network), the low antibiotic use (as reported by the European Surveillance of Antimicrobial Consumption Network) and the nation-wide implementation of effective antibiotic stewardship programmes in the Netherlands.<sup>5,6</sup> It does also not reflect the low resistance proportions of Gram-negative bacteria in Australia (these are even lower than those in the Netherlands), but possibly the position of the Australian DRI is influenced by high resistance proportions of *Staphylococcus aureus* and *Enterococcus* spp. in this country, compared with many other countries.<sup>7</sup> In both examples, the DRI does not seem to reflect reality.

The explanation for the respective positions of the Netherlands and the USA is quite likely the following: while prescribers in the Netherlands may see no reason to adapt their antibiotic prescription patterns in the community to resistance proportions seen in mainly healthcare-associated pathogens, studies have shown that clinicians in the USA tend to prescribe broad-spectrum antibiotics in the community at such a high rates if they adapted community antibiotic prescribing to the resistance proportions in healthcare-associated pathogens (although this should not be done).<sup>8-10</sup> The respective positions of Australia and the USA are difficult to understand, as they do not correspond with the lower resistance rates, both in Gram-negative and Gram-positive pathogens, in Australia, than in the USA, despite comparable antibiotic use rates in these countries.<sup>11</sup> We propose that Klein *et al* investigate how developing separate DRIs for the community and the hospital sectors would influence conclusions.

Furthermore, DRIs might be counterproductive in reaching the fourth objective of the Global Action Plan, that is, 'optimising the use of antimicrobial medicines in human and animal health'. Even more important than its complexity, which makes it difficult to understand why

a certain country has a certain DRI, we fear that the DRI may convey the wrong message. Indeed, a low DRI may intuitively be interpreted as a low level of antimicrobial resistance, which is not necessarily the case. A country with high resistance levels may have a low DRI when it uses broad-spectrum antibiotics routinely, as shown above by the example of the USA.

To take it even further, a low DRI may be the result of resistance levels that are actually low and broad-spectrum antibiotics being used without a good reason. In both instances, these countries with low DRI will be seen as performing well. This may be perceived as encouraging by politicians and as reassuring by clinicians, who could continue prescribing broad-spectrum antibiotics when they are not necessary. This issue is briefly touched on by Klein *et al*: 'a country with high per capita drug use would not have a high DRI, if resistance rates to the most frequently used drugs were low'. However, the consequence of condoning broad-spectrum antibiotics is well known. It is widely accepted that high and broad-spectrum antibiotic use should be curtailed in order to decrease selection of antibiotic-resistant and especially multidrug-resistant microorganisms. The DRI does not provide information on use of broad-spectrum antibiotics and in which countries it is common, which might give the false impression that an indiscriminate use of broad-spectrum antibiotics is a good thing, as it leads to a very good, low DRI.

Therefore, we conclude that the DRI in its present form is not a useful tool to communicate to a wide audience. First, because its complexity makes it difficult to interpret, and second because the DRI may promote the unnecessary use of broad-spectrum antibiotics, potentially reversing many good initiatives undertaken to overcome and counter the global problem of antimicrobial resistance. As restrictive use of antibiotics is one of the cornerstones in the fight against antimicrobial resistance, we should not use indicators whose interpretation may promote the opposite.

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