Q&A

GLASS method for estimating attributable mortality of antimicrobial resistant bloodstream infections

Why DALYs were chosen as metric to estimate the health impact of AMR?

Is WHO considering only health impact of resistant infections? Why not the economic?

Why is the protocol focusing only on estimating mortality and not morbidity?

Can the approach be used to estimate attributable mortality of other syndromes?

Are the three cohorts necessary?

Is the protocol designed to capture both community and hospital origin infections?

Will WHO implement the protocol at country level?

1. **Why were DALYs chosen as metric to estimate the health impact of AMR?**

DALY is becoming increasingly common in the field of public health and health impact assessment (HIA). It not only includes the potential years of life lost due to premature death, but also includes equivalent years of 'healthy' life lost by virtue of being in states of poor health or disability. In so doing, mortality and morbidity are combined into a single, common metric, allowing the comparison of health hazards and providing an evidence-based tool for healthcare policy prioritization and for monitoring intervention effects. The DALY was first conceptualized in a work carried out with the WHO and the World Bank known as the Global Burden of Disease Study, which was published in 1990, and it was subsequently adopted in 1996 as the formal WHO method to estimate impact of health conditions.

2. **Is WHO considering only health impact of resistant infections? Why not the economic?**

Estimating the health impact is the first step towards a complete calculation of the overall burden of diseases. Since its development, the DALY measure has been used widely in both national and global disease burden and economic and cost-effectiveness studies. The WHO recommends the use of DALYs in cost-effectiveness studies for the purpose of comparability. DALY losses and costs can be estimated directly for determine the economic burden of a disease or to rate the appropriateness of different intervention approaches, using the incremental cost-effectiveness ratio to determine which intervention will offer the best value for money invested.

3. **Why is the protocol focusing only on estimating mortality and not morbidity?**

For this specific protocol, bloodstream infections were chosen as target condition to study, as per the reasons listed during the presentation. Considering the complexity of implementation of prospective cohort studies, and the acute nature of bloodstream infections, it was decided to prioritize the measurement of the outcome that has the highest impact over patients' health. It was chosen therefore to not overburden investigators with an excessive number of epidemiological approaches, but to focus on the development of a methodology that secured the generation of high-quality mortality estimates. Morbidity estimates will be available through the routine GLASS data collection, by applying recommended tools that will help countries to produce representative quality estimates of AMR rates in the defined population. Also, because the sample size needed to generate mortality estimates is generally larger than the one to estimate morbidity, the latter can be generated by the proportion of infected patients enrolled in the cohorts.

4. Can the approach be used to estimate attributable mortality of other syndromes?

Yes. Case definitions need to be carefully adopted, and clinical variables to be collected have to be modified based on the condition under study. Moreover, for syndromes that are more likely to cause long-term sequalae or chronic illnesses, longer follow up periods must be considered. However, the epidemiological principles used by the method presented can be adapted for any type of study looking at attributable mortality of a wide range of resistant infections, in the specific defined population.

5. Are the three cohorts necessary?

The choice of comparator cohorts to include in a study looking at the impact of AMR BSI could be informed by the way interventions could change the occurrence of AMR BSIs. If one considers that interventions (like antimicrobial stewardship) would reduce the number of AMR BSIs but replace (some of) them by drug-susceptible BSIs, patients with a drug-susceptible BSI would be an appropriate control group (replacement scenario). However, if interventions (like routine infection prevention and control measures not specifically aimed at resistant infections) would reduce the number of AMR BSIs, and would either leave unchanged or reduce the number of drug-susceptible BSIs, then AMR and susceptible BSIs are independent entities (additive scenario), and non-infected
patients should be the control group of choice. There is no definitive evidence indicating which scenario is more likely, and it may actually be different depending on the setting, level of resistance in the population, the causative pathogen, and whether the BSI is community-associated or hospital-associated.

6. Is the protocol designed to capture both community and hospital origin infections?

Yes. Because infected patients can be enrolled in cohort 1 and 2 based on the first positive blood sample result, independently from the length of hospital stay, it is possible to follow both community and hospital origin infections outcomes. The definition used to define origin is the same applied by GLASS routine surveillance approach, where a community origin BSI is a BSI confirmed in a patient who has been admitted to a hospital for two or less calendar days, while an hospital origin BSI is a BSI confirmed in a patient that has been admitted to a hospital for more than two calendar days. Moreover, through the protocol patient's enrolment form, information is collected on patient transfer from other facilities, to allow for a clearer classification of infection origin.

7. Will WHO implement the protocol at country level?

The protocol offers a master template that can be used by any government, research institute or consortium, academia, health care facility that is interested in implementing the study at local, regional or national level.