UPDATING THE 2006 WHO GUIDELINES

More appropriate tolerable additional burden of disease
Improved determination of annual risks
Norovirus and *Ascaris* infection risks
Extended health-protection control measures
Treatment and non-treatment options

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INTRODUCTION

Since the publication of the WHO *Guidelines for the Safe Use of Wastewater, Excreta and Greywater – Volume 2: Wastewater Use in Agriculture* in 2006 an improved method for determining annual disease and infection risks has been developed (Karavarsamis & Hamilton 2010); dose-response data have been published for norovirus and *Ascaris lumbricoides* (Teunis et al. 2008; Navarro et al. 2009); the default value for the tolerable additional burden of disease due of $\leq 10^{-6}$ DALY loss per person per year (pppy) used in the Guidelines has been questioned (Mara & Sleigh 2010c); and a step-by-step guide to using the QMRA-Monte Carlo programs has been prepared (Mara & Sleigh 2010d). These points are discussed in more detail below, together with their implications for the use of health-protection – i.e., pathogen reduction – control measures which may or may not include wastewater treatment.

SELECTION OF A MORE APPROPRIATE VALUE FOR THE MAXIMUM TOLERABLE ADDITIONAL BURDEN OF DISEASE

The first task in any health-risk assessment is to establish the maximum tolerable additional burden of disease – i.e., the maximum DALY loss per person per year (pppy). The 2006 WHO Guidelines use a value of 10^{-6} pppy for this, but is this the most appropriate value to use, especially in low-income countries?

The Guidelines [volume 2, section 4.5] state that:

> *Wastewater treatment may be considered to be of a low priority if the local incidence of diarrheal disease is high and other water-supply, sanitation and hygiene-promotion interventions are more cost-effective in controlling transmission. In such circumstances, it is recommended that, initially, a national standard is established for a locally appropriate level of tolerable additional burden of disease based on the local incidence of diarrheal disease – for example, $\leq 10^{-5}$ or* ***$\leq 10^{-4}$ DALY [loss] per person per year*** [emphasis added].

This is really the key to the adoption of the 2006 Guidelines in low- and middle-income countries since setting a tolerable maximum additional burden of disease of 10^{-4} DALY loss pppy, for example, means that the design disease risk and the design infection risk are both 2-log units higher, and the required pathogen reductions 2 log units lower, than for the 10^{-6} DALY loss pppy adopted as the 'default' value in the 2006 WHO Guidelines. So, is a maximum tolerable additional DALY loss of 10^{-4} pppy acceptable or not?

Reasons in favour of a maximum tolerable additional DALY loss of 10^{-4} pppy

1. The reason why the 2006 Guidelines use a value of 10^{-6} DALY loss pppy is because it is used in the third edition of the WHO *Drinking-water Quality Guidelines* (WHO 2008) since it corresponds very closely to the fatal waterborne 70-year lifetime cancer risk of 10^{-5} per person accepted by US EPA (Munro & Travis 1986). This 70-year risk of 10^{-5} per person is equivalent to an annual risk of 1.4×10^{-7} per person. Whether this is a reasonable level of acceptable risk can only be judged by knowing how many Americans die each year from cancer. Horner et al. (2009) give the 2006 age-adjusted mortality rate from all causes of cancer for both sexes and all races as 181.07 per 100,000 population – i.e., a fatal all-cancer incidence of 1.8×10^{-3} pppy. Thus the EPA-accepted fatal waterborne-cancer risk of 1.4×10^{-7} pppy is four orders of magnitude lower than the actual fatal all-cancer incidence of 1.8×10^{-3} pppy. A DALY loss of 10^{-4} pppy would be equivalent to a fatal waterborne lifetime cancer risk of 10^{-3} per person and thus to an annual risk of ~10^{-5} per person, which is two orders of magnitude lower than the actual fatal all-cancer incidence of ~10^{-3} pppy and therefore surely safe enough.

2. The current global incidence of diarrhoeal disease is extremely high: in order-of-magnitude terms it is 0.1–1 pppy (Table 1). A tolerable diarrhoeal disease risk of 10^{-2} pppy, equivalent to a 10^{-4} DALY loss pppy, is 1–2 orders of magnitude lower than the current diarrhoeal-disease incidence. For an individual it is equivalent to an additional episode of diarrhoeal disease once every 100 years (essentially once per lifetime), which is hardly a matter of significant public health concern – see also Haas (1996) who comments on US EPA's use of a waterborne-disease infection risk of 10^{-4} pppy (Macler & Regli 1982) as follows:

It is becoming apparent that some key factors used for computing the 1:10,000 level of acceptable risk may not be correct. … the total burden of waterborne illness associated with current water treatment practice in the United States may be as high as several million cases per year. This would translate to an annual illness rate of perhaps 1:100, suggesting that the current benchmark [of 1:10,000] *may be far too stringent.*

TABLE 1. Diarrhoeal disease (DD) incidence per person per year in 2000

World region	DD incidence in all ages	DD incidence in 0–4 year olds	DD incidence in 5–80+ year olds
Industrialized countries[a]	0.2	0.2–1.7	0.1–0.2
Developing countries	0.8–1.3	2.4–5.2	0.4–0.6
Global average	0.7	3.7	0.4

[a] In some industrialized countries diarrhoeal disease incidence is much higher – for example, 0.92 pppy for 'infectious gastroenteritis' in Australians of all ages (Hall et al. 2005) and 0.79 pppy for 'acute gastroenteritis' in Americans of all ages (Mead et al. 1999) – i.e., in the developing-country range shown in the table.
Source: Mathers et al. (2002).

In low- and middle-income countries diarrhoeal diseases caused a total DALY loss of 59 million in 2001 (Lopez et al. 2006, Ezzati et al. 2006). Thus in 2001, for the then total developing-country population of 4,940 millions (UNFPA 2002), the DALY loss due to diarrhoeal diseases was:

$$\frac{\text{59 million DALYs lost per year}}{\text{4,940 million people}} = \sim 0.0119 \text{ pppy}$$

An additional DALY loss of 10^{-4} pppy would increase this to 0.0120 pppy – i.e., an increase of just under 1%. Such an increase is epidemiologically insignificant (and, in any case, would be extremely difficult to detect).

Thus it seems perfectly reasonable to accept a maximum additional DALY loss of 10^{-4} pppy for wastewater use in agriculture.

IMPROVED METHOD FOR ESTIMATING ANNUAL INFECTION RISKS

The improved Karavarsamis-Hamilton method of estimating annual infection risks from QMRA-Monte Carlo simulations is as follows:

1. Using the appropriate dose-response equation in an appropriate QMRA-Monte Carlo computer program, an estimate of median annual infection risk is determined by a Monte Carlo simulation in which the number of iterations is set equal to the number of days of exposure per year.
2. This is repeated 9,999 times, so that there are 10,000 estimates of annual infection risk.
3. The median and 95-percentile values of these 10,000 estimates are then calculated in order to provide a much more robust estimate of the median and 95-percentile annual infection risks.

Thus the program determines 10,000 estimates of median annual risk based on what happens in any one year of exposure, rather than (as in the procedure used in the Guidelines) a much less robust estimate of median annual risk determined from 10,000 estimates of annual risk based on what happens on any one day of exposure. This approach results in similar values for estimates of median annual risks, but much lower estimates for 95-percentile annual risks, and there is much less 'spread' of results (Table 2).

NOROVIRUS INFECTION RISKS

Recently it has become possible to use QMRA-Monte Carlo techniques to estimate norovirus infection risks (Mara and Sleigh 2010a,c). The dose-response data needed to do this were published by Teunis et al. (2008), so it was not possible for norovirus to have been considered as a reference viral pathogen in the 2006 WHO Guidelines.

TABLE 2. Unrestricted irrigation: comparison of the Karavarsamis-Hamilton method and the method used in the 2006 WHO Guidelines for estimating annual rotavirus infection risks from the consumption of wastewater-irrigated lettuce by 10,000 Monte Carlo simulations[a]

Wastewater quality (*E. coli* numbers per 100 ml)		Rotavirus infection risk pppy estimated by the method of Karavarsamis and Hamilton (2010)	Rotavirus infection risk pppy estimated by the method used in the 2006 WHO Guidelines
10^3–10^4	Median risk:	0.36	0.30
	95%-ile risk:	0.39	0.71
	Minimum:[b]	0.30	1.1×10^{-2}
	Maximum:[b]	0.44	0.97
100–1000	Median risk:	4.5×10^{-2}	3.5×10^{-2}
	95%-ile risk:	4.9×10^{-2}	0.11
	Minimum:	3.5×10^{-2}	1.0×10^{-3}
	Maximum:	5.5×10^{-2}	0.27
10–100	Median risk:	4.6×10^{-3}	3.5×10^{-3}
	95%-ile risk:	5.0×10^{-3}	1.2×10^{-2}
	Minimum:	3.5×10^{-3}	9.5×10^{-5}
	Maximum:	5.7×10^{-3}	3.0×10^{-2}

[a]Assumptions: 100 g lettuce eaten per person per 2 days; 10−15 ml wastewater remaining on 100 g lettuce after irrigation; 0.1−1 rotavirus per 10^5 *E. coli*; no pathogen die-off; N_{50} = 6.7 ± 25% and α = 0.253 ± 25%.
[b]The lowest and highest values of the 10,000 risk simulations.

Norovirus (NV, formerly called Norwalk or Norwalk-like virus) is the major viral pathogen causing diarrhoeal disease in adults – in contrast rotavirus mainly affects children under 5, and commonly under 2 years of age, although NV does cause diarrhoea in children (Patel et al. 2008). It is therefore a better 'reference' viral pathogen than rotavirus for wastewater-use studies as young children are less exposed than adults, either as fieldworkers (although they may play in wastewater-irrigated fields while their mothers work in them) or as consumers (children under 2, especially, eat less wastewater-irrigated foods). That norovirus is a more suitable reference viral pathogen than rotavirus is illustrated by the fact that in the USA during 1998–2007 there were 1,773 confirmed foodborne norovirus outbreaks, but only 4 confirmed foodborne rotavirus outbreaks (CDC 2009).

Using a DALY loss per case of 9×10^{-4} per case of NV disease (Kemmeren et al. 2006) and an NV disease/infection ratio of 0.8 (Moe 2009), the tolerable NV disease and infection risks corresponding to a tolerable DALY loss of 10^{-4} pppy are:

$$\text{Tolerable NV disease risk} = \frac{\text{Tolerable DALY loss pppy}}{\text{DALY loss per case of NV disease}} = \frac{10^{-4}}{9 \text{ x } 10^{-4}} = 0.11 \text{ pppy}$$

$$\text{Tolerable NV disease risk} = \frac{\text{Tolerable NV disease risk pppy}}{\text{NV disease/infection ratio}} = \frac{0.11}{0.8} = 0.14 \text{ pppy}$$

The NV dose-response dataset of Teunis et al. (2008) was used in place of the beta-Poisson equation in the QMRA-MC computer program developed to determine median NV infection risks pppy. The resulting estimates of median risk obtained are given in Table 3, which shows that a reduction of 4 log units results in an NV infection risk of 0.25 pppy, which is only marginally higher than the tolerable NV infection risk of 0.14 pppy determined above. Table 3 also includes, for comparison, rotavirus infection risks – these are broadly similar to the norovirus infection risks.

TABLE 3. Unrestricted irrigation: median norovirus and rotavirus infection risks per person per year from the consumption of 100 g of wastewater-irrigated lettuce every two days estimated by 10,000 Karavarsamis-Hamilton Monte Carlo simulations[a]

Wastewater quality (*E. coli* per 100 ml)	Median norovirus infection risk pppy	Median rotavirus infection risk pppy
10^7–10^8	1	1
…		
10^3–10^4	0.25	0.36
100–1000	2.9×10^{-2}	4.5×10^{-2}
10–100	2.9×10^{-3}	4.6×10^{-3}

[a]Assumptions: 10–15 ml wastewater remaining on 100 g lettuce after irrigation; 0.1–1 norovirus and 0.1–1 rotavirus per 10^5 *E. coli*; no pathogen die-off; N_{50} = 6.7 ± 25% and α = 0.253 ± 25% for rotavirus; and dose-response data (Teunis et al. 2008) ± 25% for norovirus.
Source: Mara & Sleigh (2010a).

ASCARIS INFECTION RISKS

Ascaris dose-response data were published by Navarro et al. (2009), so it was not possible to have used *Ascaris* as a reference helminthic pathogen in the 2006 WHO Guidelines. Even though the 2006 WHO guideline value for helminth eggs of ≤1 egg per liter of treated wastewater is based on epidemiological data, it is nevertheless very useful to be able to determine required log unit reductions of *Ascaris* (which is generally the commonest helminth and the eggs of which are able to survive for very long periods of time in the environment) by QMRA and thus to split these between wastewater treatment and post-treatment health-protection control measures (Table 5), as is done for viral, bacterial and protozoan pathogens, since this allows for a lower level of wastewater treatment.

For a tolerable DALY loss of 10^{-4} pppy, a DALY loss per case of ascariasis of 8.25×10^{-3} (Chan, 1997) and, as a worst-case scenario, an *Ascaris* disease/infection ratio of 1 (i.e., all those infected with *Ascaris* develop ascariasis), the tolerable *Ascaris* infection risk is given by:

$$\frac{\text{Tolerable DALYs lost pppy}}{\text{DALY loss per case of ascariasis}} = \frac{10^{-4}}{8.25 \times 10^{-3}} = 1.2 \times 10^{-2} \text{ pppy}$$

Median *Ascaris* infection risks pppy from the consumption by children under 15 of raw carrots irrigated with wastewaters containing specified numbers of *Ascaris* eggs were determined by a QMRA-Monte Carlo computer program based on the Karavarsamis-Hamilton method and using the values of N_{50} and α determined by Navarro et al. (2009) for use in the beta-Poisson equation. The resulting estimates of median *Ascaris* infection risk are given in Table 4, which shows that 1 egg per liter results in an *Ascaris* infection risk of ~6×10^{-3} pppy, which is just below the tolerable *Ascaris* infection risk of ~10^{-2} pppy determined above. Thus, in ascariasis-hyperendemic areas (~1000 eggs per liter of raw wastewater) a 3-log unit reduction of *Ascaris* eggs is required.

TABLE 4. Unrestricted irrigation: median *Ascaris* infection risks for children under 15 from the consumption of raw wastewater-irrigated carrots estimated by 10,000 Karavarsamis–Hamilton Monte Carlo simulations[a]

Number of *Ascaris* eggs per liter of wastewater	Median *Ascaris* infection risk pppy	Notes
100–1000	0.86	Raw wastewaters in hyperendemic areas.
10–100	0.24	Raw wastewaters in endemic areas.
1–10	2.9×10^{-2}	Treated wastewaters.
1	5.5×10^{-3}	Wastewater quality required to comply with the 1989 and 2006 WHO Guidelines.
0.1–1	3.0×10^{-3}	Highly treated wastewaters.
0.1	5.5×10^{-4}	Wastewater quality recommended by Blumenthal et al. (2000) to protect children under 15.
0.01–0.1	3.0×10^{-4}	Treated wastewaters in non-endemic areas

[a]Assumptions: 30–50 g raw carrots consumed per child per week; 3–5 mL wastewater remaining on 100 g carrots after irrigation; N_{50} = 859 ± 25% and α = 0.104 ± 25%; no *Ascaris* die-off .
Source: Mara & Sleigh (2010b).

HEALTH-PROTECTION CONTROL MEASURES

Table 5 extends the corresponding table in the 2006 WHO Guidelines. It divides the measures into four categories: wastewater treatment, on-farm options, post-harvest options at local markets, and in-kitchen produce-preparation options.

Treatment and non-treatment options

The use of a maximum tolerable burden of disease of 10^{-4} DALY loss pppy results in log unit pathogen reductions that are two orders of magnitude lower than those required for 10^{-6} DALY loss pppy, and this can be used to have a correspondingly lower degree of wastewater treatment – for example, treatment to achieve a pathogen reduction of only 1–2 log units.

Wastewater treatment processes to achieve a pathogen reduction of 1–2 log units are simple and relatively inexpensive. For large schemes anaerobic and facultative ponds would be sufficient in most cases, and for small schemes (as in urban agriculture, for example) processes such as a three-tank system would be suitable (on any one day one tank is filled, one allowed to settle, and one is used).

TABLE 5. Health-protection control measures and associated pathogen reductions

Control measure	Pathogen reduction (log units)	Notes
A. Wastewater treatment	1–7	Pathogen reduction depends on type and degree of treatment selected.
B. On-farm options		
Crop restriction (i.e., no food crops eaten uncooked)	6–7	Depends on (a) effectiveness of local enforcement of crop restriction, and (b) comparative profit margin of the alternative crop(s).
On-farm treatment:		
(a) Three-tank system	1–2	Operated in sequential batch-fed mode.
(b) Simple sedimentation	0.5–1	Sedimentation for ~18 hours.
(c) Simple filtration	1–3	Value depends on filtration system used.
Method of wastewater application:		
(a) Furrow irrigation	1–2	Crop density and yield may be reduced.
(b) Low-cost drip irrigation	2–4	2-log unit reduction for low-growing crops, and 4-log unit reduction for high-growing crops.
(c) Reduction of splashing	1–2	Farmers trained to reduce splashing when watering cans used (splashing adds contaminated soil particles on to crop surfaces which can be minimized).
Pathogen die-off	0.5–2 per day	Die-off between last irrigation and harvest (value depends on climate, crop type, etc.).
C. Post-harvest options at local markets		
Overnight storage in baskets	0.5–1	Selling produce after overnight storage in baskets (rather than overnight storage in sacks or selling fresh produce without overnight storage).
Produce preparation prior to sale	1–2	(a) Rinsing salad crops, vegetables and fruit with clean water.
	2–3	(b) Washing salad crops, vegetables and fruit with running tap water.
	1–3	(c) Removing the outer leaves on cabbages, lettuces, etc.
D. In-kitchen produce-preparation options		
Produce disinfection	2–3	Washing salad crops, vegetables and fruit with an appropriate disinfectant solution and rinsing with clean water.
Produce peeling	2	Fruits, root crops.
Produce cooking	5–6	Option depends on local diet and preference for cooked food.

Sources: EPHC/NRMMC/AHMC (2006), WHO (2006), Amoah et al. (2007), Abaidoo et al. (2010) and Keraita et al. (2010).

However, most wastewater currently used in agriculture is untreated. In many low-income countries the use of untreated wastewater is either unrecognized or illegal, or the authorities choose in practice to ignore it, but this situation is not sustainable – clear policies are needed to balance the agricultural benefits and the associated risks to human health of wastewater use. Ensink and van der Hoek (2009) recommend a set of practical and easily enforceable measures to minimize the health risks associated with the use of untreated domestic wastewater:

- only produce that is cooked before being eaten can be grown with untreated wastewater,
- root crops, such as potatoes, onions, and carrots, cannot be grown with untreated wastewater,
- vegetables should be cultivated and irrigated using the ridge-and-furrow method,
- biannual treatment of fieldworkers and their families with antihelminthic drugs, and
- general improvements in water supply and sanitation, including in local produce markets, in order to improve post-harvest practices and thus produce quality.

Some simple on-farm treatment processes and methods of wastewater application, and in-market hygiene practices, are listed in Table 5. Further information is given by Abaidoo et al. (2010), Seidu and Dreschel (2010), Ilic et al. (2010) and Keraita et al. (2010).

A PRACTICAL EXAMPLE OF QMRA IN A DEVELOPING COUNTRY: APPLICATION TO LETTUCE CONSUMPTION IN URBAN GHANA – NOROVIRUS INFECTION RISKS

Exposure to wastewater pathogens present in wastewater-irrigated foods varies with differences in consumption patterns which need to be accounted for in the risk calculations. In the 2006 WHO Guidelines the consumption pattern used was 100 g of lettuce consumed on alterate days, as used by Shuval et al. (1997). However, Seidu et al. (2008) reported that people in urban Ghana commonly consume ~10–12 g of lettuce in ready-to-eat street-vended food on each of four days per week. NV infection risks for a DALY loss of 10^{-4} pppy and for this Ghanaian consumption of lettuce were determined by 10,000 Karavarsamis-Hamilton Monte Carlo simulations for various wastewater qualities (Table 6). A 3-log unit NV reduction achieves an NV infection risk of 0.3 pppy, which is a little higher than the tolerable NV infection risk of 0.13 pppy; however, a 4-log unit reduction is perfectly feasible as it could be easily achieved by simple treatment (1 log unit) and produce disinfection (3 log units) (*cf.* Table 5).

TABLE 6. Unrestricted irrigation: median norovirus infection risks per person per year from the consumption of 10–12 g of wastewater-irrigated lettuce on four occasions per week estimated by 10,000 Karavarsamis-Hamilton Monte Carlo simulations[a]

Wastewater quality (*E. coli* per 100 ml)	Median norovirus infection risk pppy
10^7–10^8	1
…	
10^4–10^5	0.31
10^3–10^4	3.6×10^{-2}

[a]Assumptions: 10−15 mL wastewater remaining on 100 g lettuce after irrigation; 0.1−1 norovirus per 10^5 *E. coli*; no pathogen die-off; dose-response data (Teunis et al., 2008) ± 25%.

Source: Mara and Sleigh (2010a).

REFERENCES

- Abaidoo, R. C., Bakang, J. A., Drechsel, P., Keraita, B., Kinane, M. and Beernaerts, I. (2010). *Final Report of the KNUST/FAO/WHO/IDRC Project on Evaluation of Non-treatment Options for Maximizing Public Health Benefits of WHO Guidelines Governing the Use of Wastewater in Urban Vegetable Production in Ghana*. Kumasi: Kwame Nkrumah University of Science and Technology.
- Amoah, P., Drechsel, P., Abaidoo, R. C. and Klutse, A. (2007). Effectiveness of common and improved sanitary washing methods in West Africa for the reduction of coli bacteria and helminth eggs on vegetables. *Tropical Medicine & International Health* **12** (s2), 40–50.
- Blumenthal, U. J., Mara, D. D., Peasey, A., Ruiz-Palacios, G. and Stott, R. (2000). Guidelines for the micro-biological quality of treated wastewater used in agriculture: recommendations for revising the WHO guidelines. *Bulletin of the World Health Organization* **78** (9), 1104–1116.
- CDC (2009). 'OutbreakNet' – Foodborne Outbreak Online Database. Atlanta, GA: Centers for Disease Control and Prevention – available online at: http://wwwn.cdc.gov/foodborneoutbreaks/Default.aspx.
- Chan, M-S. (1997). The global burden of intestinal nematode infections – fifty years on. *Parasitology Today* **13** (11), 438–443.
- Ensink, J. H. J. and van der Hoek, W. (2009). Implementation of the WHO guidelines for the safe use of wastewater in Pakistan: balancing risks and benefits. *Journal of Water and Health* **7** (3), 464–468.
- EPHC/NRMMC/AHMC (2006). *National Guidelines for Water Recycling: Managing Health and Environmental Risks*. Canberra, ACT: Environment Protection and Heritage Council, the Natural Resource Management Ministerial Council and the Australian Health Ministers' Conference.
- Ezzati, M., van der Hoorn, S., Lopez, A. D., Danaei, G., Rodgers, A., Mathers, C.D. and Murray, C. J. L. (2006). Comparative quantification of mortality and burden of disease attributable to selected risk factors. In *Global Burden of Disease and Risk Factors* (ed. A. D. Lopez, C. D. Mathers, M. Ezzati, D. T. Jamison and C. J. L. Murray), pp. 241–396. New York, NY: Oxford University Press.
- Haas, C. N. (1996). Acceptable health risk. *Journal of the American Water Works Association* **88** (12), 8.
- Hall, G., Kirk, M. D., Becker, N., Gregory, J. E., Unicomb, L. et al. (2005). Estimating foodborne gastroenteritis, Australia. *Emerging Infectious Diseases* **11** (8), 1257–1264.
- Horner, M. J., Ries, L. A. G., Krapcho, M., Neyman, N., Aminou, R. et al. (2009). *SEER Cancer Statistics Review, 1975–2006*. Bethesda, MD: National Cancer Institute.
- Ilic, S., Drechsel, P., Amoah, P. and J. LeJeune, J. (2010). Applying the multiple-barrier approach for microbial risk reduction in the post-harvest sector of wastewater irrigated vegetables. In *Wastewater Irrigation and Health: Assessing and Mitigating Risks in Low-income Countries* (ed. P. Drechsel, C.A. Scott, L. Raschid-Sally, M. Redwood and A. Bahri), pp. 239–259. London: Earthscan.
- Karavarsamis, N. and Hamilton, A. J. (2010). Estimators of annual probability of infection for quantitative microbial risk assessment. *Journal of Water and Health* **8** (2), 365–373.
- Kemmeren, J. M., Mangen, M.-J. J., van Duynhoven, Y. T. H. P. and Havelaar, A. H. (2006). *Priority Setting of Foodborne Pathogens: Disease Burden and Costs of Selected Enteric Pathogens* (RIVM Report 330080001/2006). Bilthoven: National Institute for Public Health and the Environment.
- Keraita, B., Drechsel, P. and Konradsen, F. (2010). Up and down the sanitation ladder: Harmonizing the treatment and multiple-barrier perspectives on risk reduction in wastewater irrigated agriculture. *Irrigation and Drainage Systems* **24** (1–2), 23–35.
- Lopez, A. D., Mathers, C. D., Ezzati, M., Jamison, D. T. and J. L. Murray, C. J. L. (2006). Measuring the global burden of disease and risk factors, 1990–2001. In *Global Burden of Disease and Risk Factors* (ed. A. D. Lopez, C. D. Mathers, M. Ezzati, D. T. Jamison and C. J. L. Murray), pp. 1–13. New York, NY: Oxford University Press.
- Mara, D. D. and Sleigh, P. A. (2010a). Estimation of norovirus infection risks to consumers of waste-water-irrigated food crops eaten raw. *Journal of Water and Health* **8** (1), 39–43.
- Mara, D. D. and Sleigh, P. A. (2010b). Estimation of *Ascaris* infection risks in children under 15 from the consumption of wastewater-irrigated carrots. *Journal of Water and Health* **8** (1), 35–38.
- Mara, D. D. and Sleigh, P. A. (2010c). Estimation of norovirus and *Ascaris* infection risks to urban farmers in developing countries using wastewater for crop irrigation. *Journal of Water and Health* **8** (3), 572–576.
- Mara, D. D. and Sleigh, P. A. (2010d). *Quantitative Microbial Risk Analysis: The 2006 WHO Guidelines and Beyond – How to Use the QMRA-Monte Carlo Computer Programs in Wastewater-use Planning*. Leeds: School of Civil Engineering, University of Leeds – available online at: http://www.personal.leeds.ac.uk/~cen6ddm/QMRAzip/QMRA_How-to-use-the-programs.pdf.
- Macler, B. A. and Regli, S. (1992). *Use of Microbial Risk Assessment in Setting U.S. Drinking Water Standards* (Report No. EPA 814/S-92-001). Washington, DC: Office of Water, U. S. Environmental Protection Agency.
- Mathers, C. D., Stein, C., Ma Fat, D., Rao, C., Inoue, M., Tomijima, N., Bernard, C., Lopez, A. D. and Murray, C. J. L. (2002). *Global Burden of Disease 2000 – Version 2: Methods and Results*. Geneva: World Health Organization.
- Mead, P. S., Slutsker, L., Dietz, V., McCaig, L. F., Bresee, J. S. et al. (1999). Food-related illness and death in the United States. *Emerging Infectious Diseases* **5** (5), 607–625.
- Moe, C. L. (2009). Preventing norovirus transmission: how should we handle food handlers? *Clinical Infectious Diseases* **48** (1), 38–40.
- Munro, N. B. and Travis, C. C.. (1986). Drinking-water standards: Risks for chemicals and radionuclides. *Environmental Science and Technology* **20** (8), 768–769.
- Navarro, I., Jiménez, B., Cifuentes, E. and Lucario, S. (2009). Application of helminth ova infection dose curve to estimate the risks associated with biosolids application on soil. *Journal of Water and Health* **7** (1), 31–44.
- Patel, M. M., Widdowson, M-A., Glass, R. I., Akazawa, K., Vinjé,J. and Parashar, U. D. (2008). Systematic literature review of role of noroviruses in sporadic gastroenteritis. *Emerging Infectious Diseases* **14** (8), 1224–1231.
- Seidu, R., Heistad, A., Amoah, P. Drechsel, P., Jenssen, P. D. and Strenström, T-A. (2008). Quantification of the health risk associated with wastewater reuse in Accra, Ghana: A contribution toward local guidelines. *Journal of Water and Health* **6** (4), 641–671.
- Seidu, R. and Drechsel, P. (2010). "Cost-effectiveness of interventions for diarrhoeal disease reduction among consumers of wastewater-irrigated lettuce in Ghana." In *Wastewater Irrigation and Health: Assessing and Mitigating Risks in Low-income Countries* (ed. P. Drechsel, C.A. Scott, L. Raschid-Sally, M. Redwood and A. Bahri), pp. 261–283. London: Earthscan.
- Shuval, H., Lampert, Y. and Fattal, B. (1997). Development of a risk assessment approach for evaluating wastewater reuse standards for agriculture. *Water Science and Technology* **35** (11–12), 15–20.
- Teunis, P. F. M., Moe, C. L., Liu, P. et al. (2008). Norwalk virus: how infectious is it? *Journal of Medical Virology* **80** (8), 1468–1476.
- UNFPA (2002). *The State of World Population 2001: Demographic, Social and Economic Indicators*. New York, NY: United Nations Population Fund – available online at: http://www.unfpa.org/swp/2001/english/indicators/indicators2.html
- WHO (2006). *Guidelines for the Safe Use of Wastewater, Excreta and Greywater – Volume 2: Wastewater Use in Agriculture*. Geneva: World Health Organization.
- WHO (2008). *Guidelines for Drinking-water Quality, Third Edition Incorporating the First and Second Addenda – Volume 1: Recommendations*. Geneva: World Health Organization.

Note: A 'QMRA Beginner's Guide', with detailed instructions how to use the QMRA-MC computer programs, is available at: http://www.personal.leeds.ac.uk/~cen6ddm/QMRAbeginners.html.