

# An Integrated Risk Model of a Drinking-Water–Borne Cryptosporidiosis Outbreak

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A dynamic risk model is developed to track the occurrence and evolution of a drinking-water–borne cryptosporidiosis outbreak. The model characterizes and integrates the various environmental, medical, institutional, and behavioral factors that determine outbreak development and outcome. These include contaminant delivery and detection, water treatment efficiency, the timing of interventions, and the choices that people make when confronted with a known or suspected risk. The model is used to evaluate the efficacy of alternative strategies for improving risk management during an outbreak, and to identify priorities for improvements in the public health system. Modeling results indicate that the greatest opportunity for curtailing a large outbreak is realized by minimizing delays in identifying and correcting a drinking-water problem. If these delays cannot be reduced, then the effectiveness of risk communication in preemptively reaching and persuading target populations to avoid exposure becomes important.

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**KEY WORDS:** *Cryptosporidium*; cryptosporidiosis; risk model; drinking water; integrated assessment; risk communication

## 1. INTRODUCTION

While progress continues to be made in the United States and most developed countries in providing a safe and reliable water supply, a number of problems pose ongoing threats to public health. Among these are protozoan pathogens, such as *Cryptosporidium parvum* and *Giardia lamblia*. These pathogens are difficult to detect and remove from water, leading to periodic outbreaks of gastrointestinal illnesses. In response, the water supply industry, as well as regulatory and public health agencies, have undertaken extensive efforts to understand and man-

age the occurrence and impact of these pathogens in drinking water.

Because of imperfect monitoring and treatment, drinking water utilities have adopted a multibarrier approach to risk minimization, involving watershed protection, water treatment, and public education/notification. Public education is considered to be a virtual barrier to waterborne epidemics, reducing exposure to contaminated water by encouraging consumers to adopt averting behaviors during water quality emergencies.

In this study, the factors affecting the severity of waterborne cryptosporidiosis outbreak are examined using an integrated risk model<sup>4</sup> that incorporates the

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<sup>4</sup> Creation of the model was originally motivated by a project designed to identify those aspects of waterborne cryptosporidiosis most necessary for communication by water utilities to the public as part of mandated data collection/reporting, whether under the U.S. Environmental Protection Agency (EPA) Information Collection Rule,<sup>(1)</sup> for Consumer Confidence Reports,<sup>(2)</sup> or as part of emergency communications in the case of an outbreak or treatment failure.

following factors: (1) environmental and ecological processes that generate and disperse microbial pathogens in source waters, (2) engineering processes that affect the chances of removing pathogens from the water, (3) monitoring activities, (4) population health status and vulnerability to infection, (5) medical and institutional factors, (6) communication of risk messages, and (7) consumers' cognitive processes and behavioral responses. The risk model links these factors in realistic sequences with plausibly timed feedbacks. The model is unusual in its full integration of natural and social science factors. After briefly reviewing background material concerning the issues and parameters of drinking-water-borne cryptosporidiosis transmission (Section 1), the integrated risk model is presented (Section 2), followed by its application to evaluating strategies for epidemic prevention (Section 3).

### 1.1. Cryptosporidiosis

Cryptosporidiosis is an acute gastrointestinal disease, caused in humans by the single-celled intracellular protozoan parasite *Cryptosporidium parvum*.<sup>5</sup> The illness is self-limiting in immunocompetent individuals, with symptoms of fulminating, watery diarrhea, cramping, vomiting, and fever, usually clearing within 1 to 2 weeks. In immunocompromised patients, however, cryptosporidiosis is not self-limiting; it often becomes chronic and debilitating, sometimes even fatal.

Most *Cryptosporidium* infections are mild or asymptomatic and do not result in cryptosporidiosis.

### 1.2. Endemic Levels

Cryptosporidiosis became reportable nationally to the Centers for Disease Control and Prevention (CDC) in 1996. Incidence is widespread, with 90% of the states reporting cases in 1997. Between two and three thousand cases of cryptosporidiosis were reported in the United States each year from 1995 through 1997, though none of these cases were transmitted via drinking water. The most commonly identified mode of transmission was swimming pool fecal accidents.<sup>(3)</sup>

It should be noted, however, that there is a severe underreporting problem with cryptosporidiosis.<sup>(4,5)</sup> Additionally, medical practitioners are generally unfamiliar with its diagnosis.<sup>(6)</sup> Not all stool samples from infected patients contain oocysts

(which are necessary for positive diagnosis); and it is difficult to identify and enumerate oocysts even when they are present.<sup>(7)</sup> Typically, only the most severe cases become part of the medical record.

Perz, Ennever, and Le Balncq<sup>(8)</sup> estimated the conditional probabilities of a symptomatic case of cryptosporidiosis being reported, for adults and for children, with and without AIDS. Applying their correction factors, 2,400 reported cryptosporidiosis cases implies between 330,000 and 880,000 actual cases. Other authors have estimated the endemic rate of cryptosporidiosis in industrialized countries as 1% to 2%<sup>(9)</sup> and 0.2%,<sup>(10)</sup> which would put the annual incidence in the United States in the 0.5 to 5 million range. Coprologic and serologic prevalence surveys produce even higher estimates.<sup>(9)</sup>

### 1.3. Population Immunity Level (Herd Immunity)

"Herd immunity" is the medical term for a population's resistance to a pathogen, resulting from immunity developed during previous infection of a portion of the population. Previous exposure (even repeated exposures) to *Cryptosporidium* confers at best an incomplete resistance to infection, increasing the infective dose<sup>6</sup> 20- to 60-fold.<sup>(11,12)</sup>

### 1.4. Sources and Exposure Pathways

*C. parvum* is dispersed in the form of an environmentally resistant oocyst, with an effective diameter of 4 or 5 $\mu$ , a slightly negative charge, and a density between 1 and 1.06 gm/cm<sup>3</sup>.<sup>(13)</sup> Oocysts are excreted in large numbers in the feces of infected warm-blooded animals.

Many animal hosts for this parasite have been identified, with the most common being neonates of cattle and sheep. About 30% of U.S. beef calves (with and without diarrhea) were found to be infected with *Cryptosporidium* in 1993.<sup>(14)</sup> The probability of detecting oocysts on a farm increases with the number of calves sampled and herd size. In farms with 100 to 200 cows, that probability approaches 1 as the number of calves sampled exceeds 15.<sup>(15)</sup>

Manure entrained in farm runoff can be washed into surface and groundwater, carrying the oocysts into drinking-water sources. Outbreaks of water-

<sup>5</sup> Other species of this genus have also been implicated in human cryptosporidiosis, but less frequently than *C. parvum*.

<sup>6</sup> The authors of the dose-response study distinguish between "infection," passing oocysts in stool; and "disease," having two or more enteric symptoms. The "infective dose" refers to infection only. The "morbidity ratio" (i.e., proportion infected) refers to the disease state.

borne cryptosporidiosis, including the massive 1993 Milwaukee outbreak, have been attributed (without conclusive evidence, as Walker *et al.*<sup>(13)</sup> point out) to contamination by bovine manure. Point-source waste discharges from slaughterhouses and dairies can also be sources of oocysts.

In a primarily forested and agricultural watershed in Washington State, Hansen and Ongerth<sup>(16)</sup> observed a proportional relationship between flow rate and oocyst concentration, suggesting that soils contaminated by animal wastes are reservoirs of oocysts. Studies in larger watersheds have failed to demonstrate this correlation, implying that, in watersheds with both point and nonpoint oocyst sources, the nonpoint-source oocyst signature may be obscured.

Another widespread source of *Cryptosporidium* oocysts is treated human sewage, discharged into bodies of water eventually used for drinking water. Oocysts are *not* completely removed by conventional wastewater treatment<sup>(17–20)</sup> or by most conventional drinking-water treatments.<sup>(21)</sup> More recent analyses point to treated sewage effluent, and not livestock manure, as the major source of the Milwaukee outbreak.<sup>(20,22,23)</sup>

Large outbreaks of cryptosporidiosis are not always due to pulses in source water oocyst contamination. Sometimes failures can be traced to drinking-water treatment processes, such as inadequate filter curing (Milwaukee),<sup>(24)</sup> inadequate coagulation and flocculation<sup>7</sup> (Milwaukee), placing filters off-line and on-line without backwashing<sup>8</sup> (Carrollton, Georgia),<sup>(26)</sup> and recycling backwash waters<sup>9</sup> (Milwaukee).

### 1.5. Drinking-Water–Borne transmission

Oocysts in water samples are severely underreported. Existing sample concentration analysis and immunofluorescent techniques have low recovery rates,<sup>10</sup> generally in the 5% to 25% range. Other serious problems include an inability to distinguish between live and dead oocysts, poor reproducibility,

<sup>7</sup> Coagulation and flocculation are the addition of chemicals to water, followed by agitation, to increase the size of small particles so that they will be more readily removed by settling or filtration.

<sup>8</sup> Backwashing cleans filters by flushing them in the opposite direction of the normal flow, in order to clear out captured particulate matter. Up to 10,000 oocysts/100 L were detected in the backwash waters during an outbreak in the United Kingdom.<sup>(19,25)</sup>

<sup>9</sup> Many water treatment plants are designed to send backwash water back into the drinking-water treatment process after coagulation and/or settling.

<sup>10</sup> A recovery rate compares a measurement result with the actual value of the sample contents. It is determined from tests on “spiked” samples of known concentration.

**Table I.** Detection of *Cryptosporidium* Oocysts in Finished Drinking-Water Samples in the United States

Positive samples (percent)	Number of treatment plants sampled	Number of samples	Reference
13.4	72	262	29
27	66	83	30
17	1	26	31
7 <sup>a</sup>	33	55	32
7.1	130	1,237	33
8(13 <sup>a</sup> )	1	24	17

<sup>a</sup> Presumed positive samples: oocysts seen, but sporozoites (internal contents of oocysts) not seen in microscopic preparations.

and cross-reactivity with nonpathogenic strains of *Cryptosporidium*.<sup>(4,5)</sup>

Keeping in mind these problems, it is remarkable that *Cryptosporidium* oocysts have been detected in 65% to 97% of surface waters tested throughout the United States.<sup>(27,28)</sup> Moreover, there is considerable circumstantial evidence of low-level (nonepidemic) transmission of *Cryptosporidium* through drinking water. Low concentrations of oocysts have been detected in finished drinking water (Table I), and *C. parvum* has been implicated in several large drinking-water–borne outbreaks in the United States, since the first reported one in 1984 (Table II).

The Milwaukee outbreak<sup>(35)</sup> increased awareness that existing federal turbidity standards did not ensure protection against *Cryptosporidium*. Many utilities voluntarily adopted more stringent turbidity goals. Perhaps because of improved operating procedures, or perhaps because of difficulties in detecting cryptosporidiosis outbreaks,<sup>(36)</sup> <sup>11</sup> there have been no major drinking-water–borne outbreaks reported in the United States since 1994<sup>(3)</sup> <sup>12</sup> (see Fig. 1). Although a few years without detected outbreaks do not substantiate a trend, there is reason to believe that the water utility activities—including those of the American Water Works Association (AWWA)/EPA sponsored Partnership for Safe Water<sup>(38)</sup>—have contributed to a decline in outbreaks.

### 1.6. Drinking-Water Treatment

In two surveys of U.S. drinking water, 14% to 33% of samples tested positive for oocysts, albeit

<sup>11</sup> For example, Okun, Craun, Edzwald, Gilbert, and Rose<sup>(37)</sup> estimated that, in New York City, 1,000 excess cases of cryptosporidiosis could easily be absorbed by the health care system without triggering an alert, given the background incidence of diarrhea.

<sup>12</sup> Not counting single-house or single-tap incidents with few victims.

**Table II.** Drinking-Water–Borne *Cryptosporidium* Outbreaks in the United States from 1984 to 1996

Year	Location	Cases	Water source	Water treatment	Problem	Monitoring results
1984	Braun Station, TX	2,000	Well	Chlorinated	Contaminated with sewage	No coliforms detected
1987	Carrollton, GA	13,000	River	Conventional coagulation, flocculation, sedimentation, filtration, and chlorination	Mixers down, improper flocculation, filters brought on-line without backwashing	No coliforms detected, oocysts detected, source of oocyst contamination not identified
1992	Jackson County, OR	3,000	Springs and river	Chlorination only and package filtration plant	Poor filtration and high turbidities	No coliforms detected
1992	Berks County, PA (picnic area)	551	Well	Chlorination	Influenced by surface water	
1993	Milwaukee, WI	403,000	Lake	Conventional coagulation, flocculation, sedimentation, filtration, and chlorination	Loss of coagulation process, increase in turbidity, recycling backwashing	No coliforms detected, oocysts detected; source of oocyst contamination not identified
1993	Cook County, MN	27	Lake	Pressure filtered and chlorinated	Backflow from toilet and septic tank drainage	
1994	Clark County, NV	103 HIV+ and AIDS patients	Lake	Conventional coagulation, flocculation, sedimentation, filtration, and chlorination	Recycling backwash	No coliforms detected, oocysts detected in source, backwash, and treated water after outbreak during more intensive monitoring
1994	College Place, WA	134	Well	Untreated	Contaminated with irrigation water	Oocysts detected; source of oocyst contamination not identified

Note: Incidents involving a single tap or home are not included in the table. Sources: Rose *et al.*<sup>(4)</sup> and Craun, Hubbs, Frost, Calderon, and Via.<sup>(34)</sup>

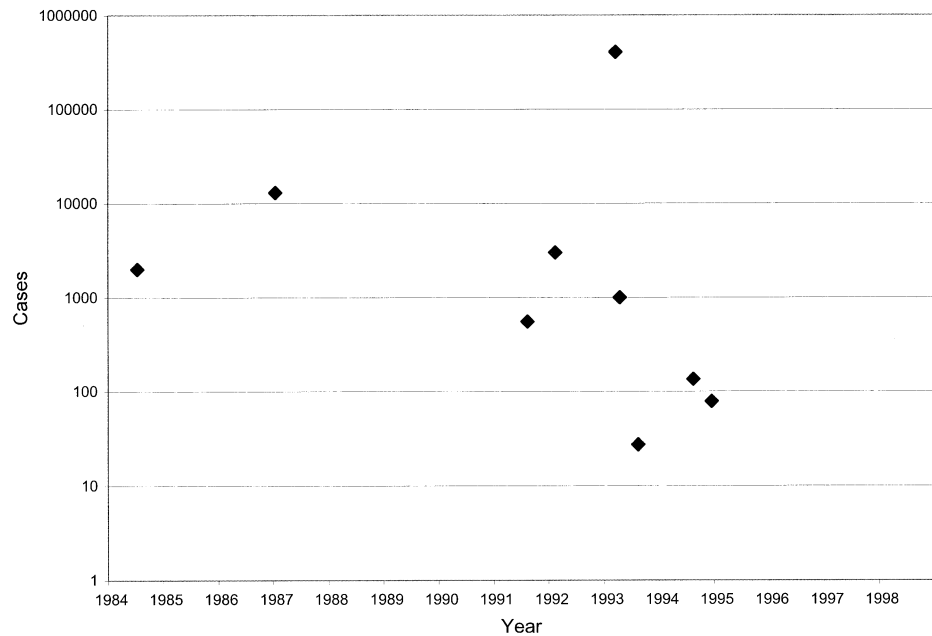
at low levels.<sup>(4)</sup> *Cryptosporidium* oocysts are quite resistant to the disinfectants typically used in water treatment.<sup>(28)</sup> As a result, the most important process for oocyst removal has been filtration, especially optimized filtration, preceded by flocculation and sedimentation. Ozonation is more effective than chlorination in inactivating oocysts,<sup>(4)</sup> but small concentrations of oocysts are found even in water that has been subjected to advanced treatment processes.<sup>(19,39)</sup> That said, overall health risk is thought to depend more on the frequency of failure of advanced treatment processes than on their typical performance.<sup>(40)</sup>

### 1.7. Epidemiological Detection/Attribution

The major cryptosporidiosis outbreaks involving treated public drinking water in the United States

have all had long lag times between the contaminating events and recognizing the ensuing epidemic. The delays have lasted from two weeks to a year.<sup>(7,23,24,35,41,42)</sup> In the 1994 Las Vegas (Clark County) outbreak, the cause wasn't discovered until weeks after the epidemic had peaked.<sup>(18)</sup> No boil-water advisory was ever issued. The outbreak lasted approximately 7 months, and people continued to become infected as long as 14 weeks after the first suspicion that an outbreak had occurred.<sup>(42)</sup> Moreover, Nevada was one of the few states where cryptosporidiosis was already reportable at that time; otherwise, the outbreak might not have been detected at all. Although the reporting requirement produced records that later allowed reconstruction of the outbreak, it did not provide timely enough feedback to stop it.

In the 1993 Milwaukee outbreak, the waterborne nature and the etiologic agent were not recog-



**Fig. 1.** Cases of waterborne cryptosporidiosis reported in the United States (after Craun *et al.*,<sup>(34)</sup> Rose,<sup>(19)</sup> and Levy *et al.*<sup>(3)</sup>).

nized until at least 2 to 3 weeks after the onset. One analysis estimated that Milwaukee was already experiencing waterborne cryptosporidiosis for a year prior to detecting the epidemic.<sup>(23)</sup> Rather than arising from formal procedures of water-quality monitoring and disease surveillance, institutional awareness of the Milwaukee outbreak developed because a pharmacist alerted the health department that his store had experienced a run on antidiarrheal drugs. That suspicion was then reinforced by media reports of absenteeism among hospital employees, students, and schoolteachers, as well as increased emergency room visits for diarrheal illness.<sup>(42,43)</sup>

## 2. INTEGRATED RISK MODEL FOR DRINKING-WATER-BORNE *CRYPTOSPORIDIUM* EXPOSURE

### 2.1. The Integrated Risk Model as an Influence Diagram

Although various representations of expert knowledge are possible, we have chosen to use influence diagrams.<sup>(44,45)</sup> Influence diagrams are directed graphs, whose nodes reflect variables determining the overall risk. Two nodes are linked when the value of the variable in one node depends on the value of the variable in the other. The influence diagram representation was chosen because it allows the expression of diverse variables and probabilistic relationships (reflecting its Bayesian roots), needed for problems like microbial

contamination of water, and because it permits sophisticated calculations while still presenting a transparent graphical interface. Such integrated assessments have been used with various complex systems in which multiple factors determine the magnitude of risks and the effectiveness of control strategies.<sup>(46,47)</sup>

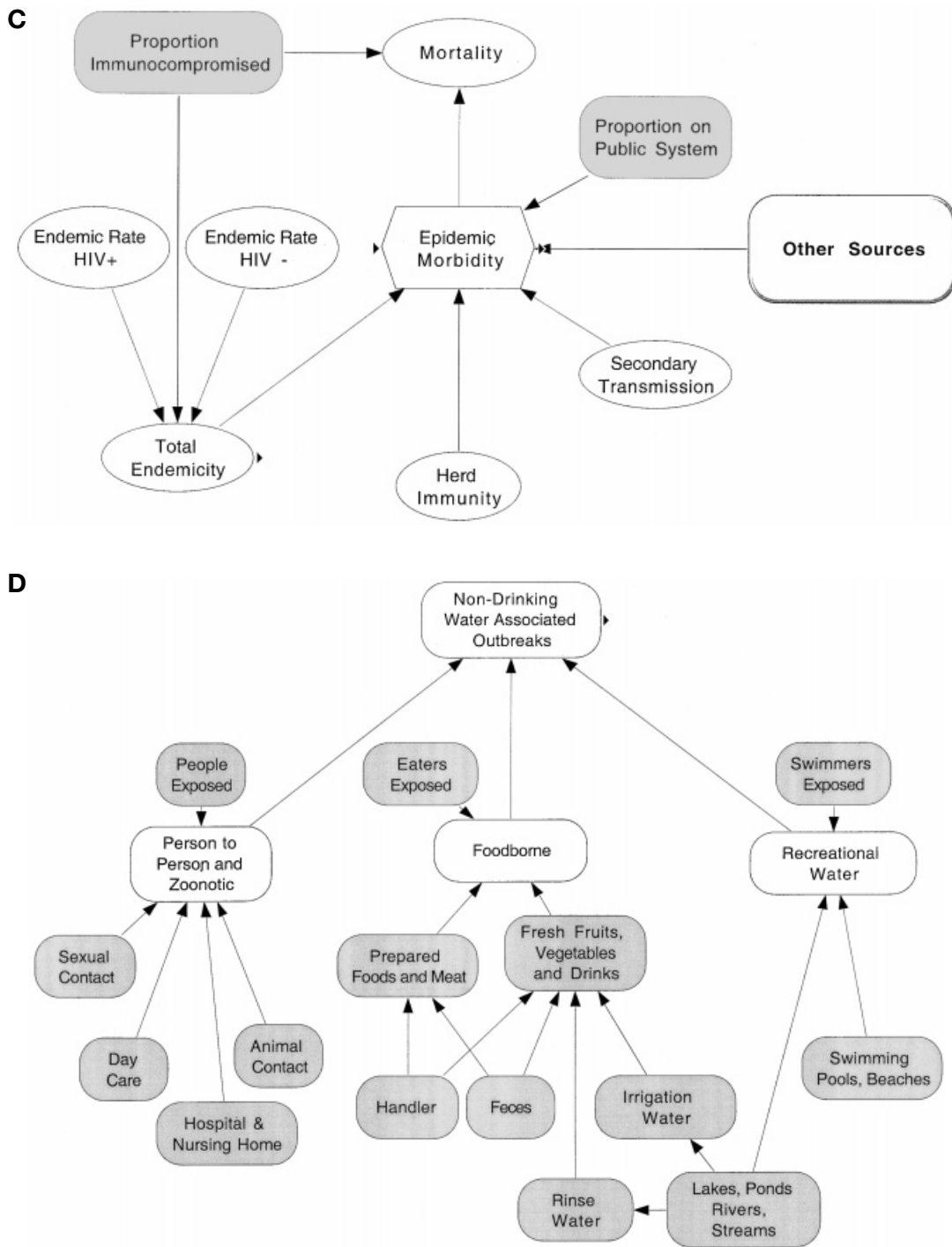
The risk model is called an “expert model,” in that it covers all relevant factors, as identified by experts.<sup>13</sup> In addition to being used for system modeling (as it is here), the expert model can also provide a standard for evaluating the “mental models” of the lay public in order to identify their informational needs.<sup>(47,48)</sup> Such communication objectives are part of the project for which this model was originally created.

### 2.2. Model Organization

Figure 2 depicts the integrated risk model for drinking-water-borne outbreaks of cryptosporidiosis in the United States. Each node in the model represents a factor affecting the magnitude of epidemic risk, and contains a mathematical expression or subroutine that relates it to the connected nodes. The ellipse-shaped nodes contain probabilistic statements; the rectangular nodes represent decision variables; and the hexagonal nodes contain objective functions. Key parameter definitions, assumed values, uncer-

<sup>13</sup> Its elements and structure were reviewed by a panel of experts in waterborne cryptosporidiosis: Jennifer Colbourne (Thames Water Authority), Charles N. Haas (Drexel University), and Joan B. Rose (University of South Florida).





**Fig. 2.** Waterborne *Cryptosporidium* transmission temporal risk model: (A) Top level diagram: water utility; medical establishment; and consumer awareness, communication, and behavior. (B) Module dealing with the contamination of drinking water and the utility’s efforts to treat the water. (C) Health effects module identifies key determinants of epidemic morbidity. (D) Sources of cryptosporidiosis infection other than drinking water.

**Table III.** Key Model Input Variables

	Assumed value	Range	Distribution	Reference
Calibration parameters				
Present in finished water			If present in intake = 0, then 0 Else if utility treatment options = "none," then 1 Else if utility treatment options = "standard," then Bernoulli (0.05) Else if utility treatment options = "enhanced," then Bernoulli (0.001)	4, 19, 49
Constants				
Proportion immunocompromised	0.0076			19, 50, 51
Uncertain parameters				
Endemic rate HIV+		0.013–0.75	Lognormal(0.1, 2)	52, 53
Endemic rate HIV–		0.0032–0.070	Lognormal(0.015, 1.7)	53, 54, 55
Herd immunity		0.3–0.7	Normal(0.5, 0.07)	53, 56, 57, 58
Secondary transmission		0.04–0.1	Normal(0.07, 0.01)	59, 60, 61
Mortality			Epidemic morbidity * triangular(0.45, 0.5, 0.7) * proportion immunocompromised	19
Scenario control variables				
Consumption of treated water		0.45–0.55 <sup>a</sup> 0.01–0.05 <sup>b</sup>	If consumer awareness ≤ 1, then 1 Else beta(200, 200) with ranges indicated at left	62, 63, 64
Time to develop utility awareness (days)		1–29		
Time to switch from standard to enhanced treatment (days)		1–29		

<sup>a</sup>Typical compliance with boil-water notice.

<sup>b</sup>Nearly complete compliance.

**Table IV.** Key Awareness Variables

Variable	Range	Algorithm	Reference
Utility awareness	0 = no known or suspected problem 1 = a trigger event has occurred, health risk is indeterminate 2 = health risk is no longer suspected 3 = Level I health risk possible for immunocompromised 4 = Level II health risk possible for general population 5 = a confirmed outbreak	If health department awareness = 2, then 5 Else if average(health department awareness) > 1.25, then 4 Else if routine testing (for <i>crypto.</i> in source water) = 2 and routine testing (for <i>crypto.</i> in finished water) = 2 and trigger event = 1, then 4 Else if routine testing (for <i>crypto.</i> in finished water) = 2 and trigger event = 1, then 3 Else if trigger event = 0 and routine testing (for <i>crypto.</i> in source water) = 1, then 2 Else if routine testing (for <i>crypto.</i> in source water) = 1 or trigger event = 1, then 1 Else 0	65
Medical awareness	0 = not aware of epidemic 1 = suspicious of epidemic 2 = convinced of epidemic	If epidemic morbidity (time – 14] > 5 * total endemicity, then 2 Else if epidemic morbidity (time – 14) > 3 * total endemicity, then 1 Else 0	7
Health department awareness	0 = indicates no known or suspected problem 1 = indicates health risk strongly suspected 2 = indicates health risk confirmed	Medical awareness time (– 7)	
Consumer awareness	0 = not aware 1 = aware but confused about what to do 2 = aware and understands what to do	If tap test = 2, then 2 Else if media coverage, (time – 1 = 2), then 2 Else if media coverage ≤ 1, then 1 Else if info sources > 0.01, then 1 Else if utility communique (time – 1) ≤ 3, then 1 Else if utility communique ≤ 2 and media coverage ≤ 1, then 0	

tainty ranges, distribution types, and supporting literature citations are given in Tables III and IV.

The model follows the evolution of an epidemic over 30 days. The presumption for the simulation is that a treatment failure has occurred and infective doses of oocysts are reaching consumers. The model tracks the development of awareness of a problem, and the steps employed to combat it.

There are built-in lags representing time-dependent processes, such as how long it takes to receive or confirm lab results, the incubation period between consumption of oocysts and development of symptoms, and the time between medical confirmation and epidemiological analysis of disease occurrences. The time dimension and associated lags are crucial to assessing how interventions affect the transmission of the disease.

Figure 2A, the top-level or master diagram, references two “modules,” or groups of nodes: Contamination of Drinking Water and Health Effects. (Node and module names are highlighted in the text by underlining.) Schematics for these two modules are in Figs. 2B and 2C, respectively. The Health Effects module itself contains another module, Other Sources (Fig. 2D).

### 2.3. Model Details

Reading Fig. 2B from the left to right, the contamination event (Source of *Cryptosporidium*) determines whether *Cryptosporidium* is present in groundwater or surface water (Present in Groundwater/ Present in Surface Water). Source water contamination is tracked from intake through treatment and distribution to the tap (Present in Utility Intake, Present in Finished Water, Present at Tap). The chance of infectious doses of oocysts being present in finished water depends on the type of treatment options active at each time step (Utility Treatment Options). The Utility Treatment Options change with the level of Utility Awareness. The treatment options are: “none,” “standard,” and “enhanced.” Section 3.2 examines the impact of filtration down-time on the development of an epidemic by varying the time it takes to switch from standard to enhanced treatment during a contamination event.

Drinking water can also become contaminated after leaving the treatment plant (Distribution System Contamination). This option is included for model generality, allowing users to calibrate the model to specific outbreaks. It was inactive in the simulations of Section 3. (Such outbreak-specific nodes are shaded gray in Fig. 2.)

Analogously, groundwater is tracked from a con-

tamination event at a recharge area, through Subsurface Attenuation to Present in Private Wells. Well Vulnerability represents the fraction of the population with contaminated wells. No effective treatment for *Cryptosporidium* is expected between well and tap. The value of the variable Present in Private Wells is probabilistically related to presence in groundwater (modified by Subsurface Attenuation) and presence in surface water (modified by Well Vulnerability). The fraction of the population on publicly supplied, treated surface water is captured in the variable Water Source Type (set at 100% surface water in our simulations), which enables the separate calculation of surface and ground water contamination problems, and the eventual summation of their medical consequences in the Health Effects module.

The left half of Fig. 2A deals with institutional behaviors, such as the utility’s water-testing protocol, weekly reports from the health department, and other relevant sources of information (such as a Trigger Event, e.g., disruption in the treatment process, or heavy rains or floods). Together, these factors determine *when* the utility learns about the *Cryptosporidium* contamination, expressed as the level of Utility Awareness. The level of Utility Awareness changes over the course of a model run. Current water-testing analyses (Routine Testing Results) may take a week to complete and a second week to confirm,<sup>(4)</sup> seriously retarding Utility Awareness. However, knowledge of a Trigger Event is assumed to be available immediately.

Any increase in the level of Utility Awareness initiates Special Studies—confirmatory tests the results of which are received 10 days later. A Joint Task Force—whose suggested membership<sup>(65)</sup> consists of utility, health department, state environmental authorities, AIDS groups representatives and other concerned parties—is convened at the request of the utility or the health department.<sup>14</sup> After evaluating the Special Studies results and level of Utility Awareness, the Joint Task Force issues warnings via the media (Media Coverage). A Utility Awareness level of 4 or 5 prompts the issuance of a boil-water notice.

Consumers can passively receive information about *Cryptosporidium* risk from the media (Media Coverage) and the utility (Utility Communicate), or actively seek information from point-of-use water-quality tests (Tap Test, Well Test) or from Info

<sup>14</sup> In communities lacking this arrangement, the health department is responsible for a boil order, not the utility. The utility communicates its concerns to the health department, and the latter decides when to begin and end the boil order.

Sources (e.g., Internet web sites, telephone hot lines, or library services). The value of these variables determines Consumer Awareness for Public Systems and Consumer Awareness for Private Wells (center right, Fig. 2A).

Media Coverage has three levels: “no alert,” “background information,” and “saturation coverage” (e.g., boil-water alerts and medical updates). The level is determined by Utility Awareness and Health Department Awareness, as well as the pronouncements of the Joint Task Force. Consumer Awareness can also be affected by a Miscellaneous Announcement. This variable permits modeling cases where some person or office outside of the usual chain of communication makes a pronouncement that affects consumer behavior. The model includes a 1-day lag in Consumer Awareness development to represent information penetration through the population.

Consumers drink tap water until notified of the emergency situation, whereupon some adopt proper averting behaviors and others do not. It is assumed that about half of the consumers continue to drink contaminated water after receiving a boil-water notice in the simulations below,<sup>15</sup> based on observations of boil-water alert compliance<sup>16</sup> during previous waterborne epidemics.<sup>(60,62,63)</sup> (Later, in Section 3.2, the effect on morbidity of intensive public education that increases the level of compliance to nearly complete is investigated.)

Consumption of contaminated water leads to adverse Health Effects. The heart of the Health Effects module (Fig. 2C) is the Epidemic Morbidity calculation of cumulative morbidity ratio (the fraction of the exposed population that develops cryptosporidiosis). It is determined by the consumption of contaminated water, the endemic level in the population, the immune status of consumers (which contributes to the calculation of the endemic level, Total Endemicity), Herd Immunity, exposures to *Cryptosporidium* from Secondary Transmission, and Other Sources (Fig.

<sup>15</sup> A beta distribution with parameters  $x = 200$ ,  $y = 200$ , and range of 0.45–0.55 is used to simulate uncertainty in the fraction of consumers drinking the water.

<sup>16</sup> In an economic analysis, Kocagil *et al.*<sup>(63)</sup> assumed that after an advisory, 34% do nothing, 22% do something inappropriate, and 44% demonstrate correct averting behavior. Angulo *et al.*<sup>(62)</sup> surveyed a community after a boil-water alert and found 31% drank unboiled water after receiving the order, 1% didn't know about the order, and 10% got the order 10 days too late. Of the 226 households surveyed by Laughland *et al.*<sup>(60)</sup> after a giardiasis outbreak, 53% said they boiled drinking and cooking water once the boil-water order was given.

**Table V.** Epidemic Intensities of United States Cryptosporidiosis Outbreaks

Year	Location	Number exposed	Number infected	Proportion infected
1983	Texas	5,900	2,006	0.34
1987	Georgia	32,400	12,960	0.40
1992	Oregon	160,000	15,000	0.09
1993	Minnesota	39	27	0.69
1993	Wisconsin	1,600,000	403,000	0.25 <sup>a</sup>

Note: Data from Rose *et al.*<sup>(4)</sup> and Morris *et al.*<sup>(23)</sup>

<sup>a</sup> Other estimates for this outbreak include Griffen, Dunwoody, and Zabala: 0.39,<sup>(66)</sup> Guerrant: 0.52,<sup>(10)</sup> and Haas and Rose: 0.14.<sup>(58)</sup>

2D). These Other Sources include Person-to-Person and Zoonotic, Foodborne, and Recreational Water transmission. As can be seen from Table V, the morbidity ratio for historic outbreaks varies across them and, sometimes, across studies of the same one.

Herd Immunity is a lumped parameter, reflecting the percentage of people consuming infectious doses of oocysts who fail to develop cryptosporidiosis. It includes the partial immunity that develops from previous exposure as well as the observed dose-independent morbidity ratio<sup>17</sup> of about 50%.<sup>(58,67)</sup>

Total Endemicity, or the nonepidemic background infection level, is a weighted average of the reported endemic rates in industrialized countries for people with and without AIDS.<sup>(52,53)</sup> The user specifies the value of Proportion Immunocompromised, which can include transplant patients and persons undergoing chemotherapy, as well as those with AIDS.

Some portion of the endemic rate of cryptosporidiosis is probably due to drinking-water contamination. Recent studies have shown that between 27% and 54% of treated municipal water supplies are normally contaminated with small numbers of oocysts. The health risk associated with consumption of filtered or unfiltered public drinking water with these levels is unclear.<sup>(69)</sup> Goldstein *et al.*<sup>(42)</sup> investigated the

<sup>17</sup> A normal distribution is assumed with a mean of 0.5 and a standard deviation of 0.07. In a clinical trial on healthy adults, doses of 1,000 to 1,000,000 oocysts infected 100% of the test group, although only 30% showed cryptosporidiosis symptoms. “Infection” was defined as the excretion of oocysts in the stool (See Table VI). The median infective dose (obtained by regression) was 132 oocysts. The lowest dose tested was 30 oocysts.<sup>(67)</sup> Haas and Rose<sup>(58)</sup> interpreted these data to indicate a dose-independent morbidity ratio of approximately 0.5. Typically, one sees a dose-response function for infection rather than disease;<sup>(40,49,68)</sup> however, the present model tracks clinical disease, as subclinical infections would not become part of the medical surveillance record.

**Table VI.** Experimental Infection and Disease Rates in Healthy Volunteers Without Previous Exposure to *Cryptosporidium*

Intended dose of oocysts	Subjects excreting oocysts (percent)	Subjects with enteric symptoms <sup>a</sup> (percent)	Subjects with cryptosporidiosis <sup>b</sup> (percent)
30	20	0	0
100	37.5	37.5	37.5
300	66.7	0	0
500	83.3	50	33.3
10 <sup>3</sup> –10 <sup>6</sup>	100	71.4	28.6

Source: DuPont *et al.*<sup>(67)</sup>

<sup>a</sup> Fever, nausea, vomiting, abdominal pain or cramps, gas, tenesmus, but not diarrhea.

<sup>b</sup> Infection, diarrhea, plus one or more enteric symptom(s).

potential risk of infection and death for persons with HIV infection exposed to *Cryptosporidium* in drinking water. Their case-control study found that persons with HIV infection who drank any unboiled tap water were four times more likely to have had cryptosporidiosis than persons who drank only bottled water (odds ratio, 4.22). For persons with CD4+ cell counts less than 100 cells/mm<sup>3</sup>, the association between drinking unboiled tap water and cryptosporidiosis was even stronger (odds ratio, 13.52).

The overall rate of Secondary Transmission of cryptosporidiosis has been estimated to be 7%.<sup>(60)</sup> Secondary transmission rates are around 5% when the index case is an adult and 40% if a child.<sup>(59,61)</sup>

In two recent waterborne outbreaks in North America, the mortality rates in HIV+ patients with cryptosporidiosis ranged from 50% to 68% within 6 months of infection; 62% had cryptosporidiosis listed on their death certificates. AIDS patients with CD4+ counts below 50 are especially vulnerable. Cryptosporidiosis in these patients often involves biliary colonization and death within 1 year.<sup>(19,70)</sup> The Mortality node gives an order-of-magnitude estimate of the cumulative 1-year mortality rate. It depends on the size of the immunocompromised population.

Medical Awareness represents the state of alert of physicians in the field. It is a function of Epidemic Morbidity. Given the difficulty of identifying a waterborne outbreak against a high background of diarrheal diseases,<sup>(36,53)</sup> the model assumes that Epidemic Morbidity exceeding three times Total Endemicity triggers increased Medical Awareness. This awareness variable lags morbidity by 2 weeks (the sum of the incubation period of the disease; the time needed

to complete stool sampling and testing; and the time required to record, summarize, and report the data).

Physicians report confirmed cryptosporidiosis cases to the health department, which collects and analyzes these reports. A (rather optimistic) 1-week lag is assumed between cases reporting and completing the epidemiological study. This lag time reflects how long it takes individual disease reports—from laboratories, hospitals, and physicians—to reach the health department, get entered in a database, and be analyzed to reveal evidence of a waterborne etiology. No lag time is assumed between the development of Utility Awareness and Health Department Awareness, reflecting current response plans.

As mentioned in Section 1, a long lag time between a contaminating event and the detection of an epidemic is the norm. Section 3 illustrates how the development of Utility Awareness and the speed with which a utility corrects a treatment problem can have significant impacts on the magnitude of an epidemic.

The model is implemented in Analytica™, a software environment that facilitates uncertainty propagation.<sup>18</sup> Model parameters can be specified as probability distributions. Values from these distributions are sampled in each model run. After a user-specified number of runs is completed—500 in the examples shown in Section 3—results are reported probabilistically.

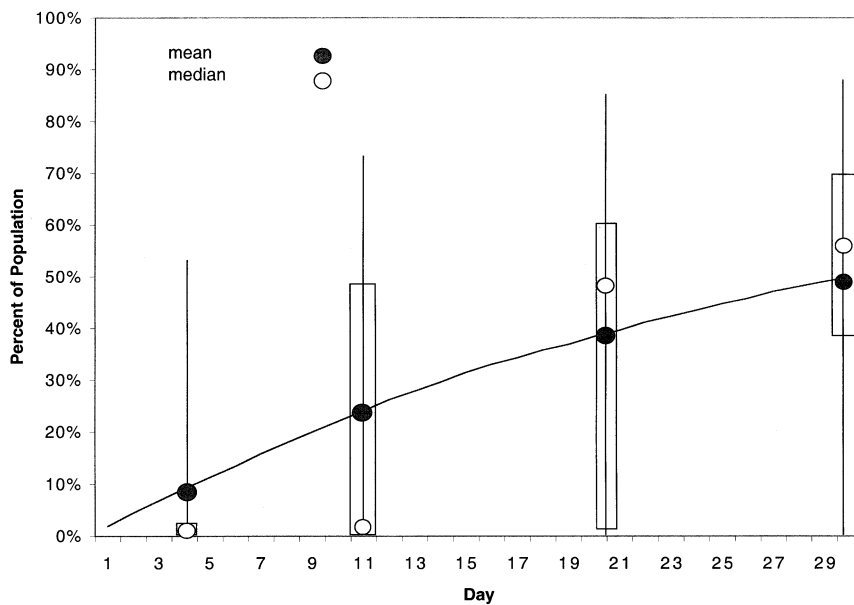
## 2.4. Unusual Features of the Model

This model differs from many epidemic risk models<sup>(67,71)</sup> in that it includes communication, psychological, and institutional variables, as well as the timing of events.

Source water is treated as either “contaminated” or “not contaminated.” This simplification is adequate for the present use, tracking the events leading to or mitigating an epidemic. A more precise measurement of oocyst concentrations, however, would be needed for applications such as evaluating watershed protection options.

The studies establishing the dose-response relationship for *Cryptosporidium* typically define morbidity as a patient passing oocysts in the stool.<sup>(12,68)</sup> Given the health effects focus of the present model, morbidity is defined as clinically defined cryptospor-

<sup>18</sup> A free demonstration copy of Analytica™ can be obtained at <http://www.lumina.com/software>. The integrated risk model is available upon request from the authors, and a PowerPoint® presentation, containing much of the documentation for the model, is on the web at: [http://hdgc.epp.cmu.edu/models-icam/cryptosporid\\_model\\_USA.htm](http://hdgc.epp.cmu.edu/models-icam/cryptosporid_model_USA.htm).



**Fig. 3.** Cumulative percent epidemic morbidity for the base-case model run: predicted cumulative epidemic morbidity for when the contamination event is not discovered. (Box plots show the probability distribution for the result, with the boxes spanning the interquartile range, and the lines the 90% confidence region.)

ridiosis (diarrhea plus one other gastrointestinal symptom), because the transitory infective condition typically does not receive medical attention and as such is not comparable with reported morbidity ratios from the historic cryptosporidiosis epidemics.

Although the model could be calibrated to specific outbreaks, the demonstrations that follow are intended to reveal how the general structure and practices of the U.S. public health resources perform in a water treatment failure situation. The following section describes applications of the model that identify key variables affecting the occurrence, timing, and magnitude of an epidemic.

### 3. RESULTS

#### 3.1. Base-Case Morbidity

An undetected epidemic is presented for the base case. In this scenario, the contamination event begins on Day 1 and continues for 30 days. The expected cumulative epidemic morbidity rate (Fig. 3) increases from the assumed endemic level of 2% to a maximum near 50% (with wide probability bands, indicated by box plots).<sup>19</sup> This result is in line with the historical epidemic intensities listed in Table V, which range from 14% to 69%.

<sup>19</sup> The incubation period of cryptosporidiosis varies from around 2 to 10 days, with the most frequently reported period being 7 days.<sup>(23,72)</sup> The figure does not show the lag time because, here, the morbidity is the fraction of the population who is infected and will become ill after the incubation period.

For most of the simulated outcomes of the 500 sample runs, there is very little morbidity through Day 11 (with a median epidemic morbidity around 2%, equal to the assumed endemic level). Morbidity rates for the remaining simulations, however, were high enough to make the *mean* epidemic morbidity at Day 11 approach 25%. The expected magnitude of the outbreak grows significantly between Day 11 and Day 21, with most simulation runs yielding 50% epidemic morbidity or more. Expected epidemic morbidity levels off between 50% and 55% by day 30.

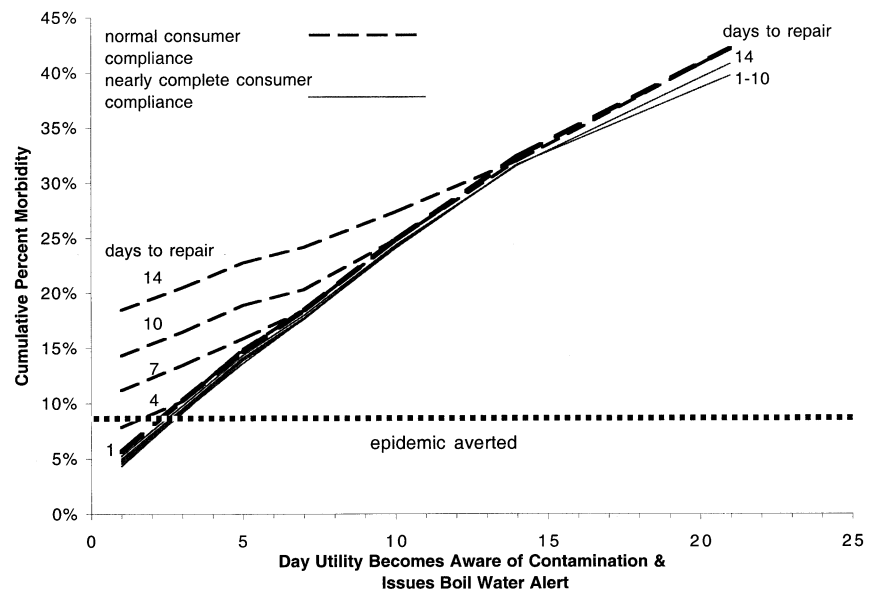
#### 3.2. Curtailing a Cryptosporidiosis Epidemic

Historic cryptosporidiosis epidemics have occurred in the United States despite modern water treatment technologies, an infrastructure of responsible parties, accepted control measures, and established lines of communication. The current model clarifies how this was possible, and permits evaluation of suggested intervention strategies.

The CDC now recommends a much more vigilant program of community health surveillance and water-quality monitoring to facilitate the early detection of emerging epidemics.<sup>(65)</sup> The potential efficacy of these efforts are explored below.

Figure 4 shows how mean epidemic morbidity (y axis) is affected by variations in several factors:

1. The time it takes for the utility to become aware that its finished water is contaminated and to issue a boil-water notice (*x* axis).



**Fig. 4.** Effects of utility awareness, utility response time, and consumer compliance level on average cumulative epidemic intensity.

2. The degree of consumer compliance with a boil-water alert (“normal” compliance<sup>20</sup> is indicated by dashed lines, and “nearly complete compliance”<sup>21</sup> by solid curves)
3. The time it takes the utility to repair the damage and stop releasing contaminated water (the two families of five curves, for repair times of 1, 4, 7, 10, and 14 days). Note: four of the five solid lines fall on top of each other and are not distinguishable in the figure.

The morbidity level defining an “epidemic” is set to four times the endemic level (horizontal broken line), consistent with the present model definition of Medical Awareness.

For normal consumer compliance (dashed lines), an epidemic is averted only if utility awareness develops on Day 1 *and* repair time does not exceed 4 days, or if awareness develops by Day 2 *and* repair time does not exceed 3 days (on average).

By contrast, when the level of consumer compliance is nearly complete, an epidemic can be avoided if the utility is informed of the breakdown by Day 2, regardless of how long it takes to fix the problem. Thus, a high level of consumer compliance would give the utility considerably more time to execute repairs and flush the system.

<sup>20</sup> From the base-case, noncompliance of  $\beta(x = 200, y = 200)$ , and range 0.45–0.55.

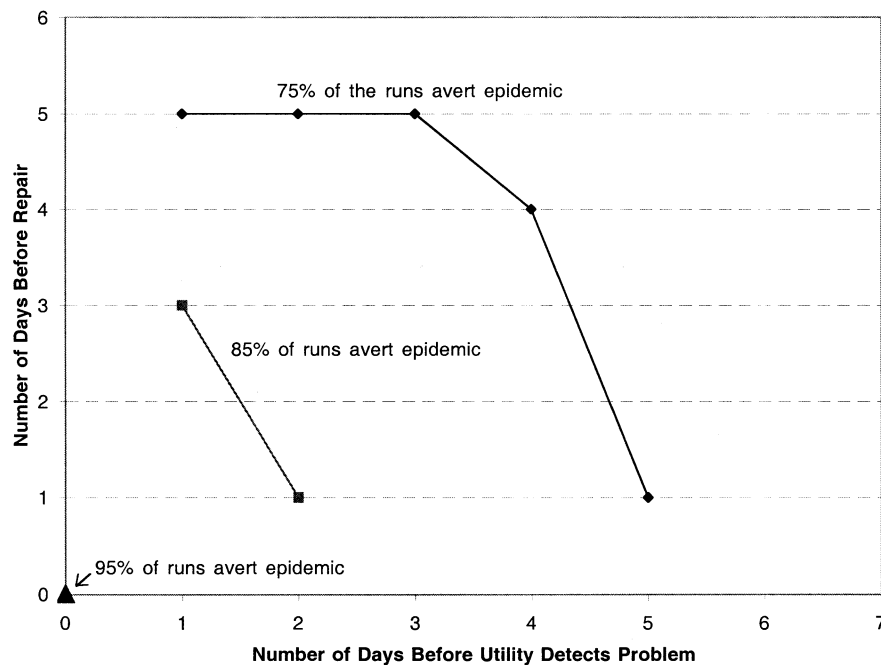
<sup>21</sup> Noncompliance is modeled as  $\beta(x = 200, y = 200)$ , with range 0.01–0.05.

The most striking effect of the difference in compliance level is seen in situations where the problem is recognized quickly but it takes more than a week to repair the system. In such cases, a boil-water notice and the associated mobilization would avert an epidemic under nearly full-compliance, but not under normal compliance.

### 3.3. Implications of Uncertainty in the Results

As mentioned previously, there are wide error bars on the model output (Fig. 3) as a result of the propagation of parameter uncertainty. The scenario results (Fig. 4) were reported in terms of average population morbidity over 500 runs per scenario. Figure 5 shows another way to conceptualize the results: namely, the chances of averting an epidemic—defined by the percentage of model runs in which an epidemic is prevented—as a function of response times. This analysis is useful for determining how fast a detection method is needed.

With normal compliance, in 75% of the runs an epidemic could be averted with the response times shown in the upper curve (25% failure to avert). When the tolerance for failure is only 5% (95% of the outcomes avert an epidemic), the awareness of a treatment problem and the repair must both occur no later than Day 0. Thus, for high reliability, immediate detection methods are required; if detection takes more than 5 days, an intolerable probability of an epidemic ( $\geq 25\%$ ) is expected, given a treatment failure.



**Fig. 5.** The effect of delays in utility awareness development and treatment process repair on the expected likelihood of preventing an epidemic, as defined by the percentage of simulation runs in which that occurs.

#### 4. DISCUSSION

In order to avert cryptosporidiosis epidemics, without changing prevailing consumer compliance behaviors, Utility Awareness must develop in the first few days following a contamination event. Unfortunately, if a utility must rely on current standard water-quality monitoring methods for *Cryptosporidium*, which typically take at least a week to complete, this seems unlikely or even impossible. As a result, under current conditions, a water authority's best chance to avoid an outbreak is to issue prophylactic boil-water notices on the basis of trigger events (rather than on confirmed treatment failure). Since many of these will turn out to be false alarms, it may, however, be difficult to secure the high compliance needed.

The results of the current simulation thus confirm the concerns raised about the adequacy of current disease surveillance systems for detecting outbreaks of waterborne disease.<sup>(34,43,73,74)</sup> Medical surveillance data, although essential for the retrospective attribution of waterborne epidemics to their source, cannot develop Utility Awareness quickly enough to prevent an epidemic. Medical surveillance has irreducible time constraints, such as the incubation period for cryptosporidiosis, the lag between the initiation of symptoms and the confirmation of a medical diagnosis by lab results, and the time needed for epidemiologists to acquire and interpret the raw data. In prac-

tice, the minimum turnaround time is 2 weeks. Figure 4 shows that that is too long to avert an epidemic.

Developing more rapid and sensitive diagnostic techniques for the detection of *Cryptosporidium* in environmental sources has been identified as a major research priority.<sup>(27)</sup> The current standard technology, the indirect fluorescent antibody (IFA) procedure, in addition to being slow, is plagued with poor recovery efficiency, lack of reproducibility, low sensitivity, and inability to determine viability or species. This has stimulated some debate regarding the appropriateness of using oocyst counts at all for short-term water treatment plant operation and management decisions.<sup>22</sup> Several alternative methods are currently under development. They include cellulose-acetate membrane filter dissolution, in vitro cell culture, lipid biomarker technology, continuous-flow cytometry with fluorescent cell sorting, and modified blood cell separation technology.<sup>(76,77)</sup>

The EPA has been developing a modified IFA approach, Method 1622. This protocol includes opti-

<sup>22</sup> Haas and Rose<sup>(75)</sup> have proposed an action level of 10 to 30 oocysts per 100 L of finished drinking water as a signal to utilities that an outbreak of cryptosporidiosis is possible. However, Craun *et al.*<sup>(34)</sup> recommend against relying on water-quality screens for oocysts for assessing epidemic potential, arguing that outbreaks have occurred when oocysts were not detected in water samples and have not always occurred when oocysts were detected.

mized filtration, immunomagnetic separation, and immunofluorescence microscopy.<sup>(76,78)</sup> It is expected to have higher recovery rates and lower detection limits than the current IFA method, with preliminary results suggesting at least twice the recovery rate (although still well below full recovery).

Another promising technology in development is a DNA chip that can detect *Cryptosporidium* by screening for DNA fragments. The chips have short DNA sequences bound chemically to a slice of glass or silicon. They identify fragments of DNA in a sample through hybridization, the bonding of homologous single strands of DNA. The technology is expected to reduce water-quality testing time to 4 hr. Fluorescent in situ hybridization methods can discriminate among *Cryptosporidium* species and may be able to determine viability, two capabilities that will have epidemiological significance.<sup>(79)</sup> The impact of fast-monitoring technology on epidemic potential justifies the priority being given to its development.

## 5. SUMMARY

An integrated risk model has been created, incorporating elements of natural and human ecology, in order to evaluate several classes of intervention strategies for waterborne cryptosporidiosis outbreaks. The model can evaluate a broad range of risk management issues. In this first illustrative application of the model, the discussion has focused on how operational practices of a utility—*Cryptosporidium* detection method, treatment deficiency repair time, and public communication/education—and consumer compliance behavior influence the development of an outbreak. The present analysis indicates that slow turnaround time and insensitive tests allow waterborne cryptosporidiosis outbreaks to occur, despite well-developed communications and response methods.

High consumer compliance with boil-water alerts can, to some extent, compensate for a utility's inability to repair a drinking-water treatment problem quickly. As a result, consumer education can be an important part of a multibarrier approach to risk minimization for drinking-water safety. The usefulness of communication though is limited by the timeliness of the message. Speeding up utilities' ability to detect *Cryptosporidium* in water samples would allow consumer communications to significantly limit the progression of an outbreak. Fortunately, increasing the sensitivity and decreasing the turnaround time for water-quality monitoring is already a priority

with research funding agencies, and several new technologies are in testing protocols. The current model strengthens the case for such investments, and also shows the limits to the containment that can be expected with current technology and procedures.

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