

Appendix A: Translation of 1986 Criteria Risk to Equivalent Risk Levels for Use with New Health Data Developed Using Rapid Methods for Measuring Water Quality.

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In 1986, the Environmental Protection Agency (EPA) published criteria for recreational waters (U.S. EPA, 1986), based on epidemiological studies which related microbial water quality, as measured by culture methods, to health effects in swimmers (Cabelli, 1983; Dufour, 1984). The case definition for gastrointestinal (GI) illness was defined by symptoms or groups of symptoms. Highly credible gastrointestinal illness (HCGI) was defined by the following symptoms or symptom groups observed in the 8-10 days after the beach visit: (1) vomiting; (2) diarrhea with a fever or disabling enough for the individual to remain home, remain in bed or seek medical advice; or (3) stomachache or nausea accompanied by a fever. These combinations of symptoms were developed to strengthen the validity of using symptoms to describe GI illness in swimmers, where the health status information was obtained by telephone interview.

In 2002, EPA initiated the National Epidemiological and Environmental Assessment of Recreational (NEEAR) study program, a series of epidemiological studies to determine the relationship between health effects in swimmers and water quality that has been measured using a new method that produces quantitative results in 2 to 3 hours (Wade et al., 2008). By 2007, seven epidemiological studies had been completed, four at freshwater beaches and three at marine beaches. These studies used a more contemporary health case definition, "NEEAR GI" (NGI), which differed from the HCGI symptoms used in the early EPA studies. Fever was no longer required to co-occur with diarrhea, stomachache or nausea to meet a case definition of gastroenteritis, NGI still used multiple symptoms to describe gastrointestinal illness. NGI was defined as any of the following in the 10-12 days after the beach visit: (1) diarrhea (three or more loose stools in a 24 hour period); (2) vomiting; (3) nausea and stomachache; (4) nausea or stomachache, and interference with regular activities (missed time from work or school, or missed other regular activities as a result of the illness).

One of the major differences between the early and recent studies is the broadening of the definition of an adverse health episode to include illnesses with gastrointestinal symptoms without fever as a pre-requisite (with the exception of vomiting, which with or without fever is sufficient for an illness episode in both HCGI and NGI). This was done to capture episodes of gastroenteritis caused by viral infections (e.g., norovirus) which can often present with mild or no fever. Furthermore, this is consistent with definitions used in several recent longitudinal studies of gastroenteritis (Payment et al., 1991; Colford et al., 2002). International experts have also suggested that a uniform international definition which does not require a fever and should include vomiting or diarrhea constituting greater than or equal to 3 soft stools in a 24 hour period (Majowicz et al., 2008). An additional difference was the extension of the risk period for NGI by an average of approximately 2 days to 10-12 days. This was done to capture the longer incubation period for illnesses caused by some infectious organisms such as *Cryptosporidium*.

The significant differences between the HCGI and NGI case definitions or health endpoints create a dilemma with regard to the risk level used to develop previous criteria for managing beach water quality. In the early EPA epidemiological studies (1986) the issue of risk level was resolved by using a simple algebraic equation that contained three known factors (1) the average density of the then current bacterial indicator, fecal coliforms; (2) the average density of the proposed indicator (enterococci or *E. coli*); and (3) the standard density of fecal coliforms required for the beach water quality standard of 200 cfu per 100 mL. Knowing these factors made it easy to calculate what the equivalent standard would be for the proposed indicator. This approach was used to develop the 1986 U.S. EPA criteria (Dufour and Schaub, 2007). Based on these new standards and the health relationships that were derived for the proposed indicator, the implied attributable risk was 8 illnesses per 1,000 primary contact recreators in freshwater and 19 illnesses per 1,000 primary contact recreators in marine water.

The question now is, how can one select a risk level using the new case definition for gastroenteritis that will be “as protective as” the currently used risk level under the old case definition? A logical approach to translating the currently used risk levels based on the HCGI case definition (8 illnesses per 1,000 primary contact recreators for freshwater and 19 illnesses per 1,000 primary contact recreators for marine waters) to the NGI definition used in the NEEAR studies would be to equate a translation factor to the ratio of the non-swimmer illness rates from the NEEAR study relative to the non-swimmer illness rates from the 1986 data, thus retaining a constant relative risk. The non-swimming illness rates of the two populations will give the best estimate of any inherent changes in the background illness rates that may have occurred in the time between the 1986 and the 2009 studies, and provide an estimate of the effect of changing the case definition for gastroenteritis. Relative risk is the ratio of risk among an exposed population to that in an unexposed population (the baseline risk). The non-swimmer illness rates represent the baseline. For relative risk to remain constant in the translation from HCGI to NGI, the respective swimmer illness rates must follow in proportion to the respective baseline illness rates. Non-swimmer HCGI rates from the 1970 – 1980 EPA epidemiological studies (Cabelli, 1983; Dufour, 1984) can be compared with the non-swimmer NGI rates obtained from the NEEAR study data (Wade et al., 2008; Wade et al., 2010). The non-swimmer HCGI rate from all of the early EPA studies (Cabelli, 1983; Dufour, 1984) is 14 gastrointestinal illnesses per 1000 participants. The non-swimmer NGI rate from the NEEAR study data is 63 gastrointestinal illnesses per 1000 non-swimmer participants (Wade et al., 2009; Wade et al., 2010). For a new criterion value to be “as protective as” the 1986 criteria, the relative risk of the two respective criterion values must be equal.

The acceptable risk limit of 8 HCGI per 1,000 primary contact recreators in freshwater refers to *attributable* risk, calculated by subtracting the illness rate in non-swimmers from that in swimmers. The non-swimmer value must be added to the attributable risk value to obtain the total number of illnesses in swimmers. The relative risk can be calculated by:

$$RR = \frac{\text{attributable illness rate in swimmers} + \text{illness rate in non-swimmers}}{\text{illness rate in non-swimmers}}$$

Relative risk implied by the 1986 criteria for HCGI is:

$$RR = (8 + 14) / 14 = 1.57 \text{ for freshwater}$$

In order to answer the question, what would an equivalent acceptable risk be for the same relative risk based on NGI in the NEEAR study, rearrange the above equation to obtain an Equivalent Risk Value (ERV) using a non-swimmer NGI (NS NGI) rate of 63 per 1,000 in place of the NS HCGI rate of 14 per 1,000. Using the freshwater relative risk as an example, this gives:

$$\begin{aligned}\text{ERV} &= 1.57 (\text{NS NGI rate}) - \text{NS NGI rate} \\ &= 1.57 (63) - 63 \\ &= 36\end{aligned}$$

Thus, an attributable risk of 36 NGI per 1,000 primary contact recreators represents an acceptable risk equivalent to 8 HCGI illnesses per 1,000 primary contact recreators.

The ERV for 19 GI illnesses per 1,000 primary contact recreators or any other suggested criterion value can be calculated the same way. First, calculate a relative risk value for the acceptable risk and then use the relative risk value to calculate an ERV using the NGI value for non-swimmers. A second, simpler way to calculate the ERV is to use the multiplication factor equal to the ratio of the NS NGI illness rate to the NS HCGI illness rate. That value is $63/14=4.5$. This is the translation factor for calculating the new risk level. Simply multiply the old criterion value by the translation factor to obtain an ERV that is “as protective as” the current criteria. For example, to determine the ERV for 8 GI illnesses per 1,000 primary contact recreators, simply multiply 8 by 4.5 to obtain 36.

The translation factor of 4.5 represents the risk of NGI relative to HCGI and is key to this suggested approach to translating NGI risk in terms of HCGI. An approximate 95% confidence interval for this factor can be calculated to be 3.3 to 6.2. This assumes that non-swimmer illness rates observed at the study areas (beaches) are representative of the variation in background illness among all coastal areas, and that this variation is described by a beta distribution (a common assumption when dealing in the variability of incidences which must fall in the range 0 to 100%).

Another question that must be addressed is, which risk level is to be translated, the freshwater level or the marine water risk level? A direct comparison of the risk estimates for fresh and marine beach waters was carried out as described by Altman and Bland (2003) indicated that there were significant differences in the estimated risk levels only for limited range of *Enterococcus* CCE (approximately in the range of 100-126 CCE per 100 mL). Furthermore, a direct test of the slope parameters also shows that there is no difference in the slopes ($p=0.44$), or the rate of increase in risk per unit increase in enterococci CCE, between marine and freshwater beaches. A comparison based on the likelihood ratio test (as described by Wade et al., 2008), resulted in the same conclusion. For the likelihood ratio test the combined model was estimated with terms that allowed beach specific effects for the indicator term and the swimming term. However, this model was no better than a model with only a single term for each of these parameters ($p=0.19$).

A likelihood ratio test was conducted the combined model was estimated with terms that allowed beach specific effects for the indicator term and the swimming term. However, this model was no better than a model with only a single term for each of these parameters ($p=0.19$).

In effect, there was little evidence for differences in risk estimates obtained from separate models from marine and freshwater beaches and the beach-specific separate models showed no statistical improvement over a single combined model. On the basis of these, we present risk levels based on the combined model (Figure 1). Results from the marine and freshwater studies indicate that exposure-response relationships are sufficiently similar to allow combining the newly-developed freshwater and marine water data to give a single relationship between health effects and water quality measured with a new rapid method. The relationship between swimming-associated NGI per 1000 swimmers and water quality developed from the combined marine and freshwater data is defined by the equation:

$$\text{Swimming associated NGI} = -27.31 + 23.73(\text{mean Log}_{10} \text{qPCR CCE}/100\text{mL})$$

which, for the purpose of calculating the qPCR CEE (quantitative polymerase chain reaction calibrator cell equivalents) concentration for a new water quality criterion, is re-arranged to:

$$\text{mean Log}_{10} \text{qPCR CCE per 100mL} = (\text{NGI} + 27.31) / 23.73.$$

If the 8 illnesses per 1,000 primary contact recreators is translated into a NEEAR case definition level, the ERV is given by 36 illnesses per 1000 primary contact recreators. Substituting the ERV of 36 for SAI in the equation above gives:

$$\text{mean Log}_{10} \text{qPCR CCE per 100 mL} = (36 + 27.31) / 23.73 = 2.67$$

$$\text{Antilog}(2.68) = 465 = \text{geometric mean (qPCR CCE per 100 mL)}$$

Thus, the risk level equivalent to 8 HCGI per 1,000 primary contact recreators is 36 NGI per 1,000 primary contact recreators and this relates to a geometric mean (GM) qPCR CCE per 100 mL value of 471 per 100 mL in terms of the NEEAR case definition.

An approach for translating the currently accepted risk levels for fresh and marine waters to equivalent risk levels appropriate for use with the new rapid qPCR method has been proposed in this document. The approach is appealing because:

- The approach is based on relative risk, which can be used with any case definition.
- The approach can be applied to any risk translation if a health, water quality relationship is available.
- The approach is not dependent on what indicator or method is used to measure water quality.

References

- Altman, D. G., Bland, J. M. 2003. Interaction revisited: the difference between two estimates. *BMJ*, 326, 219.
- Cabelli, V.J. 1983. Health Effects Criteria for Marine Waters, US Environmental Protection Agency, EPA-600/1-80-031, Research Triangle Park, NC.
- Colford, J.M., Rees, J.R., Wade, T.J., Khalakdina, A., Hilton, J.F., Ergas, I.J., et al., 2002. Participant blinding and gastrointestinal illness in a randomized, controlled trial of an in-home drinking water intervention. *Emerging Infectious Disease*, 8(1): 29-36.
- Dufour, A.P. 1984. Health Effects Criteria for Fresh Recreational Waters, U.S. Environmental Protection Agency, EPA-600/1-84-004, Cincinnati, OH, 1984.
- Dufour, A. Schaub, S. 2007. The Evolution of Water Quality Criteria in the United States 1922- 2003, In: *Statistical Framework for Recreational Water Quality Criteria and Monitoring*, Wymer, LJ, (Editor), John Wiley & Sons, Chichester, England.
- Majowicz, S.E., Hall, G., Scallan, E., Adak, G.K., Gauci, C., Jones, T.F., O'Brien, S.O., Henao, O., and Sockett, P.N. 2008. A common symptom-based case definition for gastroenteritis. *Epidemiology and Infection*, 136: 886-894
- Payment, P., Richardson, L., Siemiatycky, J., Dewar, R., Edwardes, M., and Franco, E. 1991. A randomized trial to evaluate the risk of gastrointestinal disease due to consumption of drinking water meeting current microbiological standards. *Am. J. Public Health*, 8(16): 703-708.
- Wade, T.J., Calderon, R.L., Brenner, K.P., Sams, E., Beach, M., Haugland, R., Wymer, L., Dufour, A. 2008. High Sensitivity of Children to Swimming-associated Gastrointestinal Illness. *Epidemiology*, 19(3): 375-383.
- Wade, T.J., Dufour, A.P. 2009. Considerations on Combining Marine and Freshwater Data from the NEEAR Water Studies, Internal ORD Document, March, 2009.
- Wade, T.J., Sams, E., Brenner, K.P., Haugland, R., Chern, E., Beach, M., Wymer, L., Rankin, C.C., Love, D., Li, Q., Noble, R., Dufour, A.P. 2010. Rapidly measured indicators of recreational water quality and swimming-associated illness at marine beaches: a prospective cohort study. *Environmental Health*, 9: 66, retrieved from <http://www.ehjournal.net/contents/9/1/66>
- U.S. Environmental Protection Agency. 1986. Ambient Water Quality Criteria for Bacteria -1986, EPA440/5-84-002, Office of Water, Washington DC

Figure 1. Swimming-Associated GI illness and Daily Average *Enterococcus* qPCR CCE. All subjects, marine and freshwater beaches combined (Intercept= -0.02730777, Slope= 0.02372795)

