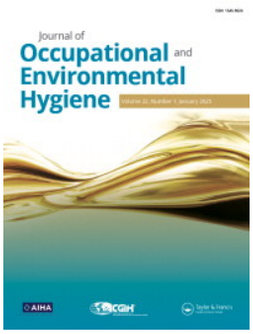

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REPORT

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A risk-risk tradeoff approach for incorporating the public's risk perceptions into quantitative microbial risk assessment

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ABSTRACT

In public health, risk experts often define acceptable risk targets without community input. We developed a novel method for applying behavioral microeconomics to integrate individuals' risk preferences into risk assessment. To demonstrate this methodology, we explored a risk-risk tradeoff case scenario: increased asthma risk from increased cleaning and disinfection (C&D) and increased infection risk from decreased C&D for healthcare staff. Utilizing a risk-risk tradeoff (RRTO) framework, two datasets were informed with RRTO survey data describing the risks individuals would accept for one outcome to offset risk in another (i.e., "risk target"). A quantitative microbial risk assessment (QMRA) was deployed to output "critical concentrations," viral concentrations on surfaces that yield risk targets for a single contaminated surface touch and a work shift. Critical concentrations were over four orders of magnitude larger for single-touch scenarios. Critical concentrations across risk target datasets were similar. Using the RRTO framework to inform QMRA advances the incorporation of individuals' risk preferences in risk analyses outside economics.

KEYWORDS

Asthma; behavioral economic; disinfection; occupational health

Introduction

Quantitative microbial risk assessment (QMRA)

Quantitative microbial risk assessment (QMRA) is a framework that includes four components: hazard identification, exposure assessment, dose-response assessment, and risk characterization (Haas et al. 2014) and is used to estimate a "risk" (i.e., probability of a negative health outcome) for a variety of public health and engineering purposes, including informing environmental monitoring strategies, treatment goals, and comparing intervention outcomes (Ryan et al. 2014; Hamilton et al. 2019; Wilson et al. 2021a; Gerrity et al. 2023). QMRAs often utilize environmental microbiology data from literature or experimental or field studies; mathematical relationships regarding the fate and transport of microbes in environments; the role of human behaviors in fate, transport, and exposure; and dose-response relationships to relate an environmental concentration of a pathogen with an anticipated health risk (Hamilton et al. 2019; King et al. 2022; Heida et al. 2024). While "risk" can be used in a variety of ways (e.g., as solely a probability of a negative health outcome or as a more complex concept including values and perceptions (Slovic 2000)), the terms "risk threshold" and "acceptable risk" were used herein as terms referring to a threshold or acceptable probability of a negative health outcome, namely infection with the chosen index pathogen.

Risk targets

Historically, a variety of "acceptable" risk targets, also referred to in the literature as "levels," or "goals,"

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Table 1. Examples of QMRA risk targets and associated scenarios and references.

Risk Threshold		Scenario Details	References
Annual Risk	1/10,000 annual risk	• Used in drinking water contexts, including DPR in Arizona, California, Texas, and Colorado • US EPA, WHO, Health Canada, USDS-ARS	(Burch et al. 2022; Environmental Protection Agency (EPA)) 2002; Hamilton et al. 2006; Health Canada 2019; Hynds et al. 2014; Leschevallier and Buckley 2007; Owens et al. 2020; Regli et al. 1991; World Health Organization 2011)
Per Event	1/100 1/1,000	• Exploring contamination of hands by handwashing water, using a risk threshold of 1/1,000 for the main analysis and additional comparison thresholds of 1/100 and 1/10,000	(Verbyla et al. 2019)
	1/10,000	• Used in QMRAs as a reference point for single fomite touch • Used in CDC communication about COVID-19 risks posed by fomites relative to other transmission routes	(Harvey et al. 2021; Wilson et al. 2021b)
	1/1,000,000 per event risk	• Risk associated with contaminated fomites in healthcare – used to determine level of cleaning needed	(Ryan et al. 2014; Wilson et al. 2021b; Reynolds et al. 2022)
Per Day	2.7×10^{-7} Daily infection risk	• Used in California to inform log removal values for direct potable reuse water	(State Water Resources Control Board 2019)

have been determined by experts in the areas of microbial and chemical risk assessment (Slovic 2000) in environmental health contexts. In quantitative microbial risk assessment (QMRA), specifically, these risk targets guide environmental monitoring strategies and treatment goals by defining the $\log_{10}$ reductions in environmental concentrations needed to achieve a specific risk target. Risk characterizations from QMRAs inform necessary controls and monitoring strategies for protecting public health. The most common risk target in microbial risk assessment is 1/10,000, an annual risk target for infection from ingesting drinking water and a threshold used for comparisons in other QMRA contexts, such as exposure to contaminated fomites or contamination of hands from handwashing with unclean water (Table 1; Verbyla et al. 2019). In the context of drinking water, this target informs by how many $\log_{10}$ microbial concentrations in surface water sources used for drinking water must be reduced to achieve this goal. Interventions offering a specific $\log_{10}$ reduction can then be combined and are assumed to have an additive effect. The needed reductions to meet a risk target are referred to as "log reduction targets" (LRTs), or the number of "log credits" needed in sum to achieve a risk target (Jahne et al. 2023). A similar approach was taken with direct potable reuse (DPR) standards (Salveson and Soller 2019), using a 1/10,000 annual infection risk target and/or a 2.7×10^{-7} daily infection risk target (Table 1; State Water Resources Control Board 2019). Other examples of risk targets, scenarios in which they have been applied, and associated references can be found in Table 1.

While some risk targets are firm, others are more flexible. For example, during the COVID-19 pandemic, risk scores were used in the Google Apple Exposure Notification (GAEN) API for digital contact tracing to determine whether an individual needed to quarantine or not if exposed to someone with illness. One proposed method was to use flexible risk targets, giving more individualized decision-making to specific communities utilizing the application (app) and offering the ability of the app to change risk targets given differentials in the prevalence of disease in the population (Wilson et al. 2022a). Other studies have used various risk targets to compare estimated infection risks that are less conservative (e.g., 1/1,000) than the U.S. EPA annual drinking water threshold of 1/10,000, using real-world risks that the public has usually internalized, such as through consuming food with the potential to be contaminated to inform a risk comparison (Lim and Jiang 2013). In recreational water exposure contexts, illness risk targets are set at 36/1,000 or 32/1,000 (Office of Water 2012).

Some use a QMRA approach to (1) environmental microbial concentrations are defined that relate to a risk threshold (termed "critical concentrations" (Hamilton et al. 2019; Rasheduzzaman et al. 2019) or "threshold concentrations" (Dean and Mitchell 2020)) or (2) treatment goals that achieve critical concentrations and a risk threshold (Schoen and Garland 2017; Rasheduzzaman et al. 2019; Dean and Mitchell 2020). The outcome variable is simulated over a range of input values to examine the parameter space of iterations associated with a greater-than-target risk. The focus of this work is on estimating "critical

concentrations" with a Monte Carlo approach for relating microbial concentrations to defined risk thresholds.

A vital component to the ongoing discourse on QMRA is how to inform the choice of risk target value(s) for infectious disease decision-makers. Traditionally informed by experts or epidemiological observations, there is a need to improve the engagement of the general public in risk decision-making for ethical reasons (i.e., people in positions of power and privilege deciding acceptable risks for marginalized and underrepresented communities and inherent bias in all human judgment, even those of experts (Shrader-Frechette 1995)), but also to guide efficient and fair resource allocation (i.e., ensuring sufficient financial resources are directed toward maintaining or achieving a desired risk level for an environmental hazard). The choice of risk benchmarks/targets is inherently a value-based policy judgment that is context- and population-specific. However, involving the public in these deliberations can introduce heuristics and biases (Kahneman et al. 1982) that may, for example, suggest a desired outcome from risk management efforts that is unachievable, such as setting a risk target of zero. Nevertheless, while engaging the public in the risk management process can be challenging, Slovic (2000) argues it is worth pursuing, as experts who set risk targets are not immune to the heuristics and biases to which the public often fall victim, and those in positions of power, such as experts, may have higher risk tolerance than those facing the risks on a frequent or even everyday basis (Slovic 2000). This is especially true if the demographics of decision-makers do not reflect the actual proportions of females or underrepresented minorities, who may be more risk-averse relative to White males (Slovic 2000). Additionally, including communities in the risk management process can better inform resource allocation, especially in the face of competing risks, discussed below in the Risk-risk Tradeoffs in Public Health section.

In the field of healthcare, the idea of involving individuals in decisions regarding their risks is more acceptable and indeed is growing, helped by the use of patient decision aids (Breslin et al. 2008; Stacey et al. 2011; Sepucha et al. 2013; Bonner et al. 2021) that support shared decision-making in which patients collaborate with healthcare providers to make healthcare decisions that are in their best interest. Exploring methodologies in public health contexts for involving individuals in identifying their acceptable risk level, and further, to better understand these decisions, is needed to advance diversity and equity in microbial risk assessment.

Behavioral economics and decision-making psychology

One way in which to elicit tolerable risks from individuals to assess tolerable risk distributions across a population is through methods rooted in behavioral economics and decision-making psychology (Viscusi et al. 1991; Krueger 2013; Fischhoff and Broomell 2020). A common method is a willingness-to-pay (Jordan and Elnagheeb 1993; Steigenberger et al. 2022) approach which elicits the monetary value individuals place on the outcome, i.e., an increased or decreased risk of an adverse event. However, when there are competing outcomes related to an intervention or policy or where populations are income-constrained, a risk-risk tradeoff (RRTO) approach may be more appropriate, as weighing outcomes monetarily may increase the cognitive burden for participants relative to comparing the risks, themselves (Van Houtven et al. 2008; Nielsen et al. 2019). Choosing on one single dimension (risk) also reduces the likelihood of scope insensitivity (that is, being unresponsive to changes in the size of the good or service being valued), compared to the use of two dimensions (money and risk) (Carson and Mitchell 1995; Jones-Lee et al. 1995; Fetherstonhaugh et al. 1997; Beattie et al. 1998). Using this methodology, tolerance for one risk outcome to maintain a lower risk in another outcome can be quantified and used to inform further analyses, without the need to use a monetary approach that elicits, for example, willingness to pay. It should be noted that RRTOs have been shown to work in non-standard settings, such as in the context of climate risk in the UK (Mussio et al. 2024) and heatwave-related mortality risks in India (Chilton et al. 2024). In the context of fatal risks, the value of a statistical life (VSL) (McDonald et al. 2016; Nielsen et al. 2019) (i.e., a willingness of a society to pay for a given individual's small reduction in risk of mortality) (Colmer 2020) can be calculated through an indirect approach based on risk-risk tradeoffs. This contrast with a direct approach, which uses willingness to pay to calculate VSL, has been used within more familiar contexts of transportation safety (Nielsen et al. 2019) and risks of other outcomes, such as cancer and other illnesses (McDonald et al. 2016), and environmental risks (Mussio et al. 2024). The indirect approach uses the outcome of the RRTO which elicits the relative value of two risks to an individual. This can be considered

as a context premium that summarizes how much more or less individuals value specific changes in one risk compared to another risk and can be used to calculate a context-specific VSL.

There are two current approaches to conducting an RRTO study, both having their own advantages and disadvantages depending on the risks, the population targeted, and statistical efficiency considerations. In the first approach, a series of single sets of risk tradeoffs are used (Wilson et al. 2022b) while in the second a multiple risk list is used (Nielsen et al. 2019). In the former, information can be obtained to infer the range of acceptable risks across individuals in a population through a subset of randomly chosen questions, while in the latter, information can be gathered about the actual risk target of the individual directly by asking participants to move through a list of risk tradeoffs where one of the risks increases, until the point at which they choose to accept the other risk (their "switch point" or "indifference point") is found. Responses can then be aggregated to estimate an average switching point, which could be used to protect the population at a risk threshold that satisfies a given proportion of individuals' acceptable risks.

Risk-risk tradeoffs in public health

RRTOs could, in principle, be introduced into risk assessments aimed to inform public health interventions, for example in cases whereby an intervention decreases a risk for a health outcome of concern while increasing a risk for another (Heida et al. 2022; Wilson et al. 2022b). An example of this is seen in cleaning and disinfection in healthcare, where increased frequency or intensity of cleaning, especially with certain products, can increase asthma-related risks for healthcare workers (Caridi et al. 2019; Starke et al. 2021) and decreased cleaning and disinfection could translate to increased risks for healthcare-associated infections (Aw et al. 2017). While cleaning can theoretically reduce asthma-associated symptoms by removing dust that could later be resuspended affecting indoor air quality, cleaning and disinfection in healthcare often creates an unavoidable tradeoff for those conducting the cleaning and disinfection due to the frequency and intensity necessary to protect patients from healthcare-associated infections. Other tradeoffs include pathogen inactivation with chlorine and chloramine disinfection in the treatment of wastewater for water reuse and subsequent disinfection by-product formation and tradeoffs between chemical and microbial contaminants in building plumbing systems (Furst et al. 2018; Tolofari et al. 2022). There may be multiple competing outcomes introduced by an intervention, such as increased water heater temperature settings to decrease *Legionella* growth potential but posing higher energy costs and scalding risks (Heida et al. 2022). Another example includes the use of residential water reuse systems for sustainability benefits but potentially increased microbial infection risks (Schoen et al. 2014).

Study objective

To handle these complex RRTO setups that usually do not involve money (and where it traditional economic and monetary valuation methods may be less useful or equitable), new methodologies in QMRA are needed. Using indifference points, described above, to inform risk targets would allow for the inclusion of individuals' acceptable risks in QMRAs used to inform a risk threshold and, subsequently, critical concentrations and/or intervention performance goals. Exposure and dose-response assessment from the QMRA framework can be used to elucidate critical concentrations that yield risk thresholds informed directly by RRTO study output. This advances the current state-of-the-art of risk assessment in several ways. (1) It creates a way in which individuals can quantitatively inform risk thresholds based on their values and willingness to accept risk. (2) It frames risk thresholds within the context of competing risks, where an acceptable risk is not elicited in isolation from potential negative consequences of decreasing this risk through intervention. Rather, it addresses a larger system in which addressing one risk may come at the "cost" of increasing risk in another health outcome. These improvements are vital to the advancement of QMRA, to address increasingly complex microbial exposures and intervention decision-making (Heida et al. 2022) and to protect the health of those who bear the "cost" of interventions that, while aimed to reduce microbial risks, could be associated with other negative health outcomes (Wilson et al. 2023a).

The objective of this study was to demonstrate how results from RRTO surveys (namely, indifference points) could be used to incorporate individuals'

tolerable risks into the setting of risk targets for risk assessments and subsequent intervention design. The focus of this demonstration is on an occupational RRTO for healthcare professionals: increased risk of infection due to decreased cleaning and disinfection versus increased risk of asthma development due to increased cleaning and disinfection. Respiratory health disease related to cleaning and disinfection exposures for healthcare workers has been documented for over 30 years, with some evidence of a dose-response relationship (i.e., increased cleaning frequency posing increased respiratory health risk) (Wilson et al. 2023b). In healthcare environments, however, consistent cleaning and disinfection is imperative for reducing healthcare-associated infections, including the potential for occupational infections among healthcare workers (Aw et al. 2017). This introduces an important tradeoff and a need for strategic cleaning and disinfection interventions aimed at balancing these opposing risks.

Methods

This study involved, first, the fitting of distributions to RRTO survey data to randomly sample from the distributions to generate two simulated data sets of indifference points. Summary statistics were then used to calculate different potential risk targets from these indifference point data sets. QMRA was conducted to calculate what concentrations of the virus on surfaces would yield these risk targets (herein, "critical concentrations") assuming either a single contact with a contaminated surface or an entire shift worth of contact with contaminated surfaces. The overall workflow is summarized in Figure 1.

First, a scenario was used from a prior occupational health RRTO study involving 69 nurses, which explored increased infection risk from contaminated surfaces due to decreased cleaning/disinfection and increased asthma risk from increased cleaning/disinfection (Wilson et al. 2022b). Due to a lack of data on the scenario of interest, data from a prior RRTO survey given to UK students ($n = 162$) were also used to apply to the occupational health RRTO scenario (Nielsen et al. 2019), accessible through collaborators of the research team. Data from two scenarios in this survey data were used to demonstrate a proof of concept for using the RRTO framework in microbial risk assessment.

In the first stage, distributions were fit to RRTO survey data so that large datasets ($n = 10{,}000$) could be generated to simulate indifference points yielded from a survey of a large cohort. Second, summary statistics of these generated points were used to set risk targets. These risk targets were used in a QMRA to calculate critical concentrations. In the case of the RRTO scenario for this study, the critical concentration of interest was a concentration of SARS-CoV-2 virus (viral particles/cm^2) on contaminated surfaces in the workplace. These steps are visually summarized in Figure 1.

The pathogen of interest was SARS-CoV-2 since this was used in a previous RRTO survey to inform estimated infection risks from contaminated surfaces (Wilson et al. 2022b). While fomites do not pose the greatest transmission risk for SARS-CoV-2 (Jones 2020; Centers for Disease Control and Prevention 2021; Miller et al. 2021; Pitol and Julian 2021; Wilson et al. 2021a, 2021b), COVID-19 transmission via fomites (hand-to-contaminated surface contact followed by hand-to-mouth contact) has been documented (Xie et al. 2020) with potential for transmission through contact with the eyes (Eriksen et al. 2021) and nose (Ahn et al. 2021) and has spurred recent increases in cleaning and disinfection exposure (Kuehn 2020; Wilson et al. 2023a). Other pathogens could be substituted to investigate how specific pathogens or their associated health outcomes drive RRTO indifference points and critical concentrations.

Risk-risk tradeoff scenario

In RRTO scenarios, participants are presented with baseline risks (probabilities of the competing outcomes), usually associated with a geographical area (Nielsen et al. 2019) or place (e.g., a given hospital facility (Wilson et al. 2022b)). The specific risk values and data used in this example come from a study of UK students for a different contextual RRTO scenario. These data were used to inform simulated indifference points given the lack of data for occupational health RRTO that could inform a more representative distribution of indifference points.

The data used to inform simulated RRTO survey data originated from a survey that asked participants to imagine living in an area that posed road accident injuries and the competing risks of these outcomes in other areas: risks (probabilities) of non-fatal injuries (non-serious *vs.* serious) and fatal injuries (Nielsen et al. 2019), with more details described in the following section. Potential responses to a survey were simulated in which respondents would hypothetically asked to imagine working in a healthcare environment with given baseline risks (probability of occupational

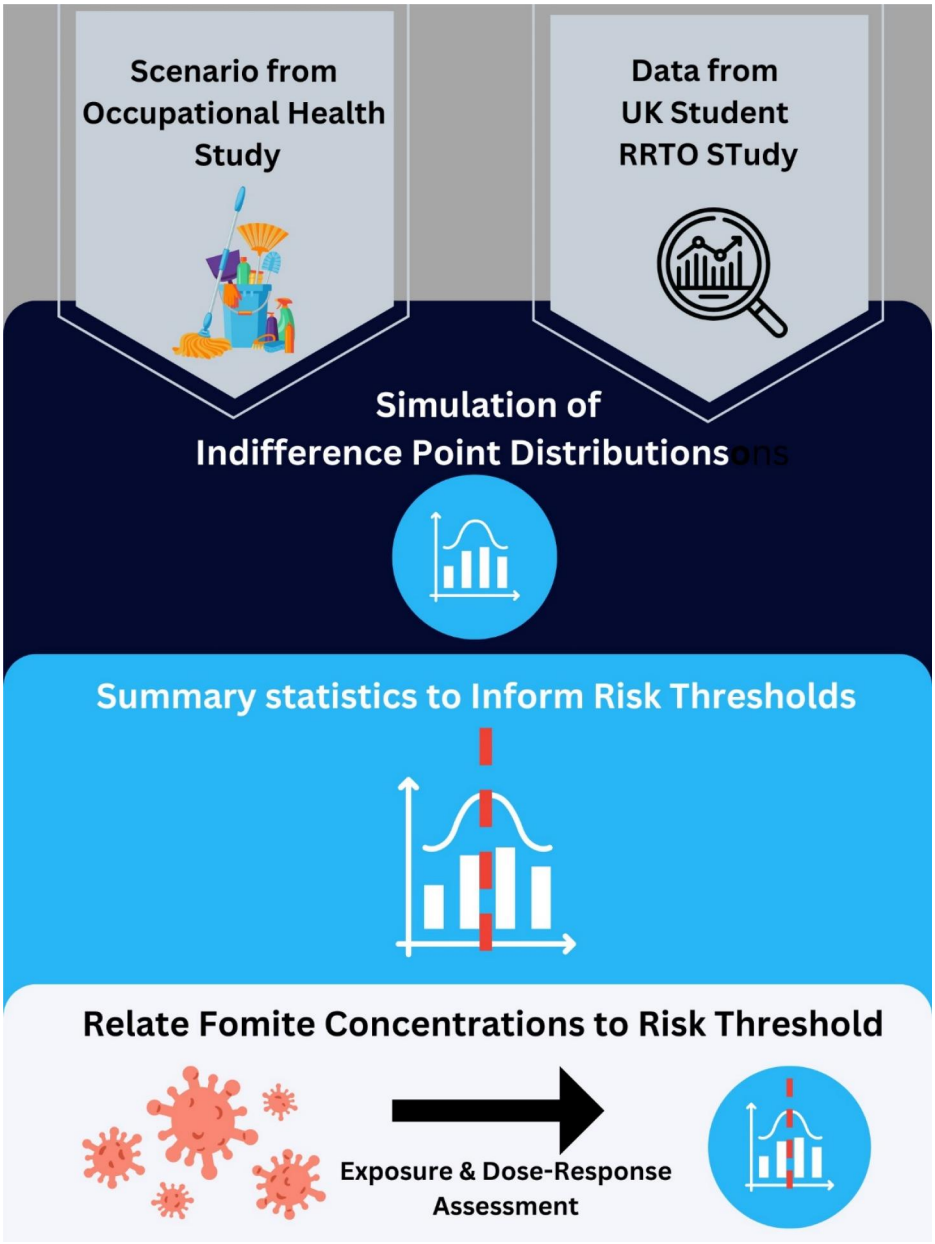

Figure 1. Study flow. This shows the use of an occupational health scenario and data from a prior RRTO study to inform the simulation of indifference points, the calculation of summary statistics with simulated indifference points to generate thresholds, and the use of exposure assessment and dose-response assessment to determine the viral exposure levels necessary to yield determined risk target.

infection and probability of occupational asthma) and presented with three options: (1) choosing another healthcare work environment that increases the risk of occupational infection risk while maintaining a risk of occupational asthma; (2) choosing another healthcare environment that increases the risk of occupational asthma while maintaining a risk of occupational infection; and (3) indicating that they are equally happy with either option (i.e., working in either healthcare environment). If they choose option 1 or 2, they are then asked how much risk of occupational asthma onset or infection they would be willing to accept in one healthcare environment to maintain their risk in the other outcome in that same work location before deciding to choose the alternative option (working at the other healthcare environment). If none of these risk options were high enough, a participant could indicate the risk they would be willing to take on before switching healthcare work environments (Table 2).

The RRTO survey data used to simulate a distribution of indifference points is similar to the hypothetical scenario in the following ways. (1) Participants were presented with two competing outcomes and had to choose between an increase in one outcome or

Table 2. Example of indifference points in risk-risk tradeoff (RRTO) survey.[a]

Healthcare Environment 1		Healthcare Environment 2	
Occupational asthma from increased cleaning and disinfection	5,005 in 100,000	Occupational asthma from increased cleaning and disinfection	5,000 in 100,000
Infection from contaminated surface	600 in 100,000	Infection from contaminated surface	605 in 100,000
Indifference point choices (risk of occupational asthma), where one option is selected with a check mark	• 5,005 in 100,000 (original choice) • 5,355 in 100,000 • 5,730 in 100,000 • 6,561 in 100,000 • 7,511 in 100,000 • 9,201 in 100,000 • 11,272 in 100,000 • 14,776 in 100,000 • 19,368 in 100,000 • 27,164 in 100,000 • 38,099 in 100,000 • _____ in 100,000	Indifference point choices (risk of infection from contaminated surfaces), where one option is selected	• 605 in 100,000 (original choice) • 641 in 100,000 • 721 in 100,000 • 858 in 100,000 • 1,083 in 100,000 • 1,450 in 100,000 • 2,057 in 100,000 • 3,093 in 100,000 • 4,929 in 100,000 • 8,328 in 100,000 • 14,913 in 100,000 • _____ in 100,000

[a]Participants do not see this full table in the survey. Rather, they are presented with scenarios of competing risks and then presented with a list of indifference point choices after specifying a preference (Healthcare Environment 1 or Healthcare Environment 2). If they indicate they are happy with either option, indifference points are not presented.

the other to avoid an increase in the competing outcome. (2) Participants then chose a maximum probability of the outcome for which they are willing to increase their risk to avoid an increase in the competing outcome. The RRTO survey data are different from the hypothetical scenario in that the probabilities would likely be vastly different (i.e., microbial infection risks for our scenario would be much lower than road accident injuries) and the spatial framing is different (i.e., imagining oneself working in different healthcare environments that pose varying occupational infection or occupational asthma risks is different than imagining being in different cities with varying road accident injury rates). However, the most important similarity that makes these RRTO data useful for modeling distributions of indifference points is the fact that the indifference points reflect a probability of an outcome that one will accept to maintain risk in a competing outcome, useful for this study in setting a risk threshold in a microbial risk assessment.

Simulation data set generation & target setting

Indifference point data for three tradeoff scenarios were explored: Area 1 *vs.* Area 2, Area 1 *vs.* Area 3, and Area 2 *vs.* Area 3. Data from two scenarios that yielded similar distributions of indifference points were used to generate two different sets of simulated indifference points, which will be called "distribution 1" (using data from the "Area 1 *vs.* Area 2" scenario) and "distribution 2" (using data from the "Area 1 *vs.* Area 3" scenario). More than one distribution was used to explore how slight distribution differences may translate to risk targets and subsequent critical concentration differences.

Lognormal, Weibull, Exponential, and Gamma distributions were fit to each of two data sets, separately, using the "fitdist" function from the *fitdistrplus* package in R (Delignette-Muller and Dutang 2015). These candidate distributions were chosen based on a visual inspection of the indifference points and literature describing the right-skewness anticipated for acceptable risks since people tend to be risk-averse as opposed to being risk-seeking (Bougherara et al. 2021). To identify a superior distribution, distribution fits were visually compared over histograms of the data; goodness-of-fit statistics for Kolmogorov-Smirnov, Cramer-von Mises, and Anderson-Darling tests were compared (where a smaller statistic is favorable); and Akaike's Information Criterion (AIC) and Bayesian Information Criterion (BIC) were compared (where smaller AICs and BICs are favorable).

The superior distributions for each of the three data sets were used to generate 10,000 indifference points (total of 20,000 points, 10,000 points per distribution), right-truncated at 1 since probabilities cannot exceed 1. Within the code, a seed was set to ensure the same 10,000 points were selected per run of the model to make the results replicable for those running the code. The 1st and 5th percentiles, median, and mean of these randomly generated points were calculated to inform acceptable risk targets. Exposure and dose-response models were then run to estimate 10,000 infection risks given 10,000 different potential microbial concentrations on surfaces, incorporating variability and uncertainty in exposure factors. For a set of 10,000 infection risks, the smallest concentration that yielded a risk below the risk threshold was identified. This was then done 50,000 times (50,000 sets of 10,000 infection risk data points) to yield 50,000 critical concentrations per risk threshold. The mean

critical concentration per risk threshold was calculated. An example of one set of 10,000 infection risks and the identification of the critical concentration can be seen in Figure 2.

Exposure and dose-response models

The exposure scenario of interest for the RRTO scenario is that of contact with a contaminated surface with subsequent hand contact with the face. Two ways in which fomite transmission has been explored in QMRA include risks from a single fomite touch (Ryan et al. 2014; Wilson et al. 2018, 2021b) and risks throughout a longer exposure period, such as a day or work shift (Beamer et al. 2015; Contreras et al. 2020; King et al. 2022). These two approaches were explored to investigate how exposure scenarios drive differences in a critical concentration that meets a given risk target.

Single fomite touch

A single fomite touch model using equations originally informed by Julian et al. (2009) was used to estimate the dose from a single hand-to-surface contact followed by a hand-to-face (mucosa of the mouth, eyes, or nose) contact. To calculate the concentration of the pathogen on the hand (C_{hand}, viral particles/cm^2 of skin) following a single fomite touch, Equation 1 was used to account for fomite-to-hand transfer efficiency:

$$C_{hand} = C_{surface} TE_{FH} S_H \quad (1)$$

where fomite-to-hand transfer efficiency is TE_{FH} (unitless fraction), the fraction of the hand used for a hand-to-fomite contact is S_H (unitless fraction), and the concentration of the pathogen on the surface is $C_{surface}$ (viral particles/cm^2). Because this contact is assumed to occur on the scale of seconds to microseconds (with a transfer efficiency for a single non-prolonged touch), time is not included as a parameter.

For pathogen concentrations on the surface, a wide distribution was used for $\log_{10}$ concentration (Uniform, min = −5, max = 5) to evaluate which concentrations yielded risks above set thresholds. The range of this distribution was informed by iterative runs evaluating a $\log_{10}$ range of concentrations that would yield risks below and above the defined risk thresholds. Surface-to-hand transfer efficiency (TE_{HS})

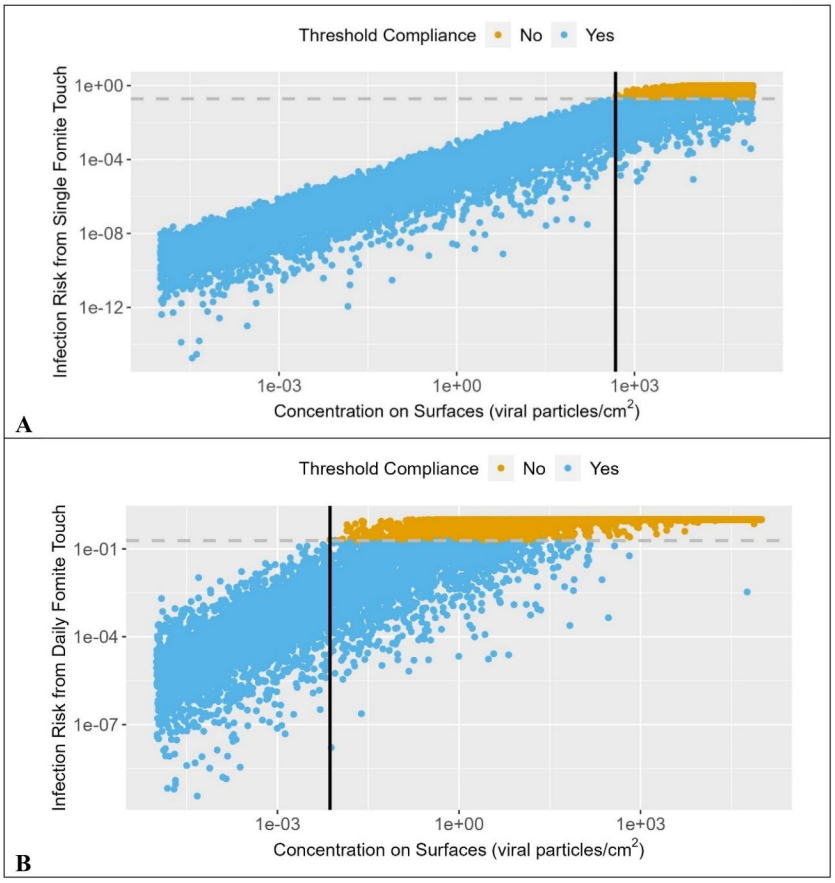

Figure 2. Example of one set of 10,000 infection risks to identify a critical concentration given a specific risk threshold (in this case, 0.19 probability of infection) for (A) single fomite exposure and (B) daily fomite exposure.

was informed by parameters from a Beta distribution fit to transfer efficiencies for enveloped virus from Anderson and Boehm (2021). Fraction of the hand used for the hand-to-fomite contact (S_H) was informed by AuYeung et al. (2008), using the minimum of the front partial fingers divided by 5 (0.04/5 = 0.008, capturing the size of a fingertip) and the maximum of the full front palm with fingers configuration (0.25).

To then calculate the number of viral particles ingested during a hand-to-mouth contact (*Dose*, number of viral particles), Equation 2 was used to account for hand-to-mouth transfer efficiency:

$$Dose = C_{hand} A_{hand} TE_{HF} S_F \quad (2)$$

where hand-to-mouth transfer efficiency is (TE_{HM} (unitless fraction), the fraction of the hand used for a hand-to-mouth contact is S_M, (unitless fraction), and total hand surface area is A_{hand} (cm^2)) of a single hand.

Total hand surface area (A_{hand}) was informed by the U.S. Exposure Factors Handbook (*U.S. Environmental Protection Agency Exposure Factors Handbook* 2011), which has been utilized to inform total hand surface area parameters in other QMRA models for adults in the general U.S. population (Beamer et al. 2015). Distribution minimum and maximum used by Beamer et al. (2015) for combined hand surface area was divided by two to represent surface area of a single hand. Transfer efficiency for hand-to-facial mucosal membrane contact (TE_{HF}) was informed by viral transfer efficiency data from Rusin et al. (2002), using a mean from Rusin et al. (2002) and a standard deviation for this same data later reported by Abney et al. (2022), as it was missing from the original data reported by Rusin et al. (2002). Fraction of the hand used for hand-to-face contact (S_F) was informed by AuYeung et al. (2008), assuming a single finger touch (AuYeung et al. 2008), where minimum and maximum fractions for the front partial fingers were divided by 5 to estimate fraction of hand surface area used for a single fingertip. Information for all parameters can be found in Table 3.

Daily fomite touch

A model developed by Beamer et al. (2015) and utilized by Contreras et al. (2020) was utilized to estimate a dose from an entire day of hand-to-surface and hand-to-mouth, -eyes, and -nose contacts (assumed duration of 12 hr corresponding to a common duration of a healthcare worker's shift) (Equation 3; Stimpfel and Aiken 2013). The Beamer et al. (2015) model included similar parameters as that for the single fomite touch with additional parameters including hand-to-surface transfer efficiency, surface area of a facial mucosal membrane touch ($A_{mouth}, A_{eyes}, A_{nose}$), inactivation of virus over time (λ, min^{-1}), and the frequency of hand-to-fomite touches (H_{surf}) and hand-to-face touches ($H_{mouth}, H_{eyes}, H_{nose}$, contacts/min). A steady state concentration on the hand is first estimated with Equation 3a, where gains to the hand result from transfer of virus from the fomite to the hand during contacts and losses from the hand result from inactivation of virus on the hands, transfer of virus from the hands during fomite and face contacts.

$$C_{hand} = \frac{H_{surf} TE_{SH} C_{surface} S_H}{\lambda + (H_{surf} TE_{HS} S_H) + TE_{HF}(H_{mouth}(A_{mouth}/A_{hand}) + H_{eyes}(A_{eyes}/A_{hand}) + H_{nose}(A_{nose}/A_{hand}))} \quad (3a)$$

For ease of reading, the fraction of the hand used for the contact can be simplified (e.g., $S_M = A_{mouth}/A_{hand}$) (Equation 3b). However, Equation 3a is provided since parameters were informed for specific surface areas of the hand used for the mouth, eyes, and nose contacts (Table 3).

$$C_{hand} = \frac{H_{surf} TE_{SH} C_{surface} S_H}{\lambda + (H_{surf} TE_{HS} S_H) + TE_{HF}(H_{mouth}(S_{mouth}) + H_{eyes}(S_{eyes}) + H_{nose}(s_{nose}))} \quad (3b)$$

Table 3. Model parameters.

Parameter		Variable	Units	Distribution/Point Value	Source
Single-Touch and Daily Dose Models	Fraction of total hand surface area for surface-to-hand or hand-to-surface contact	S_H	Unitless (fraction of cm^2/cm^2)	Uniform (min = 0.008, max = 0.25)	(AuYeung et al. 2008)
	Fraction of total hand surface area for hand-to-face contact	S_F	Unitless (fraction of cm^2/cm^2)	Uniform (min = 0.008, max = 0.012)	(AuYeung et al. 2008)
	Total hand surface area	A_{hand}	cm^2	Uniform (min = 445, 535)	(U.S. Environmental Protection Agency Exposure Factors Handbook 2011; Beamer et al. 2015)
	Transfer efficiency for fomite-to-hand contact	TE_{FH}	Unitless (fraction of $\frac{organisms/cm^2}{organisms/cm^2}$)	Beta ($\alpha = 0.64$, $\beta = 3.1$)	(Anderson and Boehm 2021)
	Transfer efficiency for hand-to-facial mucosal membrane contact (mouth, eyes, nose)	TE_{HF}	Unitless (fraction of $\frac{organisms/cm^2}{organisms/cm^2}$)	Normal ($\mu = 0.3390$, $\sigma = 0.1318$), range 0-1	(Rusin et al. 2002; Abney et al. 2022)
	Log_{10} pathogen concentration on surface	$C_{surface}$	log_{10} organisms/cm^2	Uniform (min = −5, max = 5)	[a]
	Dose-response parameter	k	Probability of initiating infection/organism	2.46×10^{-3}	(Pitol and Julian 2021)
Daily Dose Models Only	Inactivation rate	λ	hr^{-1}	Uniform (min = 0.05, max = 0.198)	(Kwon et al. 2021)
	Transfer efficiency for hand-to-surface contact	TE_{HS}	Unitless (fraction of $\frac{organisms/cm^2}{organisms/cm^2}$)	Beta ($\alpha = 0.64$, $\beta = 3.1$)	(Anderson and Boehm 2021)
	Hand-to-surface contact rate	$H_{surface}$	Contacts/min	Lognormal (geomean = 4.1, geosd = 1.6), range 0–9.8	(Beamer et al. 2015; Contreras et al. 2020)
	Hand-to-mouth contact rate	H_{mouth}	Contacts/hr	Normal ($\mu = 2.9$, $\sigma = 2.5$), range 0-10	(Wilson et al. 2021c)
	Hand-to-eyes contact rate	H_{eyes}	Contacts/hr	Normal ($\mu = 2.4$, $\sigma = 1.9$), range 0-6	(Wilson et al. 2021c)
	Hand-to-nose contact rate	H_{nose}	Contacts/hr	Normal ($\mu = 2.5$, $\sigma = 2.2$), range 0–10.4	(Wilson et al. 2021c)
	Area of hand-to-mouth contact	A_{mouth}	cm^2	Uniform (min = 3.56, max = 6.42)	(AuYeung et al. 2008; U.S. Environmental Protection Agency Exposure Factors Handbook 2011)b
	Area of hand-to-eyes contact	A_{eyes}	cm^2	Uniform (min = 3.56, max = 6.42)	(AuYeung et al. 2008; U.S. Environmental Protection Agency Exposure Factors Handbook 2011)[b]
	Area of hand-to-nose contact	A_{nose}	cm^2	Uniform (min = 3.56, max = 6.42)	(AuYeung et al. 2008; U.S. Environmental Protection Agency Exposure Factors Handbook 2011)[b]
	Shift duration	T	hr	12	(Stimpfel and Aiken 2013)

[a]Assumed a large range in order to identify which concentrations yield acceptable risks.
[b]Min and max were informed by the smallest and largest assumed fraction of total hand surface area used multiplied by the smallest and largest total hand surface areas assumed, respectively.

A dose was then estimated based on the amount of virus transferred to facial mucosal membranes over the modeled duration (T, min) (Equation 4). The assumed duration was 12 hr, representing a 12-hr shift for a healthcare worker, informed by Stimpfel and Aiken (2013).

$$Dose = ((H_{mouth}A_{mouth}) + (H_{eyes}A_{eyes}) + (H_{nose}A_{nose}))C_{hand}TE_{HF}T \quad (4)$$

Distributions for transfer efficiency for surface contacts (TE_{SH} and TE_{HS}) distributions were informed by the Beta fit for the enveloped virus from Anderson and Boehm (2021). Transfer efficiency for hand-to-mouth, -eyes, or -nose contacts is assumed to be the same as transfer efficiency for hand-to-mouth contacts used in the single fomite model, due to lack of data describing transfer efficiencies for hand-to-nose and -eye contacts. Hand-to-surface contact rate (H_{surf}) was informed by a distribution used by Beamer et al. (2015), using a maximum informed by Contreras et al. (2020). Contact rates with the mouth, eyes, and nose were informed by Wilson et al. (2021c) using

mean, standard deviation, minimum, and 99th percentile (used to inform the maximum) contact frequencies reported for adults during non-eating behaviors to inform truncated Normal distributions. The surface area of the hand used for mouth, eye, and nose contacts was informed by information on fractions of the hand used for single fingertip contacts and the anticipated range of hand surface area: The smallest fraction of the hand used for a fingertip contact multiplied by the smallest single hand surface area to inform the minimum ($0.008 \times 445\,cm^2 = 3.56\,cm^2$) and the largest fraction of the hand used for a fingertip contact multiplied by the largest single-hand surface area to inform the maximum ($0.012 \times 535\,cm^2 = 6.42\,cm^2$). Inactivation rate ($\lambda$) was informed by the minimum and maximum half-lives listed for indoor conditions on surfaces across seasons (3.5 to 12.86 hr), assuming first-order decay to calculate decay rate (hr^{-1}) ($0.693/12.86\,hr = 0.05\,hr^{-1}$, $0.693/3.5\,hr = 0.198\,hr^{-1}$). Information for all parameters can be found in Table 3.

Estimating infection risk

Estimated doses were then related to estimated infection risks ($P_{infection}$) using an exponential dose-response curve (Equation 5), where the dose-response curve parameter, k, was informed by Watanabe et al. (2010), using an exponential model fit to a pooled data set (Data sets 1 and 2) from rSARS-CoV (DeDiego et al. 2008) and murine hepatitis virus strain 1 (MHV-1) (De Albuquerque et al. 2006) infection in mice (Watanabe et al. 2010). The k parameter represented the probability that an organism will survive and arrive at a site where an infection can be initiated. While a more updated k value was available that was informed by outbreak data (Parhizkar et al. 2022), this outbreak was likely driven by inhalation of bioaerosols and therefore likely is an overestimate for fomite-mediated risks which are generally lower and not the driver of COVID-19 outbreaks. The k value utilized here has been used in other QMRAs of COVID-19 transmission from fomites (Pitol and Julian 2021).

$$P_{infection} = 1 - e^{-k \cdot Dose} \quad (5)$$

Data from the literature was used to compare expected concentrations on surfaces to the critical concentrations to calculate what $\log_{10}$ reduction would be needed with a cleaning or disinfection protocol to achieve a critical concentration that yields the risk target. These data came from real-world measured concentrations on public surfaces, including a gym water fountain (6.78×10^{-3} gc/cm^2) (Zhang et al. 2022), an office surface (1.48×10^{-1} gc/cm^2) (Zhang et al. 2022), a classroom desk (7.95×10^{-2} gc/cm^2) (Zhang et al. 2022), a bus surface (1.68×10^{-1} gc/cm^2) (Zhang et al. 2022), a liquor store handle (102.43 gc/cm^2) (Harvey et al. 2021), and a grocery store handle (11.55 gc/cm^2) (Harvey et al. 2021). Reported units were in genome copies (gc)/cm^2, however, so a ratio of infectious viral particles: gc of 1/1,000 was assumed, in range with those assumed in other SARS-CoV-2 fomite transmission models (Harvey et al. 2021). Data from healthcare environments, specifically, exist but are in units of gc/sample (Guo et al. 2020), with uncertainties in the surface area that was swabbed. Other modeling studies have used these data with assumptions regarding potential distributions of sampled surface areas (King et al. 2022), but those assumptions are not made in this study as the goal is for simple point value comparisons for demonstration purposes.

Results

Distribution fitting and indifference point generation

For all datasets, the Lognormal distribution was identified visually as a superior fit and was superior across all goodness-of-fit tests and in comparisons of AICs and BICs (Figures S1–S3). Distribution parameters for these Lognormal distributions can be found in supplemental materials. The 1st and 5th percentiles, mean, and median per distribution can be seen in Table 4. The risk targets using the 1st and 5th percentiles were identical between indifference point distributions 1 and 2. The median and mean of indifference points were both larger for distribution 2 (Distribution 1: median – 0.10, mean – 0.11; Distribution 2: median – 0.15, mean – 0.19). Summary statistics from the simulated data were comparable to those of the original data sets (Table 4), but it should be noted that limited options were available for participants (Table 2), reflected in the original data, whereas simulated data included continuous risk values. This is addressed further in the limitations section.

Critical concentration results

Critical concentrations were greatest for single fomite contacts, and more than four orders of magnitude larger in some cases than those for the daily fomite

Table 4. Simulated risk targets for critical concentration demonstration.[a]

Indifference Point Data Source		1st Percentile	5th Percentile	Median	Mean
Distribution 1 (Area 1 vs Area 2 scenario)	Simulated	0.03	0.04	0.10	0.11
	Observed	0.05	0.06	0.09	0.12
Distribution 2 (Area 1 *vs*. Area 3 scenario)	Simulated	0.03	0.04	0.15	0.19
	Observed	0.05	0.05	0.11	0.21

[a]Indifference point distributions are points at which an individual switches from accepting a given risk in one outcome to offset the increase in another. In this case, these points represent an accepted risk of occupational infection to avoid increased risk of occupational asthma.

Table 5. Critical concentrations (viral particles/cm^2) per risk target and exposure scenario.[a]

	Daily Infection Risk Scenario		Single-Touch Infection Risk Scenario	
Risk target	Indifference Point Distribution 1	Indifference Point Distribution 2	Indifference Point Distribution 1	Indifference Point Distribution 2
1st Percentile of Indifference Points	6.8×10^{-4} viral particles/cm^2	5.8×10^{-4} viral particles/cm^2	45 viral particles/cm^2	39 viral particles/cm^2
5th Percentile of Indifference Points	9.7×10^{-4} viral particles/cm^2	9.9×10^{-4} viral particles/cm^2	65 viral particles/cm^2	66 viral particles/cm^2
Median of Indifference Points	2.4×10^{-3} viral particles/cm^2	3.7×10^{-3} viral particles/cm^2	161 viral particles/cm^2	247 viral particles/cm^2
Mean of Indifference Points	2.8×10^{-3} viral particles/cm^2	4.9×10^{-3} viral particles/cm^2	186 viral particles/cm^2	330 viral particles/cm^2

[a]Green cells indicate critical concentrations above all real-world concentration comparison points and orange indicates critical concentrations below some real-world concentration comparison points after adjusting for anticipated infectious viral particle to genome copy ratios.

contact model: 45 to 330 viral particles/cm^2 for the single fomite model and 5.8×10^{-4} to 4.9×10^{-3} viral particles/cm^2 for the daily contact model (Table 5). For both the single fomite contact and daily fomite contact models, critical concentrations that yielded risk targets informed by the 1st and 5th percentiles of individual indifference points were just under 1 $\log_{10}$ smaller than the critical concentration that yielded the risk target informed by the mean indifference point (Table 4). In comparing distributions 1 and 2, critical concentrations across risk targets were similar. For example, using a risk target of 0.11 (mean of indifference points for distribution 1) *vs*. 0.19 (mean of indifference points for distribution 2) yielded a critical concentration of 2.8×10^{-3} *vs*. 4.9×10^{-3} viral particles/cm^2, respectively, for the daily exposure and 186 *vs*. 330 viral particles/cm^2 for the single exposure scenario, respectively. Because microbial concentration data tend to be Lognormally distributed (Canales et al. 2018), these critical concentration differences between the two indifference point data sets were negligible. However, this difference could become important when dealing with more virulent pathogens.

In comparison to concentrations reported in the literature (with the assumption that there is a ratio of 1,000 gc to infectious particles), all single-touch critical concentrations were above all real-world concentration comparison points, implying that the risk targets for single-touch scenarios are already being achieved without additional cleaning or disinfection. For daily exposure critical concentrations, all critical concentrations were smaller than some concentrations reported in the literature after the ratio adjustment, such as those for the liquor store handle and the grocery store handle (Table 5). This implies that some high-touch surfaces in public environments may be posing daily exposure risks above the risk targets associated with the daily exposure critical concentrations we yield in this RRTO experiment. For example, the most conservative risk target (using the 1st percentile of indifference point distribution 1) would require a 2.2 $\log_{10}$ reduction on a liquor store handle to achieve a risk target of 0.03 for daily infection risk, assuming all other contact surfaces throughout the day had a similar viral burden. However, it should be noted that the infection risk targets informed by our simulated indifference point distributions are much larger than those typically used in QMRAs (e.g., 1/10,000 or 1/1,000,000 as comparison points for infection risks from single or daily touch scenarios) (Ryan et al. 2014; Wilson et al. 2018; Contreras et al. 2020; Wilson et al. 2021b). It is unknown whether the public's or occupational groups' acceptable risks for contact with contaminated fomites are on the order of 1/10,000 or 1/1,000,000, or if they are on the order of those in this demonstration (closer to 1/100 and 1/10, Table 4). Therefore, these results do not inform cleaning protocols but, rather, demonstrate how indifference point data could be used for such a purpose.

Discussion

To the knowledge of the authors, this study represents the first application of RRTO surveys to inform

QMRAs. This study demonstrates that utilization of RRTO methodologies previously used in behavioral, environmental, and health economics holds promise for incorporating individual and community perspectives into QMRAs, ultimately driving community-based intervention goals in public health settings. Increasing methodologies for incorporating voices in risk analysis offers opportunities to address inequities in power that have traditionally been inherent in the risk analysis process: experts making risk target choices on behalf of individuals with relatively little to no say in the microbial infection risks they accept daily.

RRTO surveys in microbial risk contexts are underutilized compared to other contexts, such as risks from cancer or transportation (McDonald et al. 2016; Nielsen et al. 2019). As RRTO methodologies are translated to study microbial risk perceptions, the opportunity for incorporating RRTO survey outputs in QMRAs, as well as increasing the diversity of voices in these surveys will increase. However, risks typically estimated by QMRAs and currently utilized thresholds (Table 1) can be as small as 1/1,000,000. Imagining risks on this level may increase the potential for heuristics and biases, making indifference points from RRTO surveys less reliable than for scenarios with larger risks (e.g., 1/100). Priming and training individuals on probabilities and risk is a successful strategy for understanding small risks (Nielsen et al. 2019). Another consideration is variability in risk acceptability based on imagining risk for oneself *vs.* for others (Lu et al. 2018; Batteux et al. 2019) or the framing of the competing risks methodologically (Holzmeister and Stefan 2021). In this scenario, the focus was on how healthcare workers would view risks or themselves, but acceptable risks may change based on considerations of occupational risks for others or healthcare-associated infections for patients. As a novel area of study, future work needs to evaluate how to incorporate multiple framings of competing risks into acceptable risk elicitation for informing risk assessment methodologies.

Limitations

While the translation of methodologies from other disciplines for eliciting acceptable risks holds promise, this study also demonstrates some challenges, including a lack of RRTO survey data for microbial risk tradeoffs. Additionally, it is possible that framing effects in RRTO surveys (Anderson et al. 2007; Nielsen et al. 2019) could influence distributions of indifference points and, subsequently, greatly impact risk targets that guide QMRA. Because the indifference points in this study are simulated, they cannot be applied directly to informing cleaning and disinfection protocols to maintain infection risks at a given acceptable level and are continuous, while survey data may give a limited set of acceptable risk options (Table 2). More real-world data are needed to inform distributions of indifference points for informing risk thresholds, which is a promising avenue of research. Both RRTO methodological advancements and large data sets from RRTO surveys are needed to increase the reliability and accessibility of indifference points for use in QMRA.

Additionally, the issue of heuristics and biases aside, critical concentrations that would likely yield extremely small risks would likely be immeasurable, necessitating a reliance on the assumed performance of interventions that could provide "log credits" toward achieving a theoretical concentration that would yield a small risk target, an approach utilized in the context of drinking water and direct potable reuse (Soller et al. 2018). This introduces an increased need for data regarding ranges of performance for a variety of controls at our disposal to decrease microbial exposures.

Conclusions

Microbial risk targets informed by both individuals' acceptable risks and framing of risk-risk tradeoffs hold promise in giving a larger voice to communities in the development of future QMRAs and subsequent policies. The reliance on expert judgment alone in risk assessment has been criticized, given that these judgments hold bias and may not reflect the values of the communities that face the risks being addressed (Resnik 2021). This study demonstrated an approach that holds promise for incorporating the community's voices into QMRA, but this demonstration was with a limited and simulated data set that does not reflect acceptable risks for our scenario of interest (infection risk in the face of cleaning and disinfection tradeoffs). More data and methodology advancement are needed to improve the reliability of risk targets gleaned from RRTO surveys for informing QMRAs. Methods by which individuals can voice their acceptable risk levels can empower communities that otherwise would be protected at risk levels defined by non-community members.

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Authors' contributions

AW conceived the project and led modeling and writing. KH and MV contributed to the intellectual development on needs for risk target advancement in QMRA and contributed to writing. JY and AA conducted literature review, created Table 1, and contributed to manuscript editing. IM and SC shared the RRTO survey data set, provided behavioral economic expertise to the development of the project, and contributed to the writing.

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Data availability statement

Data and code are available via a Creative Commons License at https://github.com/awilson12/risk_threshold_paper.

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