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Quantifying malaria risk in travellers: a quixotic pursuit

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Every year, millions of travellers visit countries in which malaria is endemic. To help inform prevention guidelines, there have been many attempts to quantify malaria risk in travellers. Unfortunately, the data needed to accurately calculate such risk do not exist. Current methods and datasets can provide approximations, but as we will explain, they greatly underestimate the true risk value. Presenting such underestimates as precise measurements and using them as the basis for policy decisions has the potential to cause real harm or death to travellers from a disease easily preventable by chemoprophylaxis. Instead, a more holistic approach to determining malaria risk is needed to best protect travellers. Such an approach could include a qualitative assessment of surveillance data and individual characteristics of the traveller.

It is common to use attack rates to estimate risk. However, in the travel medicine literature, the methods used to calculate malaria attack rates to approximate individual risk[1–3] are flawed. For example, authors often determine the number of cases of imported malaria from an endemic area to non-endemic countries reported in national surveillance systems, divide by the estimated total number of travellers from non-endemic countries to this region, and use the resulting quotient to make recommendations on chemoprophylaxis for travellers. Such a calculation has limitations that have been acknowledged in passing, but as we will describe, these limitations are actually quite major and if overlooked can result in very dangerous and erroneous conclusions.

A basic epidemiologic tenet is that for rates and risks, the numerator and denominator should be derived from the same at-risk population. When looking at all travellers to a specific malaria-endemic country, there are potentially three risk groups—those who visited non-endemic areas (Figure 1A), those who visited endemic areas while taking antimalarials for prophylaxis, and those who visited endemic areas without taking chemoprophylaxis (Figure 1B). Those who travelled to a non-endemic area are not at risk for malaria, and therefore should not be in the numerator or denominator.

The total number of malaria cases among travellers includes malaria diagnosed during travel, malaria diagnosed after travel, undiagnosed malaria that was self-treated, and malaria causing death abroad. In addition, if travellers on chemoprophylaxis are included in the

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denominator, the corresponding numerator must include those who were bitten by an infective mosquito but were protected from developing disease by malaria prophylaxis (malaria averted) (Figure 1C). If the rate of malaria in only unprotected individuals is desired, then the numerator should not include cases averted, and the denominator should not include those who were on prophylaxis. (Figure 1D).

The data used to derive numerators and denominators for malaria rate calculations are also problematic. Data sources used to quantify the total number of travellers to specific countries, such as airport surveys or data from national or international tourism databases[4] usually do not discriminate between travellers to non-endemic versus endemic parts of the destination country or between travellers who take prophylaxis and those who do not. Different countries also use different methods for estimating travel volume, including individual passenger arrivals at ports of entry or overnights stays at hotels by persons holding a foreign passport, making comparisons across countries less reliable. Numerators are often derived from national surveillance data in travellers' home countries,[5] but cases can be underreported there. Travellers who died, were diagnosed during travel, or who empirically self-treated are frequently not captured by their home country surveillance systems, nor are malaria cases averted by prevention measures. National surveillance data may also be unable to pinpoint the location of parasite acquisition, particularly for travellers to countries with geographically varied malaria transmission, trips spanning multiple countries, or those with imprecise travel histories. Furthermore, time spent during travel in a malaria-endemic area, an essential element for calculating rates or risk, is usually not available from surveillance data.

Pairing a falsely small numerator (missing cases of malaria self-treated, diagnosed or died abroad, or averted) with a falsely large denominator (including travellers visiting malaria-free regions or taking chemoprophylaxis) will inevitably underestimate the true malaria risk, potentially by several orders of magnitude (Figure 1E). Malaria prophylaxis recommendations and policies based on such underestimations, particularly when presented as precise calculations, can put travellers at increased risk for malaria. This is akin to stopping an effective vaccination program when coverage rates are high because incident cases appear to be declining.

As health practitioners and scientists, we must value data-driven policies and practice evidence-based medicine. It is therefore incumbent upon the travel medicine community to use appropriate methods and to make recommendations that truly reflect the uncertain quality and limited availability of the evidence. Given that the optimal data to calculate meaningful malaria rates and risk do not exist and are unlikely to be available, attempts to quantify malaria risk should be put aside.

A more holistic approach is instead needed. Keeping in mind the described limitations, numbers of cases in surveillance systems and travel volume data can be used to qualitatively inform the guideline process, particularly when considered in the context of additional information such as sub-national endemic country surveillance data. Examples and further details of such qualitative assessment can be found in the United States Centers for Disease Control and Prevention's Yellow Book.[6] Then, when deciding on malaria prevention

recommendations for an individual traveller, travel medicine professionals should take into account both local malaria rates and patient details, such as type of travel or past medical history. To protect travellers as well as possible, it is essential that we follow basic epidemiologic principles so as to have an accurate understanding of where and when malaria transmission occurs. This knowledge will help to ensure travellers receive the best possible recommendations for malaria prophylaxis.

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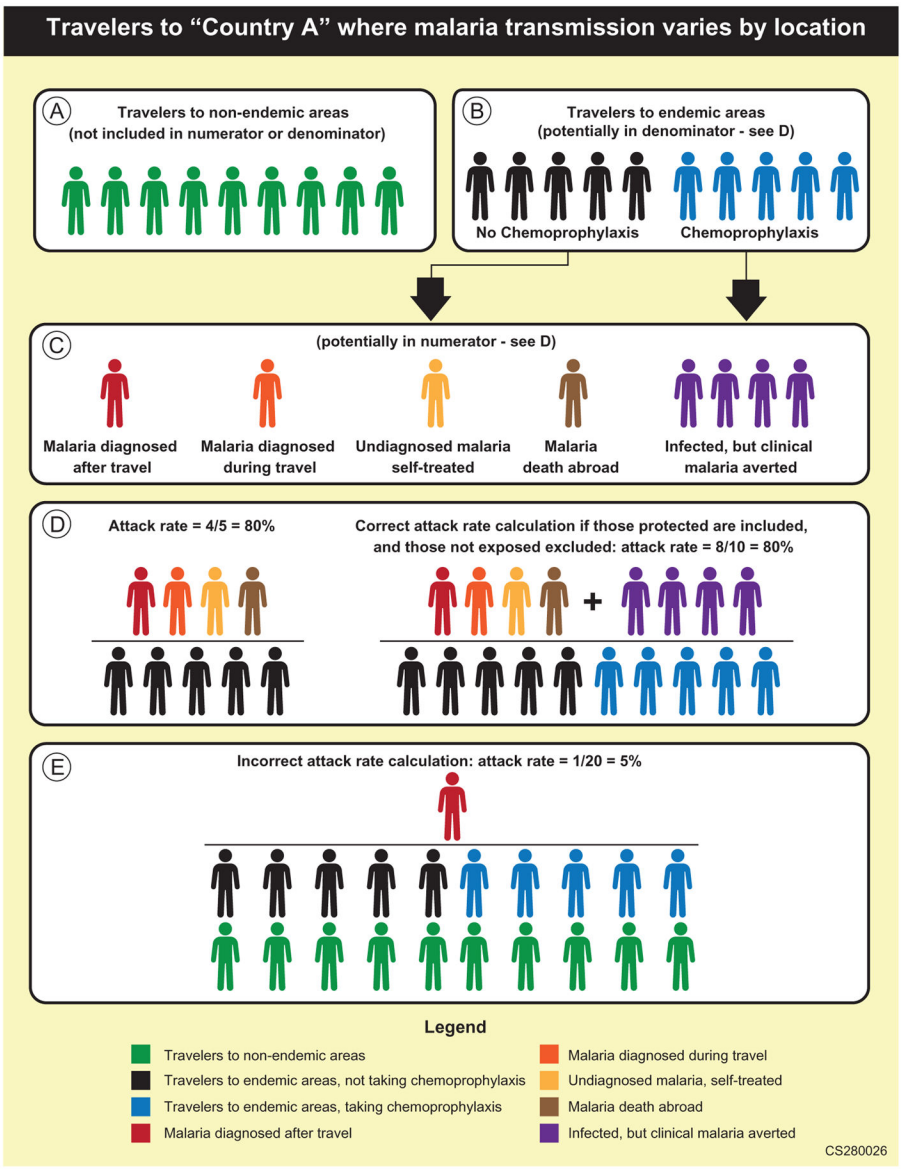

Figure 1.
Calculation of attack rates for travelers to malaria endemic areas