Adoption of a microbial health-based target for Australian drinking water regulation
Joanne O’Toole, Martha Sinclair, Katherine Gibney and Karin Leder

ABSTRACT

The health-based targets of 1 in 10,000 for infection and $10^{-6}$ disability adjusted life years (DALYs) per person per year are increasingly being considered, or have already been adopted, to define microbial safety targets for water. The aim of this paper is to convey information about how these two targets compare by converting each of the target values to a common metric. The metric chosen for viral (rotavirus and norovirus) and protozoan (Cryptosporidium) reference pathogens is the estimated maximum number of annual drinking water-associated cases of acute diarrhoeal disease tolerated. For the reference bacterial pathogen Campylobacter, sequelae to acute diarrhoeal illness have also been considered in estimating the tolerable number of cases for the DALY target. Also investigated is whether non-compliance with targets would be detected as a waterborne disease outbreak by the health surveillance system in an extreme hypothetical situation whereby all tolerable cases per annum occurred as a single event. The paper highlights that verification of compliance with targets cannot be demonstrated by the absence of reported drinking water-associated outbreaks alone and concludes that introduction of a quantitative health-based outcome for drinking water in Australia would help improve water quality management by providing a common goal directly linked to health outcomes.

Key words | DALY, health-based targets, water safety

INTRODUCTION

Currently, Australia is considering adoption of a microbial health-based target for its drinking water supplies. The target being considered is $10^{-6}$ disability adjusted life years (DALYs) per person per year, the same target as defined in the World Health Organization guidelines for drinking water quality (WHO GDWQ) (WHO 2011) and already adopted in Australian guidelines for water recycling (AGWR) (NRMCC/EPHC/AHMC 2006). To date, only Canada has adopted this target to set drinking water treatment goals (Health Canada 2013). The alternative microbial health-based target, which underpins the USEPA drinking water standards, is 1 infection per 10,000 people per year (Macler & Regli 1993) and is the basis of drinking water regulation in the Netherlands (Anonymous 2001, 2005) and New Zealand (Ministry of Health 2008).

As a consequence of the proposed extension of using the $10^{-6}$ DALY target for drinking water regulation in Australia, questions have arisen about the implications of its adoption and the applicability of the alternative target of 1 infection per 10,000 people per year. Although currently there is no prescribed microbial health outcome target for drinking water regulation in Australia (NHMRC 2004), some larger urban water authorities have nevertheless adopted 1 infection per 10,000 people per year as their operational target for drinking water treatment. Adoption of this target has often occurred under the guise of industry best practice, sometimes without full understanding of the underpinnings of the target itself. Wide familiarity with the $10^{-6}$ DALY target might be expected because it has been embedded in recycled water guidelines since 2006, but deliberate supplementation of drinking water with recycled water from sewage effluent has not yet occurred in Australia, so implementation of the target has been limited to non-potable recycled water applications. Hence, many water authorities
are newly considering the relevance of the numerical value for drinking water drawn from conventional sources, some of which contain partially or secondary treated wastewater and thus, effectively represent situations of unintended indirect potable reuse.

As part of the process of considering incorporation of a health-based target in Australian drinking water guidelines, a research study was funded to quantify the average burden of single cases of diarrhoeal disease (DALY per case) associated with selected reference pathogens (designated human-infectious species from each of bacterial, viral and protozoan classes) *Campylobacter*, rotavirus, norovirus and *Cryptosporidium*, using Australian epidemiological and clinical data (Gibney et al. 2014). Accordingly, it is now possible to compare the estimated maximum tolerable number of cases of diarrhoeal disease transmitted by drinking water for each target using Australian data for these reference micro-organisms.

The aim of this paper is to convey information about how the two health-based targets compare by converting each of the health-based target values to a common metric. The metric chosen for rotavirus, norovirus and *Cryptosporidium* is the estimated tolerable maximum number of annual drinking water-associated cases of acute diarrhoeal disease. While this metric allows for a valid direct comparison of target values in relation to these reference micro-organisms, where acute diarrhoeal disease is generally the only/most significant disease end point, this is not the case for *Campylobacter*. This is because an estimated high burden of disease is associated with sequelae such as Guillian–Barré syndrome (GBS), reactive arthritis (ReA) and post-infectious irritable bowel syndrome (PI-IBS), which can develop following the diarrhoeal illness. Accordingly, for *Campylobacter* we present three different values for the DALY target for comparison purposes: estimated tolerable maximum number of cases of acute diarrhoeal disease; estimated maximum number of cases of acute diarrhoeal disease inclusive of the related disease burden (db) of GBS and ReA; and, finally, the estimated maximum number of cases of acute diarrhoeal disease incorporating the estimated related db of GBS, ReA, as well as PI-IBS.

Acknowledging that both the infection and DALY health-based targets are expressed as annual targets, we then use the estimated maximum number of annual drinking water-associated cases tolerated by each target to investigate a hypothetical situation whereby drinking water-associated cases are not spread throughout the whole year but occur as a single event per water supply. By ‘loading’ all of the tolerable drinking water-associated cases per water supply onto a single event, such as might occur as a consequence of a short duration drinking water contamination event (whether resulting from source water contamination and inadequate water treatment or from distribution system contamination) we can explore whether non-compliance with either of these targets would be detected by the health surveillance system as a waterborne disease outbreak in this most extreme hypothetical situation.

Such an exploration is valuable when communicating the implication of adoption of a health-based target for drinking water, whether an infection or DALY target, to water managers. This is because it allows for enhanced understanding of the relationship between infection and DALY target values and more loosely defined or ‘de facto’ health-based targets such as ‘non-detection of drinking water-associated outbreaks of diarrhoeal disease by the routine health surveillance systems’. Both infection and DALY targets in combination with quantitative microbial risk assessment (QMRA) processes can be used to estimate the amount of water treatment that is required to meet target values, but this is impossible to perform or verify with more loosely defined health-based targets because of their lack of sensitivity and/or specificity. Furthermore, while water managers have familiarity with the need to collect data about the concentration of pathogens in source waters for input to QMRA processes and also appreciate the importance of maintaining operational controls of water treatment processes (e.g., maintenance of chlorine residuals) to meet health targets, these considerations are separate to the process of selecting a health target to implement. The analysis presented here serves to elaborate on the connection between health target selection and implementation. It also highlights the reasoning which underlies drinking water treatment and control, which is to reduce the number of cases of drinking water-associated diarrhoeal disease to an agreed on, predetermined, acceptable level.
While this evaluation uses Australian data it is also relevant to other jurisdictions contemplating adoption of the WHO drinking water DALY target and those interested in exploring the relationship between an infection and DALY health-based target. Data for other jurisdictions can be directly compared with Australian data and computations adjusted accordingly.

COMPARING THE MAXIMUM TOLERABLE NUMBER OF CASES OF DRINKING WATER-ASSOCIATED DIARRHEAL DISEASE THAT EACH TARGET PERMITS

For the 1 infection per 10,000 people per year target, to convert the maximum tolerable number of infections to numbers of cases of diarrheal disease, information about the proportion of infected persons that develop disease is required. For the DALY target, information required to estimate the maximum tolerable number of cases is a ‘DALY per case’. The ‘DALY per case’ is the average burden of a single case of disease and it is different for each microorganism, reflecting the severity and duration of disease outcomes and whether or not the disease comprises acute effects only, or a combination of acute and longer-term effects.

The relationship between the infection and DALY targets and the estimated maximum tolerable number of cases of diarrheal disease associated with consumption of drinking water for each target is shown in Figure 1. Transition percentages from infection of susceptible persons to disease states used for Campylobacter (50%) and Cryptosporidium (70%) are the same as those used in WHO (2011) and in AGWR (NRMMC/EPHC/AHMC 2006) guidelines, with these values originating from studies conducted in the Netherlands (Havelaar et al. 2000) and USA (Okhuysen et al. 1998), respectively. For rotavirus, the transition percentage in WHO GDWQ (50%) differs from that used in AGWR (88%), with the latter attributed (Havelaar & Melse 2006) to a hospital study in the early 1980s pertaining to children less than 36 months old (original reference source not specified but believed to be Schaap et al. 1985), as cited in Koopmans & Van Asperen (1999)). A value of 50% for transition frequency, as used in WHO GDWQ, is consistent with transition frequency values used by others (Gerba et al. 2016). Both 50–88% transition frequencies have been used.
to estimate the maximum number of cases tolerated by the infection target shown in Figure 1. DALY per case values are given for the three reference pathogens used in the WHO and AGWR guidelines (Campylobacter, rotavirus, Cryptosporidium) and norovirus based on Australian data (Gibney et al. 2014). Of note is that for rotavirus only, the estimation of the maximum number of cases tolerated by each target pertains to the Australian 2010 under 5-year-old population because this is the section of the population primarily affected by this virus and subsequent immunity is conferred to those that have been infected (NRMMC/EPHC/AHMC 2006). The DALY per case value presented and used for rotavirus calculations in Figure 1 was determined using 2010 data and is for an unvaccinated under 5-year-old population despite rotavirus vaccination having been available free of charge to all Australian infants born after 1 May 2007 (Gibney et al. 2014). As vaccine uptake becomes close to universal for this age group in Australia, DALY per case values will decrease, potentially resulting in an increase in the tolerable maximum number of cases of viral gastroenteritis. Calculations for norovirus (a candidate reference virus but not used in either AGWR or WHO GDWQ) were also included because clinical data about norovirus were available and although causing less severe disease than rotavirus, norovirus is the most prevalent cause of viral gastroenteritis in Australia. Indeed, a recent systematic review showed that norovirus contributes substantially to the global burden of acute gastroenteritis (AGE) across all settings and age groups, causing an estimated 18% (95% confidence interval 17–20) of all cases of gastroenteritis (Ahmed et al. 2014). The norovirus transition percentage (68%) used to ‘convert’ maximum tolerable number of infections to estimated maximum tolerable number of cases of diarrhoea associated with consumption of drinking water is based on work by Teunis et al. (2008), and is consistent with results (67% of infected persons developing viral gastroenteritis) obtained in a more recent study (Attmar et al. 2014).

As shown in Figure 1, the $10^{-6}$ DALY per person per year target is more lenient than the target of 1 infection per 10,000 people per year for all micro-organisms, except in the case of Campylobacter when PI-IBS is included and 95% credibility interval (CrI) of the DALY per case estimate is factored into calculations. The estimated tolerable total number of cases for the DALY target is 862 with a 95% CrI of 512–2,087 cases when the db of ReA, GBS and PI-IBS are included, compared with the infection target with an estimated maximum tolerable number of cases of 670.

WATER TREATMENT

Required pathogen percentage removal and/or inactivation for adequate water treatment for the infection target is calculated according to the difference between the maximum numbers of infections tolerated by the health target and the estimated number of infections predicted to arise from consumption of untreated drinking water. Similarly, for the DALY target, the difference between the maximum db tolerated by the health target and the estimated burden of disease per annum estimated using QMRA determines the water treatment requirements. Differences are calculated separately for each class of pathogen (i.e., bacteria, viruses and protozoa) because of their differential responses to water treatment and disinfection processes. Determination of the water treatment train to meet the relevant health target is based upon the predominating pollution sources in the catchment and the treatment processes best suited for their removal and/or inactivation.

Reference pathogens are selected as plausibly representing human-infectious pathogens that are the most prevalent, most difficult to remove by water treatment and most virulent waterborne agents in their class. In determining water treatment requirements for reference pathogens, all other members of the class can be assumed to also be adequately controlled. Selection of reference pathogens is also governed by other considerations such as the availability of relevant data. For example, the AGWR acknowledges that there is no single virus that represents an ideal reference pathogen for this class and uses an amalgam of dose–response data for rotaviruses and occurrence data for adenovirus. This decision is justified by rotaviruses having the highest pathogenicity of candidate viruses, the availability of Australian cell culture data for adenovirus in sewage and, because adenovirus appear more resistant to disinfection than other viral agents (NRMMC/EPHC/AHMC 2006). Similar rationale for rotavirus selection as a reference virus, but for drinking water, is presented in WHO GDWQ with enteroviruses, not adenoviruses, preferred to provide
source water occurrence data based on there being a routine culture-based analysis for measuring infective particles and their high concentration in waters contaminated by human waste (WHO 2011). Norovirus was not included in AGWR as a reference pathogen based on there being no dose–response model at the time of guideline formulation, as well as the lack of availability of a routine culture-based method measuring infective particles. This situation has since changed with the availability of 50% human-infectious dose for norovirus (Teunis et al. 2008; Atmar et al. 2014), now allowing for an estimate of the number of resultant infections/db of this viral pathogen for a given source water quality for comparison with the target value. However, there is still no routine culture-based method for quantifying norovirus infectious units in source water. This limitation is referred to in the WHO GDWQ as a barrier to selection of norovirus as a reference viral pathogen, necessitating the use of another human-infectious virus candidate for the estimation of their concentration in source waters (WHO 2011).

Numbers of infections arising from consumption of untreated drinking water are obtained by independently applying QMRA processes to the water supply in question, which requires information about the concentration of reference pathogens in source water, volume and frequency of exposure to drinking water, numbers of each pathogen required to initiate infection (dose–response) and the proportion of the population that is susceptible to infection. To convert the number of infections arising from consumption of untreated drinking water to DALYs for comparison with a DALY target value, additional information is required: transition percentage from infection to disease state and estimates of DALY per case estimates for each reference pathogen.

Because a higher number of cases of diarrhoeal illness is tolerated when the DALY rather than the infection target is applied for Campylobacter, rotavirus, norovirus and Cryptosporidium, calculated water treatment log 10 pathogen removal/inactivation requirements to achieve target compliance with the DALY target are less stringent than for the infection target (with the possible exception of Campylobacter when PI-IBS is included in the DALY per case estimate of db). However, this does not have a practical impact on water treatment requirements. In contrast to viruses and protozoa, bacterial pathogens as represented by the reference pathogen Campylobacter do not drive water treatment requirements due to their lesser persistence and the greater ease with which they are removed/inactivated. Accordingly, Australian water supplies currently using the target value of 1 infection per 10,000 people per year to set their operational targets for drinking water treatment and complying with it will, as a matter of course, also comply with the $10^{-6}$ DALY per person per year health-based target.

Achievement of the selected health-based target depends not only on the design capability of the drinking water treatment system, but on ensuring the reliability of the day-to-day performance of the system. Thus, water safety plans, operational controls and process monitoring assume a crucial role in ensuring that the required levels of overall system performance are consistently achieved. In addition, it is essential to maintain and manage the water distribution system effectively to prevent recontamination of treated water.

The role of health-based targets in drinking water regulation is to limit the number of cases of drinking water-associated illness to predetermined acceptable levels. While it is important to prevent peak contamination events to avert waterborne outbreaks, it is also important to ensure that water treatment and distribution system protection is continuously effective to limit the number of sporadic cases during baseline (normal) conditions (i.e., endemic disease). This is because per annum, endemic disease may represent a greater proportion of drinking water-associated disease than outbreaks and, accordingly, a higher db. In countries such as Australia with a low level of endemic diarrhoeal disease, even specially designed high-quality epidemiological trials have limited ability to detect drinking water-associated cases of diarrhea (Sinclair et al. in press). Routine disease surveillance systems are even less sensitive and, at best, will only detect a proportion of drinking water-associated outbreaks.

**HEALTH TARGETS EXPRESSED AS A PROPORTION OF PATHOGEN-SPECIFIC GASTROENTERITIS CASES**

Table 1 shows the tolerable number of cases per year for each health target expressed as a proportion (%) of total
cases of gastroenteritis estimated for each of these four pathogens annually in Australia. These results show that the infection target of 1 infection per 10,000 people per year allows for less than 1% of estimated diarrheal disease per annum for each pathogen to be attributable to consumption of drinking water. The $10^{-6}$ DALY per person per year target allows for up to approximately 6% of diarrhoeal disease caused by Cryptosporidium to be associated with consumption of drinking water and approximately 2% for norovirus. The DALY target for drinking water-associated Campylobacter disease represents less than 1% of the estimated total annual cases of Campylobacter-associated diarrhoeal disease. For rotavirus, the DALY target represents approximately 0.5% of the estimated total annual cases of diarrhoeal disease in the unvaccinated under 5-year-old population.

These calculations represent the waterborne proportion of gastroenteritis for each pathogen that would be predicted if the entire Australian population consumed drinking water which barely complied with the relevant health-based target. The current level of waterborne disease in Australia is unknown, and although few disease outbreaks from public drinking water supplies have been recorded, the limitations of health surveillance systems mean that the occurrence of unrecognised outbreaks in some small water supplies remains a possibility even if the estimated maximum annual number of cases occurred as a single event.

### COMPLIANCE WITH HEALTH-BASED TARGETS AT AN INDIVIDUAL WATER SUPPLY LEVEL

Figure 1 gives the estimated maximum tolerable number of diarrhoeal cases per year associated with drinking water consumption for the whole of Australia to meet each of the two targets. Table 1 shows the small percentage of the total that they represent. When disease transmission through a single source such as drinking water occurs at levels similar to or below the background level of disease transmission from all sources, the limits of health surveillance to detect drinking water-associated cases have been reached. If it is assumed that a water treatment failure could lead to the maximum tolerable number of cases per annum occurring at one time, the number of cases representing non-compliance with the health target for a population of 1,000 is extremely small (e.g., two cases of waterborne norovirus would constitute non-compliance with the $10^{-6}$ DALY target). When this is considered against the ‘background’ rate of illness for this pathogen (which can be calculated as 98 cases per year or an average of two cases

<table>
<thead>
<tr>
<th>Reference pathogen</th>
<th>Total estimated number AGE Australia (Gibney et al. 2014)</th>
<th>Number of tolerable AGE cases for infection target expressed as % of estimated number of AGE cases in column 2</th>
<th>Number of tolerable AGE cases for DALY target expressed as % (95% CrI) of estimated number of AGE cases in column 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter</td>
<td>774,003</td>
<td>0.09%</td>
<td>0.96% (0.69–1.44%)a</td>
</tr>
<tr>
<td>Campylobacter (burden of disease of GBS and ReA included)</td>
<td>774,003</td>
<td>0.09%</td>
<td>0.54% (0.43–0.70%)b</td>
</tr>
<tr>
<td>Campylobacter (burden of disease of GBS, ReA and PI-IBS included)</td>
<td>774,003</td>
<td>0.09%</td>
<td>0.11% (0.07–0.27%)c</td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>195,495</td>
<td>0.80%</td>
<td>5.71% (3.81–7.61%)a</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>172,739d</td>
<td>0.07% (0.012%f)</td>
<td>0.31% (0.25–0.61%)a</td>
</tr>
<tr>
<td>Norovirus</td>
<td>2,180,145</td>
<td>0.07%</td>
<td>1.71% (1.28–2.56%)a</td>
</tr>
</tbody>
</table>

*Calculations consider db for AGE only.
*Calculations incorporate db for GBS and ReA.
*Calculations incorporate db for GBS, ReA and PI-IBS.
*Total GE cases among <5-year-olds in 2010.
*Number of tolerable AGE cases based on 50% transition from infection to disease (WHO 2011).
*Number of tolerable AGE cases based on 88% transition from infection to disease (NRMMC/EPHC/AHMC 2006).
per week if spread evenly over the year in a population of 1,000) it is evident that such an event is unlikely to be recognised either by local health professionals or by the much less sensitive routine surveillance systems for infectious disease. Even in a population of 1,000,000, and again making the assumption that all cases occur simultaneously, 2,000 cases of norovirus gastroenteritis (representing non-compliance with the $10^{-6}$ DALY target) might not be recognised as being drinking water associated, depending upon the severity of diarrhoea and the proportion of affected people seeking medical care, variation in incubation periods, geographical spread of cases and/or the presence of any concomitant non-drinking water outbreaks.

Accordingly, the absence of waterborne outbreaks of gastroenteritis alone does not assure target compliance, particularly for water supplies serving small populations when single or few excess cases per year represent non-compliance with the target. Thus, assurance must be additionally achieved by using a multi-barrier approach to water supply management and using QMRA as a means of appropriately directing efforts to reduce pathogen risks throughout the water supply system.

The ability of individual Australian water authorities to comply with a $10^{-6}$ DALY per person per year microbial target will vary. For smaller water authorities, more stringent operational controls and possibly additional water treatment processes to those currently implemented may be required. Larger water authorities already using a target value of 1 infection per 10,000 people per year to set their operational targets for drinking water treatment and with a multi-barrier approach to water supply management will achieve compliance with the $10^{-6}$ DALY per person per year target. Others, using alternative but nonetheless rigorous operational targets but ones not specifically linked to a quantitative health-based end point, are also likely to comply with, or at least approach compliance with, a $10^{-6}$ DALY per person per year microbial target. Smaller water authorities are likely to have more difficulty demonstrating compliance with the target, associated with insufficient water quality monitoring data for input to QMRA processes. Default ranges in pathogen levels for source waters and treatment performance currently available (despite problems or shortcomings) are being further developed, and provide a means to determine required water treatment processes using QMRA for target compliance where collection of relevant data for individual water supplies is not feasible.

While the best available data have been used here to estimate the maximum tolerable number of cases for each target, derived numbers should be regarded as approximations because of the inherent variability and uncertainty of input data. Nevertheless, they allow the relative magnitude of case numbers and proportions of total gastroenteritis for the two target values to be compared and provide valuable information. Also, while 95% credibility limits are given for the DALY per case estimates, reflecting the variability in clinical input data used for their determination, the infection and DALY target values themselves are expressed as single maximum values (1 infection per 10,000 persons per year and $10^{-6}$ DALY per person per year, respectively). Furthermore, transition percentages from infection to disease states for the selected reference pathogens from the literature likewise are point estimates, allowing the maximum tolerable number of cases for the infection target to be expressed only as a single (estimated) number.

This discussion should not be construed as advocating the adoption of a particular microbial health-based target because of its stringency or leniency. Rather, it highlights the principle behind health-based target adoption and shows the infection target to be more stringent than the DALY target. It also serves to highlight that adoption of the $10^{-6}$ DALY per person per year target for drinking water in Australia will not preclude water authorities that currently use the infection target as their ‘working target’ from continuing to surpass the DALY target if this is already the case, or from future adoption of water management practices that reduce microbial risks even further than is required for target compliance.

While issues such as data shortfalls (e.g., dose–response data for a range of relevant pathogens; pathogen concentration in source waters; proportion of the population susceptible to infection) for QMRA or the QMRA process itself are important for determining appropriate water treatment, they are common to both the infection and DALY targets. Also they are somewhat separate to the principle of adopting a quantitative health-based target for drinking water, so have not been elaborated on here. When using
the infection target, infection is the end point of computations with the value obtained using QMRA directly compared with the target value of 1 infection per 10,000 people per year to determine water treatment requirements. When using the DALY health-based target, further computations are required before a comparison of QMRA values and the target value can be made. These include sequential conversion of the estimated number of infections based on concentrations of pathogens in source water to number of symptomatic cases, followed by conversion to burden of disease per pathogen expressed as total DALYs per annum using DALY per case estimates. We have used the estimated maximum number of annual drinking water-associated cases of acute diarrhoeal disease tolerated by each of the infection and DALY targets (including sequelae for Campylobacter) as the metric for comparison, even though this represents an additional ‘conversion’ step for the infection target, not usually performed. However, in doing this we have used the same transition percentages (from infection of susceptible persons to disease states) as used in the QMRA process when converting the estimated number of infections associated with consumption of untreated drinking water to estimated case number and then, to estimated DALYs.

CONCLUSION

Introducing a quantitative health-based outcome target for drinking water in Australia would be an improvement in terms of water quality management. While verification of compliance with a target of either 1 infection per 10,000 people per year or $10^{-6}$ DALY per person per year cannot be demonstrated by the absence of reported drinking water-associated outbreaks alone (particularly for water supplies serving small populations where the maximum estimated number of tolerable cases per annum in absolute terms is very low), introduction of a quantitative target provides a common goal directly linked to health outcomes for all drinking water supplies. Available evidence suggests that the $10^{-6}$ DALY per person per year microbial target will be met by larger, well-resourced urban water authorities in Australia who are already using and complying with the infection target. Also, some smaller water supplies will already be meeting the infection and/or the DALY target based on high microbial quality of their source water and good water treatment and operational practices. Others, based on poor source water quality and/or limited funds to determine and/or install and operate appropriate water treatment processes, may not be able to immediately meet DALY target values but may achieve this through incremental staged improvements in water supply treatment and operation.

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