Bell Island Wastewater Treatment Plant

Quantitative Microbial Risk Assessment

Prepared for Stantec

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Executive summary

Nelson's Bell Island Wastewater Treatment Plant's consent is to be replaced. To help inform the decisions to be made on the appropriate degree of treatment, a Quantitative Microbial Risk Assessment (QMRA) for human health has been carried out for sixteen sites in the Waimea inlet and Tasman Bay. These include four water uses: (i) primary contact recreation; (ii) secondary contact recreation; (iii) consumption of raw shellfish flesh (collected locally); (iv) consumption of raw flesh of scallops, collected from Tasman Bay. Three virus groups have been used: adenoviruses for item (ii); enterovirus and norovirus for the other uses.

The discharge of treated wastewater from Bell Island generally poses low risk of illness associated with swimming and harvesting of local shellfish consumed raw, provided that sufficient log-removal of viruses is incorporated in the treatment system.

Furthermore, these factors combine to indicate that in the normal course of events, minimal risks attend to either recreational water users or to consumers of raw shellfish associated with the treatment plant's discharge. Only when substantially increased levels of viral infection in the community exist do risks become significant for lower levels of virus removal efficacy in the wastewater treatment plant. Such events seem rare, for example the sustained elevated influent virus concentrations observed at the Mangere wastewater treatment plant in May-June 1999 have not recurred in the regular, ongoing monitoring since then.

Provided adequate removal efficacy is attained by the Wastewater Treatment Plant (2 log removal), the daily illness risk associated with recreational water contact or scallop collection will be well below the appropriate NOAEL levels adopted in national guidelines. Greater log-reductions are required to adequately reduce the illness risk associated with other shellfish flesh consumption, at least 3 log.

This assessment has taken a precautionary approach at several points, specifically: (i) through incorporation of occasional very high influent virus concentrations, such as can occur when there is an undetected viral illness outbreak in the contributing community; (ii) adopting the most potent form of the viruses' dose-response function; (iii) basing recreational water contact on children's health risk (greater than adults' risk).

1 Introduction

The consent for Nelson's wastewater treatment plant (WWTP) is under review. A key feature concerns the desirable level of effluent disinfection, having regard to possible human health risks for recreational water uses (swimming, kiteboarding, windsurfing or kayaking), and for consumers of local shellfish and scallops eaten raw.

Predictions from a Quantitative Microbial Risk Assessment (QMRA) offer an ideal means of analysing these risks, and projecting these risks into the future. Indeed, the use of QMRA to determine risk to human health is recommended by the New Zealand recreational water quality guidelines (MfE/MoH, 2003, at page 3): When treated wastewater discharges are close by, compliance with a faecal indicator threshold "…is not a guarantee of safety" and (ibid., at page 4): "the relationship between indicator bacteria and key pathogens (such as viruses and protozoa) must be established for that treatment". These statements have resulted in the use of QMRA methods to assess the risk of infection and illness faced by individuals who may be exposed to pathogens in the receiving waters or through consumption of shellfish harvested locally, e.g., Napier (McBride 2011), Hokitika (Stott & McBride 2011), New Plymouth and Motueka (McBride 2012 & 2015). Viruses are the principal pathogens for waters impacted by treated sewage, as is the case for the Bell Island scheme.

This report explains the approach taken, the rationale underlying the procedure, the selection of key model parameters and the results obtained. Some technical detail is contained in the Appendices, and brief technical detail appears in footnotes. A glossary of key terms is given in section 7 (on page 23).

A key feature of this QMRA approach is appropriate accounting for virus removal by wastewater treatment. One way of doing this is to define a tolerable illness risk at key sites and work backward to predict the virus removal efficacy required at the treatment plant. That approach ("inverse QMRA") is not followed here, because: (i) there is no set agreement on what constitutes a tolerable risk, and (ii) there are mathematical difficulties in applying such an approach to a complex setting such as the southern Tasman Bay. Instead, six levels of wastewater treatment plant virus removal are assumed and risks are calculated for each of them. These levels of wastewater treatment are 10-fold, 100-fold, 1,000-fold and 10,000-fold, 100,000-fold and 1,000,000-fold. In engineering and science studies these levels are commonly denoted as "log-removals" (log being shorthand for logarithms[1]) and the four levels would correspond to the log-removals of 1, 2, 3, 4, 5 and 6. Essentially, the log number is the number of zeroes in the removal efficacy figures. For example, 1,000-fold removal is "log 3".

[1] These logarithms are to base 10, so "log" denotes the unambiguous technical term "$\log_{10}$".

2 Methods: Conducting the QMRA

Quantitative Microbial Risk Assessment (QMRA) consists of four basic steps:

1. Select the hazard(s), i.e., the pathogen(s) of concern—exposure to which can give rise to illness.
2. Assess exposures to the pathogens at key sites.
3. Characterise the pathogens' dose-response.
4. Calculate and communicate the health risks.

The "Quantitative" aspect of QMRA has particularly to do with item 4—calculating risks—in which we use Monte Carlo statistical modelling. This calls for repetitive sampling from distributions and ranges of key variables, rather than just using single average values.[2] This approach is particularly important given that the majority of the risk is caused by combinations of inputs toward the extremes of their ranges, the combined effects of which may not be detected when using averages.

2.1 Selecting the pathogens of concern

In addressing this issue extensive use has been made of: international literature and previous New Zealand studies.

2.1.1 Pathogens of concern and associated potential illnesses

Pathogens present in sewage that can cause illness are many and varied.

Many of the illnesses that may be contracted from exposure to waters contaminated by human-derived treated wastewater are not "notifiable". Reporting for some that are[3] may not necessarily capture or represent much of the disease burden.[4] So, when considering such matters, microbiological water quality guidelines developed both in New Zealand (MfE/MoH 2003) and internationally (WHO 2003) are based on a range of investigations that have led to the understanding that risks associated with wastewater-contaminated water comprise two types of infection and illness:

1. Gastrointestinal disease, via
    - 1.1 ingestion during recreational water-contact, and
    - 1.2 consumption of raw shellfish flesh.
2. Respiratory ailments, via
    - 2.1 inhalation of aerosols formed when water-skiing, windsurfing, kiteboarding or kayaking.

Ear, nose, throat and skin infections have generally not been included in QMRA studies to date, not least because while there is some evidence of associations between these ailments and microbial water quality (Charoenca & Fukioka 1994), dose-response models have not been developed (WHO 2003, p. 55).

Table 2-1 lists potential waterborne diseases and their aetiological agents (i.e., pathogens), derived from the ANZECC guidelines (ANZECC & ARMCANZ 2000). It also indicates whether our assessment of the pathogen should be based on contact recreation or shellfish consumption exposure routes, and gives a brief rationale for this assessment.

[2] Using a simple-averages approach can substantially underestimate human health risk.
[3] See the list at http://www.health.govt.nz/our-work/diseases-and-conditions/notifiable-diseases
[4] For example, "acute gastroenteritis" is notifiable but is subject to the requirement that "not every case of acute gastroenteritis is necessarily notifiable, only those where there is a suspected common source or from a person in a high risk category (a food handler or an early childhood service worker) or single cases of chemical, bacterial, or toxic food poisoning such as botulism, toxic shellfish poisoning (any type) and disease caused by verotoxin or Shiga toxin-producing *Escherichia coli*.

Table 2-1: Screening of treated wastewater-borne microorganisms of public health significance.

Pathogen	Include?	Main disease caused	Rationale
Bacteria			
Campylobacter spp.	No	Gastroenteritis	Poor survival in seawater.
Pathogenic *E. coli*	No	Gastroenteritis	Low concentration expected in treated wastewater.
Legionella pneumophila	No	Legionnaires' disease	No evidence of environmental infection route.
Leptospira sp.	No	Leptospirosis	Low concentration expected in treated wastewater.
Salmonella sp.	No	Gastroenteritis	Low concentration expected in treated wastewater.
Salmonella typhi	No	Typhoid fever	Rare in New Zealand.
Shigella sp.	No	Dysentery	Low concentration expected in treated wastewater.
Vibrio cholerae	No	Cholera	Rare in New Zealand.
Yersinia enterolitica	No	Gastroenteritis	Low concentration expected in treated wastewater.
Helminths			
Ascaris lumbricoides	No	Roundworm	Rare in New Zealand.
Enterobius vernicularis	No	Pinworm	Low concentration expected in treated wastewater.
Fasciola hepatica	No	Liver fluke	Rare in New Zealand.
Hymnolepis nana	No	Dwarf tapeworm	Rare in New Zealand.
Taenia sp.	No	Tapeworm	Rare in New Zealand.
Trichuris trichiura	No	Whipworm	Rare in New Zealand.
Protozoa			
Balantidium coli	No	Dysentery	Low concentration expected in treated wastewater.
Cryptosporidium oocysts	No	Gastroenteritis	Will be removed by proposed wastewater treatment processes.
Entamoeba histolytica	No	Amoebic dysentery	Rare in New Zealand.
Giardia cysts	No	Gastroenteritis	Moderate survival in seawater but will be removed by proposed wastewater treatment processes.
Viruses			
Adenoviruses	Yes (SW only)[5]	Respiratory disease[6]	Very infective. Significant concentrations may be present in wastewater.
Enteroviruses	Yes (SW and SF)	Gastroenteritis	Less infective, but health consequences can be more severe than for exposure to adenovirus.
Hepatitis A virus	No	Infectious hepatitis	Minimal concentration in treated wastewater; very infective. Can affect recreational water users in contaminated waters.
Noroviruses	Yes, exploratory only (SW & SF)	Gastroenteritis	Increasing evidence of its prevalence in treated wastewater. Clinical trials and dose-response now available. However, it hasn't been possible to culture in the laboratory until now.[7] This makes assessment of treatment efficacy problematic.
Rotavirus	No	Gastroenteritis	Limited evidence of waterborne infection in NZ; infection in children would be of concern.[8] Difficult to translate units used in clinical trial (Focus Forming Units, FFU, Ward et al. 1986) to those used in culture methods. See section 2.1.3 for detailed justification for its omission.

[5] "SW" = swimming; "SF" = shellfish.
[6] Adenoviruses can also cause pneumonia, eye infections and gastroenteritis.
[7] A new culture-based method has recently been published—Jones et al. (2014): http://www.ncbi.nlm.nih.gov/pubmed/25378626.

A notable feature of Table 2-1 is the selection of human viral pathogens. In general terms, for sites impacted by WWTPs processing well-treated human-derived wastewater (e.g., Mangere WWTP), there is widespread agreement that human viruses are the principal aetiological agent causing gastrointestinal disease among water users and consumers of raw shellfish, e.g., Lodder & de Roda Husman (2005), Sinclair et al. (2009).[9] Accordingly, bacteria and protozoa have been excluded from consideration in this QMRA on the expectation that the WWTP wastewater treatment plant effectively removes these larger microbes—Nelson City (via the Nelson Regional Sewerage Business Unit, NRSBU) is committed to providing a high level of wastewater treatment. However, viruses are more difficult to remove through wastewater treatment processes, and are therefore the focus of this QMRA.

2.1.2 Selected viruses

The relative merits of the candidate viruses (for which some form of identified dose-response curve is available) are addressed in Table 2-2.

Gastrointestinal illness

Enteroviruses (coxsackie virus and echovirus) and norovirus are the pathogens-of-choice. Enteroviruses are included for three reasons:

1. Their evaluation is by culture, whereas to date noroviruses have had to be analysed by qPCR methods,[10] and the ratio of infectious/total virus numbers can be expected to vary through the wastewater treatment process.

2. Enteroviruses can cause longer-term illnesses.

3. Clinical trial data and associated infection dose-response relationships based on culture methods are available.

Note that the enumeration of noroviruses poses difficulties in terms of assessing WWTP removal efficacy and subsequent infectivity (da Silva et al. 2007, Hewitt et al. 2011, Sima et al. 2011, Flannery et al. 2012, Doré et al. 2013, McBride 2014a). QMRAs based on noroviruses have been conducted elsewhere in New Zealand, e.g., Napier and New Plymouth (McBride 2011, 2012).[11] We assume that the removal of noroviruses through the WWTP will be at least as effective as that inferred for enteroviruses.

Respiratory illness

For this illness category, we have only one choice: adenovirus. We are not aware of any other respiratory agents, appropriate to treated wastewater, for which dose-response information is available. Its merits and drawbacks are listed in Table 2-2.

[8] Rose & Sobsey (1993) have documented a rationale for concern about potential contamination of shellfish by rotavirus, but risk appears to have been over-estimated [they equated FFU (Focus Forming Units) with actual numbers of virions].
[9] This is not necessarily true for agricultural wastes in rural settings, where bacteria and protozoa predominate—with few exceptions (hepatitis E, some rotaviruses), animal viruses are not pathogenic to humans.
[10] "qPCR" refers to quantitative Polymerase Chain Reaction, a molecular laboratory test that essentially counts the number of virions in a sample, whether infectious or inactivated.
[11] "Norovirus" subsumes the term "Norwalk virus". The clinical trial reported and analysed by Teunis et al. (2008) was for the original Norwalk virus (genotype group GI.1)—it had been stored in a laboratory for some years. Since the time of the first identified norovirus outbreak (in Norwalk, Ohio, 1968) a number of similar caliciviruses have been identified, in genogroups I–V. Current practice is to regard the infectivity of GI.1 norovirus as equivalent to all noroviruses that affect humans (particularly GI and GII).

Table 2-2: Comparison of the merits and limitations of viruses for which dose-response information is available.

Virus	Advantages	Disadvantages
Gastrointestinal		
Enterovirus	Can induce more serious long-term effects compared to other viruses (Haas et al. 1999, DRG 2002, Simpson et al. 2003). Its inclusion is warranted given that it can cause more serious longer-term illnesses.[12]	Restricted to echovirus 12, the only enterovirus for which an infection dose-response relationship is available. Nevertheless, enterovirus by culture captures more than just echovirus, so, for example, would also capture Coxsackie virus. Meaning of "dose" not clear, giving rise to two quite different infection ID_{50} values (54 and 1052).[13] See Appendix C.
Norovirus	Reported to be the most common aetiological agent in receiving waters (e.g., Sinclair et al. 2009). Infection ID_{50} is in the order of 20 virions (among susceptible people), but the dose-response curve rises steeply from the origin, such that ~20% of people may become infected after ingestion of just one virion—see Figure B-1(b), emphasising that a precautionary approach should be taken when modelling this virus.	Efficacy of wastewater treatment in removing infectious noroviruses is difficult to establish. Restricted to Norwalk virus—norovirus genotype I.1. But note that an outbreak study (Thebault et al. 2013) identified other genotypes to be, if anything, at least as virulent. In the absence of results to the contrary, and taking an appropriate precautionary approach, noroviruses in treated wastewater are assumed to be not aggregated - were they to be aggregated, health risks would be lessened. May require a conversion from the PCR method used in the clinical trial (Lindesmith et al. 2003, Teunis et al. 2008), as described in McBride et al. (2013).
Rotavirus	Particularly affects children. The most infective virus for which published dose-response data is available. Has been used as a "model virus" in earlier QMRAs, for Warkworth (Stott & McBride 2009), Army Bay (Palliser 2011), Snell's Beach (Palliser & Pritchard 2012).	Not as prevalent in treated wastewater as noroviruses. Doses in the one available clinical trial (Ward et al. 1986) were measured in terms of "Focus Forming Units" (FFU), with the lowest "dose" set at 0.009 FFU. So FFU numbers need to be multiplied by an unknown factor to index doses of discrete virions (see the approach taken in a USA-wide study, McBride et al. 2013). See section 2.1.3 for details.
Hepatitis A	A serious illness. Dose-response function indicates virulence (infection ID_{50} = <2).	Present in very low numbers in treated wastewater relative to noroviruses.
Coxsackie (an enterovirus)	May particularly affect children (Suptel 1963).	Studied by Couch et al. (1965) for coxsackie A21 so restricted to respiratory illness response. Present in low numbers in treated wastewater. Dose-response function (Haas et al. 1999) indicates moderate virulence (infection ID_{50} = 48).
Respiratory		
Adenovirus	Found routinely in treated wastewater (DRG 2002, Simpson et al. 2003, Thompson et al. 2003, Hewitt et al. 2011). Very resistant to disinfection (is double-stranded DNA). A common cause of gastrointestinal illness (especially the 40/41 complex). Can be applied to respiratory infections, and therefore be relevant for surfers and/or water-skiers.	Dose-response only for adenovirus 4, a respiratory aetiological agent. Haas et al. (1999) report fitting a single-parameter exponential model to data reported by Couch et al. (1966a) giving rise to an infection ID_{50} less than 2 virions. However, most adenoviruses are not respiratory agents. Applying the adenovirus 4 dose-response model to all adenoviruses for gastrointestinal illness appears to over-estimate the dose-response for that form of illness (we can expect more substantial response of the human body's defences to gastrointestinal infection compared to respiratory infection). Applying the model to only the respiratory portion of total adenoviruses requires assumptions about their proportional presence in treated wastewater (Kundu et al. 2013). The latter authors also considered other studies by Couch et al. (1966b, 1969).

[12] For example, coxsackievirus type B (an enterovirus) is now recognised as the most common viral aetiological agent associated with heart disease (Haas et al. 1999).

[13] Infection ID_{50} is a quantity derived from clinical trials of pathogen infectivity. It is the pathogen dose that would result in 50% of an exposed population becoming infected.

2.1.3 Why not select rotavirus?

As noted in Table 2-2, rotavirus has been used in Auckland-region WWTP QMRA exercises (Warkworth, Army Bay, and Snell's Beach), in the period 2009-2011. In these exercises, it was used as a "model virus", representing general pathogenicity, i.e., including the likes of norovirus.[14]

Since that time an infection dose-response function for norovirus has been identified (and used in other places[15]) and a fuller understanding of the enterovirus dose-response has been gained. For such reasons these two viruses, and not rotaviruses, are now to be used both as important individual pathogens and as indicators of the possible impact of other (unknown) pathogens.

2.2 Assessing exposure

2.2.1 Predicting concentrations in the water

In consultation with Mr Garrett Hall and Dr Rob Lieffering (Stantec), sixteen sites shown in Figure 2-1 have been identified: primary recreational water contact (five sites), secondary recreational water contact (six sites), shellfish collection (four sites) and a scallop collection site in Tasman Bay.

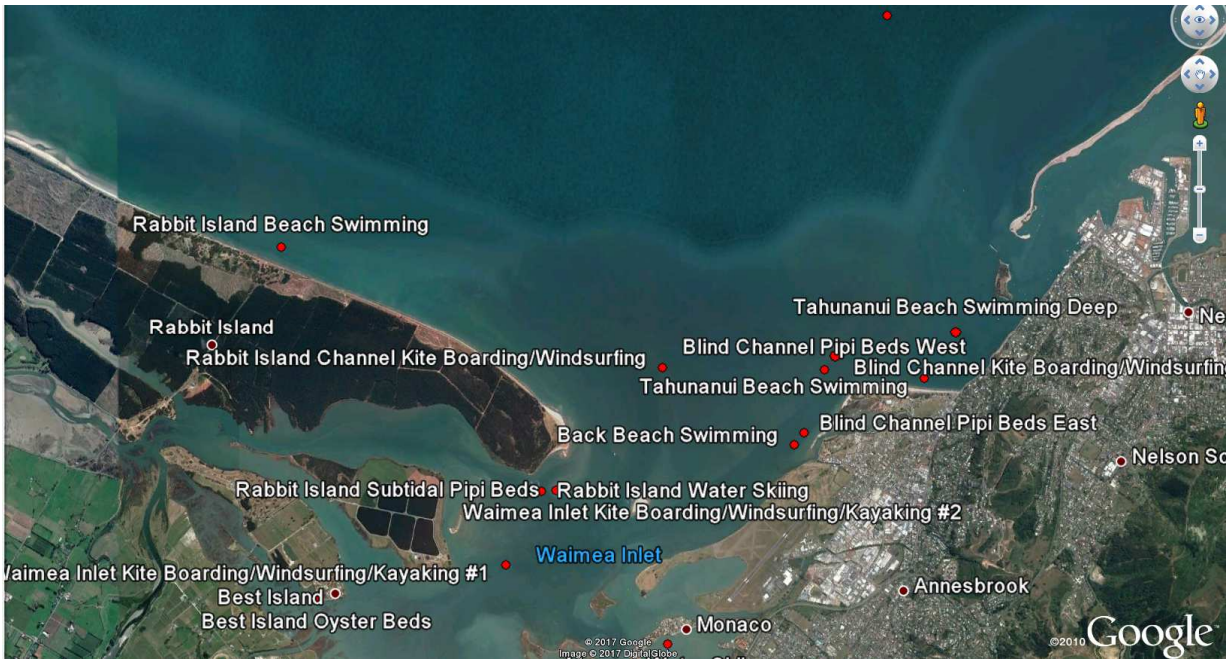

Figure 2-1: Selected assessment sites. The five primary recreational water sites are: (i) Back Beach Swimming, (ii) Monaco Swimming, (iii) Rabbit Island Swimming, (iv) Tahunanui Beach Swimming and (v) Tahunanui Beach Swimming Deep. The six secondary recreational sites are: (i) Blind Channel Kite Boarding/Windsurfing, (ii) Monaco Water Skiing, (iii) Rabbit Island Channel Kite Boarding/Windsurfing, (iv) Rabbit Island Water Skiing, (v) Waimea Inlet Kite Boarding/Windsurfing/Kayaking #1, (vi) Waimea Inlet Kite Boarding/Windsurfing/Kayaking #2. Shellfish sites are: (i) Best Island Oyster Beds, (ii) Blind Channel Pipi Beds East, (iii) Blind Channel Pipi Beds West, (iv) Rabbit Island Subtidal Pipi Beds. There is only one scallop site, which is in Tasman Bay.

[14] In so doing, the units of dose used in developing the infection dose-response function (Focus Forming Units, see Table 2-2) has been ignored, i.e., it was assumed that FFU = numbers of rotaviruses per litre of sample. This can lead to a gross exaggeration of the risk of rotavirus illness.

[15] Norovirus has been used as the pathogen for QMRA studies for Westland Milk/Hokitika (Stott & McBride 2011), Napier (McBride 2011, 2016), New Plymouth (McBride 2012), Hawera/Eltham/Whareora (Palliser et al. 2013), Akaroa (McBride 2016) and Motueka (McBride 2014b).

A hydrodynamic model has been used to predict virus dilutions at each site (MetOcean Solutions, 2013) for treated wastewater discharged from the existing diffuser offshore from Bell Island. The discharge regime is to discharge only on the ebb tide, for up to 3 hours, starting one hour after high tide, in both dry-weather and wet-weather. These simulations are for two whole years, taking account of El niño and La niña years, i.e., 1991 and 1999.

Note that, taking a precautionary approach, these dilutions include the effect only of mixing with receiving waters and do not include the inactivation (via sunlight) of the discharges microbes. That is appropriate for public health protection, particularly when it is noted that early-morning recreational water users will generally face higher microbe concentrations.

As noted earlier, six "log-removals" have been used, describing progressive reductions in virus concentration between the WWTP's influent and effluent. Reductions are driven by secondary treatment plant processes and by any ancillary installed disinfection facility (such as UV or fine membranes).

Secondary treatment alone can be expected to produce between 100-fold and 1,000-fold reduction in influent virus concentrations (pers. comm. Peter Loughran, MWH, Dunedin). Indeed, that is borne out by two Auckland-area datasets. The first comprises long-term data (2002-2016) for adenoviruses and enteroviruses enumerated in the Mangere Wastewater Treatment Plant influent and BNR effluent (Table 2-3).

Table 2-3: Summary of Mangere Treatment Plant enterovirus and adenovirus monitoring. (August 2002 to April 2016) for influent flows and for effluent from the BNR (prior to the UV dosing). Units are numbers of viruses per litre.

Virus	Minimum	Median	95%ile	Maximum	Number of data
Influent enterovirus	52	2300	9610	59000	520
BNR enterovirus	0.02	0.5	6.5	39	214
Influent adenovirus	16	1020	3670	7200	241
BNR adenovirus	0.04	0.6	6.9	21	132

However, during the microbiological investigations undertaken in 1999-2000 for the upgrades proposed for the Mangere Wastewater Treatment Plant, substantially greater influent adenovirus and enterovirus concentrations were detected for some weeks. In particular, the Scoping study component of that investigation (May and June 1999) revealed concentrations for both viruses in the period May-June 1999 that were up to 1,000 times larger than in the other component (the Surrogate study, conducted from October 1999 to March 2000). The Scoping study authors (Simpson et al. 2003) stated:

> *…anecdotal evidence of increased levels of viral infection in the community over the period of the Scoping Study. In the absence of appreciable infection in the community raw sewage virus concentrations are present at much lower concentrations.*

The data for the Scoping and Surrogate Studies are listed in Table 2-4 and summarised in Table 2-5.

Table 2-4: Virus results from the Mangere studies (1999-2000): (a) Scoping study, (b) Surrogate study. For original data see Figure 3.3.5 and Tables B1 and B6 in DRG (2002) and Figure 1 in Simpson et al. (2003). All virus enumerations are in units of $TCID_{50}$ per litre, where $TCID_{50}$ is a laboratory tissue culture technique measuring the amount of virus that produces a cytopathic effect in 50% of the cell cultures inoculated.

(a) Scoping study (DRG 2002)			(b) Surrogate study (DRG 2002)		
Date	**Adenovirus**	**Enterovirus**	**Date**	**Adenovirus**	**Enterovirus**
17-May-99	3,680,000	31,800	8-Oct-99	3,420	664
19-May-99	1,960,000	25,000	13-Oct-99	2,530	400
21-May-99	1,800,000	71,100	15-Oct-99	3,470	1,230
24-May-99	27,300,000	4,600,000	22-Oct-99	5,340	400
26-May-99	31,200,000	50,400,000	27-Oct-99	4,200	832
28-May-99	2,570,000	22,600	29-Oct-99	9,840	2,560
31-May-99	1,710,000	182,000	3-Nov-99	4,590	1,730
2-Jun-99	88,200	28,300	10-Nov-99	4,620	2,200
8-Jun-99	66,809	28,300	17-Nov-99	4,660	2,150
10-Jun-99	189,900	37,600	26-Nov-99	3,800	2,920
16-Jun-99	8,820,000	146,000	1-Dec-99	3,420	2,900
17-Jun-99	433,000	18,200	10-Dec-99	4,120	1,890
21-Jun-99	434,000	51,000	15-Dec-99	3,410	1,820
28-Jun-99	211,000	28,700	22-Dec-99	3,100	2,600
30-Jun-99	23,600	28,900	29-Dec-99	3,560	3,220
1-Jul-99	18,200	13,100	5-Jan-00	3,480	2,440
			12-Jan-00	3,880	1,940
			19-Jan-00	3,400	3,750
			26-Jan-00	3,720	2,570
			4-Feb-00	4,700	3,570
			9-Feb-00	3,900	3,800
			17-Feb-00	4,050	3,320
			23-Feb-00	1,900	1,470
			1-Mar-00	5,860	5,500
			10-Mar-00	4,820	4,750
			16-Mar-00	5,080	3,850
			22-Mar-00	8,980	8,220
			30-Mar-00	7,610	3,470

Table 2-5: Summary statistics for the Mangere Scoping and Surrogate studies.

Study	Minimum	Median	95th percentile	Maximum
Adenoviruses ($TCID_{50}$/L)				
Scoping study	18,200	1,072,000	28,275,000	31,200,000
Surrogate study	1,900	3,975	8,501	9,840
Both studies combined	18,200	1,072,000	28,275,000	31,200,000
Enteroviruses ($TCID_{50}$/L)				
Scoping study	13,100	30,350	16,050,000	50,400,000
Surrogate study	400	2,565	5,238	8,220
Both studies combined	13,100	30,350	16,050,000	50,400,000

Because the Resource Management Act defines an "effect" to include a case of "of low probability which has a high potential impact" [RMA, section 3(e)] these rare-but-substantial concentrations have been included in the QMRA analysis. This has been implemented by fitting a "hockey stick" distribution to these data, as described in detail in Table 2-6.

2.2.2 Should secondary water uses include a primary component?

The exposure pathway for kiteboarders/windsurfers and kayakers includes only inhalation, not ingestion. Yet, these water activities can involve some regular immersion, i.e., primary contact. So it may be thought that health effects on secondary water users should include gastrointestinal illness (as for primary contact) not just respiratory effects. However, overseas studies have shown that the ingestion rate for such secondary exposure is substantially lower than for swimming (e.g., the Chicago waterways secondary exposure study, Rijal et al. 2011). For that reason, this QMRA does not include gastrointestinal illness risk for secondary water contact.

2.2.3 Predicting doses

To turn concentrations into doses we need:

1. influent virus concentrations
2. ingestion or inhalation rates for water users
3. bioaccumulation factors for shellfish.

Details on how these factors have been modelled and enumerated are given in Table 2-6.

Note that water ingestion rates by swimmers—a key component of dose-calculation—have been studied using novel biochemical procedures (Dufour et al. 2006). Dufour et al. (2006) report a clinical trial observing 53 volunteers involved in recreational swimming in an outdoor community swimming pool. Swimmers were assumed to ingest similar amounts of water during swimming in pools or in freshwater due to similar behaviours in each (frequently immersing their heads under the surface and remaining in the water for long periods of time). Cyanuric acid was used to trace water ingestion because it is present in outdoor swimming pools (as a decomposition product of chlorine-stabilising chloroisocyanurate) and passes through the human body unmetabolised. For each swimmer, the volume of water ingested during active swimming events lasting at least 45 minutes was calculated. It has become standard practice to apply these ingestion rates to coastal water recreation.[16]

[16] Personal communication: Jeff Soller, Soller Environmental, California (http://www.sollerenvironmental.com/env/main/Home.html).

Table 2-6: Distributions and inputs for the QMRA.

Component	Statistics	Distributions/comments
Influent virus concentration		Bounded "hockey stick" distribution (McBride 2005a), strongly right-skewed with a hinge at the 95%ile.
Influent enterovirus concentration, per litre	Minimum = 500 Median = 4,000 Maximum = $5x10^7$	Mimicking high values found for Mangere influent in a "Scoping study" in May-July 1999 (Table B1, DRG 2002, where missing values for 24 & 26 May were advised by Mr Peter Loughran, MWH, on 7 11/2003—these values are plotted on Figure 3.3.5 of the DRG report). Most usually the concentrations are 1,000–10,000 per litre (DRG 2002, Table B6).[a]
Influent adenovirus concentration, per litre	Minimum = 2,000 Median = 5,000 Maximum = $3x10^7$	Rationale as above. Most usually the concentrations are 1,000–10,000 per litre (DRG 2002, Table B6): 10% of these concentrations are assumed infectious for respiratory illness effects (Kundu *et al.* 2013 have noted that a minority of adenovirus strains cause respiratory illness).
Influent norovirus concentration, genome copies per litre	Minimum = 10^2 Median = 10^4 Maximum = 10^7	Typical range found for New Zealand cities (e.g., Napier, New Plymouth—McBride 2011, 2012, 2016a).Norovirus harmonisation factor included (18.5). For every unit of PCR virion detected by current PCR methods there are 18.5 PCR units in the clinical trial (Teunis et al. 2008).
Duration of swim (hours)	Minimum = 0.1 Median = 0.25 Maximum = 2	Child or adult.
Swimmers water ingestion rate, mL per hour	Minimum = 20 Median = 50 Maximum = 100	PERT distribution, for a child (adult rate is half this rate). For a review on this see Wood et al. (2015, sec. 6.2.1). This study uses children's ingestion rate, higher than for adults.
Water inhalation rate, mL per hour	Minimum = 10 Median = 25 Maximum = 50	PERT distribution. Assumed to be half the child ingestion rate.
Dose-response parameters	Proportion of adenoviruses that can cause respiratory illness = 10% (see Appendix A).	▪ Adenoviruses, simple binomial [eq. (4)]; $r = 0.4142$ (so $ID_{50,infection} \approx 2$), Pr(ill | Infection) = 0.5 (Soller et al. 2010), ▪ Enterovirus, beta-binomial [eq. (5)]: $\alpha = 1.3$, $\beta = 75$ (so $ID_{50,infection} = 53$); Pr(ill | Infection) = 1. ▪ Norovirus, beta-binomial [eq. (5)]: $\alpha = 0.04$, $\beta = 0.055$ (so $ID_{50,infection} = 26$); Pr(susceptible) = 0.74 (Teunis et al. 2008); Pr(ill | Infection) = 0.60 (Soller et al. 2010).
Shellfish meal size	α = 2.2046 β = 75.072 γ = –0.903	Using a log logistic distribution, truncated below at 5 g and above at 800 g, obtained by fitting distributions to estimates of daily intake of 98 consumers of mussels, oysters, scallops, pipi and tuatua in the 1997 National Nutrition Survey (Russell et al. 1999, McBride 2005a).
Bioaccumulation factor	Mean = 49.9 Std. dev. = 20.93	Using normal distributions, truncated at 1 and 100. The pathogen dose ingested on eating 100 grams of shellfish is BAF x the number of pathogens in the equivalent volume of water (Burkhardt & Calci (2000). The chosen factors are for F^+ coliphage in winter. The use of a normal distribution for BAFs allows half of these factors to be below 50 yet retain a precautionary approach.

[a] Those high values, persisting for over a month, have not been seen in subsequent Mangere influent virus assays. Yet were they to recur during an undetected outbreak in the contributing community, one could expect elevated illness risk.

2.3 Characterising dose-response

These relationships are mostly inferred from data reported by "volunteer studies" (i.e., clinical trials). These have been done for a restricted number of viruses. In these studies, healthy adult volunteers (typically between 50 and 100, in groups of 10 or so) are individually challenged with a pathogen dose and their infection and illness states are monitored for a few days thereafter. Occasionally data from viral illness outbreaks have been available from which dose-response information can be inferred.[17] Appendix B contains a full description of how these relationships are derived, and Appendix C discusses the special case of enteroviruses (via a clinical trial on echovirus).

Note that in order to perform QMRA calculations, comparability is required between the definition of "dose" used in the clinical trial or outbreak study and the methods used in assessing virus concentrations in treated wastewater for a particular facility. For example, noroviruses cannot be cultured, so a quantitative molecular-based lab procedure to detect the norovirus genome is used (Reverse Transcription Polymerase Chain Reaction "RT-qPCR"). Since RT-qPCR detects genetic material, the method picks up both viable and non-viable viruses. This overestimation has been accounted for in the dose-response model used in the QMRA.

2.4 Conducting the risk assessment

In order to adequately reflect limits to knowledge on key features of the risk assessment, Monte Carlo statistical modelling is used (Haas et al. 1999, McBride 2005a). In simpler models, key inputs are described by a single number (e.g., WWTP influent pathogen concentration). However, such inputs are known to be variable and some are uncertain. This variability and uncertainty has been addressed as shown in Table 2-6. The proprietary Excel plug-in product "@RISK" has been used to perform the calculations, incorporating factors that reflect these distributions and inputs (Palisade Corp 2013).[18] The models were run for 1,000 iterations for each virus for each site and for each scenario. On each iteration 100 individuals were 'exposed'.

Note that it can be appropriate to report the results in terms of infection, rather than illness (which is the approach taken for the freshwater component of the New Zealand Guidelines—MfE/MoH 2003). It was also the approach taken in a very recent QMRA study for the Great Lakes (USA—Corsi et al. 2016). These authors opined that "The probability of illness for enteroviruses could not be estimated because illness dose-response and morbidity data were unavailable". Nevertheless, we present an analysis for illness and take the precautionary assumption that all individuals who contract enterovirus infection also become ill. For the other pathogens (adenovirus, Norovirus) we take standard values of the probability of illness, given that infection has occurred. For all pathogens, the output metric is therefore an individual's illness risks, to facilitate comparison with relevant guidelines. [19,20]

Finally, note that the results obtained herein are for attributable risk, i.e., the increment in risk associated with the Bell Island discharge. As such it does not encompass risks associated with stormwater runoff or overflows.

[17] An example is a study by Thebault et al. (2013) of norovirus illness outbreaks among consumers of oysters in southern France.
[18] The @RISK models use named cells as much as possible, to facilitate checking and readability.
[19] There is insufficient time and information to also compute DALY metrics (Disability-Adjusted Life Years) as often used when assessing health risks associated with drinking-water (WHO 2011, chapter 7).
[20] The individual's illness risk (IIR) is calculated as the total number of predicted illness cases divided by the total number of exposures to potentially contaminated water or shellfish flesh. It represents the risk to an individual swimmer or shellfish consumer on any day, having no prior knowledge of any contamination from the outfall. It is calculated via the Monte Carlo modelling, for which 100 individuals are exposed on each of 1,000 separate days, i.e., 10^5 exposures. The total number of cases is 1,000m where m is the mean infection case rate over 100 people (readily calculated by the Monte Carlo software—@RISK, Palisade Corp. 2013). So, the individual's infection risk, expressed as a proportion, is $1{,}000m/10^5 = m/100$. When expressed as a percentage, IIR = m%.

3 Results

Detailed results are given in Table 4-1–Table 4-4, for Primary water contact, Secondary water contact, Shellfish harvesting, and collection of Scallops, respectively. These tables are necessarily data-rich. They contain the appropriate health risk index: The IIR%, the Individual's Illness Risk, expressed as a percentage. This is the risk faced by a random person using the receiving waters on a random day, with no foreknowledge of microbial conditions. Also shown is the 95%ile, indicating the spread of results.

4 Discussion

A key feature in interpreting these results is that to keep illness risks below an "acceptable" value, the IIR should fall below particular values:

1. Less than 1% for gastrointestinal illness (primary water contact, shellfish and scallops).
2. Less than 0.3% for respiratory illness (secondary contact).

These figures correspond to NOAEL values (No Observed Adverse Effects Level), in the New Zealand marine recreational water contact Guidelines (MfE/MoH 2003, Table H1, page H25).

Results from this QMRA show that when a 100-fold (2 log) removal efficacy is attained by the Wastewater Treatment Plant, the daily illness risk associated with recreational water contact or scallop collection will be well below the appropriate NOAEL value. Greater log-reductions are required for other shellfish flesh consumption, at least 3 log.

These results are strongly influenced by unusual levels of viral infection in the community. Such events seem rare, given that the pattern of sustained elevated influent virus concentrations at Mangere in May-June 1999 has not recurred in the regular ongoing monitoring since then. Nevertheless, precautionary public health practice is to cater for the possibility of such an event recurring.

Illness risk patterns for El niño and La niña at each of the sixteen sites are quite similar.

4.1 Recreational water contact

Enterovirus illness risk to recreational water users is generally similar to that than for norovirus illness. This a consequence of a precautionary approach in that noroviruses are assumed to be disaggregated and hence their potency is maximised.[21] Also, the proportion that are infectious in the receiving water is assumed to be similar to that obtained during the clinical trial upon which the dose-response curve is based (Teunis et al. 2008).[22] Aggregation of noroviruses markedly reduces norovirus illness risk when those viruses are present in low concentrations (McBride 2014a).

As expected, secondary water contact poses a significantly lower risk than that for primary contact.

4.2 Shellfish Risk

From Table 4-3, enterovirus- and norovirus-associated illness risks are predicted to be appreciably higher than primary contact risks. This is expected because other QMRA studies (e.g., McBride 2016a&b) have shown that shellfish associated risk is the greater of the two when both uses are in the same locality. This pattern holds despite the use of dilutions-at-depth achieved from the MetOcean Solutions, as may be expected for stratified flows.[23]

[21] The ID_{50} (concentration at which 50% of an exposed group would be infected) for disaggregated norovirus is a mean of less than 1, where the mean as averaged over the whole exposed group.
[22] Recall that noroviruses cannot be cultured and so they are assessed using a molecular method (PCR) which does not distinguish viable from inert virions.
[23] Shellfish ingest water continuously and can accumulate associated viruses in their flesh. In the MetOcean model this accumulation can occur in the intertidal regions, because the model has to retain some (false) water depth at such locations, for technical reasons.

Table 4-1: **Primary contact recreation** (for enteroviruses and noroviruses)

	La ñina, log_{10} reduction						El ñino					
	1	2	3	4	5	6	1	2	3	4	5	6
Back Beach, enterovirus												
IIR%	0.6	0.2	<0.1	<0.1	<0.1	<0.1	0.6	0.1	<0.1	<0.1	<0.1	<0.1
95%ile	1.0	<0.1	<0.1	<0.1	<0.1	<0.1	2.0	<0.1	<0.1	<0.1	<0.1	<0.1
Back Beach, norovirus												
IIR%	0.8	0.2	<0.1	<0.1	<0.1	<0.1	1.0	0.3	<0.1	<0.1	<0.1	<0.1
95%ile	4.0	1.0	<0.1	<0.1	<0.1	<0.1	8.0	1.0	<0.1	<0.1	<0.1	<0.1
Monaco, enterovirus												
IIR%	0.4	0.1	<0.1	<0.1	<0.1	<0.1	0.5	0.1	<0.1	<0.1	<0.1	<0.1
95%ile	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	1.0	<0.1	<0.1	<0.1	<0.1	<0.1
Monaco, norovirus												
IIR%	0.4	0.1	<0.1	<0.1	<0.1	<0.1	0.7	0.2	<0.1	<0.1	<0.1	<0.1
95%ile	2.0	<0.1	<0.1	<0.1	<0.1	<0.1	3.0	<0.1	<0.1	<0.1	<0.1	<0.1
Rabbit Island, enterovirus												
IIR%	0.2	<0.1	<0.1	<0.1	<0.1	<0.1	0.2	<0.1	<0.1	<0.1	<0.1	<0.1
95%ile	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Rabbit Island, norovirus												
IIR%	0.3	0.1	<0.1	<0.1	<0.1	<0.1	0.2	0.1	<0.1	<0.1	<0.1	<0.1
95%ile	1.0	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Tahuanui, enterovirus												
IIR%	0.5	0.2	<0.1	<0.1	<0.1	<0.1	0.4	0.1	<0.1	<0.1	<0.1	<0.1
95%ile	1.0	<0.1	<0.1	<0.1	<0.1	<0.1	1.0	<0.1	<0.1	<0.1	<0.1	<0.1
Tahuanui, norovirus												
IIR%	0.5	0.2	<0.1	<0.1	<0.1	<0.1	0.7	0.2	<0.1	<0.1	<0.1	<0.1
95%ile	2.0	<0.1	<0.1	<0.1	<0.1	<0.1	2.0	<0.1	<0.1	<0.1	<0.1	<0.1
Tahuanui (deep), enterovirus												
IIR%	0.3	<0.1	<0.1	<0.1	<0.1	<0.1	0.3	<0.1	<0.1	<0.1	<0.1	<0.1
95%ile	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	1.0	<0.1	<0.1	<0.1	<0.1	<0.1
Tahuanui (deep), norovirus												
IIR%	0.6	0.1	<0.1	<0.1	<0.1	<0.1	0.6	0.2	<0.1	<0.1	<0.1	<0.1
95%ile	2.0	<0.1	<0.1	<0.1	<0.1	<0.1	3.0	<0.1	<0.1	<0.1	<0.1	<0.1

Table 4-2: **Secondary recreation** (for adenoviruses).

	La ñina, log_{10} reduction						El ñino					
	1	2	3	4	5	6	1	2	3	4	5	6
Blind channel (k/w)												
IIR%	0.4	0.1	<0.1	<0.1	<0.1	<0.1	0.3	<0.1	<0.1	<0.1	<0.1	<0.1
95%ile	1.0	<0.1	<0.1	<0.1	<0.1	<0.1	1.0	<0.1	<0.1	<0.1	<0.1	<0.1
Monaco (skiing)												
IIR%	0.1	<0.1	<0.1	<0.1	<0.1	<0.1	0.1	<0.1	<0.1	<0.1	<0.1	<0.1
95%ile	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Rabbit Island (k/w)												
IIR%	0.3	0.1	<0.1	<0.1	<0.1	<0.1	0.3	<0.1	<0.1	<0.1	<0.1	<0.1
95%ile	1.0	<0.1	<0.1	<0.1	<0.1	<0.1	1.0	<0.1	<0.1	<0.1	<0.1	<0.1
Rabbit Island (skiing)												
IIR%	0.1	<0.1	<0.1	<0.1	<0.1	<0.1	0.1	<0.1	<0.1	<0.1	<0.1	<0.1
95%ile	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Waimea Inlet #1 (k/w/kayak)												
IIR%	1.3	0.3	<0.1	<0.1	<0.1	<0.1	1.0	0.2	<0.1	<0.1	<0.1	<0.1
95%ile	6.0	1.0	<0.1	<0.1	<0.1	<0.1	6.0	1.0	<0.1	<0.1	<0.1	<0.1
Waimea Inlet #2 (k/w/kayak)												
IIR%	0.7	0.2	<0.1	<0.1	<0.1	<0.1	0.8	0.1	<0.1	<0.1	<0.1	<0.1
95%ile	3.0	<0.1	<0.1	<0.1	<0.1	<0.1	3.0	1.0	<0.1	<0.1	<0.1	<0.1

k = kiteboarding. w = windsurfing.

Table 4-3: **Shellfish** (for enteroviruses and noroviruses).

	La ñina, log10 reduction						El ñino					
	1	2	3	4	5	6	1	2	3	4	5	6
Best Island, (oy), enterovirus												
IIR%	5.3	2.1	0.8	0.3	0.1	<0.1	3.3	0.9	0.1	<0.1	<0.1	<0.1
95%ile	45.0	9.0	1.0	<0.1	<0.1	<0.1	25.0	3.0	<0.1	<0.1	<0.1	<0.1
Best Island, (oy), norovirus												
IIR%	3.5	1.7	0.9	0.3	<0.1	<0.1	2.8	1.1	0.6	0.1	<0.1	<0.1
95%ile	22.0	18.0	7.0	1.0	<0.1	<0.1	2<0.1	7.0	1.0	<0.1	<0.1	<0.1
Blind channel east (p), enterovirus												
IIR%	4.3	1.3	0.3	<0.1	<0.1	<0.1	4.7	1.1	0.1	<0.1	<0.1	<0.1
95%ile	28.0	5.0	<0.1	<0.1	<0.1	<0.1	38.0	5.0	1.0	<0.1	<0.1	<0.1
Blind channel east (p), norovirus												
IIR%	4.9	1.6	0.5	0.1	<0.1	<0.1	5.5	2.0	0.6	0.1	<0.1	<0.1
95%ile	21.0	12.0	2.0	<0.1	<0.1	<0.1	22.0	16.0	3.0	<0.1	<0.1	<0.1
Blind channel west (p), enterovirus												
IIR%	9.3	3.1	0.8	0.2	<0.1	<0.1	9.9	3.1	0.7	0.2	<0.1	<0.1
95%ile	65.0	18.0	2.0	<0.1	<0.1	<0.1	69.0	2<0.1	3.0	<0.1	<0.1	<0.1
Blind channel west (p), norovirus												
IIR%	7.1	3.7	1.6	0.4	0.1	<0.1	7.5	3.9	1.7	0.4	0.1	<0.1
95%ile	24.0	21.0	12.0	3.0	<0.1	<0.1	24.0	22.0	13.0	3.0	<0.1	<0.1
Rabbit Island (p), enterovirus												
IIR%	2.4	0.8	0.2	<0.1	<0.1	<0.1	2.8	1.0	0.3	0.1	<0.1	<0.1
95%ile	11.0	1.0	<0.1	<0.1	<0.1	<0.1	12.0	2.0	<0.1	<0.1	<0.1	<0.1
Rabbit Island (p), norovirus												
IIR%	3.0	0.9	0.4	0.1	<0.1	<0.1	3.3	1.1	0.4	0.1	<0.1	<0.1
95%ile	17.0	4.0	1.0	<0.1	<0.1	<0.1	19.0	7.0	1.0	<0.1	<0.1	<0.1

“oy” = oysters, “p” = pipi

Table 4-4: **Scallops** (for enteroviruses and noroviruses).

	La ñina, log_{10} reduction						El ñino					
	1	2	3	4	5	6	1	2	3	4	5	6
Tasman Bay, enterovirus												
IIR%	1.8	0.5	0.1	<0.1	<0.1	<0.1	1.8	0.5	0.1	<0.1	<0.1	<0.1
95%ile	7.0	1.0	<0.1	<0.1	<0.1	<0.1	7.0	1.0	<0.1	<0.1	<0.1	<0.1
Tasman Bay, norovirus												
IIR%	2.9	1.0	0.2	<0.1	<0.1	<0.1	2.4	0.8	0.2	<0.1	<0.1	<0.1
95%ile	19.0	8.0	1.0	<0.1	<0.1	<0.1	18.0	7.0	1.0	<0.1	<0.1	<0.1

5 Conclusions

The discharge of well-treated wastewater from Bell Island generally poses low risk of illness associated with swimming and harvesting of local shellfish consumed raw, provided that sufficient log-removal of viruses is incorporated in the treatment system.

Furthermore, these factors combine to indicate that in the normal course of events minimal risks attend to either recreational water users or to consumers of raw shellfish. It is only when there are substantially increased levels of viral infection in the community that risks become significant, but only for lower levels of virus removal efficacy in the wastewater treatment plant. Such events seem rare.

If and when it does occur, detailed examination of the results show that when a 100-fold (2 log) removal efficacy is attained by the Wastewater Treatment Plant, the daily illness risk associated with recreational water contact or scallop collection will be well below the appropriate NOAEL levels adopted in national guidelines. Greater log-reductions are required for other shellfish flesh consumption, at least 3 log.

This assessment has taken a precautionary approach at several points, specifically through: incorporating occasional very high influent virus concentrations, such as can occur when there is an undetected viral illness outbreak in the contributing community; adopting the most potent form of the viruses' dose-response potency; and basing the calculations on risks to children (at greater risk than adults).

6 Acknowledgements

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7 Glossary of abbreviations and terms

Aetiological agent	Microorganisms and microbial toxins that cause disease in humans.
Beta-Binomial dose-response curve	A mathematically-derived infection dose-response curve for variable infectivity, in which individual doses are known.
Beta-Poisson dose-response curve	A mathematically-derived infection dose-response curve for variable infectivity, in which only mean doses are known.
Conditional illness probability	The probability of illness at a given dose given that infection has already occurred.
Conditional infection dose-response models	The (simpler) mathematical form of a dose-response equation that results when individual doses are known. (More complicated mathematical functions arise when individual doses are not known).
Hypergeometric functions	Mathematical equations that defy simple calculation, yet are important in the analysis of clinical trial data and outbreak data for the infection response of a population exposed to a pathogen, and where individual doses are randomly distributed about a known mean value.
Illness ID_{50}	The dose required to cause illness in 50% of an exposed population, who are already infected.
Infection ID_{50}	The dose required to cause infection in 50% of an exposed population.
IIR	Individual's Illness Risk: The risk faced by a random person using the receiving waters on a random day, with no foreknowledge of microbial conditions.
PCR	Polymerase Chain Reaction, a molecular technique for virus enumeration using DNA segment matching.
QMRA	Quantitative Microbial Risk Assessment.
RT-qPCR	Reverse-transcription quantitative PCR, used for RNA viruses.
Sequelae	An illness that is the result of a previous disease.
Simple binomial dose-response curve	A mathematically-derived infection dose-response curve for constant infectivity, in which individual doses are known.
Simple exponential dose-response curve	A mathematically-derived infection dose-response curve for constant infectivity, in which only mean doses are known.
$TCID_{50}$	Median Tissue Culture Infectious Dose: A laboratory culture technique measuring the amount of virus that produces a cytopathic effect in 50% of cell cultures inoculated.
Virion	Shorthand for "virus particle".

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Appendix A Virus characteristics

Adenoviruses

Respiratory viruses, particularly some adenoviruses, may also need to be considered within a QMRA. Respiratory symptoms (via inhalation of contaminated water when water skiing, or inhaling surf-generated aerosols) are sometimes associated with contact with wastewater-impacted coastal waters (WHO, 2003). In particular, a New Zealand epidemiological study at seven coastal beaches found a respiratory effect associated with the faecal indicator bacterium enterococci (McBride et al. 1998). Respiratory-associated viruses are probably the commonest causes of acute respiratory infections, for example reportedly causing around 70% of acute sore throats (Mims et al. 2004). They can be particularly resistant to disinfection (Gerba et al. 2003, Thompson et al. 2003). However, while adenoviruses are commonly found in water (Horwitz 2001), including wastewater, many strains give rise to gastrointestinal illness (e.g., the 40/41 strain complex), with a rather smaller proportion associated with respiratory symptoms. So, we should note that we have clinical trial information available only for the respiratory-illness-causing adenovirus 4 (Couch et al. 1966a&b, 1969) for which a dose-response model has been developed (Haas et al. 1999). We can expect that people are more vulnerable to respiratory agents than to gastrointestinal agents, because the human body's defences to the latter are more formidable. Fong et al. (2010) found only 3% of wastewater adenoviruses were type 4. So QMRA studies that apply the adenovirus 4 infection dose-response model to all adenoviruses (Gerba et al. 1996, Crabtree et al. 1997) have over-estimated health risk. An appropriate percentage of all adenoviruses that can give rise to respiratory effects is 10%.

Other QMRA studies in New Zealand have predicted illness via ingestion among recreational water users near marine outfalls to be rather higher than illness-via-inhalation (Stott & McBride 2011). A recent study of wet weather bypass flows at Moa Point, Wellington, has included consideration of respiratory effects, using Fong's results (Crawford et al. 2014).

Enteroviruses

Enterovirus (EV) is a single-stranded member of the picornavirus family, containing over 70 serotypes.[25] It was originally classified into 4 groups, polioviruses, coxsackie A viruses, coxsackie B viruses, and echoviruses but molecular characterisation has led to their reclassification into an enterovirus genus that includes 12 species: enterovirus A-H, J and Rhinovirus A-C. Human species of enterovirus are grouped into the four EV species A-D and the three Rhinovirus groups A-C.

Enteroviruses are often found in respiratory secretions (e.g., saliva, nasal mucus) and stools of infected persons. Poliovirus, coxsackie and echovirus can be spread through faecal-oral route. Infection can result in a wide variety of symptoms ranging from mild respiratory illness (common cold), hand, foot and mouth disease, acute haemorrhagic conjunctivitis, aseptic meningitis, myocarditis, severe neonatal sepsis-like disease, and acute flaccid paralysis. Enteroviruses are distributed worldwide and are influenced by season and climate. Infections can show a seasonal pattern with enterovirus prevalence peaking in summer and early fall in temperate areas, while tropical and semitropical areas showing no discernible seasonal trend.

[25] http://www.picornastudygroup.com/types/enterovirus/enterovirus.htm

A comparison with literature data found that E-30 (echovirus 30) was the most prevalent type detected internationally (Janes et al. 2014). Generally, enterovirus B viruses (in particular echoviruses) were the most frequently detected. Age distribution patterns were observed with 30–74% of all isolates detected in young children (< 5 years).

Surveillance and monitoring of enteroviruses has traditionally been based on culturing and serotyping. However, it is likely that concentrations may be under-reported due to differences in cell culture sensitivities (see Schiff et al. 1984a&b). Current advances in molecular techniques using RT-PCR for detection followed by sequencing of the capsid genes for typing is now the method typically used (Benschop et al. 2010).

Noroviruses

Noroviruses are a principal cause of viral gastroenteritis. They are single-stranded RNA viruses that have been classified into 5 genogroups (GI to GV). Strains I, II and IV can infect humans (particularly strain GII, see Matthews et al. 2012), while GIII infects bovine species and GV has recently been identified in mice. The GI viruses are highly infectious for a proportion of the population (Teunis et al. 2008) and spread easily by direct person-to-person or person-surface-person contact. By analogy, the GII genogroup exhibits the same behaviour. They also can be associated with waterborne gastroenteritis (Parshionikar et al. 2003) or shellfish-associated gastroenteritis (Lees et al. 1995, Thebault et al. 2013)[26] and are therefore a hazard to recreational water users (Gray et al. 1997). They have been detected in both raw and treated wastewaters (Nordgren et al. 2009), with strains of GI and GII predominating in human-derived wastewater that are typically very similar to human strains circulating in the population (van den Berg et al. 2005). Therefore, the public may be at appreciable risk whenever there is exposure to human wastes (animal viruses are generally thought to be not infectious to humans, and so other animal pathogens—bacteria and protozoa—come into play). For the purposes of the QMRA, noroviruses therefore represent the primary potential risk of infection from human-derived wastewaters via ingestion for primary contact users, such as swimmers, surfers and body boarders.

[26] These authors considered both infection and illness.

Appendix B Dose-response functions

For infection

Standard clinical trial procedures involve challenging groups of volunteers with aliquots taken from serially-diluted preparations whose well-mixed concentrations are measured. Doses in individuals' challenges are not measured. Consequently, only the average dose given to each member of a group is known. Nevertheless, by making two simple assumptions the mathematical form of the infection dose-response equation can be obtained (Haas et al. 1999, McBride 2005a):

1. The "single-hit" hypothesis: That a single pathogen, surviving the body's barriers (e.g., acidic digestion system) and reaching a potential infection site, is sufficient to cause infection.
2. Poisson distribution of pathogens in the preparation—as is appropriate for a random well-mixed population.

The mathematical result, after averaging across each group's individual Poisson-distributed doses, is the single-parameter "simple exponential" equation

$$\mathrm{Pr}_{\mathrm{inf}}(d) = 1 - \mathrm{e}^{-rd} \qquad (1)$$

where d is the average doses given to each group, "e" is the standard exponential number (the base of natural logarithms, e = 2.7183…), and r is the probability that a pathogen survives the body's defences and reaches an infection site.

Sometimes host-pathogen interactions are such that a constant value of r is implausible (e.g., because of differential immunity, or varying pathogen virulence, as indicated by lack of fit to the single-parameter model). In that case r is replaced by a standard two-parameter beta distribution with shape parameter α and location parameter β. The mathematical result is the much-more-difficult-to-evaluate[27] Kummer hypergeometric function (denoted as ${}_1F_1$):

$$\mathrm{Pr}_{\mathrm{inf}}(d) = 1 - {}_1F_1(\alpha, \alpha + \beta, -d) \qquad (2)$$

For obvious reasons, this can be called the "beta-Poisson" equation.[28] Fortunately in many cases we find that β >> 1 and α << β, in which case this equation can be well-approximated by the following equation (confusingly, also called "beta-Poisson")

$$\mathrm{Pr}_{\mathrm{inf}} = 1 - \left(1 + \frac{d}{\beta}\right)^{-\alpha} \qquad (3)$$

However, this approximation is inadequate for noroviruses because the fitted parameter doublet (α = <0.14 and β = <0.155, Teunis et al. 2008) constitute a serious breach of the approximation-validity criteria (α << β, β>>1). Analysis of clinical trial data for noroviruses therefore calls for specialist software that can evaluate (2), as reported by Teunis et al. 2008, Thebault et al. (2013).

[27] Equation (2) can't be evaluated in Excel.

[28] Because a two-parameter (α and β) beta distribution is used instead of the single parameter r and the doses are assumed random, i.e., Poisson-distributed. Strictly, β is not properly a location parameter for equation (2), but it is for its approximation equation (3) (because d is simply divided by β in that equation: increasing the value of β shifts the curve to the right).

Simplifying the infection dose-response calculations for QMRA

Good QMRA practice, especially for virulent pathogens, is to "expose" *multiple* people on each exposure occasion.[29] In that case the individual doses are known (i.e., are calculated and assigned to individuals by the model) so that there is no need for Poisson-averaging. This somewhat simplifies the mathematical development of the infection dose-response formulae such that for constant r the simple one-parameter exponential model is replaced by the simple binomial model

$$\mathrm{Pr}_{\mathrm{inf}} = 1-(1-r)^{i} \tag{4}$$

where *i* is the individual's dose.

Also, the two-parameter beta-Poisson model (the ${}_1F_1$ functional form) is replaced by the "beta-binomial" model

$$\mathrm{Pr}_{\mathrm{inf}} = 1-\frac{\mathrm{B}(\alpha,\beta+i)}{\mathrm{B}(\alpha,\beta)} \tag{5}$$

where B is the standard beta function (Abramowitz & Stegun 1972) and α and β are as defined previously. This equation can be simply evaluated in Excel.[30]

These two equations have been described by Haas (2002) as conditional infection dose-response models, the condition being that individual doses are known.

The following figures (Figure B-1a&b) give examples of these functions for adenovirus 4 and for Norwalk virus, for both conditional and unconditional infection dose-response models.

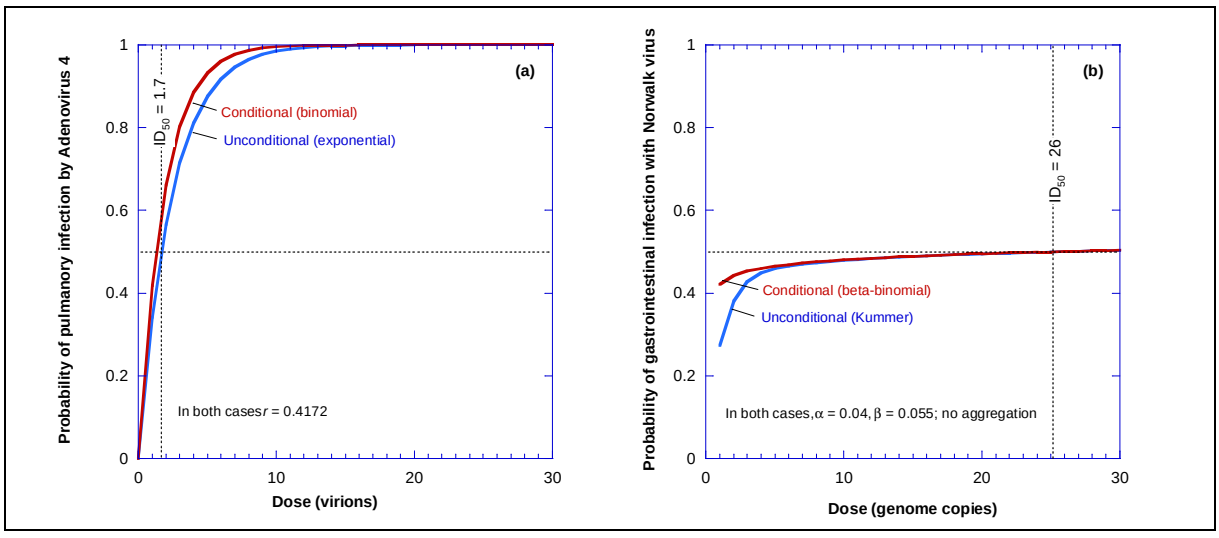

Figure B-1: Conditional and unconditional infection dose-response curves for: (a) single-parameter models for adenovirus 4, and (b) double-parameter models for Norwalk virus (only for susceptible individuals).

[29] To not do so gives rise to implausible risk profiles. For example, if only one individual is exposed per exposure occasion—as a representative of a group visiting a contaminated beach—and if the probability of infection given ingestion of one pathogen is high (say, 20%), then probabilities of infection *between* 0% and 20% are impossible. The resulting risk profile becomes extremely jagged (McBride 2005b). In such cases exposing a group of people per exposure occasion (say, 100), each with different doses (some swim for a few minutes, others for an hour or so), allows many values between 0 and 20% to be calculated.

[30] To do so we note that B(α,β) = Γ(α)Γ(α)/Γ(α+β), where Γ is the standard Gamma function (Abramowitz & Stegun 1972). Standard Excel includes the natural logarithm of the gamma function (as the function 'GAMMALN'), so that we can derive : Pr = 1 – EXP{GAMMALN(β+*i*) + GAMMALN(α+β) – [GAMMALN(α+β+*i*) + GAMMLN(β)]}.

These graphs highlight some important features of infection dose-response curves:

- The single-parameter models (e.g., Figure B-1a) rise inexorably to unit probability, precisely because their common parameter (r) is constant.
- The double-parameter models (e.g., Figure B-1b) "flatten out" well before reaching unit probability.[31]
- Whilst the relatively high infection ID_{50} for Norwalk virus (26 genome copies among susceptible individuals) occurs on the flattened top of its dose-response curve, infection probabilities are still appreciable at much lower doses.[32]
- The unconditional curves have a jagged profile around the conditional forms, yet deploying the latter in a QMRA gives rise to the same averaged risk.[33]
- Whilst the adenovirus 4 infection dose-response curve is in all respects more severe than that for Norwalk virus, for two reasons that doesn't mean that it is the most severe pathogen:

    i. adenoviruses that can cause respiratory ailments are a minor part of the total adenovirus population in sewage,[34] with most causing gastro-intestinal illness
    ii. exposure to respiratory adenoviruses (via inhalation, e.g., whilst surfing) tends to be lower than ingestion of water whilst swimming.[35]

However, having double-stranded DNA, adenoviruses are more resistant to disinfection processes.

For illness

Some individuals who become infected (e.g., as measured by serological response, or by evidence of pathogen shedding) may not go on to exhibit symptoms, i.e., they are asymptomatic. In that case, to obtain the unconditional probability of illness (given dose) we first need to calculate the conditional probability of illness given infection for each dose, denoted as $Pr_{ill|inf}$. The probability of illness is calculated as:

$$Pr_{ill} = Pr_{ill|inf}\, Pr_{inf} \tag{6}$$

Two common approaches are used for the conditional illness function:

Hazards model

Teunis et al. (1999) developed hazard models for the illness given infection, with two forms

Decreasing hazard

$$Pr_{ill|inf}(d) = 1 - \left(1 + \frac{\eta}{d}\right)^{-r} \tag{7}$$

[31] In fact these models approach unit probability only for enormous doses.
[32] The "flat top" is caused by the variable host-pathogen interactions, including a proportion of exposed population who high (but incomplete) immune. There is also another group who are completely immune.
[33] That's because applying the unconditional form to a single individual representing a group of people, as is common practice, doesn't capture the fact that, by good luck, some people at a beach will avoid exposure whilst the averaged dose is above zero (McBride 2005b).
[34] Typically, respiratory serotypes are detected less frequently than adenovirus F serotypes and so the gastro-intestinal (GI) disease-causing seroptyes tend to predominate in sewage studies (Osuolale & Okoh 2015). However, a proportion of respiratory versus GI serotypes detected will depend on the cell line used for culture assays and the target primers for molecular methods. For example, Hewitt et al. (2011) used cell line 594 and reported that culturable adenoviruses were mainly A-E types (which are respiratory and conjunctivitis serotypes) and there was still around 3 log presence in effluents.
[35] Water-contact-related respiratory illness is an area worthy of further research, particularly in the light of the respiratory illness rates reported in the one New Zealand epidemiological study on this matter—McBride et al. (1998). In that study (at seven New Zealand beaches) those rates were generally more prominent than gastrointestinal rates, a phenomenon that is not fully understood.

and

Increasing hazard $$\Pr_{ill|inf}(d) = 1 - (1 + \eta d)^{-r} \quad (8)$$

where η is a location parameter, and *r* is a shape parameter.[36]

Dose independence

Existing models of the conditional probabilities of illness (the condition being that infection has already occurred) are held in some doubt internationally. For example, the norovirus model (Teunis et al. 2008) predicts substantial infection probabilities at very low doses, but predicts substantial illness probabilities (among the infected) only at very high doses. A large body of work has taken the view that the conditional probability of illness-given-infection should be independent of dose—Schoen & Ashbolt (2010), Soller et al. (2010, 2015), Viau et al. (2011) and Boehm et al. (2015). Indeed, that approach is endorsed by WHO (2011), with the result that for the pathogens considered here the conditional illness probabilities are on the order of ½.

[36] The decreasing hazards model has only been reported for a clinical trial on adults exposed to *Campylobacter* (Teunis et al. 1999): All other conditional illness models that I am aware of infer an increasing hazards model, including a *Campylobacter* outbreak study for children (Teunis et al. 2005).

Appendix C Echovirus 12 clinical trial data analysis

Echovirus is a member of the enterovirus family. Haas et al. (1999) reported fitting a one-parameter simple exponential model to clinical trial data for an echovirus 12 study (Akin 1981),[37] with an estimated infection ID_{50} = 54 virions, corresponding to their calibrated *r* value of <0.1128.[38] Haas (1983) had earlier fitted a slightly different value to the Akin data, with *r* = <0.112 (giving infection ID_{50} = 58) and also a two-parameter beta-Poisson curve (with α = 1.3 and β = 75), so that the infection ID_{50} [= $\beta(2^{1/\alpha} - 1)$] = 53. Clearly, these approaches give consistent results with an infection ID_{50} about 50.

The beta-Poisson result was used in the QMRA performed for the Mangere wastewater treatment upgrade (DRG 2002, Simpson et al. 2003), this choice being particularly influenced by the observation that enterovirus illness can give rise to more serious consequences (i.e., sequelae) relative to other virus groups.

Akin's data were in fact preliminary results from an ongoing clinical trial, full results of which were reported three years later in Schiff et al. (1984a&b). Their 1984a paper is the proceedings of a conference held two years earlier in Herzliya Israel. It contains the Akin data. But the 1984b document (a peer-reviewed journal paper) multiplied all the doses, including those reported by Akin, by a factor of 33, to account for the re-analysis of the stock dose suspension using a more sensitive cell line[39]. These published data were analysed by Teunis et al. (1996) giving rise to a two-parameter "beta-Poisson" model (α = 0.401, β = 227.2, as reported by Teunis et al. 1996) and a higher infection ID_{50} = 1052 virions.[40]

We propose to use the beta-Poisson model (α = 1.3 and β = 75, with infection ID_{50} = 53 virions). Note that this conflicts with the approach taken in the increasingly-influential CAMRA website[41] (α = 1.06 and β = 171.3), giving rise to an infection ID_{50} = 922. This has implications for the enterovirus concentrations to be presented to this dose-response function in the QMRA calculations.[42]

[37] This widely-quoted paper (Akin 1981) seems to have been read by only a few, given its appearance only in the "grey literature", decades past. The author of this report has a copy, courtesy of Professor Haas (Drexel University), which is available on request.

[38] For the simple exponential model, algebraic manipulation shows that $ID_{50} = -\ell n(½)/r \approx 0.693/r$.

[39] At page 864 of Schiff et al. (1984b): "The original plaque assay used for determination of the titer of the echovirus-12 pool and of the various challenge doses administered to volunteers was based on the use of LLC-MK_2 cells and an agar overlay procedure; in the present study this assay was shown to be significantly less sensitive than the plaque neutralization assay involving RD cells and a soft agar overlay procedure. The latter system increased the plaquing efficiency of the challenge virus by 33-fold."

[40] For the approximate beta-Poisson model, algebraic manipulation shows that $ID_{50} = \beta(2^{1/\alpha} - 1)$.

[41] Center for Advancing Microbial Risk Assessment http://qmrawiki.canr.msu.edu/index.php?title=Table_of_Recommended_Best-Fit_Parameters#tab=Viruses

[42] The adopted dose-response function refers to echovirus 12 data gathered using the "LLC-MK_2" cell line (Schiff et al. 1984a). The CAMRA dose-response function refers to data re-analysed using "RD" cell line. Comparison of dose-response functions for other members of the enterovirus group (e.g., polio virus, hepatitis A, coxsackie) indicates that ID_{50} of the order of 50 is more tenable than of the order of 1000.

Appendix D Debate about norovirus infection dose-response

We have taken a form of norovirus infection dose-response that has become an "industry standard" in the last five years. It is based on a clinical trial, and is broadly supported by an outbreak study on French oysters (Thebault et al. 2013). That choice reflects a reasonable precautionary stance. Two recent contributors to the journal *Risk Analysis* have presented findings that norovirus may be even more infectious (Messner et al. 2014), or less infectious (Schmidt 2014) than the industry standard dose response, depending largely on the assumed degree of virus aggregation. There is currently much debate about all that. For example, another writer used data from a new clinical trial to claim that norovirus is much less infectious than the industry standard (Atmar et al. 2011, 2014) (this analysis appears to be flawed, as it ignored the role of aggregation, see McBride 2014a).

The role of noroviruses in QMRA will continue to be contentious, not least because there is a recently published procedure for their enumeration by culture (Jones et al. 2014) supplanting an earlier unsuccessful claim to such a procedure (Straub et al. 2007). This reflects the fact the QMRA is still an emerging discipline, with a number of issues that will take years to resolve. Nonetheless, experience indicates that QMRA is a more informative approach to human health risk assessment relative to that provided by levels of indicator bacteria derived from epidemiological studies at sites generally far-removed from the effects of discharges from large wastewater treatment plants.