

THESIS FOR THE DEGREE OF LICENTIATE OF ENGINEERING

Assessing the health consequences of deficiencies in water distribution
networks

A basis for future network management

VICTOR RAFAEL DE JESUS VIÑAS COS

Department of Architecture and Civil Engineering

CHALMERS UNIVERSITY OF TECHNOLOGY

Gothenburg, Sweden 2018

Assessing the health consequences of deficiencies in water distribution networks
A basis for future network management
VICTOR R. VIÑAS COS

© VICTOR R. VIÑAS COS, 2018.

Department of Architecture and Civil Engineering
Chalmers University of Technology
SE-412 96 Gothenburg
Sweden
Telephone + 46 (0)31-772 1000

Chalmers reproservice
Gothenburg, Sweden 2018

Assessing the health consequences of deficiencies in water distribution networks: A basis for future network management
VICTOR R. VIÑAS COS
Department of Architecture and Civil Engineering
Division of Water Environment Technology
Chalmers University of Technology

Abstract

Drinking water distribution networks are susceptible to incidents that may contaminate the drinking water being served to the population. Five major risks that can impact negatively the health of consumers have been identified by a literature study: intrusion, cross-connections and backflows, unhygienic repairs or maintenance works, inadequate management of storage reservoirs and biofilms. All of them have been linked to outbreaks of waterborne disease, in addition to possibly increasing the level of endemic gastrointestinal illness in society.

There are two ways to determine the association between incidents in the network and risk for disease: epidemiological studies and modelling. Epidemiological studies have been used to assess the health outcomes to certain exposures in the network, e.g., maintenance work, low pressure events, among others. Studies have linked substantially outbreaks to causes in the network; however, the association with endemic level of disease in the population has had mixed results. Quantitative microbial risk assessment (QMRA) is one of the best frameworks available to simulate the health risks these incidents have on the population.

In this thesis, the foundations for a distribution network microbial risk management framework is established. This is achieved with a systematic literature review and the development of a conceptual model, specifically for the risk of cross-connections and backflows. The systematic literature review was carried out to assess the level of epidemiological evidence for endemic disease, and evaluate the state-of-the-art of QMRA models. A conceptual model for the specific risk of cross-connections and backflows is presented, testing some scenarios to gain insights for future improvements.

Possible improvements for QMRA models, better input data and combination of modelling and epidemiological studies are discussed. One important limitation that needs to be addressed is the economic aspect of potential mitigation measures for incidents. This aspect, in conjunction with the ones previously mentioned, will be essential to overcome in order to have a functional microbial risk management framework.

Keywords: distribution network, microbial risk, epidemiological studies, QMRA, risk management

Assessing the health consequences of deficiencies in water distribution networks: A basis for future network management
VICTOR R. VIÑAS COS
Institutionen för arkitektur och samhällsbyggnadsteknik
Avdelningen för vatten miljö teknik
Chalmers tekniska högskola

Sammanfattning

Dricksvattenledningsnät utsätts för händelser och incidenter som kan förorena dricksvattnet och som kan påverka befolkningen. De fem största riskerna som kan påverka konsumenternas hälsa negativt har identifierats i en litteraturstudie: inträngning, korskoppling och backflöden, ohygieniska reparationer och underhållsarbeten i ledningsnät, undermålig hantering av reservoarer och biofilm. Samtliga dessa har knutits till utbrott av vattenburna sjukdomar, förutom att eventuellt öka graden av endemisk gastrointestinal sjukdom i samhället.

Det finns två metoder att bestämma sambandet mellan incidenter i ledningsnätet och risken för sjukdom/infektion: epidemiologiska studier och modellering. Epidemiologiska studier har använts för att utvärdera hälsoproblem för olika nivåer av exponering i ledningsnätet, exempelvis vid underhållsarbeten, låga tryck. Medans utbrott har varit väsentligt samband med orsaker i nätverket, har föreningen med endemisk nivå av sjukdom i befolkningen haft blandade resultat. Kvantitativ mikrobiell riskbedömning (QMRA) är en av de bästa metoderna för att uppskatta de hälsorisker som detta kan innebära för befolkningen.

I denna licentiatuppsats presenteras grunderna till ett ramverk för mikrobiell riskhantering för ledningsnät. Detta har genomförts genom en systematisk litteraturstudie och utveckling av en konceptuell riskhanteringsmodell, med specifikt fokus på risken för korskoppling och återflöden. Den systematiska litteraturgenomgången genomfördes främst för att undersöka om epidemiologiska bevis för endemisk sjukdom föreligger, samt att utvärdera de senaste QMRA-modellerna. En konceptuell modell för den specifika risken för korskopplingar och återflöden presenteras och testats för olika scenarier.

Möjliga förbättringar för QMRA-modeller, bättre ingångsdata och en kombination av modellering och epidemiologiska studier diskuteras. Den ekonomiska aspekten av eventuella riskreducerande åtgärder är mycket viktiga. Denna aspekt, tillsammans med de tidigare nämnda, kommer att vara avgörande för att uppnå ett funktionellt mikrobiellt riskhanteringsramverk.

Nyckelord: ledningsnät, mikrobiell risk, epidemiologiska studier, QMRA, riskhantering

List of papers

This licentiate thesis is based on research performed in the Division of Water Environment Technology, Chalmers University of Technology, between September 2015 and August 2018 under the supervision of Thomas Pettersson and Annika Malm.

This thesis is based on the work contained in the following papers.

- I. Viñas, V., Malm, A., and Pettersson, T.J.R. Overview of microbial risks in water distribution networks and their health consequences: quantification, modelling, trends and future implications. Under revision in *Canadian Journal of Civil Engineering*.
- II. Viñas, V., Malm, A., and Pettersson, T.J.R. Estimating the risk of cross-connection and backflows using QMRA: a conceptual model. Manuscript.

Acknowledgements

The road to the licentiate has been marked by bumps in the road that, at times, felt insurmountable. However, I have been fortunate enough to be surrounded by extraordinary individuals and institutions that have made it possible to achieve this milestone. I will do my best to express the extent of my gratitude in just a few lines.

I would first like to thank my main supervisor, Thomas Pettersson, for his indescribable support throughout the years. Thomas, thank you for unconditional understanding and guidance during the last three years; I would not be here without you. Thank you for teaching me so much about academia, research, and Swedish culture in general. I would also like to thank my co-supervisor, Annika Malm, for your infinite patience and perpetual positivity. Annika, I am extremely lucky to have someone as knowledgeable as you about the distribution network guiding me in the right direction. I owe to both of you the researcher I am today and all the progress I will achieve during the time remaining.

I would like to acknowledge the Göteborg Region Association of Local Authorities (GR) for their financial support of the project, in addition to contributing with their technical expertise throughout my PhD work. Without their continuous support, this project would not be possible.

The work developed so far has been carried out within the framework programme for drinking water research at Chalmers (DRICKS). I would like to express my gratitude to this wonderful group of drinking water experts for all the stimulating discussions during conferences, workshops, kick-offs and other group activities. A special thanks to Viktor Bergion for taking extra duties during our co-supervision of an MSc thesis occurring concurrently to the writing process of this document. To my long-lost DRICKS brother, Saeed, thank you for the memories.

I extend my gratitude to all my colleagues and friends at the division of Water Environment Technology. Thank you for contributing to a pleasant work environment and interesting conversations during fika. To all the WET PhD students, your capacity to create memorable moments still amazes me. A special mention to Joao, Nashita and (former officer mate) Soroush for supporting me through the really dark times of this entire process, by providing guidance, emotional encouragement and food.

A heart-warming thanks to my family in Dominican Republic and my adoptive family in Gothenburg for always being there for me. Kaj, Debdeep, Srijita, Rodolfo, Linn, Bharat, Isabelle, Fabiano, Shastry, André, Patricia, Mohamed and the Royal Flushers: this thesis would have been finished so much faster without you. I say that in jest, of course. Honestly, Gothenburg would be considerably greyer without all of you. A special shout-out to the crew in Truckstop Alaska and The Abyss for being so welcoming to a foreign metalhead: you have given me a space where I feel at home.

Gothenburg, 2018

Victor Vinas

Terminology and abbreviations

AGI	Acute gastrointestinal illness
Backflow	Situation that occurs in the presence of a cross-connection: the pressure in the non-potable source is higher than the pressure in the drinking water network allowing contamination to flow into the drinking water distribution network.
Biofilm	Aggregate of microorganisms in which cells that are frequently embedded within a self-produced matrix of extracellular polymeric substances adhere to each other and/or to a surface (e.g., pipe, reservoir wall)
Case-control	Type of observational study used to study the association between exposure and outcome, by comparing cases (groups with the desired outcome) and controls (groups without the desired outcome)
Cohort	Type of observational study that analyses a population with shared characteristics at specific points over a period of time
Cross-connection	A connection between the drinking water distribution network and a non-potable source, which can potentially cause the introduction of water/substances not intended for consumption
Cross-sectional	Type of observational study that analyses the proportion of the population with a desired outcome at a specific points of time
Ecological	Type of observational study relating risk factors and health outcomes in a population defined geographically, politically or temporally
GI	Gastrointestinal illness
Incidence	Number of new infections in a population within a specified time period
Intrusion	Event in the distribution network that occurs when inadequate pressure conditions allow for contaminated water to come into the network through physical breaches (e.g., cracks and holes)
POU	Point-of-use
Prevalence	Proportion of a population found to be affected by a medical condition at a specific point in time
QMRA	Quantitative Microbial Risk Assessment
RCT	Randomised-controlled trials - experimental study measuring changes in outcome by implementing an intervention

Contents

1	Introduction	1
1.1	Background.....	1
1.2	Aim and objectives	2
1.3	Scope.....	3
2	Theoretical Background	5
2.1	Urban water systems.....	5
2.2	Elements of the distribution network.....	6
2.2.1	Pipes.....	6
2.2.2	Valves.....	7
2.2.3	Pumps	7
2.2.4	Reservoirs.....	7
2.2.5	Hydrants.....	7
2.2.6	Configuration of the distribution network.....	8
2.3	Risk within the context of drinking water	8
2.3.1	Health risks associated to microbiological contamination	9
2.3.2	Hazards in the distribution network	10
2.4	Introduction to epidemiology	14
2.4.1	Types of epidemiological studies.....	15
2.5	The QMRA framework	17
2.5.1	Problem formulation	18
2.5.2	Exposure assessment	19
2.5.3	Health effects assessment	19
2.5.4	Risk characterization	19

2.5.5	Risk management.....	21
3	Materials and methods	23
3.1	Literature review (Paper I).....	23
3.2	Cross-connection and backflow conceptual model (Paper II).....	23
4	Summary of Thesis Contributions.....	27
4.1	Literature review	27
4.2	Cross-connection and backflow conceptual model	28
5	Discussion and Outlook	31
5.1	Epidemiological studies.....	31
5.1.1	Household interventions (RCTs).....	31
5.1.2	Observational studies.....	32
5.2	QMRA modelling.....	33
5.3	Cross-connection conceptual model.....	34
5.4	Possibilities & future work.....	34
5.5	Conclusions	36
6	References.....	37
7	Appendix.....	46

1 Introduction

A brief overview of the thesis' background is presented. The aims and objectives are stated, as well as the scope of the thesis work.

1.1 Background

Access to safe drinking water plays an essential role in the area of public health. In urban settings across the globe, centralised systems are commonly used to deliver **safe** drinking water to millions of consumers. According to the WHO (2011), water is considered safe when it “[...] does not represent any significant risk to health over a lifetime of consumption, including different sensitivities that may occur between life stages.” Dangers that can affect the water quality can be of microbiological, chemical, radiological or physical in nature. From this point onwards, the focus will be solely on microbiological contamination of the drinking water, i.e., pathogens.

An important component of any centralised system is the distribution network, which transports water from the treatment plant or an adequate water source to the consumers' taps. The distribution network is composed of many parts, e.g., pipes, valves, storage reservoirs, pumps; which work in unison to preserve the water quality and supply enough water to consumers (WHO, 2014). However, all of these parts can be vulnerable to unexpected events or mistakes during operation that can lead to contamination of the drinking water. Additionally, due to the position of the distribution network at the end of the supply chain, an incident is less likely to be detected and remediated in time (Risebro et al., 2007). Therefore, maintaining the integrity of the network is essential in preventing contamination of the treated water delivered to consumers.

Integrity of the distribution network is divided into three components: physical, hydraulic and water quality (National Research Council, 2006). First, physical integrity refers to the ability of the distribution system to act as a physical barrier against external contamination. The physical integrity can be lost if, for example, there are cross-connections with non-potable water pipes or cracks in the pipes. Secondly, hydraulic integrity is the capacity of the system to maintain adequate flow, pressure and water age. Certain events, e.g., pump shutdown and main breaks, can impact negatively the pressure and the flow, hence compromising the hydraulic integrity of the system. For a contamination event to occur, both the physical and the hydraulic integrity must be lost (Ercumen et al., 2014). Lastly, water quality integrity deals with internal chemical processes inside the pipes that can lead to a deterioration of the drinking water quality. A deterioration of the quality can lead to a contamination event itself or increase the likelihood of contamination occurring (National Research Council, 2006). An example of water quality integrity breach is the complete decay of the disinfectant residual.

Extreme consequences of distribution network contamination are waterborne disease outbreaks. Waterborne outbreaks are defined as “an incident in which two or more epidemiologically-linked persons experience a similar illness after exposure to the same water source and epidemiologic evidence implicates the water as the likely source of the illness” (CDC, 2010). In Sweden, approximately 34% of the outbreaks with known causes are associated with the

distribution network (Malm et al., 2010). This proportion is similar to the European Union level, where 31% of the outbreaks were caused by distribution network deficiencies (Risebro et al., 2007). Gastrointestinal illness (GI) is the most common illness associated to waterborne outbreaks (Messner et al., 2006).

There are different tools available to evaluate the (microbial) health risks associated to distribution networks. One method is through epidemiological studies, which are commonly performed during outbreak investigations. Their purpose is to determine the extent of the outbreak (how many were affected/infected) and identify the causes (both causative agent of the disease and events that led to the presence of this agent in the drinking water supply) (Institute of Medicine, 2000). In the last three decades, epidemiological studies have also been used to estimate the risk of disease from an endemic perspective. While outbreaks can be seen as extreme cases, the endemic level of disease is a sort of baseline level of disease in a population. Results for these studies have been mixed; some studies have found an increased risk of illness from drinking tap water while other authors have not found any association (Payment et al., 1991; Payment et al., 1997; Nygard et al., 2007; Hellard et al., 2001; Colford et al., 2005; Malm et al., 2013a). However, there is mounting evidence that malfunctioning distribution networks, as well as specific system deficiencies (i.e., pipe breaks, water outages and inadequate residual disinfectant), increase the risk of endemic GI (Ercumen et al., 2014).

Another way to analyse and assess the risks in the distribution network is through the use of computational models. Quantitative microbial risk assessment (QMRA) models have been used in conjunction with hydraulic models to quantify the consequences of different microbial risks (Teunis et al., 2010b; Yang et al., 2011; Blokker et al., 2014). Most of these models have important limitations that restrict their use, e.g., uncertainties in the input data, assumptions made about the conditions in the distribution network (turbulent flow, instantaneous mixing, etc.) (Besner et al., 2011). However, they are useful for evaluating measures that can be taken to manage the specific risks addressed in the model.

1.2 Aim and objectives

The overall aim of this thesis is to lay the foundation for a microbial risk management framework, specifically for the distribution network. The management framework would be based on QMRA modelling; which is known to have some important knowledge gaps, e.g., uncertain input data, lack of system-specific information, among others (Besner et al., 2011). There have been previous attempts at overcoming some of these limitations (e.g., (McInnis, 2004; Islam et al., 2015; Kirmeyer et al., 2014)), however to this day they remain incomplete. This thesis is a first attempt at identifying missing links between the work already done and what needs to be addressed in the future to successfully develop a comprehensive framework.

In addition to the aim, the thesis has the following specific objectives:

- Formulate a theoretical, conceptual model for assessing and managing health risks in the distribution network.
- Determine potential input data for the QMRA model from the literature.
- Present a methodology for assessment of cross-connection risk in the distribution network as a specific tool of the developed conceptual model.

1.3 Scope

Figure 1 shows the general framework for distribution network microbial risk management and where the papers presented in the thesis belong. Paper I is used as a starting point for generating reliable input data for the QMRA model. Paper II is a part of the QMRA model, in addition to covering part of the input data generation.

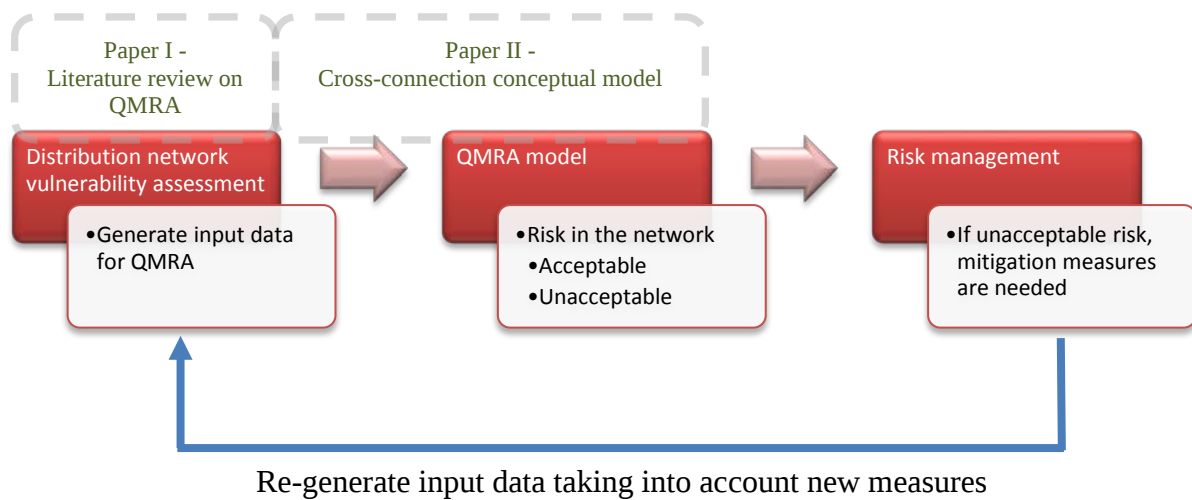


Figure 1 - Simplified scheme of a distribution network microbial risk management framework.

2 Theoretical Background

Important concepts for understanding the main contents of the thesis are introduced in this chapter. The focus is in the distribution network and the microbial risks associated with it, in addition to providing an introduction to epidemiology and the QMRA framework.

2.1 Urban water systems

Urban water systems traditionally consist of drinking water supply system, a wastewater system and, nowadays, a separate stormwater system (see Figure 2). The drinking water system extracts water from a source (surface, groundwater or combined) and prepares it for use. Drinking water is then transported to the consumers' taps. After use, the water is collected and transported through the sewage and stormwater systems towards a treatment facility, where the wastewater is processed to be suitable for discharge into the environment. In rare occasions, the wastewater will be discharged directly into the environment (usually the rain water collected in the stormwater systems).

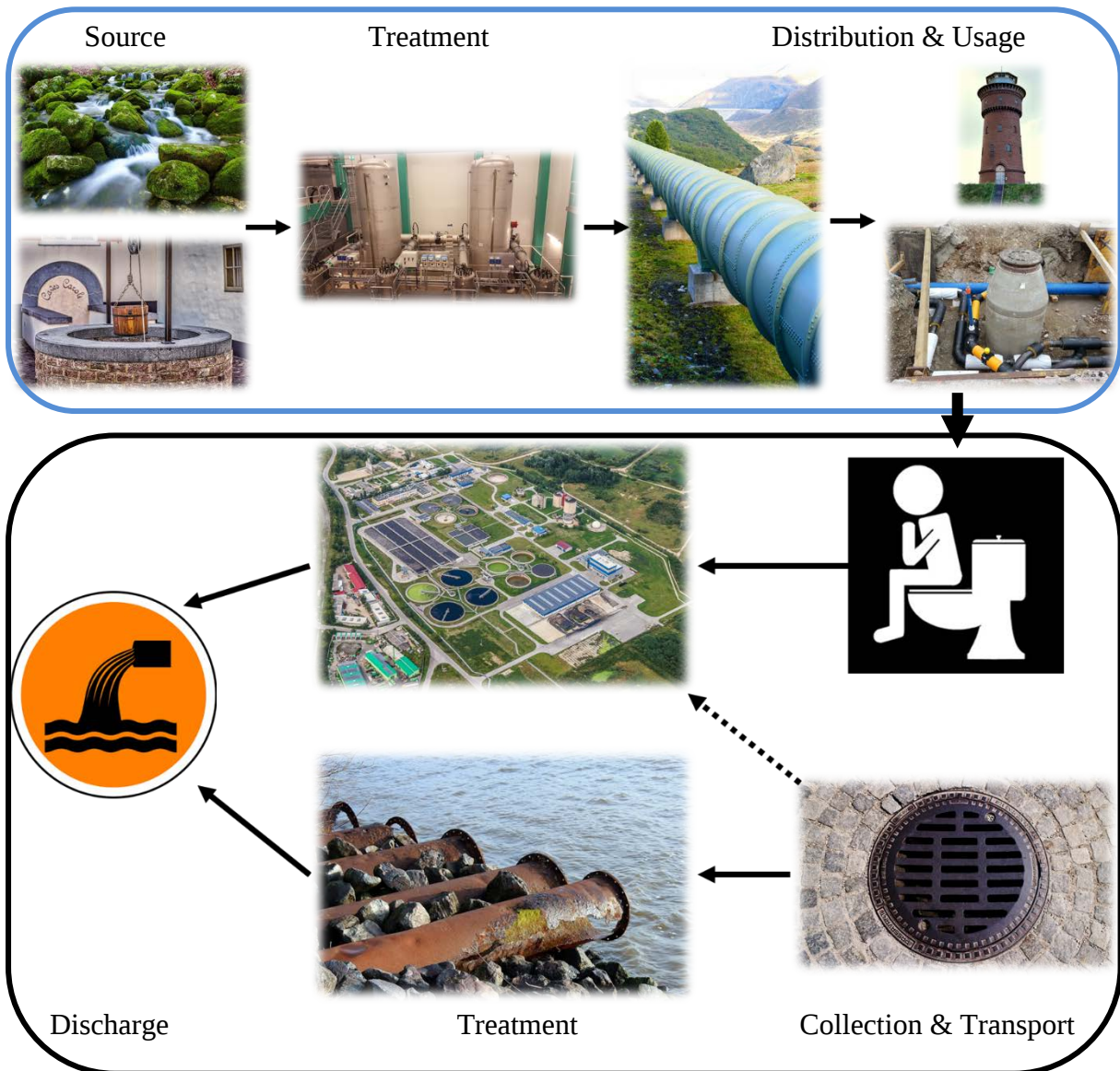


Figure 2 - Common schematic of urban water systems. The blue rounded rectangle encompasses the drinking water supply, while the black rectangle is for the wastewater network.

The water system infrastructure is usually built underground (e.g., pipes, valves, manholes, etc.), with some consideration being given to the vertical and horizontal separation relative to each other (see Figure 3). Theoretically, this prevents the drinking water system from interacting with the wastewater or stormwater system (i.e., avoiding contamination of the drinking water). In reality, interactions between the systems do occur; with varying consequences to the drinking water supply system and the impact on consumers (Besner et al., 2010a).

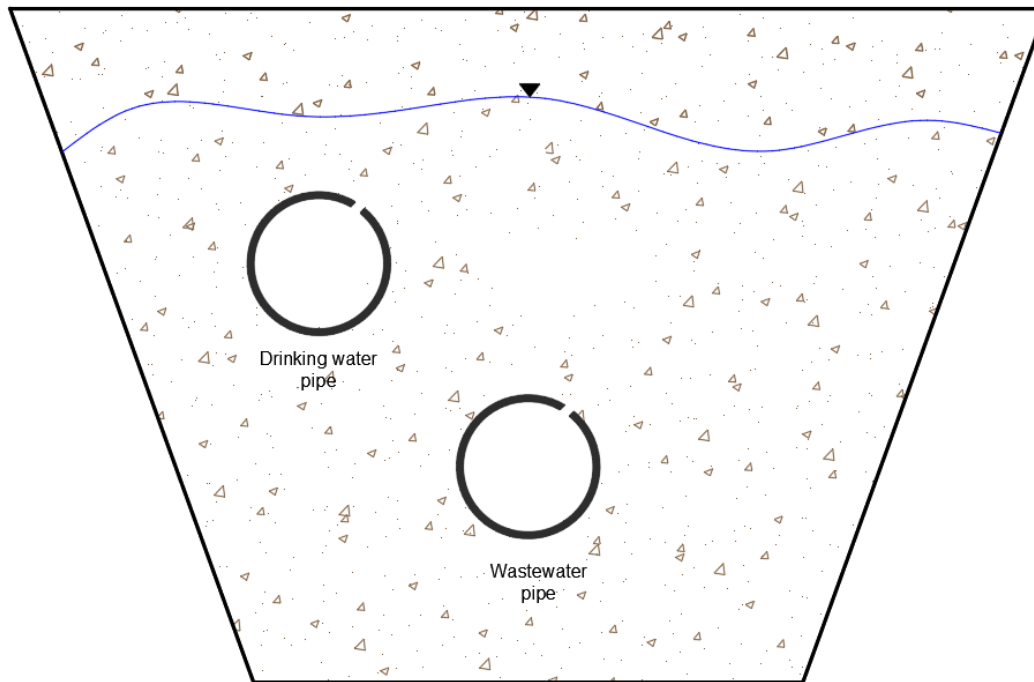


Figure 3 - Usual position of drinking water pipes compared to wastewater pipes in underground trenches. Groundwater level is shown as being over the drinking water pipe; this level will be variable, depending on environmental and seasonal conditions.

2.2 Elements of the distribution network

The distribution network consists of many components: pipes, valves, pumps, reservoirs, hydrants and other appurtenances that connect the drinking water supply to consumers' taps (National Research Council, 2006; WHO, 2014). The presence or absence of a certain component will be heavily influenced by the area the distribution network is supposed to serve. For example, the layout of the network will depend on the existing streets and roads, existing and planned land use, and where the water demand is concentrated (WHO, 2014). A pump might not be needed if the treatment plant is at a high enough elevation compared to the areas being fed. A brief description of the main components of the network is presented below.

2.2.1 Pipes

The network of pipes that transport water from a treatment facility or directly from the source to the consumers can be classified from largest to smallest as transmission mains, distribution mains, service lines and premise plumbing (National Research Council, 2006). Transmission mains usually convey drinking water from a source to a storage reservoir. Distribution mains are then used to transport water to the different parts of a city. Service lines are connected to distribution mains and carry water to the residences/buildings. Premise plumbing refers to the

pipes inside the building that distributes the water to the point of use. Premise plumbing and (partly) service lines are not considered to be part of the distribution network, since these pipes are not under the control of the water utility.

Pipes also differ in their material composition: it can be influenced by tradition, era in which they are laid, advances in material properties or production techniques, among other reasons. For example, Swedish distribution networks were mainly composed of metal pipes (galvanic steel, cast/ductile iron) until the 1970s, when plastic pipes became more widespread (Malm et al., 2013b). Plastic pipes continue to be the preferred material to this day.

2.2.2 Valves

Valves are an essential component for the proper operation of any distribution network. There are two types of valves commonly present in every network: isolation valves and control valves (WHO, 2014). Isolation valves, as their name imply, are used to isolate sections of the network during maintenance or repair work. The location of the valve also tries to minimize the inconveniences to other service areas while the work is ongoing.

Control valves are used for differing purposes. They are used to prevent adverse (i.e., too high or too low) pressure conditions in the network (e.g., pressure-reducing, pressure-sustaining and pressure-relief valve); control flow quantity and direction (e.g., flow-control valves, throttling valves, float valves and check valves); and for operational purposes (e.g., blow-off valves, air release valves).

2.2.3 Pumps

Pumps may be needed to provide the necessary energy for water to reach higher elevations within the network or increase the pressure to acceptable levels.

2.2.4 Reservoirs

Reservoirs have different functions depending on the conditions in the network. One of their main functions is to provide storage capacity for balancing variations in supply and demand throughout the day (WHO, 2014). They also serve to stabilize pressures in the network, protecting the network against surges (excessive pressure) or sudden drops. Another function is to provide emergency water during firefighting. Reservoirs can be constructed on ground or be elevated. Whether the reservoir is situated on the ground or is elevated will depend on the terrain, available locations for reservoirs and pressure requirements of the system. Reservoirs are an integral component in maintaining a well-functioning distribution network.

2.2.5 Hydrants

Hydrants' main purpose is to offer firefighters access to the water supply (National Research Council, 2006). Proper design and maintenance are required to satisfy firefighting requirements. Hydrants are also an important component of distribution network maintenance. Routine flushing programs, where large volumes of water are forced through the pipe network and exited through the hydrants, are used in many distribution networks to maintain adequate water quality. Flushing is also used during emergency situations, when the water quality has been compromised, to remove the contamination from the network.

2.2.6 Configuration of the distribution network

The distribution network can have three system configurations: branch, grid and combined (see Figure 4). The branching system is analogous to a tree branch, in that smaller pipes branch out of larger ones throughout the service area (National Research Council, 2006). An advantage of this system is a lower investment cost compared to the grid system. A major disadvantage is that numerous consumers may be affected during an incident, since the water can only take a single path to the consumers. This setup is common in rural areas and small settlements. The grid system provides loops throughout the service area, enabling the water to take two or more paths towards the consumers. This provides redundancy to the system, which minimizes the consumers affected when areas need to be isolated (VAV, 2001). It is also considered to be more expensive, since the length of the system is increased due to the loops. This setup is common in large, dense areas.

In reality, most large distribution networks are a combination of grids and branches (VAV, 2001). Dense, centric parts of the city will tend to have loops while neighborhoods in the periphery will tend to be supplied by a single branch. As mentioned previously, the choice of system will mainly be influenced by the local topography, street layout and type of community being served.

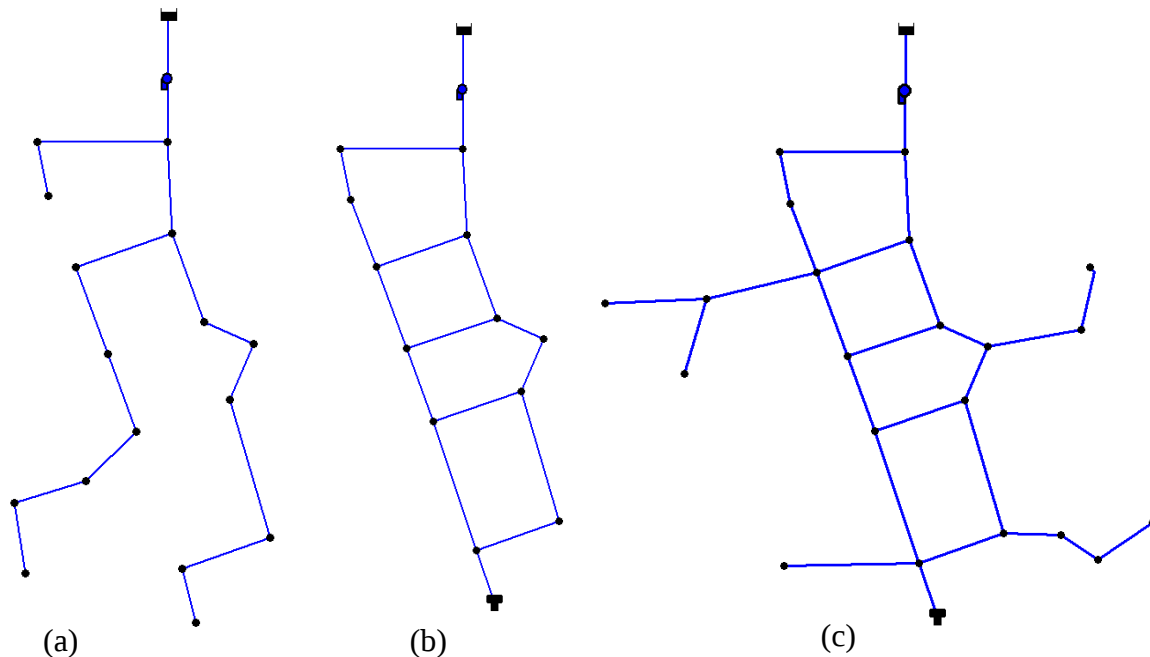


Figure 4 - (a) Branch, (b) grid and (c) combined network configurations in which the distribution network can be structured.

2.3 Risk within the context of drinking water

Risk is usually defined in multiple ways, depending on what is being evaluated (Lindhe, 2010). Within the drinking water sector, risk can be defined as a combination of probability and consequence. This can be further clarified by adding that risk can be considered to consist of (MacGillivray et al., 2006):

- An agent with the potential to cause harm (i.e., hazard);
- Uncertainty of occurrence and outcomes (expressed as the probability of occurrence);
- Consequences (what can happen);
- And a specific time frame

Risks can be of microbiological, chemical, radiological origin or physical in nature (WHO, 2011). The most evident source of contamination for microbial risks is the sewage system.

2.3.1 Health risks associated to microbiological contamination

Five major microbial risks have been identified for the distribution network (National Research Council, 2005). From higher to lower priority they consist of: cross-connections and backflows; improper maintenance and operation of reservoirs; contamination during installation, rehabilitation and repair of water mains; intrusion; and biofilms. The prioritization is based on the amount of evidence for their contribution to health risks to consumers. All of these risks have been identified as the causes for waterborne disease outbreaks (Craun, 2012; Hrudey and Hrudey, 2004; Hrudey and Hrudey, 2007; Risebro et al., 2007). A brief explanation of each risk follows below.

Cross-connections are points in the distribution network where non-potable water elements (e.g., wastewater pipe) can come into contact with the drinking water (USEPA, 2002d). When the pressure in the non-potable water source is greater than in the distribution system and there are inadequate cross-connections controls present (e.g., absence of backflow prevention valve), a backflow can occur (WHO, 2014). Cross-connections are considered one of the most serious public health risks in the distribution network (National Research Council, 2005; WHO, 2014).

Routines exist to ensure correct hygienic procedures during installation, rehabilitation and repair of water mains (Säve-Söderbergh et al., 2013; WHO, 2011; WHO, 2014). However, contamination can occur if these routines are not carried out (e.g., inadequately disinfecting newly laid pipes) (USEPA, 2002c). Unhygienic practices during installation, rehabilitation and repair of water mains were classified as a high priority issue (National Research Council, 2005).

There are different ways in which water quality can be compromised in reservoirs. Physical breaches, such as cracks in the walls/roofs of the reservoir and cross-connections can allow contamination to enter from the exterior, e.g., (Falco and Williams, 2009; Kristianstads kommun, 2015). Inadequate hydraulic design can cause long residence times, leading to complete loss of disinfectant and microbial regrowth (Clark et al., 1996; Seyoum et al., 2014; USEPA, 2002b). Improper management of reservoirs was considered a high priority issue in the first assessment report by the (National Research Council, 2005).

According to Besner et al. (2011), intrusion can be defined as the contamination of the drinking water due to adverse pressure conditions and physical breaches in the system. Three conditions are necessary for microbial contamination to occur: presence of pathogens surrounding the distribution system (*source*); occurrence of pressure transients or low-pressure events (*adverse pressure conditions*); and deteriorated physical conditions of the pipes (*physical breach*) (Hooper et al. 2008; Lindley and Buchberger 2002). Intrusion was considered a medium priority

issue by the National Research Council (2005); however, gradually it is being recognized as a major contributor to the waterborne disease burden (Besner et al., 2011; Islam et al., 2015; Murphy et al., 2016).

Biofilms are a complex collection of microorganisms, extracellular polymeric substances, organic and inorganic matter (Kauppinen et al. 2012). They are known to serve as potential reservoirs for pathogens inside the distribution system (Berry et al. 2006; Nocker et al. 2014; Wingender and Flemming 2011). Pathogenic organisms that manage to intrude the distribution network (e.g., via cross-connections and backflow into the system) can become attached to biofilms and, afterwards, become detached through shear stresses due to the water flowing. Pathogens that can be found in biofilms include *Cryptosporidium* oocysts (Angles et al. 2007; Howe et al. 2002); enteric viruses (Skraber et al. 2005; Storey and Ashbolt 2003); opportunistic pathogens (Farkas et al. 2012; Pryor et al. 2004) and bacterial pathogens (September et al. 2007; Wingender 2011). Biofilms were classified as a medium priority issue (National Research Council 2005).

2.3.2 Hazards in the distribution network

Hazards are agents that can potentially cause harm to a person. Events that lead to the presence of a hazard are known as hazardous events. From a distribution network perspective, the presence of a hazard or occurrence of a hazardous event is closely related to the loss of integrity in the network. The integrity of the distribution network can be divided into three components: physical, hydraulic and water quality.

Physical integrity relates to the capacity of the network to physically impede the entry of external contaminants (National Research Council, 2006). The main components of physical integrity are: pipes, appurtenances (e.g., hydrants, valves), reservoirs and backflow prevention devices (see Table 1). These components may induce loss of physical integrity in different manners (WHO, 2014). Pipes and reservoirs may lose their ability to act as a barrier if they develop cracks or holes. Appurtenances can become contaminated during human activities. Backflow prevention devices are a standard protective measure against cross-connections. Absence or failure of the device will also lead to loss of integrity.

There are several ways physical integrity can be preserved. Aging infrastructure is known to lead to higher frequency of pipe breaks, due to the deterioration of the pipe material (Van Abel et al., 2014). Therefore, the pipe network will need to be rehabilitated to maintain the physical integrity (Malm et al., 2013b; Winkler et al., 2018). Hygienic routines are an important measure for preserving physical integrity during repairs or maintenance work with pipes, reservoirs and appurtenances (Svenskt Vatten, 2014).

The hydraulic integrity is preserved if adequate flow, pressure and water age is maintained throughout the network. According to Swedish guidelines for general distribution networks (VAV, 2001), there exists a desirable range in which to keep the pressure in the distribution network (see Figure 5). The pressure at the connection points of the water main with the service line should not exceed 70 m (700 kPa). The lowest pressure should be: (1) 15 m over the highest tap at the connection point (2) 15 m over the ground level at a hydrant. Low pressures affect

the reliability of the supply, fire suppression and may increase the risk of intrusion. Too high pressures increase the wear on the appurtenances, increase leakage and may cause additional leakages or breakages. Pressure fluctuations must also be regulated properly to avoid abrupt surges (LeChevallier et al., 2003; Karim et al., 2003; Besner et al., 2010b).

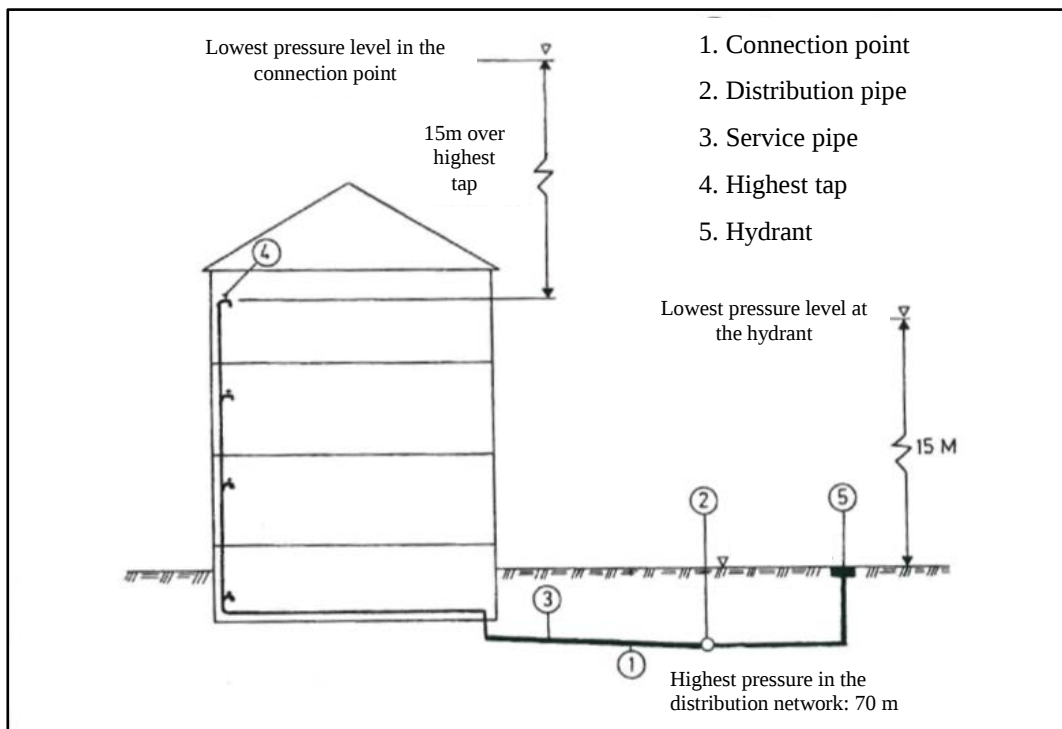


Figure 5 - Pressure requirements for Swedish distribution networks according to VAV (2001). (2) is the distribution network pipe and (4) is the service line. The highest pressure permitted in Swedish networks is 70 m at (1) connection point. The lowest pressures should be 15 m over both points (4) highest tap and (5) fire hydrant.

Water age is the time the water spends in the distribution network. Many factors that impact microbial regrowth are related to increased water age (USEPA, 2002a). For example, the longer the water stays in the network (older water) the more time the chlorine residual will have to react with naturally occurring materials in the pipes. This could lead to a scenario where there is complete decay (loss) of the residual.

Adequate water age is also dependent on mixing conditions inside the storage reservoirs. If there is incomplete mixing or if the water is not exchanged continually, pockets of stagnant water can form (Clark et al., 1996). This leads to all the negative effects of excessive water age. Therefore, reservoirs are also an important component in preserving hydraulic integrity.

Water quality integrity can be lost due to internal processes in the drinking water that lead to deterioration of the water quality (National Research Council, 2006). From a microbial perspective the two most important processes affecting water quality are biofilm growth and loss of disinfection residual. In addition to their role harbouring pathogens, biofilms can select for corrosion-inducing microorganisms in metal pipes (Farkas et al., 2012; Douterelo et al., 2014).

Theoretical Background

Water supply systems that use chlorination as a disinfection step will (usually) add sufficient disinfectant so that a “residual” remains in the drinking water after treatment. This chlorine residual (also known as disinfection residual) aids in preserving water quality in case of small contamination events inside the network (Haas, 1999; Propato and Uber, 2004). It can also be used as a proxy for disturbances in the network and to reduce the regrowth of microorganisms inside the network.

Table 1 - Integrity of the network. Partially adapted from National Research Council (2006).

Integrity	Components / Parameters	Mechanism for loss of integrity	Prevention
Physical	Pipes	• Structural failure ○ Corrosion ○ Surges • Unsanitary activity during construction, replacement, or repair	• Pipe renewal • Hygienic routines
	Appurtenances	• Corrosion • Flooded components • Unsanitary activity during construction, replacement, or repair	• Inspection programs • Hygienic routines
	Reservoirs	• Unsanitary activity during construction, replacement, or repair • Corrosion	• Inspection programs • Hygienic routines
	Backflow prevention device	• Absence of device allows backflow from cross-connection • Faulty device	• Inspection program
Hydraulic	Flow	• Pump shutdown • Scaling	• Loop network • Chemical cleaning
	Pressure	• Pump shutdown • Inadequate valve control	• Surge protection devices
	Water age	• Complete decay of residual • Stagnation in reservoirs	• Adequate mixing conditions
Water quality	Biofilm	• Long residence times	• Chlorine residual • Biologically stable water
	Disinfection residual	• Long residence times	• Booster chlorination

Theoretical Background

Microbial hazards that can intrude the network when integrity is lost are known as pathogens - infectious agents that can cause disease. Pathogens are usually grouped as bacteria, virus, protozoa (parasites), fungi and helminths (Ramírez-Castillo et al., 2015). Table 2 shows common pathogens that are known to have health effects in humans, as well as emerging pathogens. For example, the most common agents associated to waterborne outbreaks in the Nordic countries were *Campylobacter* and caliciviruses; accounting for 70% of the outbreaks with known aetiology (Guzman-Herrador et al., 2015).

Table 2 - Common pathogens that have been linked to waterborne disease. Emerging pathogens are those for which evidence is still inconclusive establishing drinking water as a route of transmission. Sources: (Ramírez-Castillo et al., 2015; WHO, 2011; Ashbolt, 2015).

Category	Common pathogens	Emerging pathogens
Bacteria	<i>Campylobacter</i>	
	<i>Salmonella</i>	<i>Aeromonas</i> spp.
	<i>Shigella</i>	<i>Helicobacter pylori</i>
	<i>Legionella</i>	<i>Listeria monocytogenes</i>
	<i>E. coli</i> pathogenic strains	<i>Pseudomonas aeruginosa</i>
	<i>Vibrio cholerae</i>	
Virus	Adenovirus	
	Calicivirus	Astrovirus
	Hepatitis A/E virus	Mamavirus
	Rotavirus	Mimivirus
	Enterovirus	
Protozoa	<i>Cryptosporidium</i>	
	<i>Giardia</i>	
	<i>Toxoplasma gondii</i>	<i>Blastocystis</i>
	<i>Nagleria fowleri</i>	<i>Isospora belli</i>
	<i>Entamoeba</i>	
Fungi	Microsporidia	<i>Candida albicans</i>
Helminth	<i>Dracunculus</i>	-
	<i>Schistosoma</i> spp.	

Microbial risks in the distribution network can lead to waterborne disease outbreaks and contribute to the endemic level of disease in the population (Guzman-Herrador et al., 2015; Murphy et al., 2016; Reynolds et al., 2008; Messner et al., 2006). Therefore, it is of utmost importance to identify, analyse and interpret the detrimental consequences of waterborne disease in society. The branch of medicine dedicated to studying these consequences is epidemiology.

2.4 Introduction to epidemiology

Epidemiology can be defined as the study of the distribution of disease and the factors that influence its frequency in human populations (Silman and Macfarlane, 2002). Epidemiology seeks, among other things, to identify factors that affect health (e.g., agents that transmit disease, environmental factors), identify sensitive groups in a population, investigate outbreaks and control epidemics (Schoenbach, 2000a). Epidemiology has a long history in the drinking water field (Stanwell-Smith, 2003), beginning in the mid-1800s with cholera outbreak investigations.

There are two main measures of disease in a population: prevalence and incidence (Schoenbach, 2000b). Prevalence is the proportion of a population affected by a disease (Eq. 1). There is no time element involved in calculating prevalence, unlike when calculating incidences.

$$\text{Prevalence} = \frac{\text{Cases}}{\text{Population (at risk)}} \quad \text{Eq. 1}$$

Incidence is the number of new infections in a population within a specified time period. It can be expressed as a proportion (cumulative incidence: Eq. 2) or as a rate (Eq. 3). Cumulative incidence can be used to calculate the level of risk for a certain population. The cumulative incidence is also known as attack rate.

$$\text{Cumulative incidence} = \frac{\text{New cases}}{\text{Population at risk for some amount of time}} \quad \text{Eq. 2}$$

$$\text{Incidence rate} = \frac{\text{New cases over a time period}}{\text{Time each person was observed, summed for population}} \quad \text{Eq. 3}$$

To estimate the increased risk of disease for a population exposed to a certain variable, three different ratios can be used. Risk ratio (RR) is the ratio of cumulative incidence in two population groups (Eq. 4). The risk ratio can also be seen as the relative risk of disease. If the $RR = 1$, the incidence is the same in the exposed group and the unexposed group: there is no association between exposure/risk factor and disease. If $RR > 1$, there is an increased risk of disease in the exposed group than in the unexposed group. If $RR < 1$, there is a reduction in risk of disease for the exposed group.

$$\text{Risk Ratio} = \frac{\text{Risk (cumulative incidence) in exposed group}}{\text{Risk (cumulative incidence) in unexposed group}} \quad \text{Eq. 4}$$

The rate ratio is a ratio between incidence rates of an exposed group and an unexposed group (Eq. 5). It is also called incidence density ratio. Rate ratio is useful when the time component is relevant for the study.

$$\text{Rate Ratio} = \frac{\text{Incidence rate in exposed group}}{\text{Incidence rate in unexposed group}} \quad \text{Eq. 5}$$

Odds ratio measures the relative odds of an outcome occurring after an exposure (Eq. 6). The numerator is the number of exposed cases divided by the number of unexposed cases. The

denominator is the number of exposed non-cases divided by the number of unexposed non-cases. An OR > 1 indicates increased odds of developing the outcome when exposed to a given variable, and an OR < 1 indicates the opposite. An OR = 1 indicates that the odds of the outcome are not affected by the variable (Szumilas, 2010).

$$\text{Odds Ratio} = \frac{\text{Odds of disease in exposed group}}{\text{Odds of disease in unexposed group}} \quad \text{Eq. 6}$$

For rare diseases, i.e., where the incidences are low, both rate ratios and odds ratio are numerically the same as the risk ratio (Schoenbach, 2000c; Silman and Macfarlane, 2002).

2.4.1 Types of epidemiological studies

There are a variety of epidemiological study designs that can be used to try to determine the relationship between risk factors and disease (see Table 3). Some study designs may be suitable to determine causes; while others can merely determine correlations or express changes in outcomes (Ho et al., 2008; Burns et al., 2011). The different designs available are: ecological, case-control, cross-sectional, cohort and randomized-controlled trials. A literature review on how these study designs have been used in the drinking water context can be found in Bylund et al. (2017).

Ecological, case-control, cohort and cross-sectional studies are collectively called observational studies (Mann, 2003). They are considered observational since the investigator does not intervene directly when collecting data on individuals. Although grouped as observational, each of the study has its own particularities, advantages and disadvantages.

Ecological studies can be used to determine correlations between risk factors and health outcomes in a certain population (defined geographically, politically or temporally) (Bylund et al., 2017; Schoenbach, 2000d). If the data is routinely collected and readily available, this study design can be carried out more quickly and less costly than other studies. However, ecological studies cannot control for potential bias (e.g., selection bias) or confounding – that is when the disease is mistakenly attributed to the risk factor/exposure being studied, due to not considering the effects of other potential factors. This restricts ecological studies from being used for hypothesis testing (i.e., cannot determine causality).

In case-control studies, the investigators group people exhibiting a desired outcome into cases and a group that does not as controls (Mann, 2003; Silman and Macfarlane, 2002). The investigators then determine which individuals were exposed to the variable of interest in both groups. Case-control studies are suitable when the disease is rare: since the investigator selects the cases, they will have a higher proportion of subjects. Studies will could also be comparatively cheaper and easier to perform (Rothman et al., 2008). Case-control studies are still prone to biases, i.e., selection bias and recall bias. Additionally, it is difficult to determine if the exposure preceded the outcome (Mann, 2003; Schoenbach, 2000d).

Cohort studies can be retrospective or prospective (Mann, 2003). A prospective cohort study involves following a population over a period of time, measuring possible risk factors that could

lead to the onset of a condition. Over the period of time, the population is observed to verify if they have developed the outcome of interest. Retrospective studies follow the same study design, with the only difference being that the exposure data has already been collected and only the development of the outcome is analysed in the present (see Figure 6). Cohort studies allow for the determination of causality. Relative risk can also be estimated with this design. However, these type of studies are resource-intensive (Bylund et al., 2017), in addition to possibly suffering from high drop-out rates. Confounding is also possibility.

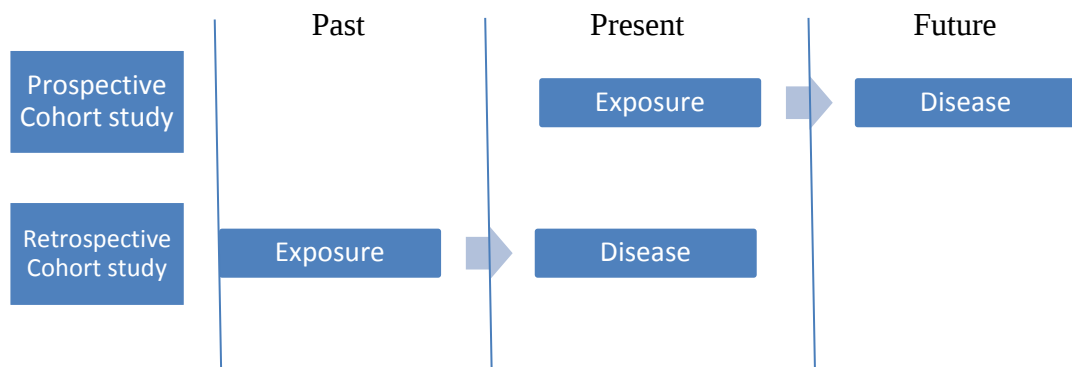


Figure 6 - Timing for measuring exposure and disease in cohort studies. Adapted from Silman and Macfarlane (2002).

A cross-sectional study collects information about a population at a specific point in time. It is used to measure the point prevalence of a disease (Silman and Macfarlane, 2002). Cross-sectional studies are usually inexpensive and quick. However, cross-sectional studies are also susceptible to misclassification and selection bias (Schoenbach, 2000d). Since all the information is collected at the same time, it may be difficult to establish if the cause preceded the effect.

Another class of study designs are experimental in nature. Randomized-controlled trials (RCTs) are considered the closest design epidemiology has to a laboratory experiment. In RCTs, the investigator directly “intervenes” in the studied population, by deciding which group is exposed to the variable of interest and which is not (Schoenbach, 2000d). RCTs provide the strongest evidence for causality of all the study designs (Ho et al., 2008). It can also provide a direct measure of the risk reduction due to the intervention (Bylund et al., 2017). In some cases, performing an RCT will be unethical; hence, alternative study designs are the only choice (Rothman et al., 2008). Additionally, RCTs are expensive and time consuming.

All of the designs previously described are commonly used in epidemiological investigations concerning association of the distribution network to disease. These represent direct and indirect measurements of microbial risk associated with distribution network deficiencies. There exists another possibility of using computational software, different modelling tools, and site-specific measurements, among other data to evaluate microbial risks and health effects due to pathogen exposure. It is encompassed in a framework known as Quantitative Microbial Risk Assessment Framework.

Theoretical Background

Table 3 - Types of epidemiological studies used to evaluate the association of the distribution network with endemic disease.

Study design	Type	Advantages	Disadvantages	Measure of association (Schoenbach, 2000d)
Ecological	Observational	If data is collected routinely, can be performed cheaply and quickly	Ecological fallacy Cannot control for confounding or other bias	Incidence Rate Ratio (IRR), Odds ratio
Case-control	Observational	Suitable for rare diseases Efficient use of resources and time	Prone to selection bias & recall bias Cannot establish sequence of exposure and outcome	Odds ratio (OR)
Cross-sectional	Observational	Can study entire populations Improved generalizability	Cannot establish sequence of exposure and outcome Prone to misclassification and selection bias	Prevalence odds ratio or prevalence ratio
Cohort	Observational	Can establish sequence of exposure and outcome Can assess several outcomes	Large sample sizes Risk for confounding Impractical for rare diseases Expensive and time consuming	Risk ratio
RCTs	Experimental	Direct measurement of risk reduction due to intervention	Expensive Time consuming	Incidence Risk Ratio (RR)

2.5 The QMRA framework

One of the most valuable methodologies available for quantification of microbial risks is the quantitative microbial risk assessment (QMRA) framework (Pettersen et al. 2016). A QMRA consists of four basic steps (WHO 2016):

- Problem formulation: the scope and purpose of the assessment is determined at this stage. Hazards, exposure pathways and health outcomes are investigated;
- Exposure assessment includes quantifying pathogen sources, magnitude and frequency of the exposure for the different scenarios being analysed;

- Health effects assessment involves estimating the health impact from the identified hazards and the population of the study (e.g., drinking water consumers);
- Risk characterization combines the exposure and health effects assessments to quantify the risk of infection. This can be represented as number of consumers infected per year, DALYs. A sensitivity analysis can also be performed in this step to determine which parameters influence the most the QMRA results.

An alternative QMRA framework presents a 5-step approach: hazard identification, dose-response assessment, exposure assessment, risk characterization and risk management (QMRAwiki, 2013; Haas et al., 2014). Risk management is the only step that is explicitly new. Here, costs and measure effectiveness are important components to make a decision after performing the previous four steps. It is important to note that in order to perform a valid assessment, uncertainties must be taken into account in each step, whether it be 4-step or 5-step QMRA. Otherwise, the results will not be representative of reality (Bouwknegt et al., 2014). A detailed explanation of each step from a distribution network perspective follows below.

2.5.1 Problem formulation

The main aim with problem formulation is to determine the scope and the purpose of the risk assessment. Effectively identifying potential hazards, in addition to contamination pathways and outcomes after exposure are all tasks to complete to have a successful problem formulation (WHO, 2016). However, already in this step some level of assumptions are needed to successfully formulate the problem.

One relevant assumption made early in the assessment is the choice of reference pathogens, since it is not possible to evaluate all possible waterborne pathogens in a single QMRA (WHO, 2016). By choosing reference pathogens, it is assumed that all other pathogen of the same type will be controlled in the same way as the reference. The reference pathogens should be the most representatives of the local conditions. For example, *Campylobacter*, norovirus and *Cryptosporidium* would be appropriate choices for reference pathogens for a QMRA performed in Sweden: epidemiological investigations support their selection (Abrahamsson et al., 2009; Guzman-Herrador et al., 2015).

To determine the exposure pathway, it is necessary to define which hazardous events or scenarios will be included in the assessment. This definition is required due to differences in potential pathways depending on which risk is assessed. For example, if the risk assessor is interested in studying intrusion and reservoir contamination, the transport inside the distribution towards the consumer can be identified in same way (see Figure 7). However, the pathogen source and pathway will differ completely.

The final step in the problem formulation is to determine which health outcome will be used to assess the risk (WHO, 2016). These can be expressed as, e.g., a yearly probability of infection or disability-adjusted life years (DALYs). The choice of health outcome will depend on the objective of the risk assessment.

2.5.2 Exposure assessment

The main goal of the exposure assessment is to quantify the sources, contamination and exposure pathways identified in the problem formulation (Haas et al., 2014). Both theoretical models (e.g., Vairavamorthy et al. (2007)) and source characterization (Besner et al., 2010a; Karim et al., 2003) have been used to quantify pathogen concentrations that could potentially contaminate the distribution network. Most of the quantification has focused on the risk of intrusion and contamination during maintenance or repair work (Yang et al., 2015; Teunis et al., 2010b; Blokker et al., 2018). Hydraulic models are also needed in order to quantify the route from the source to the consumers' tap.

Control measures to inactivate pathogens in the distribution network are limited compared to options available for the source water and treatment plant (Risebro et al., 2007). According to QMRAs already performed in the network, the following parameters achieve some kind of reduction of the pathogen concentration: disinfectant residual, dilution factor, flushing (Yang et al., 2015; Blokker et al., 2018; Teunis et al., 2010b).

For distribution network QMRAs, the basic mechanism of exposure for the consumer is through unboiled tap water intake (Yang et al., 2011; Teunis et al., 2010b; McInnis, 2004). To quantify this parameter, consumption pattern studies have been performed in variable settings, e.g., (Säve-Soderbergh et al., 2017; Roche et al., 2012; Hynds et al., 2012). Local consumption pattern studies are needed in order to accurately describe the exposure levels in the population, making the QMRA results more reliable.

2.5.3 Health effects assessment

After determining the population that will be exposed to a certain pathogen concentration, the next step will be to assess the health outcomes of these. The health effects assessment uses dose-response models to relate the dose to a probability of infection or disease (Haas et al., 2014). Dose-response models are currently available for numerous pathogens: *Campylobacter* (Medema et al., 1996; Teunis et al., 1999; Teunis et al., 2005); *Salmonella* (Teunis et al., 1999; Teunis et al., 2010a); *E. coli O157:H7* (Teunis et al., 2004; Teunis et al., 2008b); adenovirus (Teunis et al., 2016); norovirus (Teunis et al., 2008a; Messner et al., 2014); *Cryptosporidium* (Teunis et al., 1999; Teunis et al., 2002); and *Giardia* (Teunis et al., 1996; Zmirou-Navier et al., 2006).

2.5.4 Risk characterization

Risk characterization consists in combining the exposure assessment and the health effects to generate a quantitative estimation of risk. Risk estimates are most commonly expressed as yearly probability of infection and/or disability-adjusted life years (DALYs). These estimates can be used in different ways, e.g., compare the calculated risk with a regulatory target. For example, in United States the annual probability of infection allowed is set to 1/10,000 consumers (National Research Council, 2006). Consequently, if a QMRA is performed for the distribution network and the estimated risk of infection is 2/10,000 consumers per year; it could be concluded that the risk is unacceptable if compared to the health target.

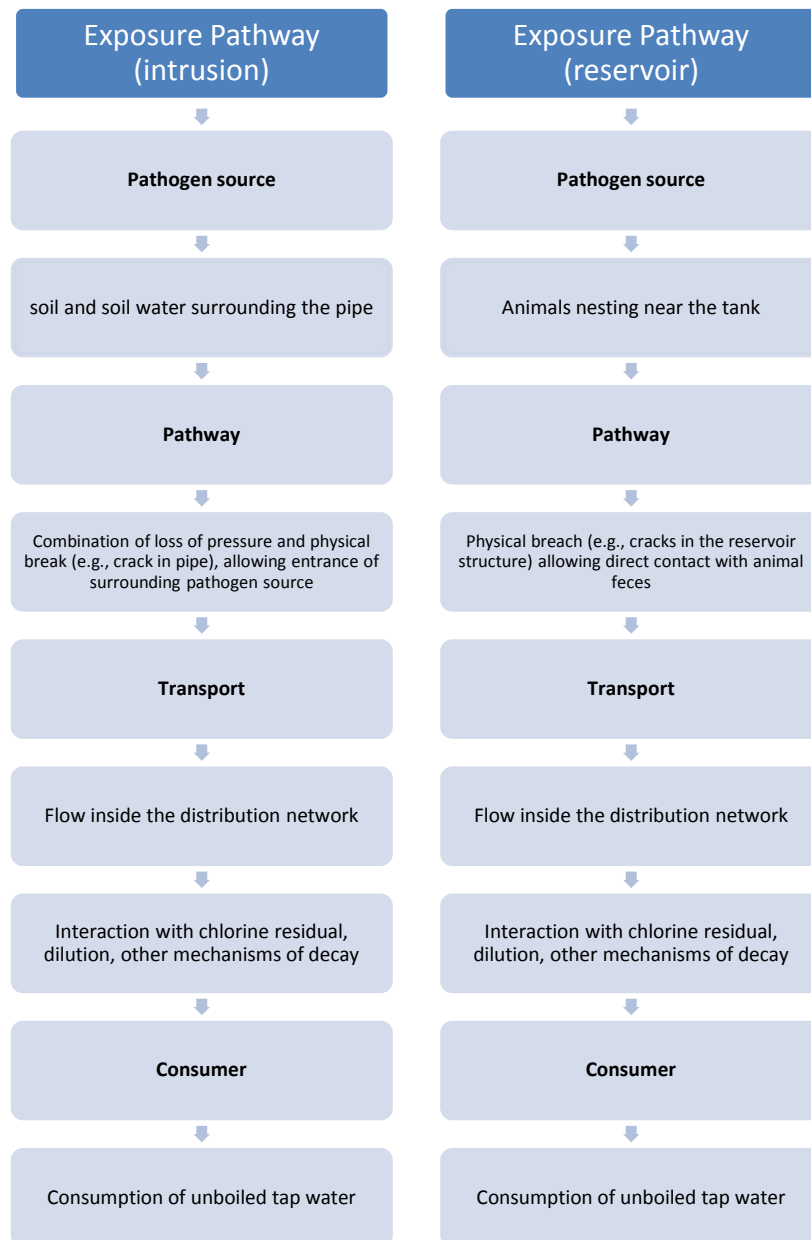


Figure 7 - Example of definition of exposure pathways for intrusion and reservoir.

In order to properly characterize the risk, uncertainties must be included in the analysis (Lindhe, 2010; Bouwknecht et al., 2014). A common way to perform uncertainty analyses in distribution network risk assessments is through Monte Carlo simulations (Teunis et al., 2010b; Torres et al., 2009; Nilsson et al., 2005; Khanal et al., 2006). Monte Carlo simulations use probability distributions as their input data, selecting random numbers from the distribution for each calculation. This process is performed for a certain number of iterations (e.g., 1 000, 10 000), obtaining a probability distribution as the result (Lindhe, 2010).

A sensitivity analysis should also be carried out for different reasons: refine the assessment, identify sources of uncertainty, and determine mitigation measures, among others (WHO, 2016). Monte Carlo simulations can also be used for this purpose; however, the standard method involves changing the input variable and noting the extent of the change in the result.

2.5.5 Risk management

The risk characterization results may be used inform decisions about managing the risk (Haas et al., 2014). For example, if the risk is deemed unacceptable mitigation measures are needed. After implementing the mitigation measure(s), a new risk estimate can be obtained by running the model with the new information. The adjusted risk estimate is then compared to the health target and evaluated accordingly. Possible mitigation measures during a contamination incident in the distribution network include (Säve-Söderbergh et al., 2017; Blokker et al., 2018):

- Isolation of the affected area
- Chlorination
- Flushing
- Boil water advisory
- Emergency water sources

3 Materials and methods

Methods used in the elaboration of Paper I and Paper II are described in this chapter. Paper I mainly consisted of a systematic literature review; hence, keywords, databases and other relevant information are given. The fault tree analysis and a secondary literature review for data collection, which are relevant for Paper II, are described in this section.

3.1 Literature review (Paper I)

A systematic literature review was performed for Paper I. The literary search was performed within three databases: Scopus, Web of Science and PubMed. Scopus and Web of Science were chosen due to their extensive collection of peer-reviewed literature. PubMed Central (PMC) was chosen due to their focus on life sciences and biomedical literature.

In order to perform the first literary search, the following keywords were used: (1) “drinking water”, (2) “distribution system”, (2) “distribution network”, (3) “disease outbreak” and (3) “gastrointestinal disease”. The keywords were combined in different ways using Boolean operators. Keywords in group (3) were truncated for some of the searches. The same search strategies were used for the three selected databases. Moreover, after performing the first search strategy in Scopus, results were refined using additional keywords e.g., water contamination, water supply, epidemic, risk assessment, etc. Keyword searches were complemented with citation searches. A summary of the search strategies used for each database can be seen in Appendix. For this thesis, the focus of the first literary search will be the endemic disease results.

For the second literary search, group (3) was changed to microbial risk assessment and the search was conducted again. Results were complemented with citation searches as well.

3.2 Cross-connection and backflow conceptual model (Paper II)

A conceptual model for estimating the risk of cross-connection and backflow in a theoretical network was developed using the fault tree methodology and literature data. Fault trees are a graphical method that allows modelling how component failures can lead to a system-wide failure (Ruijters and Stoelinga, 2015). The system failure event, usually called *top event*, will be subdivided into *intermediate events* and/or events at the end of the branch, i.e., *basic events*. Intermediate and basic events will be evaluated using logic gates, i.e., AND-gates and OR-gates, leading to the top event. Fault tree analyses have been used in probabilistic risk analyses within a drinking water context in the past (e.g., Lindhe et al. (2009); Risebro et al. (2007)); therefore, it was considered a valid methodology for the purpose of cross-connection risk estimation.

In this scenario, the top event was considered to be microbial contamination of the drinking water due to a cross-connection and backflow incident (see Figure 8 and Figure 9). For a contamination event to occur, there must be both the presence of a cross-connection (quality/source of contamination) and a backflow event (trigger of the event & magnitude of contamination). For a cross-connection to be possible, two intermediate events must occur: a

non-potable source must be put into contact with the drinking water and the competent authority fails to detect (either through having a supervision program with this goal and failing to detect or lack of supervision). The misconnection can be considered to originate from a human mistake, e.g., connecting a stormwater pipe to a point in the network, or a design failure. Human errors can be wrongful maintenance work or repair, plumbing mistakes inside residences. Design failures can include construction practices that compromise the integrity of the system (such as connecting reservoir overflows to non-drinking water pipes).

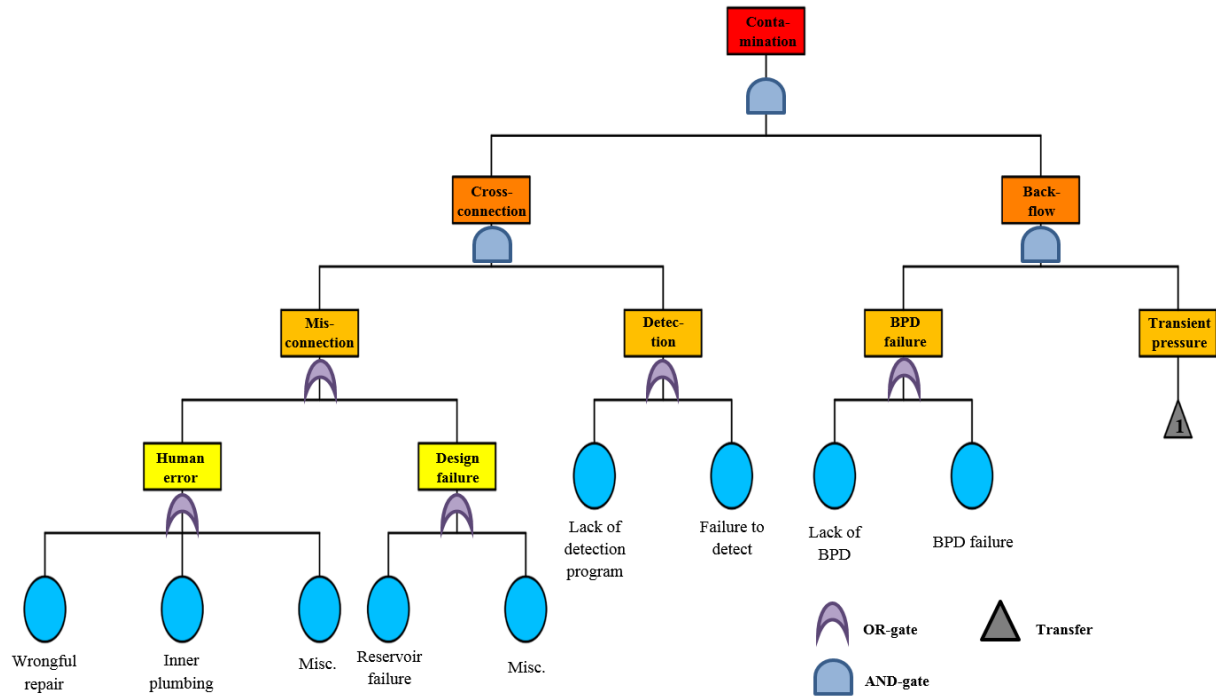


Figure 8 - Fault tree for cross-connection and backflow contamination event.

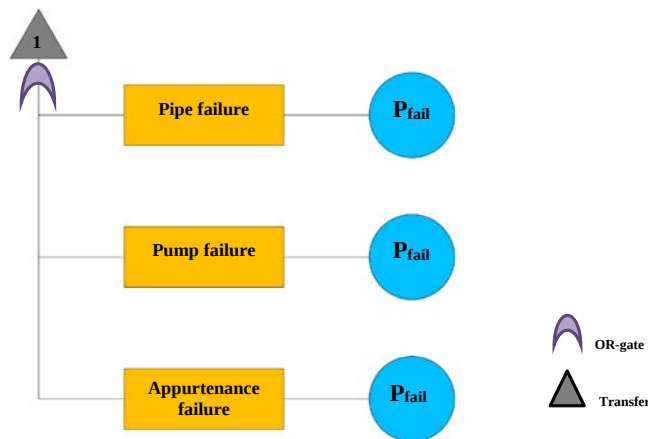


Figure 9 - Continuation of fault tree in Figure 8.

Intermediate events and basic events were generated from two main sources: TECHNEAU Hazard Database (Beuken et al., 2008) and reported outbreaks, e.g., Kristianstads kommun (2015); Mena et al. (2008); Laine et al. (2011); Falco and Williams (2009). A list of all basic events considered is presented in Table 6.

In parallel to the calculation of the probability of contamination, the magnitude of the contamination was estimated. Three levels of potential contamination were considered: (1) Endemic risk case (2) Elevated risk case - contaminated stormwater coming into the network (3) Extreme risk case - treated wastewater coming into the network. These were taken from a study for a new monitoring sensor tested in Swedish networks (Sensation III, Unpublished).

- Endemic risk case: 5-50 CFU/100ml *E.coli* (0.005-0.05 % wastewater)
- Elevated risk case: 700 CFU/100ml *E. coli* (0.7% wastewater)
- Extreme risk case: 5000 CFU/100ml *E. coli* (10% effluent wastewater)

The reference pathogens chosen were *Campylobacter*, Norovirus and *Cryptosporidium*. Concentrations were estimated using the indicator organism concentration and standard values for domestic wastewater and treated effluent (Tchobanoglous et al., 2003). Pathogen concentrations for each case are shown in Table 4.

Table 4 - Pathogen concentrations determined for each case.

Reference Pathogen	Endemic (No./L)	Elevated (No./L)	Extreme (No./L)
Campylobacter	13 – 130	1 750	25 000
Norovirus	5 – 50	70 – 700	1 000 – 10 000
Cryptosporidium	0.05 – 5	0.70 – 70	10 – 1 000

Due to the lack of site-specific distribution network, likelihood of failure was estimated from historical data (Malm et al., 2010). The endemic risk case was estimated to occur at the same frequency as an incident due to cross-connections was reported in the media. Outbreaks were estimated to occur at the frequency of reported outbreak cases due to cross-connections. Elevated risk case was considered to be 5 times more frequent scenario than extreme risk case. This assumption was based on repeated reports of outbreaks being wastewater-influenced stormwater or similar; rarely the cross-connection was reported to occur at the wastewater treatment plant. To initially test the methodology, average values for length of distribution system at a national level were used. Frequency estimations are presented in Table 5.

Table 5 - Frequency of disturbances and outbreaks caused by cross-connections and backflows. Source: Malm et al. (2010)

Parameter	Value	Additional information
Total length of distribution network in Sweden	67 000 km	The Swedish Water & Wastewater Association (2000) Government Offices of Sweden
No. of Swedish municipalities	290	
Average length of distribution network/municipality	231 km	
No. of disturbances reported 2000-2008	11 incidents	Malm et al. (2010)
No. of disturbances reported 2000-2008 (km ⁻¹ yr ⁻¹)	1.82 x 10 ⁻⁵	
Outbreaks reported 1980-2009	9 outbreaks	Malm et al. (2010)
Outbreaks reported 1980-2009 (km ⁻¹ yr ⁻¹)	4.48 x 10 ⁻⁶	Elevated risk case
Outbreaks reported 1980-2009 (km ⁻¹ yr ⁻¹)	8.96 x 10 ⁻⁷	Extreme risk case

Materials and methods

Table 6 - List of basic events in the fault tree. Further descriptions are provided.

Basic Events	Type of failure	Description
Absence of supervision	Detection	Lack of supervision program during new connections to the network, lack of sufficient staff, knowledge, etc.
Supervision failure	Detection	Supervision program fails to detect misconnection
Wrongful maintenance/repair work in the mains	Misconnection: Human error	Wrongful connection of a non-potable water pipe to drinking water pipe during regular maintenance or repair work
Building of new mains	Misconnection: Human error	Wrongful connection of a non-potable water pipe to drinking water pipe during construction of new mains
Wrongful connection in-house plumbing	Misconnection: Human error	Wrongful connection of a non-potable water pipe to drinking water pipe (service lines)
Misc. error	Misconnection: Human error	Other human mistakes
Backflow into reservoir from overflow pipe	Misconnection: Design/construction flaw	Overflow pipe connected to a non-potable drainage pipe
Misc. design	Misconnection: Design/construction flaw	Other design/construction mistakes
Backflow-prevention device failure	Backflow: Backflow-prevention device	Failure of backflow-prevention device
Absence of backflow-prevention device	Backflow: Backflow-prevention device	Lack of backflow-prevention device
Valve failure	Backflow: Hydraulic loss	Damage or destruction of network pipes due to water hammer
Pipe failure	Backflow: Hydraulic loss	Pipe burst due to increased external-stresses on pipe (e.g. traffic, soil movement, etc) in combination with a reduced pipe condition Pipe burst due to bad condition of pipe (e.g. internal /external corrosion) Low pressure in the network due to wrong settings, deficient metering or deficient control of pumps operation [VV1] Pump stoppage due to power failure/disruption and failing power back-up supply
Pump failure	Backflow: Hydraulic loss	Pump malfunctioning/failure Damage or destruction of network pipes due to water hammer, caused by absent or malfunctioning surge tanks Damage or destruction of pumping station due to human-caused accidents (car, truck or aircraft collision, landslides caused by leakage or nearby excavation)

4 Summary of Thesis Contributions

In this chapter the main findings in Paper I and Paper II are presented.

4.1 Literature review

The first main topic of the literature review in *Paper I* were the epidemiological studies. A summary of the epidemiological studies evaluating the association of the distribution network with gastrointestinal illness is listed in Table 7. Both observational (ecological, cross-sectional, case-control and cohort) and experimental (randomised-controlled trials) were carried out in distribution networks. A brief commentary on the main findings of these studies is presented below (for more details see *Paper I*).

The most common study design was the ecological study. The studies were carried out in Sweden (Nygard et al., 2004; Malm et al., 2013a), France (Beaudeau et al., 2014), and two cities in USA (Hsieh et al., 2015; Tinker et al., 2009). The studies had differing results, even when performed in the same country.

Nygard et al. (2004) investigated a multitude of potential risk factors for *Campylobacter* infections in Sweden. The authors found a positive correlation between distribution pipe length per person and increased *Campylobacter* infection. This meant that the longer the distribution pipe, higher the risk of infection. In contrast, Malm et al. (2013a) found no association between disturbances in the distribution network in the city of Gothenburg and calls to a health call centre. It was considered that most of the events in this study were low-risk (Bylund et al., 2017).

Beaudeau et al. (2014) used medical prescription data as a proxy for AGI and tested the association with several water network variables: finished water turbidity, river daily flow, source water turbidity, and daily interventions for pipe breaks. The authors tested for children and adults separately. Pipe breaks had a statistically significant in the children when performing univariate analysis, although significance was lost when combining it to other covariates in the multivariate analysis [ERR = 1.5% (-1.4% - 4.4%)]. No association at all was found for the adult population [ERR = -0.9% (-3.3% - 1.7%)].

For the ecological studies carried out in American cities, one focused on the water residence time in the network (Tinker et al., 2009) and the other on turbidity (Hsieh et al., 2015). Tinker et al. (2009) found a slight positive association between emergency visits due to GI and longer residence times. Hsieh et al. (2015) also found slight associations between emergency visits for GI and higher turbidity during spring, and for children age group. Nevertheless, the positive associations were usually linked to higher source water turbidity; thus, the distribution network was not the main factor influencing the emergency visits.

Both cohort studies identified in the search were performed in Scandinavia (Nygard et al., 2007; S  ve-S  derbergh et al., 2017). Nygard et al. (2007) found a significant association between main breaks and maintenance work in 7 Norwegian distribution networks and the affected households' incidence of GI. The authors concluded that 37% of the incidence could be

attributed to these risk factors. S  ve-S  derbergh et al. (2017) carried out a study in five Swedish municipalities studying GI during incidents in the distribution network. The authors also detected a significant positive association between disturbances in Swedish networks and acute gastrointestinal illness (AGI) and vomiting, but not for GI. The relative risk increase for AGI was 38%, within the same range as Nygard et al. (2007).

Hunter et al. (2005) performed a subsequent analysis of the control group from a larger case-control study of endemic cryptosporidiosis in UK. The authors found a strong association between low pressure events and self-reported diarrhoea [OR = 12.5 (3.5 - 44.7)]. However, it is worth mentioning that the data was extracted from a larger study of sporadic cryptosporidiosis; the study was not designed to test the hypothesis that low pressure events had an association with GI.

A cross-sectional study relating decay of chlorine residual with GI was carried out in Russia (Egorov et al., 2002). The authors calculated the relative risk due to free chlorine decay to be RR = 1.42 (1.05 – 1.91). The associations were similar when taking other parameters into account in conjunction with chlorine residual, e.g., turbidity, chloramines, total heterotrophic plate counts, etc.

There were four main intervention studies (RCTs) identified in the literature review: two carried out in Canada (Payment et al., 1997; Payment et al., 1991), one in the USA (Colford et al., 2005) and one in Australia (Hellard et al., 2001). Both Canadian studies found an increased risk from consuming tap water compared to other improved sources (point-of-use treated tap water, bottled water, and bottled water from treatment plant). Additionally, Payment et al. (1997) found that the distribution network contributed to 14-19% of excess risk of GI. Hellard et al. (2001) and Colford et al. (2005) did not detect any association in their respective studies [Hellard et al. (2001): RR = 0.99 (0.85 - 1.10); Colford et al. (2005): RR = 0.98 (0.87-1.10)]. This indicated that the contribution of the distribution network to endemic level of GI was lower than 15% and 11%, respectively (statistical strength of the studies).

The second literary search focused on QMRA methodologies. There were in total seven QMRA methodologies developed for particular risks in the distribution network, with varying degrees of complexity (see Table 8). Most of the QMRA models used some sort of hydraulic modelling to simulate the contaminant transport in the distribution network. The transport simulation determined which nodes would be affected by the contamination plume. Monte Carlo simulations were used to generate enough trial runs until a satisfactory result was obtained.

4.2 Cross-connection and backflow conceptual model

The methodology developed for estimating the risk of cross-connections and backflows could not be tested as desired, due to the lack of site-specific distribution network. However, a general proof of concept was carried out to test the methodology and gather some insights about the results. Comparing the estimates with the health target set by the US EPA of 1/10 000 infections per year, one realizes that the target is fulfilled in only one reference pathogen and one case (protozoa, endemic case). The highest infection risks were for the Nokia case (1×10^{-3} for all reference pathogens) and the bacteria reference pathogen for the endemic case (1.1×10^{-3}).

Summary of Thesis Contributions

Table 7 - Selected epidemiological studies that have addressed the contribution of tap water to endemic level of disease (Paper I).

Study	Location	Study design	Blinding	Size of the study*	Follow-up period	Results [†]	Attributable Risk
Payment et al (1991)	Canada	Cluster Randomized Controlled Trial	No	607 / 2 408	12 months	RR = 1.5 (p <0.01)	≈35% excess GI in the tap water group compared to control
Payment et al (1997)	Canada	Cluster Randomized Controlled Trial	No	1 369 / 5 253	16 months	RR = 1.15 (p <0.01)	14% - 19% excess risk of GI; 17% - 40% in children 2-5 years old
Hellard et al (2001)	Australia	Cluster Randomized Controlled Trial	Yes	600 / 2 811	12 months	RR = 0.99 [0.85 - 1.10]	No association found
Egorov et al 2002	Russia	Cross-sectional	n.a.	-- / 2 269	n.a.	RR = 1.42 [1.05 - 1.91]	Significant association between free chlorine residual and self-reported GI
Nygård et al (2004)	Sweden	Ecological	n.a.	-- / 7 280	n.a.	1. IRR = 1.11 [1.08 - 1.15] 2. IRR = 1.12 [1.08 - 1.16] 3. IRR = 1.13 [1.09 - 1.17] [‡]	Significant association of length of pipe directly proportional to increased risk of infection
Colford et al (2005)	United States	Cluster Randomized Controlled Trial	Yes	456 / 1 296	12 months	RR = 0.98 [0.87-1.10]	No association found
Hunter et al (2005)	United Kingdom	Case-control	n.a.	-- / 427	n.a.	OR = 12.5 [3.5 - 44.7]	Significant association between low pressure event and disease (p <0.01)
Nygård et al (2007)	Norway	Cohort	n.a.	1 159 / --	n.a.	RR = 1.58 [1.1 - 2.3]	Attributable fraction of 37% one week after exposure
Tinker et al (2009) [§]	United States	Ecological	n.a.	-- / 1 700 000	n.a.	1. OR = 1.00 [0.96 - 1.03] 2. OR = 0.99 [0.96 - 1.03] 3. OR = 1.07 [1.03 - 1.10] 4. OR = 1.05 [1.02 - 1.08]	Slight association directly proportional to the residence time and increased risk of disease
Malm et al (2013)	Sweden	Ecological	n.a.	-- / 500 000	n.a.	SIR = 1.08 [0.86 - 1.32]	No significant association found due to low pressure events
Beaudeau et al (2014)	France	Ecological	n.a.	-- / 400 000	n.a.	Children: ERR = 1.5% [-1.4% - 4.4%] Adults: ERR = -0.9% [-3.3% - 1.7%]	No significant association found in children No association found in adults
Hsieh et al (2015)	United States	Ecological	n.a.	Not specified	n.a.	Peak ERR = 5% [3% - 6%] GI: OR = 1.1 [0.9 - 1.5] AGI: OR = 2.0 [1.2 - 3.3] Vomiting: OR = 1.9 [1.2 - 3.0]	Positive association at approximately 6-day lag
Säve-Söderbergh et al. (2017)	Sweden	Cohort	n.a.	3 238 / 7431	n.a.		Significant association for AGI and vomiting

*Sample size is given by No. of households / No. of individuals

[†]RR: Incidence Risk Ratio. IRR: Incidence Rate Ratio. OR: Odds Ratio. SIR: Standardized Infection Ratio. ERR: Excess Relative Risk.

[‡]Result 1 is from univariate analysis; results 2 and 3 are from multivariate analyses

[§]Included more water suppliers in a subsequent study Tinker et al. 2010. Refined assessment conducted by Levy et al. (2016)

^{||}(1)OR between intermediate and short residence times and utility 1, (2) OR between intermediate and short residence times and utility 2, (3) OR between intermediate and long residence times and utility 1, (4) OR between intermediate and long residence times and utility 2

Summary of Thesis Contributions

Table 8 - QMRA performed for distribution networks. Taken from Paper I.

Study	Network site	Risk event	Pathogen	Methodology
McInnis 2004	City in North America	Intrusion	Giardia, faecal streptococci	QMRA coupled with hydraulic modelling and Monte Carlo simulations for risk characterization. QMRA modelling
Storey et al. 2004	Sweden	Biofilm	Legionella	Detachment of Legionella was determined experimentally, as well as disinfection data. Monte Carlo simulations were used for risk characterization
van Lieverloo et al. 2007	Netherlands	Multiple contamination events	Giardia, Campylobacter, Cryptosporidium and enterovirus	QMRA coupled with hydraulic modelling. QMRA coupled with hydraulic modelling.
Mena et al. 2008	United States	Cross-connection	Salmonella	Used a distribution network simulator to estimate transport of contaminated water and Monte Carlo simulations for risk characterization QMRA coupled with hydraulic modelling.
Teunis et al. 2010b*	United States	Intrusion	Rotavirus, norovirus	Used commercial software to do surge modelling, EPANET-MSX for water quality modelling coupled with Monte Carlo simulations for risk characterization QMRA coupled with hydraulic modelling.
Blokker et al. 2018†	Netherlands	Main repair	Giardia, Campylobacter, Cryptosporidium and enterovirus	Used EPANET to simulate transport of contaminated water, SIMDEUM for consumption patterns, and Monte Carlo simulations for risk characterization QMRA coupled with hydraulic modelling.
Yang et al. 2015	United States	Main repair	Norovirus, E. coli O157, Cryptosporidium	Simplified model from Teunis et al. 2010b

*Complemented by Yang et al 2011.

†Originally developed in Blokker et al. 2014

Table 9 - Yearly probabilities of infection for each scenario and each reference pathogen.

Case	P _{inf} (magnitude) Bacteria	P _{inf} (magnitude) Virus	P _{inf} (magnitude) Protozoa	P (contamination event) * 231 km	Yearly probability of infection (P _{inf} * P) Bacteria	Yearly probability of infection (P _{inf} * P) Virus	Yearly probability of infection (P _{inf} * P) Protozoa
Endemic	2.7 x 10 ⁻¹	1	1.71 x 10 ⁻²	1.82 x 10 ⁻⁵	1.1 x 10 ⁻³	4.2 x 10 ⁻³	7.19 x 10 ⁻⁵
Elevated	1	1	1	4.48 x 10 ⁻⁶	1 x 10 ⁻³	1 x 10 ⁻³	1 x 10 ⁻³
Extreme	1	1	1	8.96 x 10 ⁻⁷	2.1 x 10 ⁻⁴	2.1 x 10 ⁻⁴	2.1 x 10 ⁻⁴

5 Discussion and Outlook

The results presented in the previous chapter are scrutinised further. Important limitations are described and contextualised. Finally, current limitations of microbial risk assessments for distribution networks are addressed with proposals for future work.

5.1 Epidemiological studies

As shown in section 4.1 Table 7, a variety of study designs have been used to evaluate microbial risks in the distribution network. The results have been mixed, for reasons that are still inconclusive (National Research Council, 2006). Many of the epidemiological studies lack detailed descriptions of their study site to be able to draw comparisons among them, i.e., networks were too heterogeneous to generalise (Ercumen et al., 2014). Many also lack statistical robustness (Sinclair and Fairley, 2000; Bylund et al., 2017). Nonetheless, a meta-analysis of epidemiological studies concluded that there is a trend: malfunctioning distribution networks, as well as specific system deficiencies (i.e., pipe breaks, water outages and inadequate residual disinfectant), increase the risk of endemic GI (Ercumen et al., 2014). Specific limitations to each study are addressed in the subsections below.

5.1.1 Household interventions (RCTs)

RCTs are considered the golden standard of epidemiological studies, i.e., the best available study design to test for causal relationships of interventions (Ho et al., 2008; Walach and Loeff, 2015). It is therefore troublesome that the studies performed for the distribution network have not had uniform results. At closer inspection, though, there are several differences between the studies that might impact the results, e.g., blinding.

Hellard et al. (2001) was double blinded: both the authors and the subjects were not aware which household received a real point-of-use (POU) treatment device and which one had a sham device. Colford et al. (2005) was triple blinded: authors, participants and data analysts were all unaware of which household had a functioning POU device and which one did not. Payment et al. (1991) and Payment et al. (1997) were both un-blinded intervention studies. Blinding limits the effects of potential bias from all parties involved: subjects, researchers and data analysts (Rothman et al., 2008); hence, it might justify avoiding the comparison of results from blinded and unblinded studies. It is interesting to note that only the unblinded studies found an increased risk of GI due to drinking water, while the blinded studies did not find any association.

A unique feature of Payment et al. (1997) was that it was able to distinguish between drinking water influenced by the distribution network and water produced at the treatment plant. This was possible since the study had four different groups: regular tap water, flushed tap water, bottled water directly from treatment plant and purified treated bottled water. Future RCTs looking to study the effect of the distribution network on endemic GI could emulate this design to better quantify the risk level associated specifically with the network. Nevertheless, the bottled treatment plant water group had a considerable drop-out rate (~50%) due to taste and odour problems with the water. High drop-out rates can affect the randomization of the trial, which might lead to confounding (Rothman et al., 2008). This is undesirable since it limits the

comparability between the groups in the study and impacts the strength of the causal factor identified. Since Payment et al. (1997) is the only study to make the distinction with a “pure” distribution network group, it is crucial to minimize potential sources of error.

5.1.2 Observational studies

The most common variable directly tested for association to the risk of GI in the observational studies were low pressure events (mainly caused by pipe breaks) (Hunter et al., 2005; Malm et al., 2013a; Säve-Söderbergh et al., 2017; Beaudeau et al., 2014; Nygard et al., 2007). Low pressure events were also reasoned to be potential mechanisms for contamination of the water inside the network, even if it was not the variable being tested directly (Nygard et al., 2004; Egorov et al., 2002). This implies that maintaining adequate pressure in the network is an important measure to prevent contamination of the drinking water in distribution networks, as is suggested in the global context (Besner et al., 2010a; Besner et al., 2010b; Ebacher et al., 2011; LeChevallier et al., 2003; Karim et al., 2003; WHO, 2014).

A lower free chlorine residual in the network was found to increase the risk of GI in the Russian study (Egorov et al., 2002). This is accordance with widespread belief of the usefulness of using residual disinfectants (Haas, 1999; Karim et al., 2003; Propato and Uber, 2004). On the other hand, Malm et al. (2013a) did not find any significant association with incidents in the network, even though the residual was assumed to be below the recommended level for protection (less than 0.2 mg/L). Säve-Söderbergh et al. (2017) found an elevated risk of GI in areas affected by incidents with chlorination at the treatment plant compared to affected areas in non-chlorinated systems, which seems counterintuitive. The authors argued that this could indicate that chlorine residual concentrations are too low to protect against major incidents. Additionally, networks that do not use chlorine residuals at all (e.g., Netherlands (Smeets, 2009)) are still considered to provide safe drinking water. There could be some potential benefits in studying the effect of chlorination/chlorine residual in the network: it could serve to motivate suppliers to either improve their chlorination disinfection or focus on other aspects of their system to achieve a successful reduction in risk.

Statistical significance was also varied: Egorov et al. (2002), Nygard et al. (2004), Hunter et al. (2005), Nygard et al. (2007), Tinker et al. (2009) for long residence times, and Säve-Söderbergh et al. (2017) for AGI and vomiting found significant positive associations with distribution network variables and increased risk. Slight or no association was found in Tinker et al. (2009) for short/medium residence times, Malm et al. (2013a), Beaudeau et al. (2014) and Säve-Söderbergh et al. (2017) for GI. Egorov et al. (2002) also analysed the rate of self-reported GI for a shorter time interval and did not find a significant association with the chlorine residual. Hsieh et al. (2015) attributed a strong relationship of distribution network turbidity to source water turbidity, hence, it could be interpreted as not being associated to distribution network events per se. It is worth noting that although statistical significance is desirable to minimize false associations, it does not necessarily invalidate the study (Craun and Calderon, 2005; Schoenbach, 2000e).

Meta-analyses are a useful approach to combine the results from different studies into a single estimate, tentatively increasing the precision of the effect studied (Schoenbach, 2000f).

Ercumen et al. (2014) performed this type of analysis for the distribution network studies relating distribution network deficiencies to endemic GI. The authors found significant heterogeneity between the studies, even when further grouping them under similar site characteristics. High heterogeneity can affect the validity of the pooled estimate, therefore invalidating the meta-analysis' results. One proposed measure to address this in future studies was to include more detailed descriptions of the study site, including its operational parameters.

5.2 QMRA modelling

The QMRA models presented in section 4.1 Table 8 can be seen as first attempts at addressing the lack of comprehensive microbial risk assessment tools for the distribution network. However, there are still considerable uncertainties associated with these models that might prevent their use in risk management of distribution networks. A brief commentary follows below (refer to *Paper I* for a more detailed analysis).

Besner et al. (2011) developed a conceptual QMRA model for intrusion. The authors described in great detail the limitations at the time of each part of their model. The use of the orifice equation¹ to estimate the intrusion volume is one that has been contested through theoretical and experimental means (Yang et al., 2016; Yang et al., 2014; Fox et al., 2014; Collins and Boxall, 2013; Fox et al., 2016; Fontanazza et al., 2015). The main conclusion has been that intrusion volumes in lab experiments have been lower than the ones predicted with the orifice equation. Therefore, the risk of infection calculated with QMRA models might be overestimated due to the higher volumes obtained with the equation. While focusing solely on intrusion, many of the limitations identified by Besner et al. (2011) are shared by the other microbial risks, e.g., hydraulic modelling of transient pressures, contamination transport inside the network, etc.

When performing a QMRA, representative reference pathogens must be selected in order to make the assessment practical (WHO, 2016). The choice of reference pathogen will be determined by available information of local etiological agents, but it will also be influenced by the availability of dose-response relationships for the reference pathogens. To date, there are numerous dose-response models available: *Campylobacter* (Medema et al., 1996; Teunis et al., 1999; Teunis et al., 2005); *Salmonella* (Teunis et al., 1999; Teunis et al., 2010a); *E. coli* O157:H7 (Teunis et al., 2004; Teunis et al., 2008b); adenovirus (Teunis et al., 2016); norovirus (Teunis et al., 2008a; Messner et al., 2014); *Cryptosporidium* (Teunis et al., 1999; Teunis et al., 2002); and *Giardia* (Teunis et al., 1996; Zmirou-Navier et al., 2006). One limitation of dose-response models (specifically the ones dependent on clinical trials) is that they used healthy, adult individuals to evaluate the response to the dose (WHO, 2016). This will clearly generate an underrepresentation of the infection risk in recognized sensitive groups (Nwachuku and Gerba, 2004; Gerba et al., 1996).

¹ $Q = \frac{\pi}{4} C_d d^2 \sqrt{2g\Delta H}$ where Q is the intrusion volume, C_d is the discharge coefficient, d is the orifice diameter, g is the gravitational acceleration and ΔH is the difference between external and internal pressure head.

In addition to the inherent limitations and uncertainties of a general QMRA, there were also differences in the assumptions made by the different models. One important difference between models was the consumption pattern of individuals: Yang et al. (2015); Yang et al. (2011); and Teunis et al. (2010b) assumed that consumption occurred on one occasion at any time of the day; Blokker et al. (2018) assumed varying volumes at different times of the day. Van Abel et al. (2014) demonstrated the effect on estimated infection risk if consumption is assumed to occur in different occasions throughout the day. Therefore, properly characterizing the consumption pattern of individuals in the network is an important step in improving the validity of the assessment (Parsons et al., 2012; Hynds et al., 2012; Säve-Soderbergh et al., 2017).

5.3 Cross-connection conceptual model

Probabilities of failure were generated from recorded data in Malm et al. (2010). Since the data was aggregated at a national level, it was not possible to determine specific frequency estimates for particular networks. This might limit the applicability when implementing the method for particular distribution networks, since local data will have to be collected.

No statistical analysis was performed to assess the quality of the data used to generate the assumptions. For a working cross-connection and backflow fault tree, this could hinder its applicability at a site-specific level. However, as means for the proof-of-concept, it was deemed satisfactory.

A particular result from the test was that the endemic case had almost the same probability of infection as the Elevated risk case for *Campylobacter* (bacterial reference) and same order of magnitude for norovirus (viral reference). The only occasion where the probability of infection was below the threshold (10^{-4}) was during the endemic case, *Cryptosporidium*.

Furthermore, it would seem counterintuitive that a scenario with less magnitude would have a higher infection rate; however this was the case between elevated risk case and extreme risk case. The limiting factor for the infection was the probability of occurrence, which seem to limit yearly risk of an extreme risk case affecting the (fictional) network. However, if one takes into account that cross-connections have the potential for large magnitudes of contamination (Mena et al., 2008; Gibbs et al., 2003), then it is reasonable that the limiting factor is the probability of occurrence.

5.4 Possibilities & future work

The literature review performed for the first part of the thesis provided valuable insight in many of the limitations currently affecting QMRAs, which prevents the application of a comprehensive microbial risk management framework. To address this, future work is currently being carried out or planned.

An MSc thesis project is currently ongoing to characterize pit water surrounding the pipes during maintenance and repair work in the Gothenburg distribution network (Rudrappa and Zharkalli). This has been performed previously in North American settings (Karim et al., 2003; Besner et al., 2010a); however, it is the first time it is being evaluated in Swedish distribution networks. The generation of better site-specific data is of great relevance for improving the

reliability of QMRAs (WHO, 2016); hence, these results could be useful for estimating relevant levels of contamination that can be expected when performing works in a pit.

Epidemiological data can be seen as a direct estimate of risk, i.e., quantification of the health consequences of drinking water in a specific population or system. Epidemiological studies (mainly RCTs) have been used to inform microbial risk assessments in differing contexts (Enger et al., 2012; Eisenberg et al., 2006). Epidemiological data has also been used to calculate national estimates of the burden of disease attributable to drinking water (Messner et al., 2006; Colford et al., 2006; Murphy et al., 2016). However, to the knowledge of the author, they have not been used with distribution network QMRAs in any way.

This represents an unused opportunity to address uncertainties in QMRA results, by using these studies to calibrate distribution network QMRAs. This can be done by simulating the study area of the epidemiological study, and comparing the prevalence or incidence obtained theoretically and experimentally. The experimental risk ratios can be seen as possible values that the theoretical QMRA should adjust to. A modelling result not within an acceptable range would then be deemed as unsatisfactory, and the assumptions could be adjusted accordingly.

The conceptual model for cross-connection presented in this thesis is a first step towards a comprehensive microbial risk assessment tool. The next step will be to develop similar models for the remaining microbial risks and translating the conceptual model(s) into a computational tool. Analytica[®] (Lumina Decision Systems, USA) is the software of choice, for multiple reasons:

- The Swedish QMRA tool for source water and treatment plant is already built with this software (Abrahamsson et al., 2009);
- Common interface for suppliers that have previous experience with the Swedish tool;
- Possibility to use Monte Carlo simulations to account for uncertainties

The input data for the cross-connection method will also be validated by surveying municipalities in the Gothenburg region, collecting system specific data to compare to estimates using general information.

Costs of e.g., mitigation measures, are often ignored when evaluating health risks in the distribution network using QMRA (McInnis, 2004). To achieve a fully practical microbial risk management framework, an economic component is needed (see Figure 10). Novel methods, such as Bergion et al. (2018), can be adapted specifically for the distribution network and provide means to monetizing health effects. Hence, mitigation measures could be evaluated in economic terms, allowing for health risks to be accounted in a strategic planning context (e.g., renewal planning of pipes). This will be especially relevant in the context of aging drinking water infrastructure and the increased health risks associated with deteriorating systems (Allen et al., 2018; Van Abel, 2014).

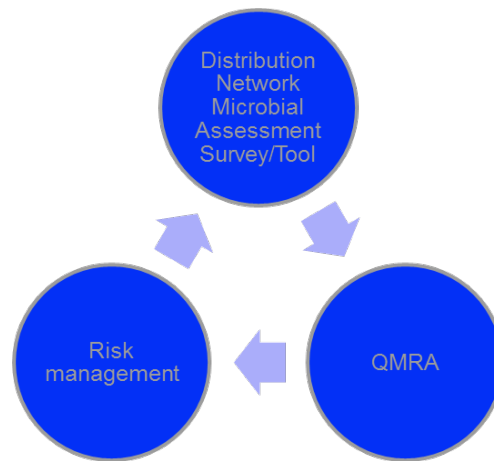


Figure 10 - Simplified risk framework for microbial risk management.

5.5 Conclusions

Microbial risks in the distribution network have been evaluated in two main ways: epidemiological studies and modelling. Outbreak surveillance has documented a significant contribution of the distribution network to the burden of waterborne disease. For the last thirty years, studies also seem to indicate that the network contributes to the endemic level of disease. Modelling capabilities have improved in the last decade. QMRAs models have been developed to evaluate risk of intrusion and maintenance work, mainly.

In summary, the main findings were:

- Epidemiological studies have linked the distribution network to endemic levels of disease (from attributable risk of 14% to 37%, depending on the study and network)
- Availability of several QMRA models for specific risks, with their strengths and limitations

Several needs were also identified:

- Improved study designs for epidemiological studies to determine the particular contribution of the distribution network
- More reliable input data for existing QMRAs
- Lack of economic dimension when performing QMRAs
- Missing integrated and simplified tool for QMRA

Future work currently ongoing or planned includes:

- Initial characterization of pit water in Swedish distribution network to use as input data for future QMRAs (MSc thesis)
- Development of computational tool for risk assessment using Analytica[®]
- Monetization of health effects and mitigation measures specifically for the distribution network
- Integration of all planned work into a comprehensive microbial risk management framework based on QMRA.

6 References

- ABRAHAMSSON, J. L., ANSKER, J. & HEINICKE, G. 2009. MRA – a model for Swedish water works (in Swedish). Stockholm: Svensk Vatten AB.
- ALLEN, M., CLARK, R., COTRUVUO, J. A. & GRIGG, N. 2018. Drinking Water and Public Health in an Era of Aging Distribution Infrastructure. *Public Works Management & Policy*, 23, 301-309.
- ASHBOLT, N. J. 2015. Microbial Contamination of Drinking Water and Human Health from Community Water Systems. *Curr Environ Health Rep*, 2, 95-106.
- BEAUDEAU, P., ZEGHNOUN, A., CORSO, M., LEFRANC, A. & RAMBAUD, L. 2014. A time series study of gastroenteritis and tap water quality in the Nantes area, France, 2002-2007. *Journal of Exposure Science and Environmental Epidemiology*, 24, 192-199.
- BERGION, V., LINDHE, A., SOKOLOVA, E. & ROSÉN, L. 2018. Risk-based cost-benefit analysis for evaluating microbial risk mitigation in a drinking water system. *Water Research*, 132, 111-123.
- BESNER, M. C., BROSEUS, R., LAVOIE, J., DI GIOVANNI, G., PAYMENT, P. & PREVOST, M. 2010a. Pressure Monitoring and Characterization of External Sources of Contamination at the Site of the Payment Drinking Water Epidemiological Studies. *Environmental Science & Technology*, 44, 269-277.
- BESNER, M. C., EBACHER, G., PREVOST, M., JUNG, B. S., KARNEY, B., LAVOIE, J. & PAYMENT, P. 2010b. *Negative pressures in full-scale distribution system: Field investigation, modelling, estimation of intrusion volumes and risk for public health*, Boca Raton, Crc Press-Taylor & Francis Group.
- BESNER, M. C., PREVOST, M. & REGLI, S. 2011. Assessing the public health risk of microbial intrusion events in distribution systems: Conceptual model, available data, and challenges. *Water Research*, 45, 961-979.
- BEUKEN, R., REINOSO, M., STURM, S., KIEFER, J., BONDELIND, M., ÅSTRÖM, J., LINDHE, A., LOSÉN, L., PETTERSSON, T., MACHENBACH, I., MELIN, E., THORSEN, T., EIKEBROKK, B., HOKSTAD, P., RØSTUM, J., NIEWERSCH, C., KIRCHNER, D., KOZISEK, F., GARI, D. W., SWARTZ, C. & MENAIA, J. 2008. Identification and description of hazards for water supply systems - A catalogue of today's hazards and possible future hazards, updated version. TECHNEAU.
- BLOKKER, M., SMEETS, P. & MEDEMA, G. 2014. QMRA in the Drinking Water Distribution System. *Procedia Engineering*, 89, 151-159.
- BLOKKER, M., SMEETS, P. & MEDEMA, G. 2018. Quantitative microbial risk assessment of repairs of the drinking water distribution system. *Microbial Risk Analysis*, 8, 22-31.
- BOUWKNEGT, M., KNOL, A. B., VAN DER SLUIJS, J. P. & EVERS, E. G. 2014. Uncertainty of Population Risk Estimates for Pathogens Based on QMRA or Epidemiology: A Case Study of *Campylobacter* in the Netherlands. *Risk Analysis*, 34, 847-864.
- BURNS, P. B., ROHRICH, R. J. & CHUNG, K. C. 2011. The Levels of Evidence and Their Role in Evidence-Based Medicine. *Plastic and Reconstructive Surgery*, 128, 305-310.
- BYLUND, J., TOLJANDER, J., LYSÉN, M., RASTI, N., ENGQVIST, J. & SIMONSSON, M. 2017. Measuring sporadic gastrointestinal illness associated with drinking water – an overview of methodologies. *Journal of Water and Health*, 15, 321-340.
- CDC. 2010. Centers for Disease Control and Prevention. Available: <https://wwwn.cdc.gov/nndss/conditions/waterborne-disease-outbreak/case-definition/2010/> [Accessed Aug 27 2018].

- CLARK, R. M., ABDESAKEN, F., BOULOS, P. F. & MAU, R. E. 1996. Mixing in distribution system storage tanks: Its effect on water quality. *Journal of Environmental Engineering-Asce*, 122, 814-821.
- COLFORD, J. J. M., ROY, S., BEACH, M. J., HIGHTOWER, A., SHAW, S. E. & WADE, T. J. 2006. A review of household drinking water intervention trials and an approach to the estimation of endemic waterborne gastroenteritis in the United States. *Journal of Water and Health*, 4, 71-88.
- COLFORD, J. M., JR., WADE, T. J., SANDHU, S. K., WRIGHT, C. C., LEE, S., SHAW, S., FOX, K., BURNS, S., BENKER, A., BROOKHART, M. A., VAN DER LAAN, M. & LEVY, D. A. 2005. A randomized, controlled trial of in-home drinking water intervention to reduce gastrointestinal illness. *Am J Epidemiol*, 161, 472-82.
- COLLINS, R. & BOXALL, J. 2013. Influence of Ground Conditions on Intrusion Flows through Apertures in Distribution Pipes. *Journal of Hydraulic Engineering*, 139, 1052-1061.
- CRAUN, G. F. 2012. The importance of waterborne disease outbreak surveillance in the United States. *Annali dell'Istituto Superiore di Sanita*, 48, 447-459.
- CRAUN, G. F. & CALDERON, R. L. 2005. How to interpret epidemiological associations. *Nutrients in Drinking Water*, 108, 108-115.
- DOUTERELLO, I., BOXALL, J. B., DEINES, P., SEKAR, R., FISH, K. E. & BIGGS, C. A. 2014. Methodological approaches for studying the microbial ecology of drinking water distribution systems. *Water Research*, 65, 134-156.
- EBACHER, G., BESNER, M., PRÉVOST, M. & ALLARD, D. 2011. Negative Pressure Events in Water Distribution Systems: Public Health Risk Assessment Based on Transient Analysis Outputs. *Water Distribution Systems Analysis 2010*. American Society of Civil Engineers.
- EGOROV, A., FORD, T., TERESCHENKO, A., DRIZHD, N., SEGEDEVICH, I. & FOURMAN, V. 2002. Deterioration of drinking water quality in the distribution system and gastrointestinal morbidity in a Russian city. *International Journal of Environmental Health Research*, 12, 221-233.
- EISENBERG, J. N. S., HUBBARD, A., WADE, T. J., SYLVESTER, M. D., LECHEVALLIER, M. W., LEVY, D. A. & COLFORD JR, J. M. 2006. Inferences drawn from a risk assessment compared directly with a randomized trial of a home drinking water intervention. *Environmental Health Perspectives*, 114, 1199-1204.
- ENGER, K. S., NELSON, K. L., CLASEN, T., ROSE, J. B. & EISENBERG, J. N. 2012. Linking quantitative microbial risk assessment and epidemiological data: informing safe drinking water trials in developing countries. *Environ Sci Technol*, 46, 5160-7.
- ERCUMEN, A., GRUBER, J. S. & COLFORD, J. M. 2014. Water Distribution System Deficiencies and Gastrointestinal Illness: A Systematic Review and Meta-Analysis. *Environmental Health Perspectives*, 122, 651-660.
- FALCO, R. & WILLIAMS, S. I. 2009. Waterborne Salmonella Outbreak in Alamosa, Colorado March and April 2008: Outbreak Identification, Response, and Investigation.
- FARKAS, A., DRAGAN-BULARDA, M., CIATARAS, D., BOCOS, B. & TIGAN, S. 2012. Opportunistic pathogens and faecal indicators in drinking water associated biofilms in Cluj, Romania. *J Water Health*, 10, 471-483.
- FONTANAZZA, C. M., NOTARO, V., PULEO, V., NICOLOSI, P. & FRENI, G. 2015. Contaminant Intrusion through Leaks in Water Distribution System: Experimental Analysis. *Procedia Engineering*, 119, 426-433.
- FOX, S., SHEPHERD, W., COLLINS, R. & BOXALL, J. 2014. Experimental proof of contaminant ingress into a leaking pipe during a transient event. *12th International Conference on Computing and Control for the Water Industry, Ccwi2013*, 70, 668-677.

- FOX, S., SHEPHERD, W., COLLINS, R. & BOXALL, J. 2016. Experimental Quantification of Contaminant Ingress into a Buried Leaking Pipe during Transient Events. *Journal of Hydraulic Engineering*, 142, 04015036.
- GERBA, C. P., ROSE, J. B. & HAAS, C. N. 1996. Sensitive populations: who is at the greatest risk? *International Journal of Food Microbiology*, 30, 113-123.
- GIBBS, S. G., MECKES, M. C. & SCARPINO, P. V. 2003. The effect of long-term wastewater cross-connection on the biofilm of a simulated water distribution system. *Journal of Environmental Engineering and Science*, 2, 85-98.
- GOVERNMENT OFFICES OF SWEDEN. Available: <https://www.government.se/government-policy/municipalities-and-county-councils/> [Accessed 27-09 2018].
- GUZMAN-HERRADOR, B., CARLANDER, A., ETHELBERG, S., DE BLASIO, B. F., KUUSI, M., LUND, V., LÖFDAHL, M., MACDONALD, E., NICHOLS, G., SCHÖNNING, C., SUDRE, B., TRÖNNBERG, L., VOLD, L., SEMENZA, J. C. & NYGÅRD, K. 2015. Waterborne outbreaks in the Nordic countries, 1998 to 2012. *Eurosurveillance*, 20, 1-10.
- HAAS, C. N. 1999. Benefits of using a disinfectant residual. *Journal - American Water Works Association*, 91, 65-69.
- HAAS, C. N., ROSE, J. B. & GERBA, C. P. 2014. *Quantitative Microbial Risk Assessment (2nd Edition)*, Somerset, NJ, USA, Wiley.
- HELLARD, M. E., SINCLAIR, M. I., FORBES, A. B. & FAIRLEY, C. K. 2001. A randomized, blinded, controlled trial investigating the gastrointestinal health effects of drinking water quality. *Environ Health Perspect*, 109, 773-8.
- HO, P. M., PETERSON, P. N. & MASOUDI, F. A. 2008. Evaluating the evidence: is there a rigid hierarchy? *Circulation*, 118, 1675-84.
- HRUDEY, S. E. & HRUDEY, E. J. 2004. *Safe drinking water : lessons from recent outbreaks in affluent nations*, London, UK, IWA Pub.
- HRUDEY, S. E. & HRUDEY, E. J. 2007. Published case studies of waterborne disease outbreaks - Evidence of a recurrent threat. *Water Environment Research*, 79, 233-245.
- HSIEH, J. L., NGUYEN, T. Q., MATTE, T. & ITO, K. 2015. Drinking water turbidity and emergency department visits for gastrointestinal illness in New York City, 2002-2009. *PLoS ONE*, 10.
- HUNTER, P. R., CHALMERS, R. M., HUGHES, S. & SYED, Q. 2005. Self-reported diarrhea in a control group: a strong association with reporting of low-pressure events in tap water. *Clin Infect Dis*, 40, e32-4.
- HYNDS, P. D., MISSTEAR, B. D. & GILL, L. W. 2012. Investigation of water consumption patterns among Irish adults for waterborne quantitative microbial risk assessment (QMRA). *Journal of Water and Health*, 10, 453-464.
- INSTITUTE OF MEDICINE 2000. *Public Health Systems and Emerging Infections: Assessing the Capabilities of the Public and Private Sectors: Workshop Summary*, Washington, DC, The National Academies Press.
- ISLAM, N., FARAHAT, A., AL-ZAHRANI, M. A. M., RODRIGUEZ, M. J. & SADIQ, R. 2015. Contaminant intrusion in water distribution networks: review and proposal of an integrated model for decision making. *Environmental Reviews*, 23, 337-352.
- KARIM, M. R., ABBASZADEGAN, M. & LECHEVALLIER, M. 2003. Potential for pathogen intrusion during pressure transients. *Journal American Water Works Association*, 95, 134-146.
- KHANAL, N., BUCHBERGER, S. G. & MCKENNA, S. A. 2006. Distribution system contamination events: Exposure, influence, and sensitivity. *Journal of Water Resources Planning and Management*, 132, 283-292.

- KIRMEYER, G. J., WATER RESEARCH FOUNDATION. & GREAT BRITAIN. DRINKING WATER INSPECTORATE. 2014. *Effective microbial control strategies for main breaks and depressurization*, Denver, CO., Water Research Foundation.
- KRISTIANSTADS KOMMUN 2015. Contaminated water in Everöd, Östra Sönnarslöv and Huaröd: Summer 2015 (in Swedish).
- LAINE, J., HUOVINEN, E., VIRTANEN, M. J., SNELLMAN, M., LUMIO, J., RUUTU, P., KUJANSUU, E., VUENTO, R., PITKANEN, T., MIETTINEN, I., HERRALA, J., LEPISTO, O., ANTONEN, J., HELENIUS, J., HANNINEN, M. L., MAUNULA, L., MUSTONEN, J., KUUSI, M. & PIRKANMAA WATERBORNE OUTBREAK STUDY, G. 2011. An extensive gastroenteritis outbreak after drinking-water contamination by sewage effluent, Finland. *Epidemiol Infect*, 139, 1105-13.
- LECHEVALLIER, M. W., GULLICK, R. W., KARIM, M. R., FRIEDMAN, M. & FUNK, J. E. 2003. The potential for health risks from intrusion of contaminants into the distribution system from pressure transients. *Journal of Water and Health*, 1, 3-14.
- LEVY, K., KLEIN, M., SARNAT, S. E., PANWHAR, S., HUTTINGER, A., TOLBERT, P. & MOE, C. 2016. Refined assessment of associations between drinking water residence time and emergency department visits for gastrointestinal illness in Metro Atlanta, Georgia. *Journal of Water and Health*, 14, 672-681.
- LINDHE, A. 2010. *Risk Assessment and Decision Support for Managing Drinking Water Systems*. PhD thesis, Chalmers University of Technology.
- LINDHE, A., ROSÉN, L., NORBERG, T. & BERGSTEDT, O. 2009. Fault tree analysis for integrated and probabilistic risk analysis of drinking water systems. *Water Research*, 43, 1641-1653.
- MACGILLIVRAY, B. H., HAMILTON, P. D., STRUTT, J. E. & POLLARD, S. J. T. 2006. Risk analysis strategies in the water utility sector: An inventory of applications for better and more credible decision making. *Critical Reviews in Environmental Science and Technology*, 36, 85-139.
- MALM, A., AXELSSON, G., BARREGARD, L., LJUNGQVIST, J., FORSBERG, B., BERGSTEDT, O. & PETTERSSON, T. J. R. 2013a. The association of drinking water treatment and distribution network disturbances with Health Call Centre contacts for gastrointestinal illness symptoms. *Water Research*, 47, 4474-4484.
- MALM, A., PETTERSSON, T. J. R. & BERGSTEDT, O. 2010. Health effects of quality disturbances in Swedish water distribution networks (in Swedish). *Proceedings of the 7th Nordic Drinking Water Conference*. Copenhagen: DANVA.
- MALM, A., SVENSSON, G., BACKMAN, H. & MORRISON, G. M. 2013b. Prediction of water and wastewater networks rehabilitation based current age and material distribution. *Water Science and Technology-Water Supply*, 13, 227-237.
- MANN, C. J. 2003. Observational research methods. Research design II: cohort, cross sectional, and case-control studies. *Emergency Medicine Journal*, 20, 54-60.
- MCINNIS, D. 2004. A relative-risk framework for evaluating transient pathogen intrusion in distribution systems. *Urban Water Journal*, 1, 113-127.
- MEDEMA, G. J., TEUNIS, P. F., HAVELAAR, A. H. & HAAS, C. N. 1996. Assessment of the dose-response relationship of *Campylobacter jejuni*. *Int J Food Microbiol*, 30, 101-11.
- MENA, K. D., MOTA, L. C., MECKES, M. C., GREEN, C. F., HURD, W. W. & GIBBS, S. G. 2008. Quantitative microbial risk assessment of a drinking water - wastewater cross-connection simulation. *Journal of Environmental Engineering and Science*, 7, 525-530.
- MESSNER, M., SHAW, S., REGLI, S., ROTERT, K., BLANK, V. & SOLLER, J. 2006. An approach for developing a national estimate of waterborne disease due to drinking

- water and a national estimate model application. *Journal of Water and Health*, 4, 201-240.
- MESSNER, M. J., BERGER, P. & NAPPIER, S. P. 2014. Fractional poisson--a simple dose-response model for human norovirus. *Risk Anal*, 34, 1820-9.
- MURPHY, H. M., THOMAS, M. K., MEDEIROS, D. T., MC, F. S. & PINTAR, K. D. 2016. Estimating the number of cases of acute gastrointestinal illness (AGI) associated with Canadian municipal drinking water systems. *Epidemiol Infect*, 144, 1371-85.
- NATIONAL RESEARCH COUNCIL 2005. *Public Water Supply Distribution Systems: Assessing and Reducing Risks - First Report*, Washington, DC, National Academies Press.
- NATIONAL RESEARCH COUNCIL 2006. *Drinking water distribution systems : assessing and reducing risks*, Washington, DC, National Academies Press.
- NILSSON, K. A., BUCHBERGER, S. G. & CLARK, R. M. 2005. Simulating exposures to deliberate intrusions into water distribution systems. *Journal of Water Resources Planning and Management-Asce*, 131, 228-236.
- NWACHUKU, N. & GERBA, C. P. 2004. Microbial risk assessment: don't forget the children. *Curr Opin Microbiol*, 7, 206-9.
- NYGARD, K., ANDERSSON, Y., ROTTINGEN, J. A., SVENSSON, A., LINDBACK, J., KISTEMANN, T. & GIESECKE, J. 2004. Association between environmental risk factors and campylobacter infections in Sweden. *Epidemiology and Infection*, 132, 317-325.
- NYGARD, K., WAHL, E., KROGH, T., TVEIT, O. A., BOHLENG, E., TVERDAL, A. & AAVITSLAND, P. 2007. Breaks and maintenance work in the water distribution systems and gastrointestinal illness: a cohort study. *International Journal of Epidemiology*, 36, 873-880.
- PARSONS, D., WHELAN, M. & BEVAN, R. 2012. Probabilistic modelling for assessment of exposure via drinking water. United Kingdom: Centre for Environmental Risks and Futures, Cranfield University.
- PAYMENT, P., RICHARDSON, L., SIEMIATYCKI, J., DEWAR, R., EDWARDES, M. & FRANCO, E. 1991. A Randomized Trial to Evaluate the Risk of Gastrointestinal-Disease Due to Consumption of Drinking-Water Meeting Current Microbiological Standards. *American Journal of Public Health*, 81, 703-708.
- PAYMENT, P., SIEMIATYCKI, J., RICHARDSON, L., RENAUD, G., FRANCO, E. & PRÉVOST, M. 1997. A prospective epidemiological study of gastrointestinal health effects due to the consumption of drinking water. *International Journal of Environmental Health Research*, 7, 5-31.
- PROPATO, M. & UBER, J. G. 2004. Vulnerability of water distribution systems to pathogen intrusion: How effective is a disinfectant residual? *Environmental Science and Technology*, 38, 3713-3722.
- QMRAWIKI. 2013. *Quantitative Microbial Risk Assessment* [Online]. Available: http://qmrawiki.canr.msu.edu/index.php/Quantitative_Microbial_Risk_Assessment [Accessed 24 September 2018].
- RAMÍREZ-CASTILLO, F. Y., LOERA-MURO, A., JACQUES, M., GARNEAU, P., AVELAR-GONZÁLEZ, F. J., HAREL, J. & GUERRERO-BARRERA, A. L. 2015. Waterborne Pathogens: Detection Methods and Challenges. *Pathogens*, 4, 307-334.
- REYNOLDS, K. A., MENA, K. D. & GERBA, C. P. 2008. Risk of waterborne illness via drinking water in the United States. In: WHITACRE, D. M. (ed.) *Reviews of Environmental Contamination and Toxicology*, Vol 192. New York: Springer.
- RISEBRO, H. L., DORIA, M. F., ANDERSSON, Y., MEDEMA, G., OSBORN, K., SCHLOSSER, O. & HUNTER, P. R. 2007. Fault tree analysis of the causes of waterborne outbreaks. *Journal of Water and Health*, 5, 1-18.

- ROCHE, S. M., JONES, A. Q., MAJOWICZ, S. E., MCEWEN, S. A. & PINTAR, K. D. M. 2012. Drinking water consumption patterns in Canadian communities (2001-2007). *Journal of Water and Health*, 10, 69-86.
- ROTHMAN, K. J., GREENLAND, S. & LASH, T. L. 2008. *Modern Epidemiology*, Wolters Kluwer Health/Lippincott Williams & Wilkins.
- RUDRAPPA, S. & ZHARKALLI, A. Unpublished. Evaluation of risk for fecal contamination of soil or water surrounding drinking water pipes (working title). Chalmers University of Technology.
- RUIJTERS, E. & STOELINGA, M. 2015. Fault tree analysis: A survey of the state-of-the-art in modeling, analysis and tools. *Computer Science Review*, 15-16, 29-62.
- SCHOENBACH, V. J. 2000a. Chapter 1: Epidemiology — Definition, functions, and characteristics. In: SCHOENBACH, V. J. & ROSAMOND, W. D. (eds.) *Understanding the Fundamentals of Epidemiology: an evolving text*. Chapel Hill: University of North Carolina at Chapel Hill.
- SCHOENBACH, V. J. 2000b. Chapter 5: Measuring Disease and Exposure. In: SCHOENBACH, V. J. & ROSAMOND, W. D. (eds.) *Understanding the Fundamentals of Epidemiology: an evolving text*. Chapel Hill: University of North Carolina at Chapel Hill.
- SCHOENBACH, V. J. 2000c. Chapter 7: Relating risk factors to health outcomes. In: SCHOENBACH, V. J. & ROSAMOND, W. D. (eds.) *Understanding the Fundamentals of Epidemiology: an evolving text*. Chapel Hill: University of North Carolina at Chapel Hill.
- SCHOENBACH, V. J. 2000d. Chapter 8: Analytic study designs. In: SCHOENBACH, V. J. & ROSAMOND, W. D. (eds.) *Understanding the Fundamentals of Epidemiology: an evolving text*. Chapel Hill: University of North Carolina at Chapel Hill.
- SCHOENBACH, V. J. 2000e. Chapter 11: Multicausality - Confounding. In: SCHOENBACH, V. J. & ROSAMOND, W. D. (eds.) *Understanding the Fundamentals of Epidemiology: an evolving text*. Chapel Hill: University of North Carolina at Chapel Hill.
- SCHOENBACH, V. J. 2000f. Chapter 14: Data analysis and interpretation. In: SCHOENBACH, V. J. & ROSAMOND, W. D. (eds.) *Understanding the Fundamentals of Epidemiology: an evolving text*. Chapel Hill: University of North Carolina at Chapel Hill.
- SENSATION III Unpublished. Evaluation of electronic tongue and other online sensors for detection of chemical and biological pollutants in the drinking water network (in Swedish).
- SEYOUM, A. G., TANYIMBOH, T. T. & SIEW, C. Optimal Tank Design And Operation Strategy To Enhance Water Quality In Distribution Systems. International Conference on Hydroinformatics, 2014 New York City, USA. CUNY Academic Works.
- SILMAN, A. J. & MACFARLANE, G. J. 2002. *Epidemiological studies : a practical guide*, Cambridge ; New York, Cambridge University Press.
- SINCLAIR, M. I. & FAIRLEY, C. K. 2000. Drinking water and endemic gastrointestinal illness. *J Epidemiol Community Health*, 54, 728.
- SMEETS 2009. The Dutch secret: how to provide safe drinking water without chlorine in the Netherlands. *Drink. Water Eng. Sci.*, 2.
- STANWELL-SMITH, R. 2003. Cholera, Chloroform, and the Science of Medicine: a Life of John Snow. *Journal of the Royal Society of Medicine*, 96, 612-613.
- SVENSKT VATTEN 2014. Manual for control programs with HACCP in the production and distribution of drinking water (in Swedish). Stockholm: The Swedish Water and Wastewater Association.

- SZUMILAS, M. 2010. Explaining Odds Ratios. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, 19, 227-229.
- SÄVE-SÖDERBERGH, M., TOLJANDER, J., MATTISSON, I., AKESSON, A. & SIMONSSON, M. 2017. Drinking water consumption patterns among adults — SMS as a novel tool for collection of repeated self-reported water consumption. *J Expos Sci Environ Epidemiol*.
- SÄVE-SÖDERBERGH, M., BYLUND, J., MALM, A., SIMONSSON, M. & TOLJANDER, J. 2017. Gastrointestinal illness linked to incidents in drinking water distribution networks in Sweden. *Water Research*, 122, 503-511.
- SÄVE-SÖDERBERGH, M., MALM, A., DRYSELIUS, R. & TOLJANDER, J. 2013. Microbiological hazards of drinking water distribution - overview of events, breakdowns, problems and procedures (in Swedish). Sweden: National Food Agency.
- TCHOBANOGLIOUS, G., BURTON, F. L., STENSEL, H. D., METCALF & EDDY, I. 2003. *Wastewater Engineering: Treatment and Reuse*, McGraw-Hill Education.
- TEUNIS, P., SCHIJVEN, J. & RUTJES, S. 2016. A generalized dose-response relationship for adenovirus infection and illness by exposure pathway. *Epidemiology and Infection*, 144, 3461-3473.
- TEUNIS, P., TAKUMI, K. & SHINAGAWA, K. 2004. Dose Response for Infection by *Escherichia coli* O157:H7 from Outbreak Data. *Risk Anal*, 24, 401-407.
- TEUNIS, P., VAN DEN BRANDHOF, W., NAUTA, M., WAGENAAR, J., VAN DEN KERKHOF, H. & VAN PELT, W. 2005. A reconsideration of the *Campylobacter* dose-response relation. *Epidemiology and Infection*, 133, 583-592.
- TEUNIS, P. F., MOE, C. L., LIU, P., MILLER, S. E., LINDESMITH, L., BARIC, R. S., LE PENDU, J. & CALDERON, R. L. 2008a. Norwalk virus: how infectious is it? *J Med Virol*, 80, 1468-76.
- TEUNIS, P. F., NAGELKERKE, N. J. & HAAS, C. N. 1999. Dose response models for infectious gastroenteritis. *Risk Anal*, 19, 1251-1260.
- TEUNIS, P. F. M., CHAPPELL, C. L. & OKHUYSEN, P. C. 2002. *Cryptosporidium* dose response studies: Variation between isolates. *Risk Analysis*, 22, 175-183.
- TEUNIS, P. F. M., KASUGA, F., FAZIL, A., OGDEN, I. D., ROTARIU, O. & STRACHAN, N. J. C. 2010a. Dose-response modeling of *Salmonella* using outbreak data. *International Journal of Food Microbiology*, 144, 243-249.
- TEUNIS, P. F. M., OGDEN, I. D. & STRACHAN, N. J. C. 2008b. Hierarchical dose response of *E. coli* O157:H7 from human outbreaks incorporating heterogeneity in exposure. *Epidemiology and Infection*, 136, 761-770.
- TEUNIS, P. F. M., VAN DER HEIJDEN, O. G., VAN DER GIESSEN, J. W. B. & HAVELAAR, A. H. 1996. The dose-response relation in human volunteers for gastrointestinal pathogens. Bilthoven, The Netherlands: National Institute of Public Health and the Environment (RIVM).
- TEUNIS, P. F. M., XU, M., FLEMING, K. K., YANG, J., MOE, C. L. & LECHEVALLIER, M. W. 2010b. Enteric Virus Infection Risk from Intrusion of Sewage into a Drinking Water Distribution Network. *Environmental Science & Technology*, 44, 8561-8566.
- THE SWEDISH WATER & WASTEWATER ASSOCIATION 2000. Facts on water supply and sanitation in Sweden. Stockholm, Sweden.
- TINKER, S. C., MOE, C. L., KLEIN, M., FLANDERS, W. D., UBER, J., AMIRTHARAJAH, A., SINGER, P. & TOLBERT, P. E. 2009. Drinking water residence time in distribution networks and emergency department visits for gastrointestinal illness in Metro Atlanta, Georgia. *Journal of Water and Health*, 7, 332-343.

- TORRES, J. M., BRUMBELOW, K. & GUIKEMA, S. D. 2009. Risk classification and uncertainty propagation for virtual water distribution systems. *Reliability Engineering & System Safety*, 94, 1259-1273.
- USEPA 2002a. Effects of Water Age on Distribution System Water Quality. Washington DC, USA: U.S. Environmental Protection Agency.
- USEPA 2002b. Finished Water Storage Facilities Washington DC, USA: U.S. Environmental Protection Agency.
- USEPA 2002c. New or Repaired Water Mains. Washington DC, USA: U.S. Environmental Protection Agency.
- USEPA 2002d. Potential Contamination Due to Cross-Connections and Backflow and the Associated Health Risks Washington DC, USA: U.S. Environmental Protection Agency.
- VAIRAVAMOORTHY, K., YAN, J., GALGALE, H. M. & GORANTIWAR, S. D. 2007. IRA-WDS: A GIS-based risk analysis tool for water distribution systems. *Environmental Modelling & Software*, 22, 951-965.
- WALACH, H. & LOEF, M. 2015. Using a matrix-analytical approach to synthesizing evidence solved incompatibility problem in the hierarchy of evidence. *Journal of Clinical Epidemiology*, 68, 1251-1260.
- VAN ABEL, N. 2014. QMRA: Exposure model sensitivity to input parameters, critical review of dose-response models, and application in assessing risk of aging drinking water distribution systems. PhD thesis, University of Washington.
- VAN ABEL, N., BLOKKER, E. J. M., SMEETS, P. W. M. H., MESCHKE, J. S. & MEDEMA, G. J. 2014. Sensitivity of quantitative microbial risk assessments to assumptions about exposure to multiple consumption events per day. *Journal of Water and Health*, 12, 727-735.
- VAV 2001. General water distribution networks: Instructions for design, renewal and calculation (in Swedish). Stockholm: The Swedish Water and Wastewater Association.
- WHO 2011. *Guidelines for drinking-water quality*, Geneva, World Health Organization.
- WHO 2014. *Water safety in distribution systems*, Geneva, World Health Organization.
- WHO 2016. *Quantitative microbial risk assessment: application for water safety management*, Geneva, World Health Organization.
- WINKLER, D., HALTMEIER, M., KLEIDORFER, M., RAUCH, W. & TSCHEIKNER-GRATL, F. 2018. Pipe failure modelling for water distribution networks using boosted decision trees. *Structure and Infrastructure Engineering*, 1-10.
- YANG, J., LECHEVALLIER, M. W., TEUNIS, P. F. M. & XU, M. H. 2011. Managing risks from virus intrusion into water distribution systems due to pressure transients. *Journal of Water and Health*, 9, 291-305.
- YANG, J., SCHNEIDER, O. D., JJEMBA, P. K. & LECHEVALLIER, M. W. 2015. Microbial Risk Modeling for Main Breaks. *Journal American Water Works Association*, 107, E97-E108.
- YANG, Y., ZHANG, T. Q. & ZHU, D. Z. 2014. Influence of porous media on intrusion rate into water distribution pipes. *Journal of Water Supply Research and Technology-Aqua*, 63, 43-50.
- YANG, Y., ZHU, D. Z., ZHANG, T., LIU, W. & GUO, S. 2016. Improved Model for Contaminant Intrusion Induced by Negative Pressure Events in Water Distribution Systems. *Journal of Hydraulic Engineering*, 142, 06016012.
- ZMIROU-NAVIER, D., GOFTI-LAROCHE, L. & HARTEMANN, P. 2006. Waterborne microbial risk assessment : a population-based dose-response function for *Giardia* spp. (E.M.I.R.A study). *BMC Public Health*, 6, 122.

7 Appendix

Summary of search strategies and results for epidemiological studies. For this thesis only results related to endemic disease were included. (Cutoff main search: Spring 2016; Cutoff secondary searches: Summer 2017)

Scopus			Web of Science			PubMed Central		
ID	Strategies	Number of Results	ID	Strategies	Number of Results*	ID	Strategies	Number of Results
SS1	"drinking water" AND ("distribution system" OR "distribution network") AND ("disease outbreak" OR "gastrointestinal disease")	595	WS1	"drinking water" AND ("distribution system" OR "distribution network") AND ("disease outbreak" OR "gastrointestinal disease")	2 (1)	PS1	"drinking water" AND ("distribution system" OR "distribution network") AND ("disease outbreak" OR "gastrointestinal disease")	74
SS2	SS1 + filtering by keywords [†]	491	WS2	-	-	PS2	-	-
SS3	"drinking water" AND ("distribution system" OR "distribution network") AND ("disease outbreak" OR "gastro*")	1 196	WS3	"drinking water" AND ("distribution system" OR "distribution network") AND ("disease outbreak" OR "gastro*")	71 (52)	PS3	"drinking water" AND ("distribution system" OR "distribution network") AND ("disease outbreak" OR "gastro*")	80
SS4	"drinking water" AND ("distribution system" OR "distribution network") AND ("outbreak" OR "gastro*")	1 858	WS4	"drinking water" AND ("distribution system" OR "distribution network") AND ("outbreak" OR "gastro*")	106 (78)	PS4	"drinking water" AND ("distribution system" OR "distribution network") AND ("outbreak" OR "gastro*")	330

*Core Collection results are shown in parenthesis.

TS2: "drinking water" AND (" distribution system" OR "distribution network") AND ("disease outbreak" OR "gastrointestinal disease") AND (LIMIT-TO (EXACTKEYWORD , "Drinking water") OR LIMIT-TO (EXACTKEYWORD , "Water supply") OR LIMIT-TO (EXACTKEYWORD , "Water quality") OR LIMIT-TO (EXACTKEYWORD , "Water Supply") OR LIMIT-TO (EXACTKEYWORD , "Water contamination") OR LIMIT-TO (EXACTKEYWORD , "Disease Outbreaks") OR LIMIT-TO (EXACTKEYWORD , "Potable water") OR LIMIT-TO (EXACTKEYWORD , "Epidemic") OR LIMIT-TO (EXACTKEYWORD , "Risk assessment") OR LIMIT-TO (EXACTKEYWORD , "Water distribution systems") OR LIMIT-TO (EXACTKEYWORD , "Water management") OR LIMIT-TO (EXACTKEYWORD , "Water sampling") OR LIMIT-TO (EXACTKEYWORD , "Biofilm") OR LIMIT-TO (EXACTKEYWORD , "Water analysis") OR LIMIT-TO (EXACTKEYWORD , "Health risk"))