NATIONAL INSTITUTE FOR HEALTH AND WELFARE

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Study on disease burden, health consequences and health-economic costs

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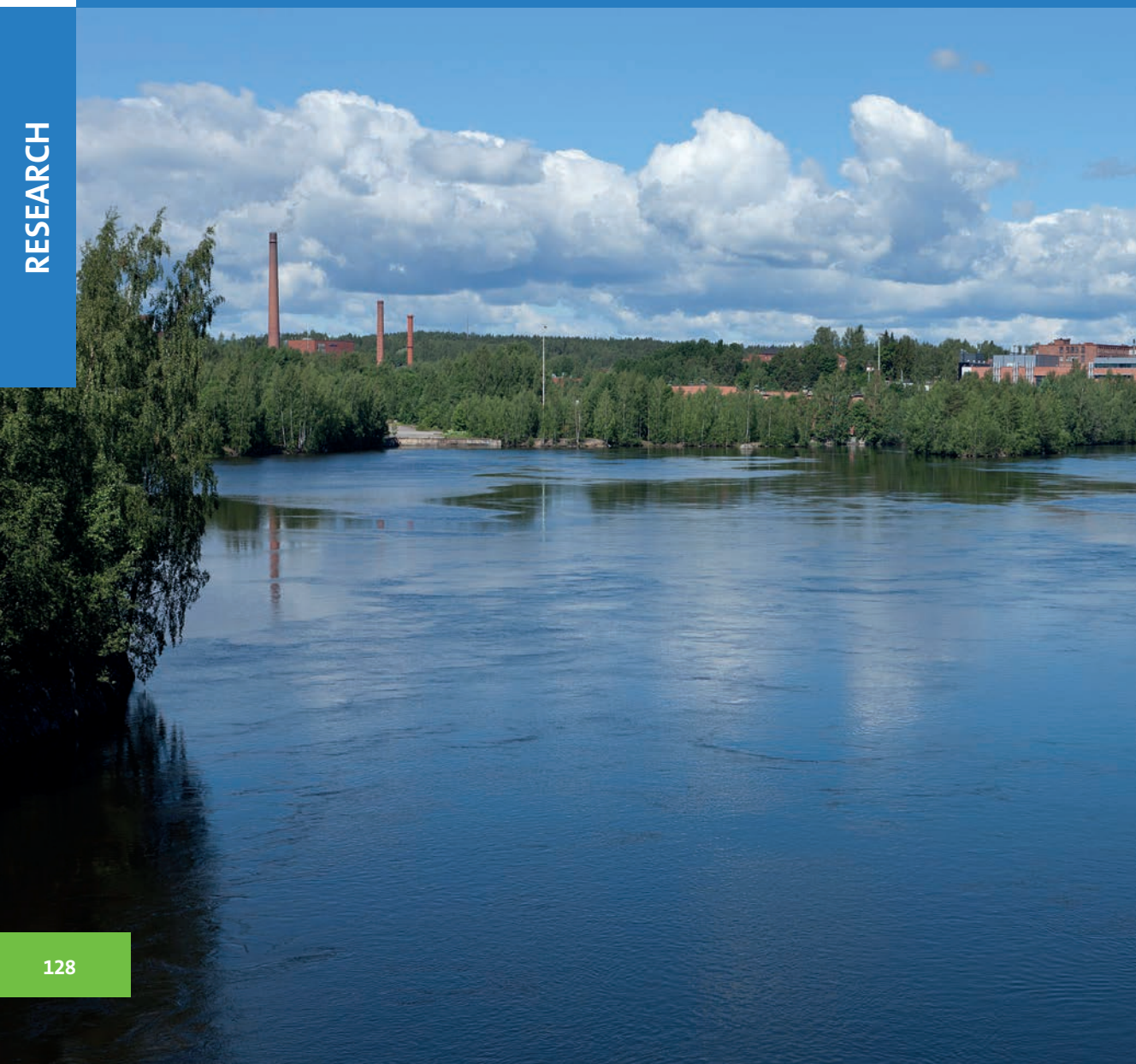

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ACADEMIC DISSERTATION

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Dedicated to the people of the town of Nokia

Abstract

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A large drinking water-associated epidemic took place in the town of Nokia, Southern Finland in November-December 2007. Water became heavily contaminated with treated waste water at the town's waste water plant. A valve connecting waste water and household water lines had been opened during plant maintenance and accidentally left open for two days, allowing large amounts of waste water to flow into the distribution network.

During the following weeks the Nokia health centre encountered a rush of patients with gastroenteritis, a total of 1222 visits being reported for the outbreak period, 28 November to 31 December 2007. Altogether 204 referrals to Tampere University Hospital were made, of which 71% involved children.

Clinical stool samples revealed seven pathogens, six of which were also detected in water samples. This diversity reflects the mechanism and the magnitude of the contamination. *Campylobacter*, norovirus and *Giardia* were considered the main pathogens.

A population-based questionnaire study was conducted to assess the burden of gastroenteritis and joint symptoms within 8 weeks from exposure. Based on technical data and modelling, the town was divided into two areas: contaminated and uncontaminated. One thousand residents from both areas were picked from the population register to form two study groups, contaminated and uncontaminated group. The control group constituted 1 000 inhabitants of another municipality located in the same city area.

In comparison to the control municipality, there were 4519 excess cases of gastroenteritis in the contaminated and 1981 in the uncontaminated area. Attack rates were 53.0% and 15.6%, respectively. The odds ratio for gastroenteritis was 7.5 (95% CI: 4.3-10.0) in the contaminated and 1.95 (1.05-3.6) in the uncontaminated group. Most subjects fell ill during the first week of the epidemic. Common symptoms included diarrhoea, vomiting, nausea, abdominal pain and fever.

Altogether 13.9% in the contaminated group and 4.3% in the uncontaminated group experienced joint symptoms within eight weeks. Arthritis-like symptoms (pain in joint movement, joint swelling, redness or warmth) were reported by 6.7% and 2.1%, respectively. The frequency of these symptoms was significantly higher than in the control group. Every gastrointestinal symptom and fever was associated with a higher frequency of joint symptoms in both contaminated and

uncontaminated groups. In the contaminated group, the odds of having joint symptoms was increased even without gastroenteritis.

Another questionnaire study, a follow-up was conducted 15 months after the epidemic to assess the persistence of gastrointestinal and joint symptoms. Study groups were based on the three original population samples, but included only subjects who responded to the first study and gave permission to be contacted again.

According to the follow-up, 54% of respondents in the contaminated group reported gastroenteritis during the epidemic. Of these, 42.7% had prolonged symptoms of loose stools and abdominal pain or distension after the acute disease. This proportion diminished rapidly during three months, but thereafter the decrease levelled off. At 15 months, 10.9% were still experiencing these symptoms.

A total of 31.8% of the subjects in the contaminated group who reported having had epidemic-related gastroenteritis reported arthritis-like symptoms after gastroenteritis. A third of these symptoms were relieved within five months, but subsequently the proportion remained almost stable. At the end of the follow-up, 19% were still experiencing arthritis-like symptoms.

Direct health-economic costs were assessed by counting the costs of health care visits to the health centre or university hospital, clinical microbiology laboratory expenses and the cost of treatment in wards in neighbouring municipalities.

The direct health-economic costs according to this study were 354 496 EUR. Medicines, the use of private sector and occupational health-care services were not included in the analysis. This figure is thus probably a minimum estimate of the direct health-economic costs of this epidemic.

In conclusion, extensive drinking water contamination in Nokia resulted in the largest published waterborne epidemic in Finland to date. In addition to high morbidity in the contaminated area, excess cases of gastroenteritis were also observed in the uncontaminated area of the town, probably due to exposure to contaminated water while visiting the contaminated area or a secondary spread of viral pathogens. An excess of joint symptoms was observed in both contaminated and uncontaminated areas, in the former also among those who did not have gastroenteritis. A substantial proportion of people had prolonged gastrointestinal and joint symptoms after the acute gastroenteritis.

Contamination of drinking water can lead to widespread outbreaks of disease and constitute potentially dangerous situations. Ensuring safe drinking water should be a high priority in communities.

Keywords: waterborne, water contamination, gastroenteritis, joint symptoms, reactive arthritis, health-economic cost

Tiivistelmä

Laine Janne. Laaja juomavesivälitteinen epidemia Pirkanmaalla 2007. Tutkimus epidemian aiheuttamasta sairastuvuudesta, oireiden kestosta ja terveystaloudellisista kustannuksista. Terveyden ja hyvinvoinnin laitos. Tutkimus 128. 120 sivua. Helsinki, Finland 2014. ISBN 978-952-302-197-6 (painettu); ISBN 978-952-302-198-3 (verkkojulkaisu)

Turvallinen juomavesi on terveyden edellytys. Puhtaan juomaveden puute on maailmanlaajuisesti merkittävä ongelma, joka etenkin kehitysmaissa on merkittävä sairastuvuuden ja myös kuolleisuuden aiheuttaja.

Kehittyneissä maissa järjestäytynyt vesi- ja jätevesihuolto on viime vuosisadalta lähtien vähentänyt juomaveden aiheuttamien epidemioiden määrää selvästi. Tästä huolimatta vesiepidemioita, myös suuria, esiintyy edelleen ja niihin liittyy merkittävää sairastuvuutta.

Suomessa vesiepidemioita on rekisteröity kattavasti vuodesta 1997. Vuosina 1997−2009 Suomessa rekisteröitiin yli 70 vesiepidemiaa (Figure 1, s.24). Suurimmissa niistä sairastuneiden määrä on ollut tuhansia, ja suurimmillaan yli puolet alueen väestöstä on sairastunut (Table 1, s. 23). Yleisimmät suomalaisissa vesiepidemioissa tavattavat taudinaiheuttajat ovat kampylobakteeri ja norovirus. Useimmiten suomalaisen vesiepidemian aiheuttaa yksi mikrobi. Poikkeuksina ovat Pyhätunturin ja Nokian epidemiat, joissa aiheuttavia mikrobeja oli useita. Molemmissa epidemioissa juomaveden saastutti jätevesi, mikä selittää runsaan mikrobikirjon.

Merkittävimpiä vesiepidemioita ulkomailla ovat olleet epidemiat Milwaukeessa (USA), Walkertonissa (Kanada) ja Bergenissä (Norja) (Table 2, s. 27). Milwaukeessa yli 400 000 asukasta sairastui Kryptosporidium-alkueläimen aiheuttamaan vatsatautiin ja epidemiaan liittyi myös kuolleisuutta. Pienen Walkertonin kaupungin juomavesilähde saastui karjan ulosteella. Tässä epidemiassa toisena taudinaiheuttajana oli enterohemorraginen *E. coli* O157:H7 (STEC). Tämän aiheuttamaan hemolyyttisureemiseen oireyhtymään sairastui 27 kaupunkilaista, ja kuusi heistä kuoli. Bergenissä havaittiin v. 2004 *Giardia*-alkueläimen aiheuttama vesiepidemia, joka sairastutti 1300 – 2500 kaupunkilaista. *Giardia*-infektion oireet kehittyvät hitaasti, ja muun muassa sen vuoksi kesti lähes kaksi kuukautta ennen kuin epidemia havaittiin.

Äkillinen vatsatauti on tavallisin vesiepidemioihin liittyvä sairaus. Noroviruksen tai kampylobakteerin aiheuttama vatsatauti on kestoltaan yleensä korkeintaan muutamia päiviä. Osa sairastuneista saattaa kuitenkin kokea jälkioireita kuten niveloireita, reaktiivista niveltulehdusta (Table 4, s. 37) tai ärtynyt paksusuoli
– oireyhtymää (Table 6, s. 43). Nämä oireet voivat kestää useita kuukausia ja saattavat myös kroonistua.

Laaja juomavesivälitteinen epidemia saattaa aiheuttaa merkittäviä kustannuksia. Koska tällainen epidemia vaikuttaa yhdyskunnan toimintaan monella tavalla, kustannuksia syntyy myös muuta kautta kuin sairastuneiden hoidosta tai vesilaitoksen

toimenpiteistä. Tehtyjen kustannusanalyysien perusteella voidaan arvioida, että epäsuorat kustannukset kuten sairauslomat tai taloudellisen toiminnan katkokset aiheuttavat yleensä välittömiä kuluja suurempia kustannuksia (Table 7, s. 47).

Nokian vesiepidemia

Nokian kaupungissa Pirkanmaalla sattui marras-joulukuussa 2007 laaja juomavesivälitteinen epidemia. Marraskuun lopussa kaupungin jätevedenpuhdistamolla tehtiin huoltotöitä. Töiden yhteydessä laitoksessa oli avattu venttiili, joka yhdisti käsiteltyä jätevettä sisältävän linjan ja talousvesiverkoston. Tämä venttiili oli töiden päätyttyä erehdyksessä jäänyt sulkematta. Venttiili oli auki kaksi vuorokautta, ja sinä aikana n. 450 m^3 käsiteltyä jätevettä sekoittui kaupunkilaisten juomaveteen.

Kaksi vuorokautta huoltotöiden jälkeen Nokialla havaittiin vatsatautitapausten nopea lisääntyminen. Koska myös veden laadusta oli valitettu, juomavettä epäiltiin osalliseksi tilanteeseen. Pian epäilyn herättyä auki oleva venttiili havaittiin ja suljettiin, ja väestölle annettiin kehotus keittää nautittavaksi aiottu vesijohtovesi.

Juomavesi oli saastunut kaupungin eteläisessä osassa, jossa asuu n. kolmannes kaupungin väestöstä (Figure 3, s. 52). Jätevesikontaminaatio oli huomattava, sillä verkostonäytteistä löytyi suuria määriä ulosteperäisiä indikaattorimikrobeja ja taudinaiheuttajia.

Nokian terveyskeskuksessa koettiin vatsatautipotilaiden ruuhka. Tilannetta vaikeutti se, että myös osa henkilökunnasta sairastui. Työntekijöitä siirrettiin terveydenhuollon kiireettömistä toimipisteistä päivystysvastaanotolle, ja naapurikunnat tarjosivat henkilökuntaansa sekä vuodepaikkojansa nokialaisten hoitoon. Tampereen yliopistollinen sairaala (Tays) varautui avaamaan vatsatautiin sairastuneille Nokialle väliaikaisen osaston, mutta osastoa ei lopulta tarvittu.

Veden käyttörajoitukset purettiin puhtaan veden alueelta 12 vrk:n kuluttua. Saastuneen veden alueella veden käyttörajoituksia jouduttiin jatkamaan 18.2.2008 saakka, 82 vuorokauden ajan.

Epidemian selvitystyö

Mikrobiologiset näytteet ja terveydenhuollon toimintayksiköissä kävijät

Tieto ulostenäytteistä löydetyistä taudinaiheuttajista saatiin Fimlab Laboratoriot oy:n (Pirkanmaan sairaanhoitopiirin kliininen laboratorio) tietokannasta. Laboratorion ylikuormittumisen välttämiseksi ulostenäytteitä ei epidemian aikana tutkittu kaikista potilaista vaan keskityttiin vaikeimmin sairastuneisiin. Virusnäytteitä tutkittiin otantana viidestä peräkkäisestä hoitoon hakeutuvasta ensimmäisellä epidemiaviikolla. Parasiittinäytteitä tutkittiin niin ikään otantana toisella epidemiaviikolla. Kun myöhemmin havaittiin *Giardia* – infektioita, *Giardia* tutkittiin kaikilta pitkittynyttä ripulia potevilta.

Vesi- ja vesijohtoverkostonäytteiden löydökset saatiin tiedoksi näytteitä tutkineista laboratoriosta.

Terveyskeskuksessa käynnistettiin epidemiapotilaiden rivilistaus. Rivilistan lisäksi epidemiapotilaiden määrä arvioitiin käyttämällä terveyskeskuksen käyntisyyrekisteriä, johon käynnit koodataan kansainvälistä ICPC-luokitusta käyttäen. Kaikki käynnit epidemiajakson aikana, joiden ICPC-koodi viittasi vatsatautiin, luokiteltiin epidemiakäynneiksi (Table 8, s. 55). Yliopistosairaalassa laskettiin epidemian vuoksi hoitoon hakeutuneiden aikuisten määrä, mutta kävijöiden henkilötietoja ei kirjattu. Lapsipotilaista käytettävissä oli määrän lisäksi myös muita tietoja.

Ensimmäinen kyselytutkimus (Q1)

Väestökyselytutkimus käynnistettiin epidemian laajuuden, taudinkuvan ja varhaisten niveloireiden selvittämiseksi. Nokian kaupunki jaettiin kahteen alueeseen: kontaminoitunut alue (saastuneen veden alue) ja kontaminoitumaton alue (puhdas alue). Poimimalla väestörekisteristä kummaltakin alueelta tuhannen asukkaan otos muodostettiin kaksi tutkimusryhmää. Kolmas tutkimusryhmä, (verrokkiryhmä) muodostettiin poimimalla tuhannen asukkaan otos Kangasalan kunnasta. Tämä kunta valittiin verrokkiväestöksi koska se Nokian tavoin sijaitsee Tampereen kaupunkialueella ja on väestöltään suunnilleen samankokoinen. Kunnat sijaitsevat kaupunkialueen eri laidoilla, joten verrokkiväestön kontaktit Nokialle (ja samalla verrokkiryhmän altistuminen saastuneelle vedelle) ovat todennäköisesti vähäisempiä kuin naapurikuntien kohdalla.

Kysely toteutettiin lomakkeella, joka postitettiin kahdeksan viikkoa tapahtuman jälkeen. Määräaikaan mennessä vastaamatta jättäneille lähetettiin muistutuskirje.

Toinen kyselytutkimus (Q2)

Toinen kyselytutkimus (seuranta) toteutettiin 15 kk:n kuluttua epidemian alkamisesta. Tutkimuksen tarkoituksena oli selvittää vatsa- ja niveloireiden kesto kontaminoituneessa ryhmässä. Kysely toteutettiin postitse lähetettyä lomaketta käyttäen. Lomake lähetettiin niille alkuperäisiin tutkimusryhmiin kuuluneille, jotka olivat vastanneet ensimmäiseen kyselyyn ja antaneet suostumuksensa uuteen yhteydenottoon. Tutkimusryhmät näin ollen pienenivät alkuperäisistä (Table 13, s. 64).

Terveystaloudellinen selvitys

Epidemian terveydenhuollolle aiheuttamia suoria kuluja tutkittiin laskemalla hoitokulut Nokian terveyskeskuksessa, yliopistosairaalassa ja naapurikuntien terveyskeskusten vuodeosastoilla sekä ulostenäytekulut. Lääkekuluja sekä yksityisen terveydenhuollon piirissä muodostuneita kuluja ei laskettu mukaan.

Tulokset

Mikrobiologiset löydökset

Epidemiapotilaista tutkituista ulostenäytteistä todettiin seitsemän eri taudinaiheuttajaa, kuusi näistä lajeista löydettiin myös vesinäytteistä (Table 11, s. 61). Yleisin todettu taudinaiheuttaja oli kampylobakteeri, toiseksi yleisin *Giardia lamblia.* Vähäinen määrä *Salmonella* -tapauksia todettiin. Norovirusnäytteitä otettiin epidemian alkuvaiheessa vain viidestä potilaasta. Kaikki viisi näytettä olivat kuitenkin positiivisia, ja epidemian kulku viittasi siihen, että myös norovirus oli keskeinen taudinai-

heuttaja tässä epidemiassa. Mikrobilöydösten perusteella epidemiajakso rajattiin ajankohtaan 28.11. – 31.12.2007, sillä tämän ajanjakson aikana tehtiin valtaosa ulosteviljelylöydöksistä. Giardian osalta kuitenkin tapaukset 31.5.2008 saakka luettiin epidemiaan liittyviksi, sillä tämän infektion itämisaika on muita vatsataudin aiheuttajia pitempi ja hitaasti kehittyvän taudinkuvan vuoksi diagnoosi usein viivästyy.

Potilasmäärät terveydenhuollon toimipisteissä

Epidemiajakson aikana Nokian terveyskeskukseen tehtiin vatsataudin takia 1222 käyntiä. Kiireisimmällä viikolla vatsatautipotilaiden määrä oli 53-kertainen epidemiaa edeltäneeseen aikaan verrattuna (Figure 4, s. 62). Yliopistosairaalaan lähetettiin 204 potilasta, joista 145 (71 %) oli lapsia.

Ensimmäinen kyselytutkimus

Ensimmäisen kyselytutkimuksen vastausprosentti oli 70.8 %. Kontaminoituneen ryhmän vastausprosentti oli 79 %, kontaminoitumattoman 73 % ja verrokkiryhmän 60 % (Table 13, s. 64). Ryhmien taustatiedot eivät eronneet merkittävästi toisistaan, joskin kontaminoituneen ryhmän vastaajilla käyttövesi tuli useammin kunnallisesta vesijohtoverkostosta kuin kahdessa muussa ryhmässä (Table 12, s. 63).

Vatsatautiin sairastuneiden osuus kontaminoituneessa ryhmässä oli kyselytutkimuksen perusteella 53 %, kun se verrokkiryhmässä oli 6.5 %. Myös kontaminoitumattomassa ryhmässä vatsatautiin sairastuneiden osuus (15.6 %) oli verrokkiryhmää korkeampi. Tutkittaessa tapausten ylimäärää Nokialla vertailemalla ilmaantuvuutta verrokkiväestöön voidaan Nokian kontaminoituneella alueella arvioida 4519 ja kontaminoitumattomalla alueella 1981 asukkaan sairastuneen vesiepidemian vuoksi.

Suurin osa sairastui viikon kuluessa tapahtumasta, eniten sairastumisia ilmaantui 1.12. (Epidemiakuvaaja, Figure 6, s. 66). Tavallisin vatsatautioire oli ripuli, jonka yleisyys kontaminoituneessa ryhmässä oli 47 %. Oksentelua koki 38 %, pahoinvointia 38 %, vatsakipua 39 % ja kuumetta 24 %. Akuutin vatsataudin mediaanikesto kontaminoituneessa ryhmässä oli kolme vuorokautta.

Kontaminoituneen ryhmän vastaajista 13.9 % ilmoitti kokeneensa niveloireita vatsataudin jälkeen kun kontaminoitumattomassa ryhmässä vastaava osuus oli 4.3 % ja verrokkiryhmässä 1.5 % (Table 14, s. 67). Niveltulehdukseen viittaavien oireiden (nivelen turvotus, kuumotus, punoitus tai kipu liikuteltaessa) yleisyys oli 6.7 %, 2.1 % ja 0.5 %. Niveloireiden todennäköisyys oli kontaminoituneessa ryhmässä verrokkeja korkeampi myös niillä, jotka eivät olleet sairastuneet vatsatautiin (Table 15, s. 68). Niveloireiden todennäköisyys oli suurempi niillä kontaminoituneen ryhmän vastaajilla, jotka joivat yli kuusi vesilasillista päivittäin, kuin alle kolme lasillista juovilla (Table 16, s. 68).

Toinen kyselytutkimus

Alkuperäiseen väestöotantaan kuuluneista kontaminoituneen ryhmän jäsenistä 615 (60.2 %) otettiin seurantatutkimukseen. Vastaus kyselyyn saatiin 323 osallistujalta (52.5 %). Heistä 174 (54 %) ilmoitti sairastaneensa epidemiaan liittyneen vatsataudin. Tiedon yhtenevyys ensimmäisessä kyselytutkimuksessa ilmoitettuun vatsatautiin oli 91.8 %.

Vatsatautiin sairastuneista kontaminoituneen ryhmän vastaajista 42,7 % (74/174) ilmoitti kokeneensa pitkittyneitä vatsaoireita (vatsan turvotusta tai kipua yhdistyneenä löysävatsaisuuteen) vatsataudin akuutin vaiheen päätyttyä. Vatsaoireisten osuus väheni nopeasti kolmen kuukauden kuluessa mutta pysyi sen jälkeen lähes muuttumattomana (Figure 7, s. 70). Seuranta-ajan lopussa 10,9 % (19/174) vatsataudin sairastaneista ilmoitti vatsaoireiden jatkuvan edelleen.

Niveltulehdukseen viittaavia oireita oli esiintynyt 31.8 %:lla (55/174) vatsatautiin sairastuneista. Kolmanneksella näistä oireet väistyivät viiden kuukauden kuluessa mutta sen jälkeen väheneminen oli hidasta (Figure 7, s. 70). Seuranta-ajan lopussa 19 % (33/174) koki edelleen niveltulehdukseen viittaavia oireita.

Terveystaloudellinen tutkimus

Nokian vesiepidemia aiheutti terveydenhuollossa 354 496 euron suorat kustannukset (Table 18, s. 72). Suurin kustannuserä oli epidemiapotilaiden hoito Nokian terveyskeskuksessa, mikä muodosti 44 % (157 573 EUR) kustannuksista. Hoito yliopistosairaalassa oli toiseksi merkittävin kustannus (42 %, 148 625 EUR). Laboratoriokustannukset muodostivat 10.2 % kustannuksista (36 263 EUR).

Pohdinta

Selvitys osoitti Nokian vesiepidemian olleen Suomen tähän asti laajin juomavesivälitteinen epidemia. Jätevedellä saastuneen talousveden alueella yli puolet asukkaista sairastui. Myös Nokian puhtaan veden alueen asukkailla havaittiin verrokkiväestöä enemmän vatsatautitapauksia. Osa puhtaan veden alueen asukkaista kävi työssä, koulussa tai päivähoidossa saastuneen veden alueella ja altistui siellä ollessaan. Lisäksi norovirus on todennäköisesti lähtenyt leviämään henkilöstä toiseen, ja norovirustartunnan on saattanut saada myös ilman suoraa altistumista saastuneelle vedelle.

Varhaiset niveloireet olivat yhdeksän kertaa tavallisempia kontaminoituneella alueella kuin verrokkiväestössä. Niveltulehdukseen viittaavien oireiden kohdalla ero oli 13-kertainen. Niveloireidenkin kohdalla havaittiin ylisairastuvuutta myös Nokian puhtaan veden alueella. Reaktiivisen niveltulehduksen esiintyvyyttä Nokian epidemian jälkeen tutkiva ryhmä totesi niveltulehduksen kuitenkin vain 21 henkilöllä (Uotila, Antonen et al. 2011). Niveltulehdusta lievemmät niveloireet näyttävät siis olevan selvästi yleisempiä kuin varsinaiset reaktiiviset niveltulehdukset.

Pitkittyneet vatsaoireet olivat yleisiä puolen vuoden ajan. Seuranta-ajan lopussa aikuisilla havaittu 11.9 % vallitsevuus sen sijaan on lähellä joissakin tutkimuksissa raportoitua ärtynyt paksusuoli -oireyhtymän luontaista vallitsevuutta aikuisväestössä. On siten kyseenalaista, oliko kontaminoituneella alueella enää havaittavissa vatsaoireiden ylimäärää seuranta-ajan lopussa väestötasolla tarkasteltuna.

Myös niveloireista enin osa väistyi puolen vuoden kuluessa. Seuranta-ajan lopussa kuitenkin vielä lähes viidennes vatsataudin kokeneista koki niveltulehdukseen viittaavia oireita. Vaikka suurimmalla osalla näistä todellisuudessa ei ollut reaktiivisen niveltulehduksen diagnoosiin riittäviä löydöksiä, oireiden pysyvyys on linjassa niveltulehduksia tutkivan ryhmän löydösten kanssa. Vuoden seurannassa kolmannes

todetuista niveltulehduspotilaista käytti edelleen reumalääkkeitä ja yli puolet kipulääkkeitä (Uotila, Antonen et al. 2013).

Nokian vesiepidemia oli mikrobilöydösten runsauden johdosta maamme oloissa ainutlaatuinen. Runsas taudinaiheuttajakirjo on ilmiö, joka yleensä on havaittu voimakkaan ulostesaastumisen aiheuttamien vesiepidemioiden yhteydessä. Jätevesi on sekoitus jopa tuhansien ihmisten ulosteista, minkä johdosta on ymmärrettävää, että sen aiheuttama vahva-asteinen kontaminaatio johtaa runsaaseen taudinaiheuttajakirjoon.

Epidemian suorat terveystaloudelliset kustannukset jäivät suhteellisen pieniksi ottaen huomioon epidemian laajuuden. Selvityksessä otettiin huomioon kuitenkin vain julkisessa terveydenhuollossa syntyneet kustannukset. Tämän vuoksi selvityksessä todetut kustannukset edustavat kustannusten vähimmäistasoa. Epidemian kokonaiskustannukset, mukaan lukien epäsuorat kulut, olivat todennäköisesti huomattavasti suuremmat kuin tässä selvityksessä havaitut. Toisen tutkimusryhmän tekemässä tutkimuksessa Nokian epidemian aiheuttamien sairauspoissaolojen kustannukset olivat merkittävästi suuremmat kuin tässä havaitut suorat terveystaloudelliset kulut (Halonen, Kivimaki et al. 2012).

Nokian talousvesijärjestelmän voimakas jätevesisaastuminen ja sitä seurannut laaja vatsatautiepidemia oli potentiaalisesti vaarallinen onnettomuus. Tilanne huomioon ottaen seuraukset olisivat voineet olla huomattavasti nähtyä vakavampia. Vakavimmissa vesiepidemioissa aiheuttajana on usein ollut enterohemorraginen *E. coli* O157:H7. Nokialla niin tältä kuin muiltakin vakavammilta taudinaiheuttajilta vältyttiin. Mikrobit, joita Nokian epidemiassa todettiin, aiheuttavat useimmille äkillisen vatsataudin, joka yleensä paranee jälkiä jättämättä. Huolimatta tästä onnekkaastakin yleiskuvasta Nokialla on henkilöitä, jotka kärsivät pitkäaikaisista tai pysyvistä, vuoden 2007 vesiepidemiaan liittyvistä terveysongelmista.

Contents

List of original papers

I Laine J, Huovinen E, Virtanen MJ, Snellman M, Lumio J, Ruutu P, Kujansuu E, Vuento R, Pitkänen T, Miettinen I, Herrala J, Lepistö O, Antonen J, Helenius J, Hänninen M-L, Maunula L, Mustonen J, Kuusi M and the Pirkanmaa Waterborne Outbreak Study Group (2011): An extensive gastroenteritis outbreak after drinking-water contamination by sewage effluent, Finland. Epidemiol Infect 139:1105-13.

II Laine J, Uotila T, Antonen J, Korpela M, Kujansuu E, Lumio J, Huovinen E, Mustonen J, Ruutu P, Virtanen MJ, Kuusi M and the Pirkanmaa Waterborne Outbreak Study Group (2012): Joint symptoms after a large waterborne gastroenteritis outbreak –a controlled, population-based questionnaire study. Rheumatology 51:513-8. http://rheumatology.oxfordjournals.org/content/51/3/513.full.pdf+html

III Laine J, Lumio J, Toikkanen S, Virtanen MJ, Uotila T, Korpela M, Kujansuu E, Kuusi M and the Pirkanmaa Waterborne Outbreak Study Group (2014): The duration of gastrointestinal and joint symptoms after a large waterborne outbreak of gastroenteritis in Finland –a questionnaire-based 15 month follow-up study. PLoS One 9:e85457. http://www.plosone.org/article/fetchObject.action?uri=info%3Adoi%2F10.1371%2Fjournal.pone.0085457&representation=PDF

IV Huovinen E, Laine J, Virtanen MJ, Snellman M, Hujanen T, Kiiskinen U, Kujansuu E, Lumio J, Ruutu P and Kuusi M (2013): Excess healthcare costs of a large waterborne outbreak in Finland. Scand J Public Health 41:761-6.

Abbreviations

AGE	Acute gastroenteritis
ECDC	European Centre for Disease Prevention and Control
HAV	Hepatitis A virus
HLA-B27	Human leucocyte antigen B27
HEV	Hepatitis E virus
HUS	Haemolytic-uremic syndrome
IBS	Irritable bowel syndrome
ICPC	International Classification of Primary Care
IGE	Infectious gastroenteritis
Kela	Finnish Social Insurance Institution
OR	Odds ratio
PCR	Polymerase chain reaction
PI-IBS	Postinfectious irritable bowel syndrome
Q1	First questionnaire study
Q2	Second (follow-up) questionnaire study
ReA	Reactive arthritis
SD	Standard deviation
STEC	Shiga-toxin producing *Escherichia coli*
TAUH	Tampere University Hospital, Finland
Tays	Tampereen yliopistollinen sairaala
THL	National Institute for Health and Welfare, Finland
WHO	World Health Organization
WHS	The Walkerton Health Study

1 Introduction

Safe drinking water is a necessity for life. Despite this long-known fact, waterborne gastroenteritis remains a significant cause of mortality, especially in the developing countries. Small (< 5 years) children are the most vulnerable, especially if they are malnourished. It has been estimated that in developing countries 4.9 per one thousand children die because of gastroenteritis every year (Kosek, Bern et al. 2003). In 2008, an estimated 1,3 million child deaths were caused by diarrhoeal diseases globally (Black, Cousens et al. 2010). Although it is not clear to what extent diarrhoeal morbidity is due to lack of clean drinking water, it is reasonable to consider that unsafe water is a prominent cause.

An extensive drinking-waterborne cholera epidemic which killed over 600 people in London in 1854 was a cornerstone in the history of waterborne epidemics in Western countries. The work of Dr John Snow in studying and controlling that epidemic is considered to be a starting-point for modern infectious disease epidemiology (Paneth 2004). The London epidemic and a later cholera epidemic in Hamburg in 1892 had an important influence in improving drinking water safety and sewage treatment in developed countries.

Since those times, the introduction of organized water distribution and sewage systems has reduced the incidence of drinking water-associated outbreaks in developed countries. Nevertheless, waterborne epidemics remain a major concern in these countries (Hrudey and Hrudey 2007). In the United States, for example, 20 million people are estimated to fall ill in consequence of waterborne infection every year (Reynolds, Mena et al. 2008). Also in Europe, waterborne epidemics are frequently noted (Miettinen 2009). However, surveillance systems vary considerably between nations and the magnitude of waterborne outbreaks is probably underestimated (Risebro and Hunter 2007). It is also unclear how much waterborne infections contribute to the endemic level of such microbes as can be transmitted by water. For example in Finland, the incidence of domestic *Campylobacter* infections is highest during the summer, a time when Finns spend time at their summer cottages and obtain water from their private wells (Nakari, Huovinen et al. 2010).

Although organized water supply systems have given protection against outbreaks, they may also constitute an efficient pathogen distribution system if contaminated. In large towns a single distribution network may involve thousands of residents. If household water becomes heavily contaminated in such circumstances, the number of people falling ill can easily be thousands. Such an epidemic is a considerable challenge to health-care system as well society overall.

Waste water effluent contaminated the household water network in the town of Nokia, Pirkanmaa County, Finland in November 2007 and an extensive epidemic of gastroenteritis took place. The purpose of this work was to study the microbial

agents, disease burden, short- and long-term health effects and health-economic costs associated with this epidemic.

2 Review of the literature

2.1 Epidemiology of waterborne outbreaks

Numerous outbreaks of infectious intestinal disease caused by contaminated drinking water have been reported in affluent nations (Craun, Craun et al. 2006; Hrudey and Hrudey 2007; Karanis, Kourenti et al. 2007; Beaudeau, de Valk et al. 2008; Kvitsand and Fiksdal 2010). Some of these epidemics have affected thousands of people (Mac Kenzie, Hoxie et al. 1994) and some have involved mortality (Auld, MacIver et al. 2004).

2.1.1 Waterborne outbreaks associated with drinking water in Finland

Finland is a country of rich water resources, 92% of the population using drinking water distributed from public waterworks (Anonymous 2013). In 2001, 52% of the distributed water was groundwater (Miettinen, Zacheus et al. 2001). The number of plants using surface water is low (74) compared to ground water (1 440). However, surface water plants produce almost a half of the water distributed, as they usually serve largest cities.

Groundwater in Finland, as elsewhere in Scandinavia, is considered to be of high quality and safe for drinking, requiring minimal or no treatment before use (Miettinen, Zacheus et al. 2001; Kvitsand and Fiksdal 2010). Surface water, in contrast, is filtered and disinfected before distribution. Despite the high quality of water resources, several outbreaks have taken place (Table 1), most of them associated with small waterworks.

Surface water runoff is a common cause of contamination and waterborne outbreaks in Finland (Vartiainen, Miettinen et al. 2003; Kuusi 2008). Such outbreaks are thus most common during spring and fall, when melting snow or heavy rainfalls increase the risk. Another important mechanism has been sewage contamination due to obstruction or flooding of the sewage system or a breakage of the sewage line.

Surveillance of food- and waterborne outbreaks in Finland dates back to 1975 (Figure 1). In the beginning reporting was voluntary. Twenty-four outbreaks associated with drinking water were reported during 1980-92, ten of these (7 670 people) being associated with community water systems (Lahti and Hiisvirta 1995). The most common mechanism in these outbreaks was sewage contamination, including one case where there was a cross-connection between sewage and household water lines. One or more of the valves normally closing this connection gave way and allowed a waste water backflow to occur (Lahti and Hiisvirta 1995).

In 1997, reporting of waterborne outbreaks became mandatory in Finland, lending greater accuracy to the surveillance system. Already during the first two

years of mandatory reporting, 14 outbreaks affecting 7 300 people were registered (Miettinen, Zacheus et al. 2001) (Figure 1). Most of the outbreaks were associated with small waterworks using groundwater without disinfection. The main reasons for contamination in these outbreaks included surface runoffs, flooding and fissures in the bedrock (Miettinen, Zacheus et al. 2001). Subsequently, during the years 1998-2009, 67 waterborne outbreaks with 27 000 disease cases were recorded (Zacheus and Miettinen 2011).

During the 1980s the etiologic microbial agents remained unknown in 58% of outbreaks, probably by reason of limited diagnostic methods at the time (Lahti and Hiisvirta 1995). In outbreaks where the etiology was defined, viruses constituted 17% of the outbreaks, followed by *Campylobacter* (13%) and *Salmonella typhimurium* (8%). After the implementation of PCR-based methods in viral diagnosis, norovirus has turned out to be the most frequent etiology (Maunula, Miettinen et al. 2005).

Since the end of the 1990s the etiologic agents in Finnish waterborne outbreaks have almost consistently been norovirus and *Campylobacter* (Miettinen, Zacheus et al. 2001; Vartiainen, Miettinen et al. 2003) (Table 1, Figure 2). In most cases, only one microbial pathogen has been associated with the outbreak. Exceptions to this rule are two outbreaks, in Pyhätunturi and Nokia, where a number of pathogens were involved. Another feature common to these two outbreaks was relatively extensive sewage contamination. Although protozoan pathogens such as *Giardia lamblia* and *Cryptosporidium* are important pathogens in waterborne outbreaks in other countries (Andersson and Bohan 2001; Smith, Reacher et al. 2006), these have mostly been absent in Finnish outbreaks. This is somewhat surprising, as these microbes certainly exist in the Finnish environment (Hanninen, Horman et al. 2005). One possible explanation is underdiagnosis of these pathogens in patient samples (Rimhanen-Finne, Jokiranta et al. 2011).

Table 1 summarises the waterborne outbreaks in Finland published in the literature. In all the studies in question, an association with drinking water was verified by epidemiological or microbiological methods, or both. There was no mortality associated with these outbreaks, with the exception of Nokia, where in one case the outbreak may have contributed to death.

Table 1. Published outbreaks associated with drinking water in Finland.

Location and year	Water source	Cause	N:o of cases	Attack rate	Microbial etiology	Detected in water	Reference
Hospital, Heinola 1986	GW	Surface water contamination	94	Not given	*Campylobacter jejuni*	Yes	(Rautelin, Koota et al. 1990)
Noormarkku 1994	GW	River water backflow to a well	1 500-3000	25-50%	Norovirus + other viruses	No	(Kukkula, Arstila et al. 1997)
Haukipudas 1998	GW	Not known	2 700	19%	*Campylobacter jejuni*	No	(Kuusi, Nuorti et al. 2005)
Heinävesi 1998	SW	Insufficient chlorination	1 700-3 100	35-64%	Norovirus	Yes	(Kukkula, Maunula et al. 1999)
Asikkala 2000	GW	Not known	463	Not given	*Campylobacter jejuni*	Yes	(Kuusi, Klemets et al. 2004)
Nurmes 2000	GW	Not known	5 500	63%	Norovirus	No	(Kuusi, Nuorti et al. 2004)
Pyhätunturi 2000	GW	Sewage line leakage	300	Appr. 14%	Several	Not known	(Vartiainen, Zacheus et al. 2001)
Eastern Finland 2004	GW	Faecal (bird) contamination	3	Not given	*Campylobacter jejuni*	Yes	(Pitkanen, Miettinen et al. 2008)
Nokia 2007	GW	Waste water backflow	6501*	22%*	Several	Yes	(Laine, Huovinen et al. 2011)

*The number of cases and attack rate in the case of the Nokia outbreak represent the figures for the whole town, not only the contaminated area. The Nokia outbreak is the subject of this dissertation and will be discussed in detail in later sections.
GW: ground water, SW: surface water.

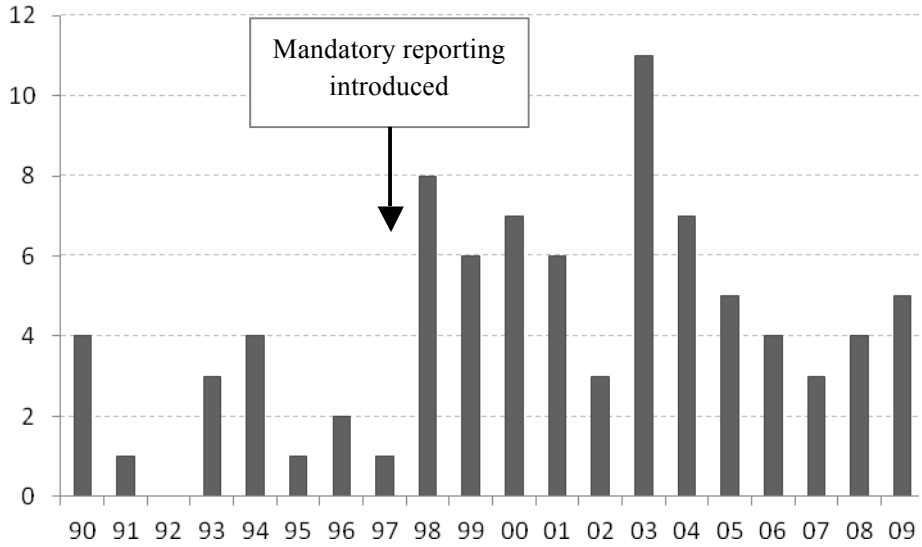

Figure 1. The annual number of waterborne outbreaks in Finland reported to the surveillance system. Reporting became mandatory in 1997. (Niskanen, Korhonen et al. 2010; Zacheus and Miettinen 2011)

2.1.2 Waterborne outbreaks associated with drinking water in Europe

Despite the growing importance of the European Centre for Disease Prevention and Control (ECDC), outbreak surveillance is still largely maintained by national institutions. There are therefore substantial variations in the number of reported outbreaks, which is probably at least in part due to differences in surveillance systems. Comprehensive data on morbidity caused by drinking water in Europe are lacking so far; instead there are outbreak reports and national summaries. Based on these data, there were at least 354 outbreaks associated with drinking water in Europe between 2000-7, affecting 47 617 people (Miettinen 2009).

In England and Wales, 19 outbreaks connected with drinking water were reported during 1992-5 (Furtado, Adak et al. 1998). All ten outbreaks associated with public systems were caused by *Cryptosporidium*. Subsequently, Smith and colleagues reviewed waterborne outbreaks during 1992-2003, finding reports of 89 outbreaks which had affected 4321 people (Smith, Reacher et al. 2006); 27% (24 outbreaks) were associated with public water supplies. After the year 2000 there was a decline in the outbreaks connected to public water supplies. The authors concluded that the risk of outbreak may be 35 times higher when using private water supplies.

Ten outbreaks were investigated in France in the years 1998-2006 (Beaudeau, de Valk et al. 2008). The total number of exposed individuals in these outbreaks was 176 700 and over 9 500 fell ill. No deaths were associated with these outbreaks. In three instances, there was a cross-connection between waste-water and tap-water

lines, and a backflow through this connection contaminated drinking water. In Italy, 2-12 drinking water-associated outbreaks were reported annually to the National surveillance system during 1998-2005 (Blasi, Carere et al. 2008).

There are a considerable number of reports of waterborne outbreaks from the Nordic countries in relation to the small populations of these countries. The probable reason for this is the relatively long history of surveillance and reasonably well-established surveillance systems (Andersson and Bohan 2001). During the last two decades of the 20th century, 116 outbreaks with 57 000 affected subjects and two deaths were reported in Sweden (Andersson and Bohan 2001). The largest of these affected approximately 11 000 people (Andersson 1991). *Campylobacter* and *Giardia* were the most common causative agents. Subsequently, norovirus (Carrique-Mas, Andersson et al. 2003; Lysen, Thorhagen et al. 2009; Riera-Montes, Brus Sjolander et al. 2011; Nenonen, Hannoun et al. 2012) and *Campylobacter* (Martin, Penttinen et al. 2006) have dominated in the etiology of Swedish waterborne outbreaks. In one norovirus outbreak, the contamination was due to a sewage pipe crack near a tap water well (Carrique-Mas, Andersson et al. 2003).

In Norway, 102 outbreaks associated with drinking water were reported in the period 1984 – 2007, 17 243 cases of illness being recorded (Kvitsand and Fiksdal 2010). Norovirus and *Campylobacter* were the most common etiologies. There was seasonality in the *Campylobacter* outbreaks, as all took place between March and November with a peak in July-September. No clear seasonality was observed in norovirus outbreaks. Largest norovirus outbreaks were, however, reported during winter. A *Campylobacter* outbreak with an attack rate up to 59% took place in the town of Røros (Jakopanec, Borgen et al. 2008). An association with consuming tap water was confirmed, but the reason for the contamination remained inconclusive. The most comprehensively studied waterborne epidemic in Norway took place in Bergen 2004 (Nygård, Schimmer et al. 2006). This epidemic will be discussed more closely in later sections.

In Denmark, a waterborne outbreak with multiple microbial agents was reported in 2007 (Table 2) (Vestergaard, Olsen et al. 2007). Simultaneous with the emergence of gastroenteritis cases, household water was observed to be of unusual colour, taste and smell. The number of persons visiting health care providers was 140. Seventy-seven yielded positive microbial findings in their stool specimens, 23 of them had 2-5 different pathogens. Altogether 19 different microbial strains were detected in stool samples, *Campylobacter* and enteropathogenic *E. coli* representing the majority of findings. The reason for water contamination was concluded to be a backflow of 27 m^3 of partially filtered waste water into the tap-water network, although the exact circumstances remained unclear. Although drinking water-associated outbreaks are said to be rare in Denmark, another outbreak of campylobacteriosis has been epidemiologically linked to tap water (Gubbels, Kuhn et al. 2012).

2.1.3 Waterborne outbreaks associated with drinking water in the United States and Canada

In the United States, 36 outbreaks connected to drinking water were reported to the federal surveillance system in 2007-8 (Brunkard, Ailes et al. 2011). The true impact is, however, assumed to be higher than the figures drawn from surveillance data. It has been estimated that up to 20 million people may contract a drinking water-associated infection annually (Reynolds, Mena et al. 2008). An average of 6 deaths per year connected to waterborne outbreaks were counted between 1991-2002 (Craun, Craun et al. 2006).

The largest reported drinking water-associated outbreak took place in 1993 in Milwaukee in 1993, where over 400 000 people fell ill with cryptosporidiosis (Table 2) (Mac Kenzie, Hoxie et al. 1994). Another significant U.S. epidemic was that at the Washington county fair in 1999. This epidemic was caused by *Campylobacter* and *E. coli* O157:H7, was implicated in 127 confirmed *E. coli* 0157:H7 infections, 14 cases of haemolytic-uremic syndrome (HUS) and two deaths (Novello 2000). According to a telephone survey, the total number of cases was estimated to be at least 2800. The source of contamination was possibly a septic tank containing faecal matter and situated near a drinking water well.

In Canada, 288 outbreaks possibly linked to drinking water were reported during the years 1974-2001 (Schuster, Ellis et al. 2005). As the surveillance system in Canada did not necessitate reporting the source of an outbreak, the connection with drinking water is registered in only a part of reported outbreaks. Furthermore, the authors concluded that this figure is probably an underestimate. In Walkerton, Ontario, a serious waterborne outbreak with *E. coli* O157:H7 and *Campylobacter* with several deaths took place in 2000 (Anonymous 2000a). This outbreak is discussed in greater detail in later sections.

Table 2. (next page). Some well-described outbreaks associated with drinking water.

Location, year	Water Source	Cause	Number of cases	Deaths	Microbial etiology	Pathogens detected in water	Epidemio-logical verification	Reference
Milwaukee, WI, USA 1993	SW	Shedding of faecal matter into water reservoir	403 000	Yes	*Cryptosporidium*	Yes	Yes	(Mac Kenzie, Hoxie et al. 1994)
Gideon, MO, USA 1993	GW	Faecal (birds) contamination	>650	7	*S. typhimurium*	Yes	Yes	(Angulo, Tippen et al. 1997)
La Neuveville, Switzerland 1998	GW	Sewage backflow	1607	No	Several	+/-	Yes	(Maurer and Sturchler 2000)
Albany, NY, USA 1999*	GW	Faecal contamination	2800	2	*E. coli* O157:H7 and *C. jejuni*	Yes	Yes	(Anonymous 1999; Novello 2000)
Walkerton, ON, Canada 2000	GW	Faecal (livestock) contamination	2300	6	*E. coli* O157:H7 and *C. jejuni*	Yes	Yes	(Anonymous 2000a)
France 2000	GW	Faecal (livestock) contamination	264	No	*C. coli,* rota- and norovirus	Yes (rota)	Yes	(Gallay, De Valk et al. 2006)
Bergen, Norway 2004	SW	Sewage contamination (?)	1300-2500	No	*Giardia lamblia* *Cryptosporidium*	+/- (see 2.1.4)	Yes	(Nygård, Schimmer et al. 2006)
South Bass Island, OH, USA 2004	GW	Faecal contamination	1450	No	Several	Yes	Yes	(Fong, Mansfield et al. 2007; O'Reilly, Bowen et al. 2007)
New Zealand 2006	GW	Sewage contamination	218	No	Several	Yes	Yes	(Hewitt, Bell et al. 2007)
Denmark 2007	NS	Sewage backflow	140	No	Several	Not stated**	Yes	(Vestergaard, Olsen et al. 2007)

GW: Ground water; SW: Surface water; *The Washington County Fair outbreak; **Faecal indicator microbes were detected in water samples

2.1.4 Three outbreaks of interest

Three outbreaks described next are noteworthy by reason of their size and clinical relevance and because they have been comprehensively studied.

Cryptosporidium outbreak in Milwaukee, spring 1993. A widespread outbreak of acute watery diarrhoea was noted among residents of the city of Milwaukee, WI, USA (Mac Kenzie, Hoxie et al. 1994). Increased turbidity was recognized at the city's southern water treatment plant. Examination of stool samples revealed *Cryptosporidium* oocysts. Ice blocks frozen during the epidemic were melted and *Cryptosporidium* oocysts were found. According to a telephone survey, 403 000 residents had fallen ill during the epidemic, giving an attack rate of 26%. *Cryptosporidium*-associated mortality during the post-outbreak period was found to have increased 13-fold compared to the pre-outbreak era (Hoxie, Davis et al. 1997). The increased mortality was concentrated among HIV-infected persons. Also elderly people were highly affected and the risk of severe disease increased with age (Naumova, Egorov et al. 2003).

Epidemiologic modelling of the outbreak suggested that shedding of *Cryptosporidium* into the sewage system by infected persons and subsequently into the raw water reservoir (Lake Michigan) created a transmission circuit. Furthermore, person-to-person transmission independent of water contributed to 10% of the illnesses (Eisenberg, Lei et al. 2005). The authors recommended increasing the distance between waste water effluent and raw water influent points in the lake.

The Walkerton outbreak 2000. In the rural town of Walkerton, Ontario, Canada, a gastrointestinal outbreak of *Escherichia coli* O157:H7 and *Campylobacter* was registered (Anonymous 2000a; Anonymous 2000b; Salvadori, Sontrop et al. 2009). The outbreak was due to contamination of the town water supply by livestock faecal residue flowing from a nearby farm. A heavy rainfall and inadequate chlorination contributed to the event. At least 2 300 residents became ill, >750 visited emergency rooms, 65 were admitted to hospital, 27 developed HUS and six died.

Two years after the outbreak, a comprehensive study was initiated to assess the possible long-term health consequences of the outbreak, named the Walkerton Health Study (WHS). Three cohorts were created from the exposed population, those who had clinically verified gastroenteritis, those who had self-reported gastroenteritis and those who remained asymptomatic during the outbreak (Garg, Macnab et al. 2005; Garg, Marshall et al. 2006). The study could also be entered after initiation and some participants dropped out, causing slight variation in the study cohorts during the follow-up. The participants visited the study clinic annually. WHS has released several reports of chronic disorders possibly associated with the outbreak; these reports will be discussed in detail in later parts of this thesis.

Waterborne Giardia-outbreak in Bergen, Norway 2004. In October 2004, an increase in confirmed *Giardia* cases was observed in the city of Bergen. A total of

1300 cases were recorded. According to prescription data, approximately 2 500 persons had received treatment for giardiasis (Nygård, Schimmer et al. 2006). Detection of the outbreak was delayed for several weeks, which increased the public health impact considerably.

A case-control study showed a connection between drinking water from city centre water network and falling ill. A dose correlation was also noted; those who drank more than 5 glasses of tap water per day had the highest risk of contracting the disease. Young women, who usually use larger amounts of water, predominated among cases (Robertson, Forberg et al. 2008). Within 15 months from the outbreak, 124 persons had continuous abdominal symptoms despite treatment, and 32.3% of these were found to have persistent *Giardia* infection (Hanevik, Hausken et al. 2007). In addition to *Giardia,* 115 cases of *Cryptosporidium* infection were confirmed (Robertson, Forberg et al. 2006).

Water samples yielded faecal indicator bacteria, but the number of *Giardia* cysts was low, at a level presumed not to cause any risk according to Norwegian experience (Nygård, Schimmer et al. 2006). The cases occurred in area served by one particular water source. Leakage in an old pipeline near the water source was discovered upon inspection of the sewage lines, this possibly being the cause of contamination. There was also a short failure in water chlorination before the onset of the outbreak (Nygård, Schimmer et al. 2006). *Giardia* cysts were found to persist in city sewage for several months, but returned to pre-outbreak levels at 18 months (Robertson, Forberg et al. 2008).

Also the Bergen cohort has been followed to check for late effects. These issues are discussed in later sections.

2.1.5 Microbial agents in drinking water-associated outbreaks

To constitute a waterborne pathogen, a microbe needs to have some certain characteristics. First, the microbe has to be able to survive in water (Robben and Sibley 2004). Secondly, the infective dose of a waterborne microbe must be low as the contaminating microbes are diluted into a large amount of water, resulting in low concentrations. Some waterborne enteric bacterial pathogens may be able to grow in an aquatic environment (Leclerc, Schwartzbrod et al. 2002). Thirdly, enteric viruses, especially norovirus and oocysts of *Giardia* and *Cryptosporidium,* are relatively resistant to disinfecting processes, ensuring better to survive in concentrations high enough to cause infection (Huang and White 2006; Ganesh and Lin 2013).

A wide variety of pathogens have been implicated in waterborne outbreaks. Figure 2 presents microbial agents involved in drinking water-associated outbreaks in Finland and the USA during recent decades. In Finland *Campylobacter* and norovirus dominated the etiology in 1998-2002 (Miettinen, Zacheus et al. 2001; Vartiainen, Miettinen et al. 2003). In the USA, the proportion of *Legionella*

outbreaks is high. The diseases associated with *Legionella* outbreaks are almost uniformly acute respiratory infections and probably caused by inhaling water aerosol contaminated with *Legionella* (Brunkard, Ailes et al. 2011). The proportion of outbreaks without identified pathogen has diminished over time in both countries. This is, most of all, due to improved diagnostic methods. Reporting of waterborne outbreaks is mandatory in both countries; despite this, probably only a portion of outbreaks is actually reported.

There are some differences in this context between continents and countries. In the WHO European region, data on 354 outbreaks from 14 countries have been summarized (Miettinen 2009). Of these, 49% were caused by viral agents, 45% by bacterial pathogens (*Campylobacter spp., Aeromonas spp,* and *Shigella sonnei*), and 5% by protozoa. As in Finland, the most common agents in other Scandinavian countries are *Campylobacter* and norovirus (Kvitsand and Fiksdal 2010). However, outbreaks due to *Salmonella, Shigella, Giardia, Cryptosporidium* and hepatitis A have occurred (Andersson and Bohan 2001; Kvitsand and Fiksdal 2010).

In England and Wales, *Cryptosporidium* was the most common waterborne pathogen during the years 1992-2003 representing 69% of outbreaks, followed by *Campylobacter* (14%) and *E. coli O157* (3%) (Smith, Reacher et al. 2006). Surprisingly, very few viral outbreaks were reported.

Although protozoan pathogens are most prevalent in developing countries, all outbreak reports of protozoan pathogens published have been from wealthy countries (Karanis, Kourenti et al. 2007). Surprisingly, 76% of these reports come from two countries, the UK and the USA. It is possible that there are true differences in epidemiology within western countries; however, a more likely explanation is differences in the level of suspicion of these pathogens. In Finland, at least cryptosporidiosis is considered to be probably underdiagnosed (Autio, Karhukorpi et al. 2012).

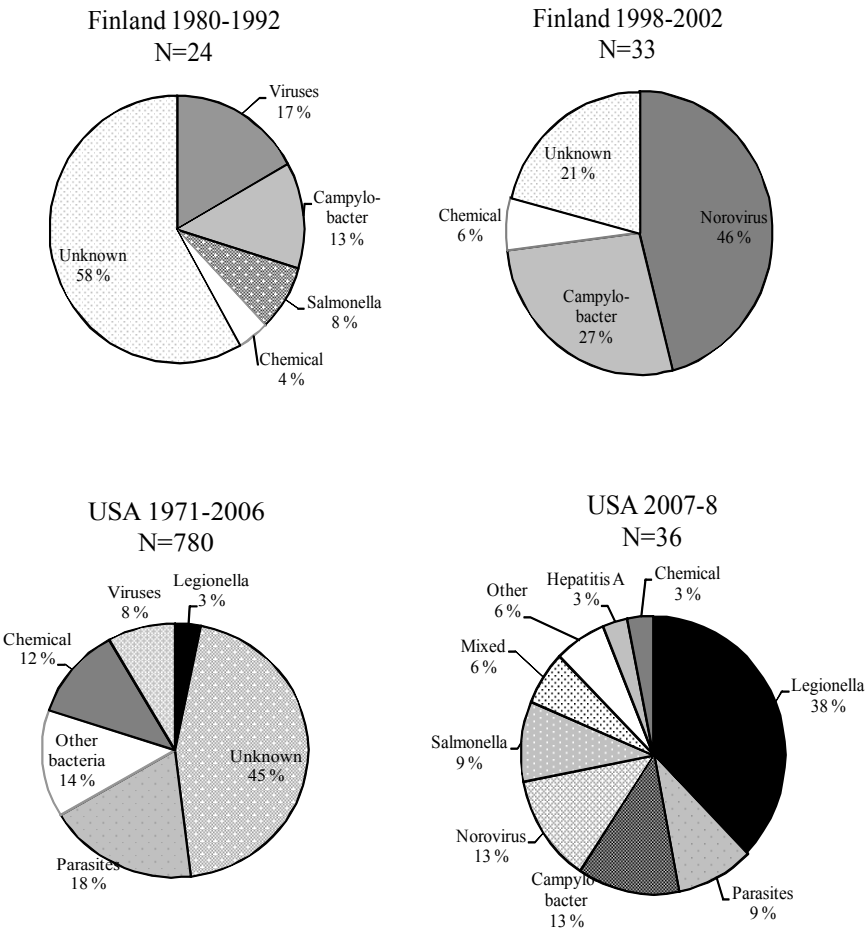

Figure 2. Microbial etiologic agents in waterborne outbreaks and their proportion in the total number of outbreaks, Finland and USA (Lahti and Hiisvirta 1995; Miettinen, Zacheus et al. 2001; Vartiainen, Miettinen et al. 2003; Craun, Brunkard et al. 2010; Brunkard, Ailes et al. 2011).

2.1.6 Methods to study outbreaks

Although most countries have a strategy for water quality surveillance, quality deficits or the presence of indicator bacteria or pathogens are not often the first indications of an ongoing outbreak. Most outbreaks have been detected by observing an unusually high number of illnesses or microbial findings conceivably of waterborne origin. Usually suspicion of an outbreak has been raised by health care providers noticing an increased number of cases (Tillett, de Louvois et al. 1998). Often, however, notification is delayed because acute gastroenteritis is a common,

usually self-limiting disease and the number of such patients tends in any case to vary sporadically.

Other officials may also contribute substantially in detecting outbreaks. Waterworks employees and environmental health officials may receive complaints of water quality and contemporary gastrointestinal illnesses, and schools, day-care centres and workplaces may observe unusual absences. Detection of an outbreak is thus a matter of team work (Kuusi 2004).

In most cases, the cause of an outbreak is not in the beginning clear. Microbial findings alone do not prove an outbreak to be waterborne as such microbes could equally well be foodborne. An epidemiologic investigation is usually needed to confirm the association. Such an investigation can be descriptive or analytic (Table 3).

Descriptive studies collect information on when, where, who and how many fell ill, what was the clinical picture and what were the findings. Data obtained by descriptive methods can then confirm the presence of an outbreak and form a hypothesis as to the cause (Tillett, de Louvois et al. 1998). For example, if all or most cases live within the area of one water supply, a waterborne cause may be suspected.

Sometimes water as a source is obvious from the beginning. If not, analytic epidemiologic studies are needed to confirm the association. Case-control or cohort methods can be used (Hrudey and Hrudey 2007). In some studies, the dose correlation between the amount of water ingested and risk of falling ill is also investigated (Kuusi, Nuorti et al. 2005). Environmental sampling may confirm the contamination of water and finding of pathogens involved in the outbreak also in water strongly supports the waterborne hypothesis. As detection methods have improved, increasingly specific data are obtained, especially regarding viral pathogens (Hanninen, Haajanen et al. 2003; Maunula, Miettinen et al. 2005).

Table 3. An example from England and Wales of analyzing the strength of evidence when assessing whether or not an outbreak is associated with drinking water (Tillett, de Louvois et al. 1998).

Evidence	
A.	A pathogen found in patient samples is also detected in water
B.	No pathogen is detected in water, but there are relevant water treatment deficiencies and/or water quality failure
C.	Evidence of an association between water and illnesses in analytic epidemiologic study (case-control or cohort study)
D.	Descriptive data suggest that the outbreak is related to drinking water and there are no other relevant explanations
Interpretation	
Strongly associated:	A+C **or** A+D **or** B+C
Probably associated:	B+D **or** C **or A**
Possibly associated:	B **or** D

2.2 Diseases associated with waterborne outbreaks

2.2.1 Acute disease and mortality associated with waterborne disease

The major clinical illness associated with a drinking water-associated outbreak is acute gastroenteritis (Brunkard, Ailes et al. 2011). The vast majority of microbial agents associated with waterborne diseases are intestinal pathogens. Acute gastroenteritis is characterized as an illness involving increased frequency of defecation (≥3 times/day), nausea, vomiting, abdominal cramping, malnutrition and systemic symptoms (e.g. fever) and lasting less than 2 weeks (Thielman and Guerrant 2004).

The incubation period for norovirus gastroenteritis is short, 10 – 51 hours (Glass, Parashar et al. 2009). The infection may present as only vomiting or only diarrhoea or a mixture of both. The presenting sign is often vomiting, followed by abdominal cramps, watery diarrhoea and general symptoms (fever, malaise, headache, myalgias). The usual duration of illness is 2-3 days but it may last up to 6 days (Glass, Parashar et al. 2009). One third of the infected may be asymptomatic. Death

due to norovirus infection is unusual and if it occurs, it is usually a result of dehydration in elderly or chronically ill persons.

Acute watery diarrhoea is a major symptom of bacterial gastroenteritis caused by *Campylobacter, Salmonella, Shigella* and *E. coli* (DuPont 2009). Vomiting is less frequent, but may be present. Fever is often observed. Diarrhoea which becomes bloody after 1-5 days is a hallmark of Shiga-toxin producing *E. coli* (STEC, e.g. O175:H7)-infection. However, gastroenteritis caused by other bacterial pathogens (*Campylobacter, Salmonella* and especially *Shigella)* may cause dysentery (DuPont 2009). Acute mortality is uncommon following infections with *Campylobacter* or non-typhoid *Salmonella*. STEC, in contrast, has been involved in waterborne outbreaks with mortality (Anonymous 1999; Anonymous 2000a).

The incubation period for giardiasis varies from 1 to 45 days, but is most often 1-2 weeks (Ortega and Adam 1997). Infection may be asymptomatic in children and persons with prior giardiasis. Symptomatic patients have loose, foul-smelling stools with increased amounts of fat and mucus. Weight loss, flatulence, abdominal cramps, bloating, nausea, anorexia and malaise are common symptoms. Fever may be present at the beginning of the infection. Transient lactose intolerance is common, occurring in 20-40% of cases. The clinical course is subtle, and patients may have had symptoms for several weeks when they seek medical attention. The disease may resolve spontaneously, but may also recur after treatment. Mortality is rarely if at all associated.

Cryptosporidiosis presents as watery diarrhoea after an incubation period of 1 week (Huang and White 2006). Abdominal cramps, vomiting, nausea and fever are also often present. The median duration of cryptosporidiosis is 5-10 days and the illness may be biphasic. The disease is self-limiting among immunocompetent persons; however, among immunocompromised individuals cryptosporidiosis can be life-threatening.

In addition to acute gastroenteritis, certain other clinical illnesses may be present. Hepatitis A virus (HAV) can be transmitted by faecal-contaminated drinking water, and such outbreaks occurred in the 1960s in the developed world. Nowadays waterborne HAV is uncommon in affluent countries. However, at least in the USA and Norway outbreaks have taken place (Kvitsand and Fiksdal 2010; Brunkard, Ailes et al. 2011).

The incubation period for HAV infection is approximately 28 days (range 15-50 d.) (Wasley, Feinstone et al. 2009). Patients may experience prodromal symptoms (nausea, malaise, vomiting, headache, fatigue, fever) 1-7 days before their urine becomes dark (bilirubinuria). A few days later jaundice, yellow discoloration of skin, sclera and mucous membranes set in. Children are often asymptomatic. The disease can last several weeks, but usually by the third week patients begin to feel improvement. The course of disease is usually benign, but fulminant hepatitis has been reported. Death from HAV infection is uncommon, especially among children.

Hepatitis E-virus (HEV) has caused at least two waterborne outbreaks during recent decades, in India in 2005 (1611 cases) and in South-western Vietnam in 1994 (over 50 cases) (Corwin, Khiem et al. 1996; Sailaja, Murhekar et al. 2009). On both occasions the outbreaks were due to faecal contamination of undeveloped water systems. No drinking water-associated HEV-outbreaks have been detected in wealthy countries (Teshale, Hu et al. 2010). HEV infection is particularly dangerous for pregnant women and is a significant cause of death to them in developing countries (Teshale, Hu et al. 2010).

2.2.2 Reactive arthritis and milder forms of joint symptoms

Reactive arthritis (ReA) is a well-known complication of bacterial gastroenteritis or venereal infection (Leirisalo-Repo 2005). In Finland, Ilmari Paronen described 344 cases of Reiter's disease already in the late 1940's (Paronen 1949). In addition to the classical triad of urethritis, eye inflammation and urethritis, he observed a variety of other manifestations, such as pleuritis, carditis and stomatitis.

There are a wide variety of symptoms which can be clinical manifestations of ReA (Carter and Hudson 2009). ReA presents classically as oligo- or monoarthritis, but polyarthritis is also possible. Extra-articular symptoms may coexist and include iritis or conjunctivitis, urethritis, tendinitis, or mucosal, skin and sometimes cardiac manifestations (Carter 2006). Systemic symptoms such as fever, malaise and weight loss may also be present. The incidence of ReA is considered to be lower among children than adults (Rudwaleit, Richter et al. 2001)

Classical triggering infections for ReA are gram-negative bacteria causing gastrointestinal or urogenital infections (*Shigella, Salmonella, Yersinia, Campylobacter and Chlamydia trachomatis)* (Leirisalo-Repo, Hannu et al. 2003). In Northern Europe, *Campylobacter* has become the most common pathogen responsible for bacterial gastroenteritis (Rautelin and Hanninen 2000). Also *Clostridium difficile* infection is considered a possible trigger of ReA (Carter 2006). The role of *Giardia* is uncertain. However, case reports and descriptions of small patient series indicate that *Giardia* may be associated with ReA or reactive arthralgia (Meza-Ortiz 2001; Carlson and Finger 2004). There is no evidence of norovirus infection leading to ReA, although such a connection was suggested in one case report (Gemulla and Pessler 2011).

HLA-B27 antigen has been considered a risk factor for ReA, but is not an essential factor as a substantial proportion of ReA cases lack the antigen and the association has not been observed in all studies (Carter and Hudson 2009). HLA-B27 antigen may rather be a risk factor for a more severe and prolonged course of ReA than for the disease itself (Leirisalo-Repo 2005; Carter and Hudson 2009).

Despite the long history of ReA literature, the definition of the disease remains unsettled (Townes 2010). Especially in the American literature, the eponym Reiter's syndrome has been widely used in the past. This is often, but not always, defined as

a triad of arthritis, eye inflammation (iritis or conjunctivitis) and urethritis. A third term is "post-infectious arthritis", originally based on whether the micro-organism could be verified from the affected joint (Hannu, Inman et al. 2006). Furthermore, expert panels have discussed whether even arthritis is required for the definition and whether extra-articular manifestations are sufficient for diagnosis (Townes 2010). As a result, there are a variety of criteria used in studies, blurring the picture of the frequency of ReA after an infection.

Population-based studies. The annual incidence of *Campylobacter* associated ReA is 4.3 per 100 000 persons in Finnish population according to one population-based controlled register study (Hannu, Mattila et al. 2002). The frequency of ReA was 7% and reactive tendinitis 1% after infection. In a population-based US study the incidence of ReA associated with *Campylobacter* was 2.1/100 000 person years and with *Salmonella* 1.4/100 000 person years. The figure for ReA associated with *Shigella* infection was 1.3 per 100 000 inhabitants according to another population-based, controlled Finnish register study (Hannu, Mattila et al. 2005). Of the cases infected with *Shigella*, 7% had ReA and 2% other musculoskeletal symptoms.

Outbreak reports. There are a substantial number of studies dealing with ReA or reactive joint symptoms after single-source, mostly foodborne outbreaks. Methods in these studies vary considerably, for example the definition used (if any), whether only self-reported symptoms are asked or is the diagnosis verified by a rheumatologist, what is the observation time, etc. The observed frequency therefore fluctuates significantly among these studies (Leirisalo-Repo 2005).

Table 4. (next page). Summary of studies of joint symptoms and ReA after food- or waterborne outbreaks. The percentages with joint symptoms or ReA are counted from the whole study sample.

Q: Questionnaire study
T: Telephone survey
CE: Clinical examination
NA: Not applicable

** Only culture-confirmed cases were included
*Only those who sought medical care were included

Triggering organism		Study type	Study sample	Joint symptoms % (N)	Self-reported ReA (N)	Verified ReA % (N)	Reference
Foodborne outbreaks							
Salmonella enterica spp.	Finland, 1992	Q	272	NA	6% (17/272)	NA	(Mattila, Leirisalo-Repo et al. 1994)
Salmonella Bovismorbificans	Finland, 1994	Q	191	26% (51/191)	NA	12% (22)	(Mattila, Leirisalo-Repo et al. 1998)
Yersinia pseudotuberculosis	Finland, 1998	Q+T	33	30% (10/33)	12% (4/33)	NA	(Hannu, Mattila et al. 2003)
Salmonella Typhimurium	Finland, 1999	Q+CE	63	40% (25/63)	NA	8% (5/33)	(Hannu, Mattila et al. 2002)
Salmonella Typhimurium	Australia, 1999	Q+CE	261*	25% (64/261)	NA	15% (38/261)	(Lee, Hall et al. 2005)
Salmonella Hadar	Spain, 2005	Q+T +CE	248	52% (130/248)	NA	5% (13/248)	(Arnedo-Pena, Beltran-Fabregat et al. 2010)
Drinking water-associated outbreaks							
Campylobacter jejuni	Norway, 1988	Q	520	21%	9%	NA	(Melby, Svendby et al. 2000)
Campylobacter jejuni	Finland, 2000	CE	350**	4% (15/350)	NA	3% (9/350)	(Hannu, Kauppi et al. 2004)
E.coli O157:H7, *C. jejuni*	Canada, 2000	Q	2299	NA	17.9%	NA	(Garg, Pope et al. 2008)

Table 4 presents studies of joint symptoms and ReA after food- or waterborne outbreaks. According to these data, symptoms suggesting or fulfilling the criteria of ReA comprise only a portion of the whole burden of joint symptoms after an outbreak. Milder forms of joint symptoms are much more common. However, as no unexposed control groups are included in these studies, it is difficult to conclude what proportion of these symptoms are excess symptoms linked to the outbreak.

Outcome. The long-term prognosis of ReA is considered to be generally favourable. However, about 25% of subjects may develop chronic spondylarthritis (Hannu, Inman et al. 2006). Symptoms of ReA lasting more than six months are often taken as a sign of chronicity (Leirisalo-Repo 2005; Carter and Hudson 2009). Chronicity may mean a sustained, relapsing or remitting course of disease.

Seventy-five males were studied in Finland 13 years after a foodborne outbreak of *Yersinia enterocolitica* in a garrison. Half of the respondents had some health problems, mainly musculoskeletal complaints. Sixteen were re-examined. In three cases a chronic connective tissue disease was diagnosed and two had ankylosing spondylitis (Lindholm and Visakorpi 1991). In a study made five years after a foodborne outbreak of *Campylobacter jejuni,* 5 subjects out of 66 (7.6%) developed chronic or relapsing rheumatic disorder (Bremell, Bjelle et al. 1991). Four of them did not have infectious symptoms during the outbreak but were confirmed as infected by either stool culture or serologic assay. In a non-outbreak study of ReA with mixed etiologies 1 out of 23 patients had ankylosing spondylitis, three radiological changes in peripheral joints and three radiological sacroilitis ten years after acute ReA (Laasila, Laasonen et al. 2003). The long-term prognosis of ReA and especially milder forms of joint complaints remains, however, a matter of further studies (Pope, Krizova et al. 2007).

2.2.3 Persisting gastrointestinal symptoms

In most cases, recovery from infectious enteritis is rapid and complete. On occasion, however, gastrointestinal symptoms may persist for months or years (Spiller and Garsed 2009). If symptoms persist for at least 12 weeks, have characteristics listed in Table 5, and no other plausible explanation, the condition is referred to irritable bowel syndrome (IBS) (Horwitz and Fisher 2001). According to one meta-analysis, the prevalence of IBS was 11.2% in an adult population (Lovell and Ford 2012). In the Finnish population, the frequency of IBS was 9.7% if three or more of the Manning criteria were required for diagnosis (Table 5), 5.5% if Rome I criteria and 5.1% if Rome II criteria were used (Hillila and Farkkila 2004).

Postinfectious irritable bowel syndrome (PI-IBS). Some IBS patients consider that the condition began after an episode of acute infectious gastroenteritis. Such a condition has been named “postinfectious irritable bowel syndrome” (PI-IBS). The proportion of PI-IBS in the whole burden of IBS is thought to be about 10% (Spiller and Garsed 2009). Vice-versa, PI-IBS develops in 4-32% of patients with bacterial

gastroenteritis. In a meta-analysis of eight studies, the frequency of IBS was estimated as 9.8% among the patients with infectious gastroenteritis versus 1.2% among the controls (OR 7.3, 95% CI: 4.7-11.1) (Halvorson, Schlett et al. 2006). In a systematic review of the literature up to 2007, the risk PI-IBS was found to diminish by time after infection (Thabane, Kottachchi et al. 2007). Pooled odds ratios for PI-IBS after an enteric infection were 7.58 at 3 months, 5.18 at 6 months, 6.37 at 12 months and 3.85 at 24-36 months in comparison to the control subjects. According to a register-based study of US military personnel having had infectious gastroenteritis within 1999-2007, 22.7% of those who had prolonged gastrointestinal symptoms continued to be symptomatic at five years (Porter, Gormley et al. 2011). In a follow-up study of verified *Salmonella* or *Campylobacter* infections, nearly 10% still had gastrointestinal symptoms 10 years after infection (Schwille-Kiuntke, Enck et al. 2011). This study was not, however, controlled and the observed proportion of symptomatic patients was close to the IBS-prevalence among general population.

In one prospective study of traveller's diarrhoea it was found that persons who had had diarrhoea during a trip were more prone to develop IBS within six months than those who remained healthy (13.6% vs. 2.4%, $p<0.0001$) (Stermer, Lubezky et al. 2006), although previous studies have suggested that IBS is not so often associated with traveller's diarrhoea as with other infectious enteritides (DuPont 2008).

Table 5. Diagnostic criteria for IBS (Fass, Longstreth et al. 2001; Horwitz and Fisher 2001; Yale, Musana et al. 2008)

Criteria	Characteristics
Manning	• Visible abdominal distension • Pain eased with bowel action • Looser stools at the onset of pain • Rectal mucus discharge • Sense of incomplete rectal emptying
Rome I	At least 3 months of recurrent or continuous symptoms: 1. Abdominal discomfort or pain and (any of these): • Pain is relieved with defecation • A change in the frequency or consistence of stools AND 2. Two or more of the following (at least ¼ of occasions or days): • Altered stool frequency • Altered stool form • Altered passage • Mucus discharge • Bloating or sense of distension
Rome II	Abdominal pain or distension of at least 12 weeks duration during the previous 12 months and at least two of the following features: • Symptoms are relieved with defecation • Onset of symptoms associated with a change in stool form • Onset of symptoms associated with a change in stool frequency
Rome III	Recurrent abdominal discomfort or pain for at least 3 days per month in the previous 3 months and associated with two or three of the following features: • Pain relieved with defecation • Onset associated with change in the frequency of bowel movements or form of the stools • Onset associated with change in the form of stools

Table 6 summarizes some key reports on the incidence of PI-IBS after water- or foodborne gastrointestinal outbreaks. Almost all these reports, including those of waterborne outbreaks, indicate an increased risk of IBS after outbreak-related infectious gastroenteritis.

Focusing on waterborne outbreaks, the occurrence of PI-IBS has been closely investigated after the outbreaks in Bergen and Walkerton.

In a study of subjects at least 16 years of age, investigators of WHS observed IBS in 36.2% of subjects with clinically verified gastroenteritis, in 27.5% with self-reported gastroenteritis and in 10.1% among controls (living in the town but not ill) 2-3 years after the outbreak (Marshall, Thabane et al. 2006). The Walkerton cohort was followed for 8 years. During that period, the prevalence of PI-IBS was 21.4% at 4 years, 14.3% at 6 years and 15.4% at 8 years among adults who had experienced either clinically suspected or self-reported gastroenteritis during the outbreak (Marshall, Thabane et al. 2010). Among subjects under 16 years of age the cumulative incidence of PI-IBS during the entire follow-up was 10.5% in the infected cohort vs. 2.5% among the uninfected (Thabane, Simunovic et al. 2010). Occurrence of dyspepsia was also investigated by WHS and an increased probability was observed 8 years after the outbreak in the acute gastroenteritis cohort compared to controls (OR 2.3, 95% CI: 1.6-3.3) (Ford, Thabane et al. 2010).

In Bergen, the proportion of patients with continuing gastrointestinal symptoms decreased from 69.5% at six months to 19.2% at 12 months among microbiologically verified cases of giardiasis (Wensaas, Langeland et al. 2010). On the other hand, according to a controlled cohort study using a questionnaire 3 years after the Bergen outbreak, the prevalence of IBS was 46.1% in the exposed group vs. 14% in the control group (RR 3.4, CI 95%: 2.9-3.8) (Wensaas, Langeland et al. 2012). Altogether 13.8% of the exposed cohort reported IBS symptoms which frequently limited their daily activities. In a study comparing abdominal symptoms between exposed (N=378) and unexposed (N=135) preschool children 1 year after the outbreak in Bergen, no difference was observed in the probability of abdominal pain or nausea (Mellingen, Midtun et al. 2010). Diarrhoea and flatulence, on the other hand, were slightly more common among the exposed.

Microbial factors in PI-IBS. PI-IBS has been considered a sequela of a bacterial gastrointestinal infection (Spiller and Garsed 2009). There are probably differences between bacterial species and strains influencing the risk of PI-IBS (Connor 2005), although the issue has not been thoroughly investigated. It is possible that PI-IBS may be more common after *Campylobacter* than *Salmonella* infection (Neal, Hebden et al. 1997).

The role of viruses in triggering PI-IBS remains controversial. In a study following a foodborne viral gastroenteritis outbreak, an increased prevalence of IBS was observed at 3 months from the outbreak among cases compared to controls (23.6 vs. 3.4) (Marshall, Thabane et al. 2007). After six months there was no difference

between the groups. However, after a waterborne norovirus outbreak in Italy, the probability of IBS was significantly higher among those infected compared to controls at 12 months (OR 11.4, CI 95%: 3.4-37.8) (Zanini, Ricci et al. 2012). On the other hand, in one study of subsequent gastrointestinal complaints after several norovirus outbreaks, the risk of gastroesophageal reflux disease was increased, but not that of IBS (Porter, Faix et al. 2012). As norovirus gastroenteritis is a very common disease and its consequences would therefore probably be easily observed, it is reasonable to assume that PI-IBS after a norovirus infection is not a major problem and if it occurs, it probably resolves in a relatively short time (Karst 2010).

Table 6. The frequency and probability of postinfectious irritable bowel syndrome associated with food- or waterborne outbreaks.

Triggering organism	Origin	Country, year	Follow-up time, months	N:o of cases	Percentage with PI-IBS	Probability OR or RR (95% CI)	Reference
E. coli O157:H7 and *C. jejuni*	WB	Canada, 2000*	24	464	36.2	OR 4.8 (3.4-6.8)	(Marshall, Thabane et al. 2006)
E. coli O157:H7 and *C. jejuni*	WB	Canada, 2000**	96	305	10.5	OR 4.6 (1.6-13.3)	(Thabane, Simunovic et al. 2010)
Salmonella Enteritidis	FB	Spain, 2002	12	677	10.0	RR 7.8 (3.1-19.7)	(Mearin, Perez-Oliveras et al. 2005)
Norovirus	FB	Canada, 2002	3***	89	23.6	OR 6.9 (1.0-48.7)	(Marshall, Thabane et al. 2007)
Giardia lamblia	WB	Norway, 2004¶	36	817	46.1	RR 3.4 (2.9-3.4)	(Wensaas, Langeland et al. 2012)
Norovirus	WB	Italy, 2009	6	186	>10	OR 11.4 (3.4-37.8)	(Zanini, Ricci et al. 2012)
Norovirus	Military bases	USA, 2004-09	<12	1718		RR 0.7 (0.3-1.5)	(Porter, Faix et al. 2012)

WB: waterborne; FB: foodborne; * The Walkerton outbreak, adults; ** The Walkerton outbreak, children; *** The cohort was followed up to 12 months but there was no difference between infected cohort and controls after 3 months; ¶ The Bergen outbreak.

Risk factors and possible pathogenetic mechanisms of PI-IBS. The long duration of acute gastroenteritis has been shown to be a risk factor for PI-IBS (Connor 2005; DuPont 2008). Female sex is also usually found to be a risk factor for PI-IBS (Spiller and Garsed 2009). Children have a smaller overall risk of PI-IBS, as do subjects over 60 years of age (Connor 2005; Spiller and Garsed 2009). A number of psychological factors have been connected with the risk of PI-IBS, for example depression, anxiety, hypochondriasis and fatigue (Dunlop, Jenkins et al. 2003; Spiller and Garsed 2009).

Researchers in the WHS have developed a risk score for PI-IBS (Thabane, Simunovic et al. 2009). According to this score, female gender, age <60 years, duration of acute diarrhoea >7 days, bloody stools, increased stool frequency (>6 per day), abdominal cramps, weight loss, fever and psychological disorders (anxiety and depression) predict developing PI-IBS.

The pathogenesis of IBS and, to an even lesser extent, of PI-IBS is poorly understood. Increased permeability was studied by researchers in WHS by lactulose-mannitol permeability testing and increased permeability was observed among those with PI-IBS compared to controls (Marshall, Thabane et al. 2004). This might cause abnormal exposure to luminal antigens and contribute to the presence of prolonged inflammation.

Duodenal biopsies from 124 patients in Bergen 15 months after a *Giardia* outbreak revealed duodenal inflammation in 57 cases (Hanevik, Hausken et al. 2007). Visceral hypersensitivity and the effect of ondaserton (serotonin antagonist) was studied in another study of patients with persisting gastrointestinal symptoms after the Bergen outbreak (Dizdar, Gilja et al. 2007). Subjects with persisting symptoms showed increased visceral hypersensitivity with lower drinking capacity and delayed gastric emptying, but ondaserton showed no effect.

As the risk of PI-IBS may be associated with the severity of the initial enteric infection, it is somewhat surprising that antibiotic treatment does not seem to lessen the risk (Spiller and Garsed 2009). In fact, antibiotic treatment would appear to be associated with an increased risk of developing PI-IBS after traveller's diarrhoea (Stermer, Lubezky et al. 2006). As the studies observing this have not been prospective and randomized, it is probable that this association was observed because severely ill patients are more likely to receive antibiotics and antibiotic treatment itself may not be the factor.

2.2.4 Other health consequences

Register-based studies have suggested that IGE may be associated with an increased risk of inflammatory bowel disease and aortic aneurysm (Ternhag, Torner et al. 2008; Gradel, Nielsen et al. 2009). IGE in childhood or adolescence is suggested to be associated with an increased probability of hospitalization due to any cause for 20

years ahead (Moorin, Heyworth et al. 2010). The risk of death by any cause after a domestic *Campylobacter* infection was found to be increased for 12 months in a register-based Swedish study (Ternhag, Torner et al. 2005). On the other hand, in a register-based study from New Zealand infectious intestinal diseases did not contribute to hospitalization due to Quillan-Barre syndrome or even ReA (Lake, Baker et al. 2004). In Finnish nationwide study of blood-culture positive *Campylobacter* infections in 1998-2007, 1 out of 76 cases developed Quillan-Barre syndrome (Feodoroff, Lauhio et al. 2011).

Several possible late effects after the waterborne outbreak of *E. coli* O157:H7 and *C. jejuni* infection have been studied by WHS group. Patients with severe gastrointestinal symptoms had a slightly increased risk of hypertension (RR 1.28, CI 95%: 1.04-1.56) at 3.7 years after the incident (Garg, Moist et al. 2005). A non-significant trend towards an increased rate of pregnancy-related hypertension in those having had gastroenteritis has been observed within five years (Moist, Sontrop et al. 2009). At eight years, the researchers found that the hazard ratio of hypertension (1.33, CI95%: 1.14-1.54) and self-reported cardiovascular disease (2.13, CI95%: 1.03-4.43) was increased among those who experienced gastrointestinal illness during the outbreak compared to asymptomatic residents (Clark, Sontrop et al. 2010). However, after linking the WHS data to register data, no increased risk of death or cardiovascular event was found within ten years among affected subjects in Walkerton (Hizo-Abes, Clark et al. 2013). The Walkerton Health Study extended to 2008; however, the cohort is planned to be followed further.

Investigators of the Bergen outbreak found a high prevalence of fatigue (46%) among verified cases of giardiasis in three years after the outbreak (Wensaas, Langeland et al. 2012). The relative risk of fatigue was 4.0 (CI 95%: 3.5-4.5) compared to controls. Those subjects whose fatigue resulted in loss of employment or delayed education were called for closer examination (N=96). Fifty-eight (60%) of them fulfilled the criteria of chronic fatigue syndrome (Naess, Nyland et al. 2012). This suggests that at least 5% of cases with giardiasis may have developed chronic fatigue syndrome, which is at least eight times the prevalence in the general population.

2.3 Costs of waterborne outbreaks

Drinking water contamination can result in an extensive outbreak imposing a substantial load on the health care system and tap water suppliers, and involving loss of working days, school absence and damage to local economic life. It is therefore to be presumed that the cost of a waterborne epidemic can be considerable.

Despite this, the costs of drinking water-associated outbreaks have not been extensively studied. The probable reason for this is the difficulty in comprehensively assessing the costs of an accident which affects society in many ways. Direct costs to the health care or water supply institutions do not give the whole picture. Indirect

costs such as loss of productivity, interruption of business, lost confidence in the authorities' capacity to provide a healthy environment and sometimes lost reputation may cause more costs than the immediate handling of the situation. These expenses are difficult to assess and may be realized only long after the outbreak.

There are only a few published economic analyses of drinking water-associated outbreaks (Table 7). Total medical costs and costs due to productivity losses after the waterborne *Cryptosporidium* outbreak (estimated 403 000 cases) in Milwaukee were studied by Corso and associates (Corso, Kramer et al. 2003). The total costs of that outbreak were estimated to be $96.2 million, of which productivity losses comprised 67%.

Laursen and associates studied the cost due to lost working days in Copenhagen during an outbreak of waterborne gastroenteritis (1455 cases); 1658 working days were lost at a cost of 1.6 million Danish crowns (214 500 EUR) (Laursen, Mygind et al. 1994). In Sweden, costs of a waterborne outbreak of *Campylobacter* in Kinna (> 3 000 cases) were analyzed, including direct costs to health care (medical care, hospitalization and laboratory costs), outbreak investigation costs, sick leaves, personal expenses (e.g. bottled water, transportation) and costs to the municipal waterworks (Andersson, De Jong et al. 1997). The total costs were estimated to be 4 749 625 Swedish crowns (542 000 EUR).

Direct health-economic costs and indirect costs (loss of workdays and loss of business) caused by a waterborne gastroenteritis outbreak (5368 cases) were evaluated in Pittsburgh, Pennsylvania (Baker, Peterson et al. 1979). The total costs of this outbreak were 338 076 $ and indirect costs made up 66% of this.

Costs per case are presented in Table 7. Costs included in these studies vary considerably and the studies were made at different times. Therefore, the data is not well comparable between studies.

Table 7. Cost (EUR) per case of illness in four waterborne outbreaks. All currencies were transformed to EUR using the exchange rate for October 2013

Location	Milwaukee, USA 1995	Kinna, Sweden 1995	Uggeløse, Denmark 1992	Sewickley PA, USA 1975
N:o of cases	403 000	>3000	1455	5368
Attack rate	26%	24%	88%	61%
Health care costs /case	58 €	56 €	NS	6 €
Productivity losses /case	118 €	57 €	147 €	31€
Other costs /case	NS	67 €	NS	NS
Reference	(Corso, Kramer et al. 2003)	(Andersson, De Jong et al. 1997)	(Laursen, Mygind et al. 1994)	(Baker, Peterson et al. 1979)

NS =not stated

3 Aims of the study

The aims of this study were to:

1. assess the burden of gastroenteritis caused by water contamination in Nokia (I).

2. describe microbiological findings of the epidemic (I).

3. assess the frequency of early joint symptoms after the epidemic and predisposing clinical symptoms (II).

4. evaluate the persistence of gastrointestinal and joint symptoms after the epidemic (III).

5. estimate the direct health-care costs of the epidemic (IV).

4 Material and methods

4.1 Setting

Nokia is a town in Pirkanmaa County, Southern Finland. In year 2007, the population was 30 016 and had been constantly growing. The centre of the town is a densely populated urban area, surrounded by wide rural area.

The water supply is arranged by municipal waterworks and some small cooperatives. The waterworks uses groundwater which is disinfected with sodium hypochlorite. Ninety per cent of the population are covered by the public water supply while the rest use private wells. Sewage is processed in the municipal waste water plant, covering 80 per cent of the population.

Primary health care is organized in the municipal health centre. The town also has a municipal hospital providing primary in-patient care and limited secondary care. Most of the latter and all tertiary care are arranged in hospitals in the Pirkanmaa Hospital District, mainly in the Tampere University Hospital (TAUH), situated in the city of Tampere, 20 km distant from Nokia. Clinical laboratory services are provided by Fimlab laboratories, which is owned and run by the hospital district. Environmental health services, including monitoring of water systems, are arranged in collaboration with five neighbouring municipalities.

Municipalities in Finland have working groups for outbreaks. Food- and waterborne outbreaks are handled and monitored by these groups in collaboration with hospital districts and national authorities. National authorities responsible for investigating food- and waterborne outbreaks are the National Institute for Health and Welfare (THL) and the Finnish food safety authority Evira.

4.2 The epidemic

4.2.1 Contamination of household water network

Routine maintenance work was carried out at the waste water plant in Nokia on Wednesday, 28 November 2007. By chance, technical problems arose in the municipal household water distribution system during that same day. During the following two days residents complained of the bad smell, taste and extraordinary look of tap water. These were first taken to be caused by harmless deposits of pipe wall loosened and discharged while repairing the clean-water pipelines.

On Friday 30 November 2007 environmental and waterworks officials received complaints of gastroenteritis and a sharp rise in the number of patients with gastroenteritis was observed in the health centre. These observations led to the

suspicion of a waterborne outbreak, a boil-water notice was issued and microbial sampling of the tap water network was initiated.

The contamination of the tap water became evident on the same day. It emerged that an inappropriate cross-connection between the town tap water and waste water effluent lines at the waste water plant had been opened during the maintenance work on Wednesday, and by mistake, left open for two days. According to flow data, approximately 450 m^3 of waste water effluent had flowed into the tap water network. This effluent had been fully treated and was ready to be discharged into the river but still contained large amounts of faecal microbes. The tap water of about a third of the town's population became heavily contaminated with faecal microbes (Figure 3). Tap water and distribution network samples revealed large quantities of faecal indicator microbes as well as pathogens.

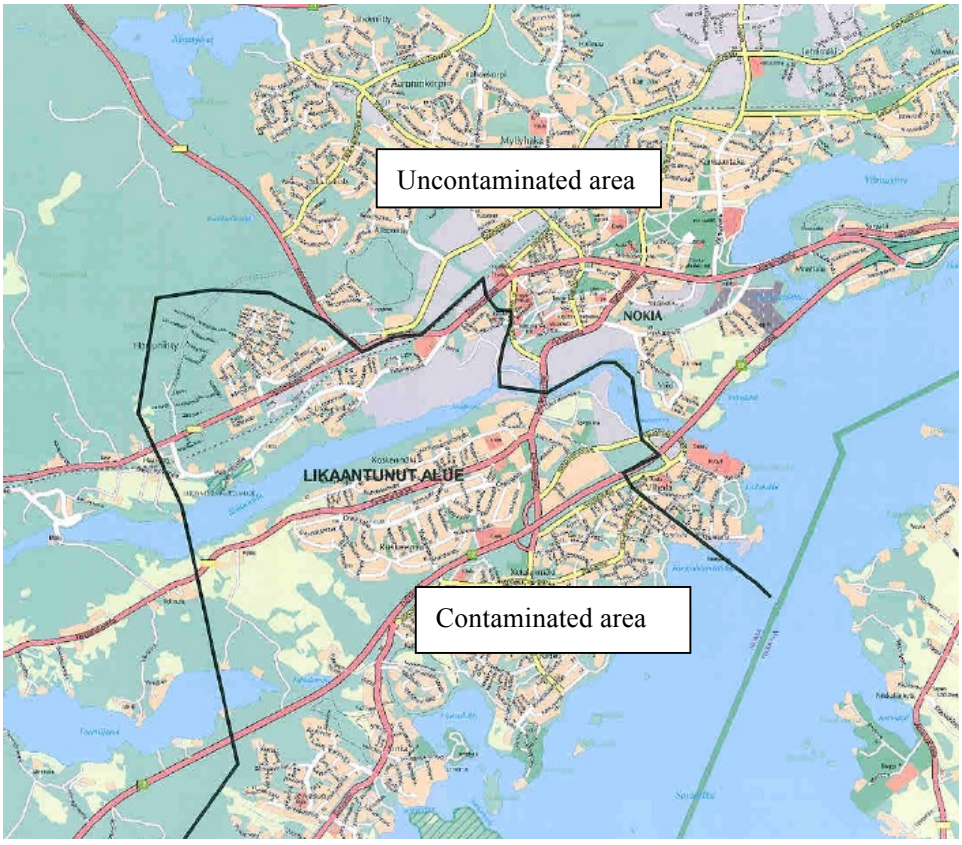

Figure 3. Map of the town of Nokia, divided into contaminated and uncontaminated areas. Reprinted by permission of the Town of Nokia, permission number 2014/1 (Nokian kaupunki Kartta ja Tontti, kaupungingeodeetin lupa 2014/1).

4.2.2 Handling of the outbreak

The authorities of the municipal health centre held the responsibility of managing the primary care of epidemic patients. The hospital district prepared to receive a number of patients needing hospital care in TAUH. The health centre and hospital district worked in close collaboration providing instructions for diagnosis and treatment of epidemic patients and ensuring sufficient resources for handling the situation. THL was officially notified on the third day of the epidemic.

Epidemic patients were treated primarily in the health centre. Adult patients needing rehydration were taken care of in the emergency department or in the municipal hospital. All children needing rehydration were referred to the paediatric clinic of TAUH. The health centre was considerably loaded with patients for the forthcoming weeks and the situation was even more difficult as personnel also became ill. In TAUH, on the other hand, the number of adult patients remained moderate and was handled without difficulties. The number of paediatric patients at TAUH was higher, but could be managed. The hospital district made preparations to open an extra ward in one of its hospitals but this was not eventually needed. The neighbouring municipalities decided to take Nokia residents needing primary inpatient care for non-outbreak related reasons into their health centre wards. An advisory telephone service was established in TAUH, run by the infection control nurses.

As data on the pathogens involved became available and most patients suffered from mild or moderate self-limiting gastroenteritis, practitioners were advised not to prescribe antibiotics, except in severe cases. Stool samples for microbial analysis were also advocated to be taken only from selected patients to avoid overloading of laboratory capacity.

The boil-water notice was withdrawn from the uncontaminated area after 12 days when the area of contamination became sufficiently reliably defined. In the contaminated area, pipeline samples repeatedly revealed pathogens despite network disinfection. Finally, after extensive procedures including shock chlorination, usage restrictions were discontinued in the contaminated area on 18 February, 82 days after the initial event. During the use restrictions, provision of drinking water was organized by municipal officers, volunteers and the military.

4.3 Microbiological data

Data on clinical microbiological samples and findings were obtained from the Fimlab database. To avoid overloading diagnostic capabilities, bacterial stool samples were not taken comprehensively but mainly from patients with severe disease. Samples for viral diagnostics were taken from five consecutive patients on the fourth outbreak day. Specimens for detection of parasites were taken as a sample from ten consecutive

patients in the second week. Subsequently, when the presence of *Giardia* became evident, all patients with loose stools were investigated for this parasite.

Bacterial pathogens (*Campylobacter, Salmonella, Yersinia and Shigella)* were examined in stool samples by culture. Shiga-toxin producing *E. coli* (STEC) was examined by culture and toxin detection. Electron microscopy and PCR were utilized for the detection of norovirus. Protozoan pathogens were investigated by microscopy of formalin-fixed samples. After the presence of *Giardia* but no other parasites became clear, only *Giardia*-antigen detection was used to investigate this parasite.

Findings up to 31 December 2007 were regarded as epidemic-related. An exception to this were the findings of *Giardia,* as the incubation time of giardiasis is longer and diagnosis is often delayed. For *Giardia,* all findings made before 31 May 2008 (six months from the outset) were considered to be epidemic-related.

A total of 293 water samples were examined for the presence of faecal indicator bacteria between 29 November 2007 and 28 August 2008; 62 water samples were examined for norovirus, 65 for adenovirus and 14 for *Giardia*. *Campylobacter*, astrovirus, hepatitis A virus and rotavirus were studied in six water samples and *Salmonella*, enterovirus and *Clostridium difficile* in three during the first week of the epidemic.

4.4 Data on the use of health services

Line-listing of patients was initiated in the health centre. However, this procedure started only on the sixth day of the epidemic, data on patients before that being added retrospectively from patient records. Patient ID, gender, age, symptoms and date of onset of illness were recorded.

The number of primary-care visits was obtained from the health centre's database. This uses the international classification of primary care (ICPC-1, WHO, Geneva). A visit was defined to be due to gastroenteritis if any of the codes D01, D09, D10, D11, D25, D70, D73 or D96 was used (Table 8).

The adult emergency department in TAUH counted the number of patients admitted because of the epidemic. This listing did not include any identification or clinical information. The paediatric emergency department, in contrast, also listed identification of patients.

Table 8. Explanation of the ICPC codes used to define a health-care visit due to gastroenteritis

ICPC-code	Symptom or disease
D01	Abdominal pain/cramps, general
D09	Nausea
D10	Vomiting
D11	Diarrhoea
D25	Abdominal distension
D70	Gastrointestinal infection
D96	Worms/other parasites

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4.5 Questionnaire studies

Two population-based questionnaire studies were conducted to assess the short- and long-term health effects of the epidemic.

4.5.1 Questionnaire 1 (Q1)

The town of Nokia was divided into two areas; contaminated and uncontaminated. This division was based on microbiological data derived from water samples and technical modelling of flow directions in the network. Two study groups were created from the population of these areas. A third, the control group was created from the population of another municipality in the county. This municipality was chosen because, like Nokia, it is a close neighbour of the city of Tampere, but situated on the opposite site of the urban area (distance 38 km). Daily connections between these municipalities are not frequent and therefore the members of the control group were less likely to be exposed to contaminated water. Basic statistical data on these two municipalities are presented in Table 9.

Table 9. Demographic characteristics of the town of Nokia and the control municipality

	Nokia	Control municipality
Distance from the centre of the city area (km)	16	18
Population*	30 951	29 828
Male gender*	49.3%	49.5%
Age in years*		
0-15	21%	22%
16-65	65%	64%
>65	14%	14%
Unemployment rate*	9%	7%
Population density (/km^2)*	108	45
Living in population centres**	91%	84%
Tap water obtained from a municipal system***	91%	82%

Demographic data obtained from the database of Statistics Finland (www.stat.fi).
* Year 2008 data; ** Year 2011 data; ***The data on water source is drawn from the Q1

One thousand participants were randomly picked from the population register for each group. Groups were matched by age and gender and only one participant per household was allowed. Participants of all ages were included.

The study was carried out using a questionnaire form mailed to participants 8 weeks after the contamination. A reminder was sent to non-responders after 3 weeks. Participants were asked whether they had fallen ill with gastroenteritis and the time of onset as well as their gastrointestinal symptoms. The occurrence of joint symptoms (pain, pain in joint movement, swelling, redness, warmth and back pain at rest) was inquired. Participants were also asked regarding tap water consumption for drinking defined as glasses per day.

A case of gastroenteritis was defined as a person suffering from acute diarrhoea (≥ 3 loose stools/day) or vomiting between 28 November 2007 and 20 January 2008. The latter date was set according the time when questionnaires were sent to recipients. In the analysis of joint symptoms all symptoms were first analyzed separately and then categorized as arthritis-like, if pain in joint movement, joint swelling, redness or warmth was present (Table 10).

4.5.2 Questionnaire 2 (Q2)

Another questionnaire study, a follow-up, was conducted at 15 months from the beginning of the epidemic, focusing on the duration of gastrointestinal and joint symptoms. The follow-up was based on the same population samples as were used in the first study. However, only those who responded to that study and gave their consent to a new contact were admitted. The study groups were therefore smaller and of unequal sizes (Table 13).

This study used a questionnaire form with informed consent. It was mailed to participants, but no reminder form was mailed to those not responding. Participants were asked whether they had fallen ill with gastroenteritis due to the water contamination during the epidemic. Then they were asked how long (stated as weeks or months) gastrointestinal and joint symptoms lasted after the acute phase of the disease, or whether they still persisted.

Loose stools, constipation, nausea, abdominal pain and abdominal distension were inquired. First these symptoms were analyzed separately, whereafter that a combination of loose stools and abdominal pain or distension was created. Although no established criteria for IBS were utilized in this study, this combination was close to the Manning and Rome I criteria for IBS (Tables 5 and 10).

Of joint symptoms, pain in joint movement and joint swelling, redness, or warmth were asked. Symptoms were categorized as arthritis-like in a manner similar to that in Q1 (Table 10).

The persistence of gastrointestinal and joint symptoms was then analyzed as remaining prevalence over time among those who reported having had gastroenteritis during the epidemic.

4.6 Health-economic data

The data on the use of health-care services were obtained in a manner similar to that described in section 4.4. The quantity of microbiological samples was collected from the laboratory's database. The time period for epidemic-related stool samples was defined as 28 November to 31 December 2007. However, all *Giardia* antigen detection tests as well as *Cryptosporidium* staining tests made from 28 November up to May 2008 were considered epidemic-related, as these tests are not usually done in normal circumstances. The excess numbers of primary care visits and laboratory tests were estimated by comparing the data on the epidemic period to the time before the

epidemic. The cut points for investigation of epidemic-related visits to health centre were set at 28 November 2007 and 6 April 2008 to ensure that most of the common effects became included in the analysis. Data on the use of private and occupational health care were not available.

Appointments at TAUH emergency departments and care in paediatric wards were traced from manual lists, as described in section 4.4. In addition, visits due to suspected ReA to the rheumatology clinic in TAUH were obtainable. All these visits were regarded as excess costs due to the epidemic.

The excess costs related to care in the wards of the municipal hospital of Nokia were not obtainable, as this hospital is usually fully occupied. Other than outbreak patients had been referred elsewhere, but costs due to this could not be traced. However, costs due to the usage of primary care wards in neighbouring hospitals were available from the municipal finance office.

The unit costs of health care services were based on average costs in the Finnish health care (T. Hujanen et al. Terveydenhuollon yksikkökustannukset Suomessa vuonna 2006. Helsinki: STAKES;2008). These figures were obtainable from the year 2006 and were multiplied by 1.033 for the year 2007.

Table 10. Summary of definitions used in this study

Concept	Definition
Acute gastroenteritis	Three or more loose stools per day and/or vomiting
Arthritis-like symptoms	Pain in joint movement or joint swelling, redness or warmth
IBS-like symptoms	Loose stools and abdominal pain or distension

4.7 Statistical methods

In the first questionnaire, the study areas were compared by χ^2 or Kruskal-Wallis rank sum test, as appropriate. Attack rates were calculated as proportion (%) of cases in the study group. The total number of cases was obtained by extrapolating the sex- and age-adjusted attack rates to the population in a study group. The attack rate was calculated from the control population to estimate the number of cases if the epidemic had not taken place. Estimation was made with age- and sex-adjustment. The bootstrap method was used to calculate confidence intervals for the total number of cases.

Crude differences between joint symptom occurrences were tested by Fisher's exact test. For all other analyses, univariate logistic regression was used with the occurrence of arthritis-like symptoms as response and fever, water use or gastrointestinal symptoms as covariate. The results were presented as percentages or odds ratio (OR) with confidence intervals.

In the follow-up questionnaire, the selection bias of the study group was analyzed in two steps. The probability of being included in the follow-up sample was studied using univariate logistic regression within all original study subjects. Thereafter the probability of responding to the survey was estimated in a similar manner. The bootstrap method was used to calculate confidence intervals for symptom prevalence at each time-point.

For the analysis of health-economic data, three time periods were created: before, during and after the epidemic; 28 November 2007 was set as starting cut-off point and 6 April 2008 as ending cut-off point. Mean burden was estimated to predict the burden during the epidemic period, if the epidemic had not occurred. A bootstrapping method was used to take account of uncertainty (Efron and Tibshirani 1994).

All analyses were made using R version 2.9 (or later versions) (R development core team. http://www.R-project.org)

4.8 Ethical considerations

According to the Finnish legislation concerning infectious disease surveillance and response, immediate outbreak investigations can be undertaken without approval from an ethics committee to ensure prompt outbreak handling. Therefore no ethical approval was required for the first questionnaire study. The follow-up study was approved by the ethical committee of Tampere University Hospital. The questionnaire form in the follow-up study included informed consent.

5 Results

5.1 Microbiological samples and findings (I)

Seven potential pathogens were found in patient stool samples during the outbreak (Table 11). All these microbes except *Shigella boydii* were also found in water or water distribution network samples, *Campylobacter* represented the most common finding. Only a few samples were investigated for the presence of norovirus. During the first epidemic week stool samples from five consecutive patients were studied for norovirus, all five proving positive.

Table 11. Microbial findings in patient stool samples. Only findings in samples taken between 28 November and 31 December are counted, except for *Giardia,* where all findings up to 31 May 2008 were included.

	N:o of clinical findings (N:o of tested)	Detected in water samples
Campylobacter species	148 (539)	+
Norovirus	7 (10)	+
Giardia	55 (872)	+
Salmonella sp.	14 (689)	+
Rotavirus	17 (31)	+
Clostridium difficile	6 (65)	+
Shigella boydii	3	n.d.

n.d.= not done

5.2 Use of health-care services because of gastroenteritis (I)

According to the data obtained from the health centre database, 1222 visits with an ICPC-1 diagnosis compatible with acute gastroenteritis were made between 28 November and 31 December 2007. The number of patients presenting with gastrointestinal complaints was substantially higher during the peak period compared to the median number of visits prior to the epidemic (Figure 4). Children under 10 years of age constituted the largest age group of health centre visitors.

A total of 204 patients were treated in the emergency departments of TAUH, 145 (71%) of them were children. TAUH maintained a telephone service for inquiries concerning the epidemic for 9 days, receiving 848 calls.

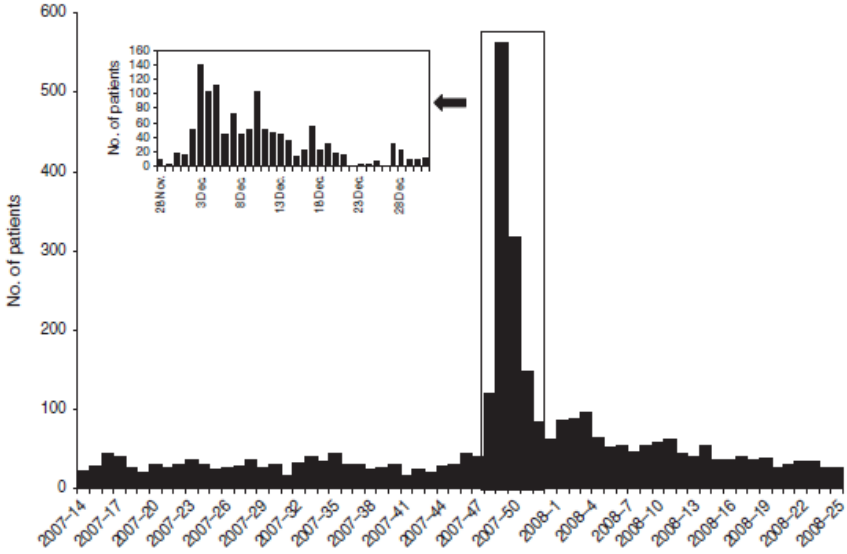


Figure 4. Weekly number of patient visits because of gastrointestinal symptoms in the Nokia health centre (original article I, copyright Cambridge University Press).

5.3 Response rates and selection (I-III)

5.3.1 Questionnaire 1 (I-II)

Taking all study groups together, the questionnaire form was returned by 2154 participants. Thirty-one forms were excluded because of insufficient content or unidentifiable respondent. The accepted response rate was therefore 70.8% (2123/3000). Background data on the study groups are presented in Table 12. The groups matched well, although household water was obtained more often from the

public supply in the contaminated group than in the two other groups. Response rates are presented in Table 13. These were interpreted as sufficiently high for the study to be considered representative.

Table 12. Background data on the study groups in the first questionnaire study.

	Contaminated N= 808	Uncontaminated N=717	Control N=598
Male gender	44.8%	44.5%	45.8
Median age	41	44	42
Household water from public system	98%	84%	82%
Consumption of tap water (glasses/day), mean (SD)	4.9 (3.1)	4.9 (3.3)	4.5 (3.0)

5.3.2 Questionnaire 2 (III)

Counting all groups together, 68.6% (1456/2123) of the respondents in the first study gave permission for a further contact and were included in Q2. The evolution of the study groups and the response rates are presented in Table 13. All study groups became stepwise smaller as a result of responding and giving permission to be contacted again. Analysis of selection during the evolution of the study groups is shown in Figure 5. There was a selection towards female gender and having had gastroenteritis or joint symptoms according to Q1. There was no further selection involved in responding to the survey.

Table 13. Evolution of the study groups and response rates in the two questionnaire studies. Q1: first questionnaire, Q2: second questionnaire

	Nokia, contaminated	Nokia, uncontaminated	Control population
Population 2007	9 538	20 478	27 259
Size of the group in Q1	1 021	979	1 000
Responded to Q1	808	717	598
Response rate in Q1	**79.1%**	**73.2%**	**59.8%**
Permission for re-contact (included in Q2)	615	498	343
-% of the original sample	*60.2%*	*50.9%*	*34.3%*
Responded to Q2	323	230	186
Response rate in Q2	**52.5%**	**46.2%**	**54.2%**
-% of the original sample	*31.6%*	*23.5%*	*18.6%*

Figure 5a-b. Selection linked to the step-wise formation of study groups in Q2. Figure 5a illustrates the probability of being included in the Q2 study (i.e. given permission to be re-contacted), Figure 5b the probability of responding. Black boxes represent calculated odds ratios and vertical lines 95% CI.

Figure 5a. Being included in Q2

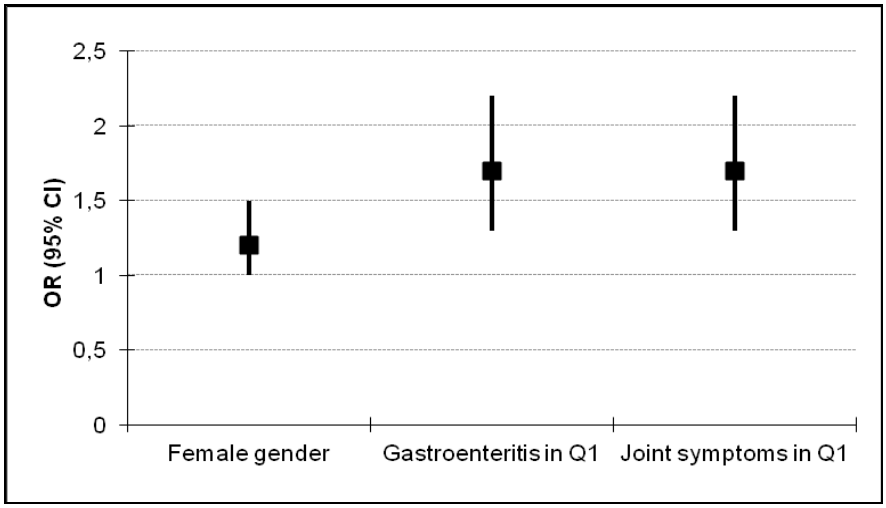
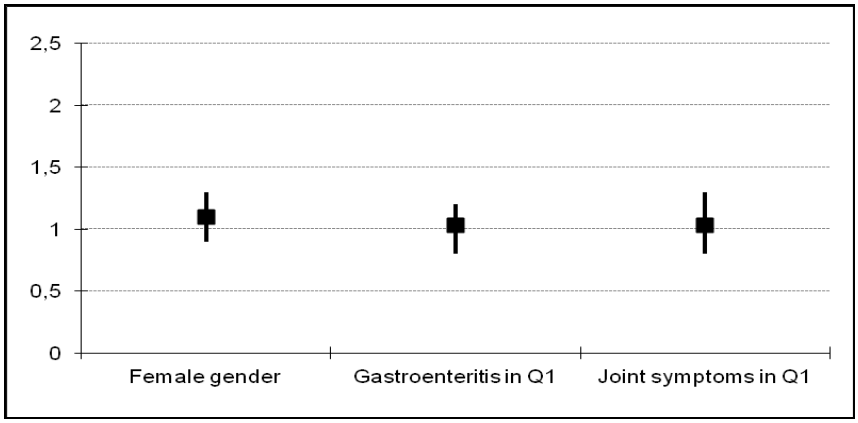


Figure 5b. Responding to Q2



5.4 Burden of gastroenteritis (I)

5.4.1 Total and excess cases of gastroenteritis

Among the participants in the contaminated, uncontaminated and control groups, 428/808, 112/717 and 39/598, respectively, fulfilled the case definition of gastroenteritis. Extrapolating these figures to the whole population of these areas, the estimated total number of cases was 5174 (95% CI: 4834-5513) in the contaminated area, 3279 (2731-3850) in the uncontaminated area and 1788 (1267-2362) among the control population. Attack rates of gastroenteritis in these areas were 53.0% (49.0-56.4), 15.6% (13.1-18.5) and 6.5% (4.8-8.8), respectively. Odds ratio for fulfilling the case definition was 7.5 (95% CI: 4.3-10.0) in the contaminated group and 1.95 (1.05-3.6) in the uncontaminated group, compared with the control group.

Comparing the number of cases in the town of Nokia to the control population, the estimated numbers of excess cases due to the epidemic were 4519 (4118-4911) in the contaminated and 1981 (1295-2671) in the uncontaminated area. Most subjects fell ill within 1 week from contamination of the household water (Figure 6)

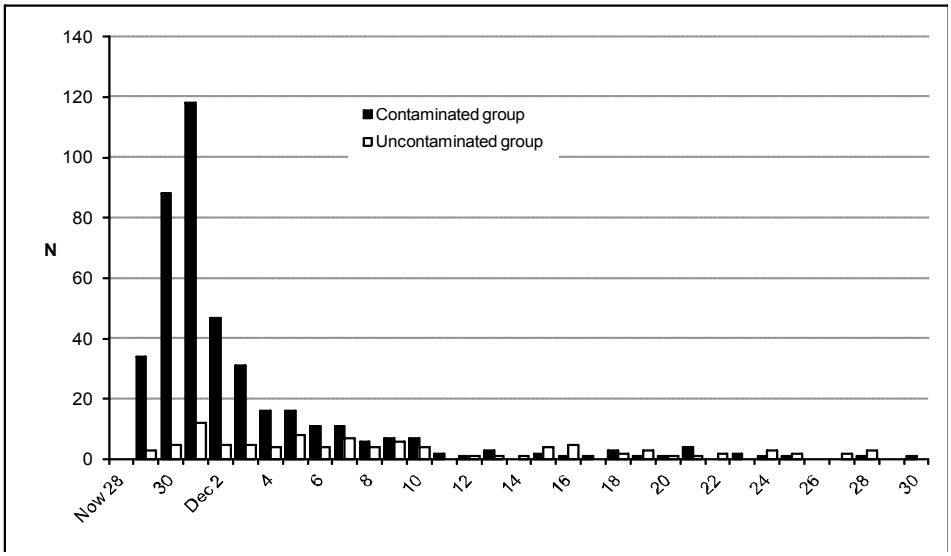


Figure 6. The epidemic curve according to the results of Q1. The bars represent the daily numbers of onsets of gastroenteritis in the contaminated and uncontaminated groups between 28 November and 31 December 2007.

5.4.2 Clinical picture of gastroenteritis

The most common gastrointestinal symptom in the contaminated group was diarrhoea, which was reported by 47% (377/808) of participants. Vomiting was reported by 38% (308/808), nausea 38% (306/808), abdominal pain 39% (317/808) and fever by 24% (191/808). The median duration of acute gastroenteritis was 3 days in the contaminated group, 2 days in the uncontaminated group and 2 days in the control group.

5.5 Joint symptoms within 8 weeks (II)

Altogether 13.9% (112/808) subjects in the contaminated group reported having had some form of joint symptoms within eight weeks after the onset of exposure, a figure 9.3 times higher than in the control group (P= <0.001); 6.7% (54/808) reported arthritis-like symptoms, against 0.5% (3/598) in the control group (p<0.001). In the uncontaminated group, the proportions were 2.4% (17/717) and 2.1% (15/717), respectively. Also in the uncontaminated group the frequencies of these symptoms were significantly higher than in the control group (Table 14)

Table 14. Prevalence of joint symptoms in the three study groups within eight weeks from the contamination. P-values stand for the difference against the control group.

	Contaminated group N=802	p	Uncontaminated group N=717	p	Control group N=598
Any joint symptom	13.9% (112)	<0.001	4.3% (31)	0.003	1.5% (9)
Joint pain	9.2% (74)	<0.001	2.4% (17)	0.015	0.7% (4)
Arthritis-like symptoms	6.7% (54)	<0.001	2.1% (15)	0.016	0.5% (3)
Back pain at rest	4.8% (39)	<0.001	1.4% (10)	0.160	0.5% (3)

Every type of gastrointestinal symptom and fever reported by the subjects in the contaminated group predicted arthritis-like symptoms. The odds ratios for arthritis-like symptoms were 6.1 (95% CI: 2.8-13.1) for acute gastroenteritis, 4.1 (2.3-7.4) for vomiting, 7.9 (3.7-17.0) for diarrhoea, 5.2 (1.6-16.8) for blood in faeces and 3.8 (2.2-6.6) for fever, in comparison to absence of that gastroenteritis symptom. In the uncontaminated group, the corresponding values were 13.5 (4.6-39.7), 5.4 (1.9-15.0), 11.4 (4.1-31.4), 13.0 (1.1-155) and 5.7 (1.8-18.5) (Table 2 in publication II).

The probability of joint symptoms, except for back pain at rest, was also increased among those participants in the contaminated group who declared no gastrointestinal symptoms. This phenomenon was not seen in the uncontaminated group (Table 15).

Table 15. Probability of joint symptoms among study subjects without gastrointestinal symptoms in the contaminated and uncontaminated groups. Comparisons are made against the control group.

Symptom	Contaminated group	Uncontaminated group
	OR (95% CI)	
Any articular symptom	4.0 (1.8-9.0)	1.5 (0.6-3.6)
Joint pain	7.3 (2.1-24.8)	1.7 (0.5-6.8)
Arthritis-like symptoms	3.0 (0.9-9.9)	1.1 (0.3-4.1)
Back pain at rest	1.7 (0.5-6.4)	1.6 (0.5-5.6)

5.6 Water use and the probability of joint symptoms (II)

The odds of having joint symptoms according to the amount of tap water used for drinking was elevated in those ingesting more than 6 glasses per day compared to those ingesting fewer than three glasses; 3-6 glasses of daily consumption was not associated with increased probability of joint symptoms (Table 16).

Table 16. Odds ratio (95% CI) for having joint symptoms according to the amount of tap water used for drinking. Categories 3-6 and >6 glasses per day were compared to those consuming fewer than 3 glasses per day. All comparisons were done within the contaminated group.

	Amount of tap water used for drinking (glasses/day)		
Symptom	<3 (N=223)	3-6 (N=339)	>6 (N=168)
Any joint symptom	1	1.3 (0.8-2.2)	2.1 (1.2-3.7)
Arthritis-like symptoms	1	1.1 (0.6-2.3)	2.0 (1.0-4.2)
Back pain at rest	1	2.6 (1.0-6.9)	4.9 (1.8-13.1)

5.7 Persistence of symptoms in the contaminated group (III)

According to the follow-up questionnaire made 15 months after the contamination, 54% (174/323) of subjects in the contaminated group recalled having experienced acute gastroenteritis during the epidemic. The concordance between Q1 and Q2 in reporting gastroenteritis was 91.8%.

5.7.1 Persistence of gastrointestinal symptoms

Altogether 42.7% (74/174) of those in the contaminated group who reported having had gastroenteritis during the epidemic noted persisting loose stools and abdominal pain or distension after the acute gastroenteritis. The remaining prevalence of these symptoms decreased rapidly during the first three months, but thereafter the decrease levelled off (Figure 7). At the end of the follow-up (15 months) 10.9% (19/174) were still suffering from these symptoms. The proportion with these symptoms was 8.9% in children under 16 years and 11.5% among adults.

5.7.2 Persistence of joint symptoms

Altogether 31.8% (55/174) of those in the contaminated group suffering gastroenteritis during the epidemic reported arthritis-like symptoms after falling ill with acute gastroenteritis. A third (33%) of these symptoms were relieved within five months (Figure 7). Thereafter the prevalence of arthritis-like symptoms declined very slowly until the end of the follow-up. At fifteen months, 19% (33/174) of those who had experienced gastroenteritis still had arthritis-like symptoms.

Fig 7a

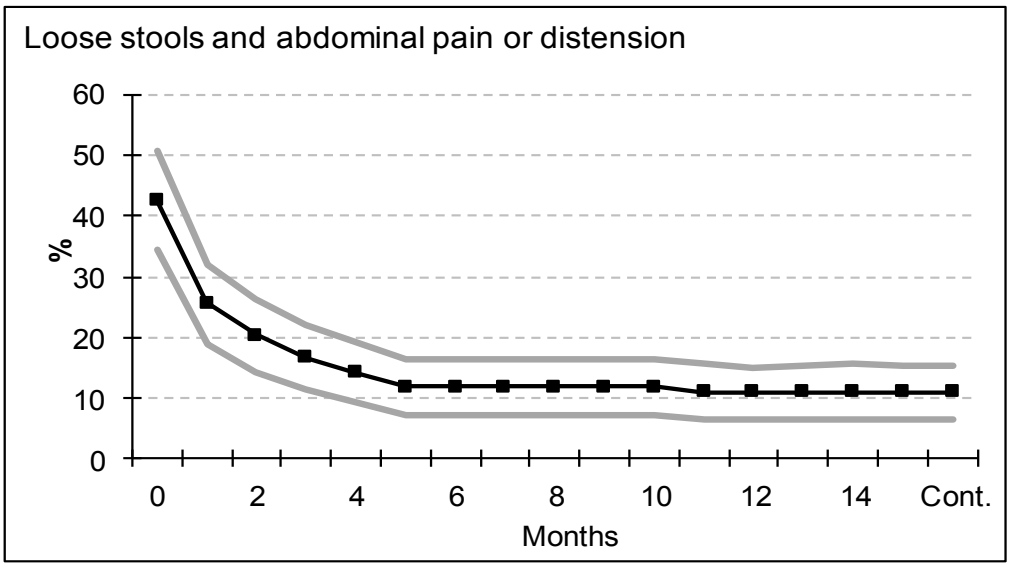


Fig 7b

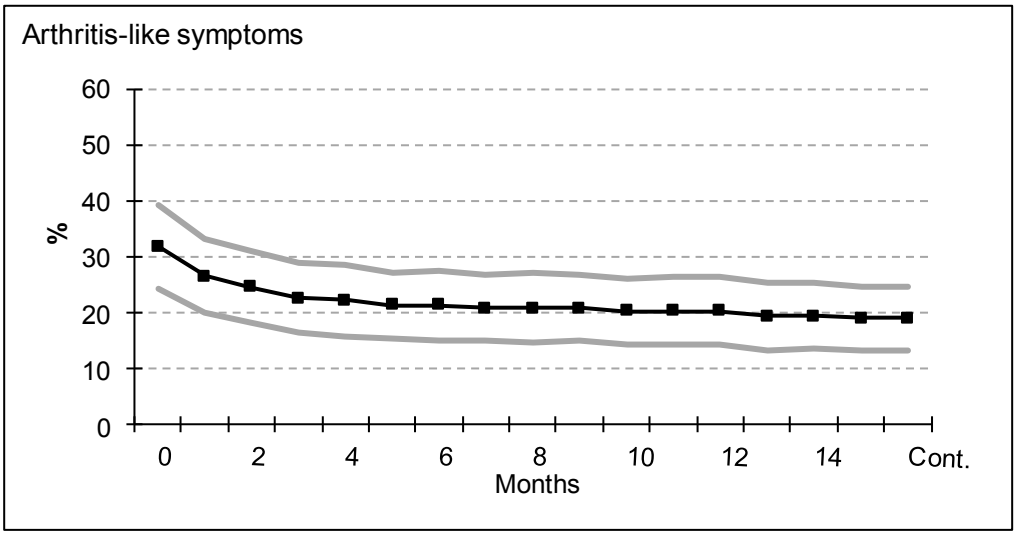


Figure 7. The prevalence of remaining IBS-like symptoms (Fig 7a) and arthritis-like symptoms (Fig 7b) by month among subjects in the contaminated group who experienced gastroenteritis during the epidemic (N=174). Data from the follow-up questionnaire (Q2). Black boxes represent the point-prevalence and grey lines 95% CI.

The prevalence of arthritis-like-symptoms was approximately five-fold higher at 3 months and 15 months among those who had prolonged IBS-like symptoms after acute gastroenteritis compared to subjects without IBS-like symptoms (Table 17).

Table 17. The prevalence of arthritis-like symptoms among subjects with or without gastrointestinal symptoms after acute gastroenteritis during the epidemic.

	Arthritis-like symptoms	
	At 3 months	At 15 months
With IBS-like symptoms	54.3% (19/35)	52.2% (12/23)
Without IBS-like symptoms	10.9% (6/55)	10.4% (7/67)
p-value	<0.001	<0.001

5.8 Health-economic costs (IV)

The epidemic caused an estimated 354 496 EUR direct health-care costs (Table 18). Dividing this figure by the number of excess cases of gastroenteritis (6500) in the town of Nokia, the costs per case were 55 EUR.

Care in the municipal health centre in Nokia constituted 44% (157 573 EUR) of the costs. Unit costs were 118.9 EUR for an emergency department visit, 62.9 EUR for a scheduled visit to a doctor and 27.8 EUR for a visit to a nurse. Care in TAUH accounted for 42% (148 625 EUR) of the costs, of which care of children amounted to 70% (104 183 EUR). The unit costs in TAUH varied widely (196.3-752.0 EUR), depending on the care needed and whether it was a question of an emergency visit or a scheduled appointment with a rheumatologist.

The neighbouring municipalities charged 12 035 EUR for the care of Nokia inhabitants, making 3.4% of the direct health-care costs. The microbiological examination of stool samples made up 10.2% (36 263 EUR) of the costs. The average cost per sample was 18 EUR.

Table 18. Details of the health-care expenses included in the study.

	Excess cost (€)
Nokia health centre	
Emergency department	98 448
Scheduled doctor's appointment	44 981
Nurse's appointment	14 144
Tampere University Hospital	
Emergency department	
-children	44 562
-adults	18 131
Scheduled appointment with a rheumatologist	
-first visit	13 946
-control visit	12 365
In-patient care of children	59 621
Neighbouring municipal wards	12 035
Stools samples	
Bacterial culture	13 702
Faecal ova and parasite microscopy	15 820
Giardia antigen detection test	4 641
Cryptosporidium staining test	2100
Total of direct excess health-care costs	**354 496**

6 Discussion

6.1 Study design

A prospective, population-based, controlled cohort design was used in this study. Three representative study groups were created from the National population register. The division of the town into contaminated and uncontaminated areas was made by assessing the contaminated area by flow data and modelling the probable flow directions in the network. Although this assessment may not be completely precise, data from the epidemiological studies showed the assessment to be close to correct.

Epidemiological studies concerning drinking water-associated outbreaks usually utilize case-control or cohort designs (Tillett, de Louvois et al. 1998; Hrudey and Hrudey 2007). Roughly, case-control studies seek an answer to a question "why me", in the case of an infectious disease outbreak the cause of the outbreak. In sudden large waterborne outbreaks, drinking water as a causative factor may be obvious already from the beginning, as was the case in Nokia. In such circumstances, case-control studies may not be needed to show the connection. Cohort studies deal with the question "what will happen to me". Studying a cohort of persons exposed or falling ill provides data of immediate and later (health) consequences.

Control groups are not frequently used in outbreak cohort studies. When the illness in question is a common one, as is gastroenteritis in a waterborne outbreak, an uncontrolled study tends to overestimate the burden, as these illnesses also occur in normal circumstances. In Walkerton, the control group was created of local residents who did not fall ill during the outbreak (Garg, Macnab et al. 2005). In such a case, a control group matches well with the ill population; however, control subjects have probably also been exposed and may have had a symptomless infection. Asymptomatic infection may also have later consequences similar to those in symptomatic infection and this kind of control group may therefore underestimate the influence of an outbreak.

The control population in this study was chosen from another municipality in the same city area. The municipality in question was chosen because of its location on the opposite edge of the urban area and daily connections between these two municipalities would thus be minimal. Otherwise, these two communities are more or less alike (Table 9). This design enables reliable conclusions as to excess morbidity associated with the epidemic. Furthermore, it makes it possible to observe the outbreak morbidity in the uncontaminated part of the town.

Questionnaires, either by mail or telephone, are usually used to collect data in analytic outbreak studies. This method makes it possible to include large number of subjects; however, observations rely on self-reported perceptions. In the case of large outbreaks, information bias may distort the findings towards the expected.

Questionnaire studies may also be vulnerable to selection bias; those who fell ill are probably more prone to respond to a survey. In addition, if the time between the incident and the survey is protracted, recall bias may become significant (Hunter and Syed 2001).

Descriptive epidemiology describes the findings, in infectious disease outbreaks usually the number of cases, microbes found and clinical symptoms. In this study, comprehensive data on clinical microbiological findings were collected. The service of the clinical laboratory of TAUH (Fimlab) is district-wide and represents the vast majority of laboratory diagnostics in the area. The data from the health centre is representative as being derived from prospective line-listing and a database. Paediatric epidemic patients referred to TAUH were listed and comprehensive data collected by the researchers of the paediatric study branch (Rasanen, Lappalainen et al. 2010). Exact data on adult patients treated in the wards of TAUH were missing, as the patients could not be traced. However, these patients would have been admitted only to wards of either infectious diseases or gastroenterology. Therefore, the clinical impression of only a few adult inpatients in TAUH can be taken to be relatively reliable.

6.2 The water contamination

Faecal contamination is a frequent cause of drinking water-associated outbreaks. Usually faecal contamination is caused by runoff of faecal material in consequence of heavy rainfall, melting snow, sewage line breakage or blockage (Miettinen, Zacheus et al. 2001; Vartiainen, Miettinen et al. 2003; Hewitt, Bell et al. 2007). Water reservoirs (e.g. water towers) may be inadequately maintained, leaving the possibility of animals or their faecal matter entering the reservoir (Angulo, Tippen et al. 1997; Pitkanen, Miettinen et al. 2008).

In the Nokia case, the mechanism of faecal contamination was exceptional. Faecal contamination was caused by a backflow of treated waste water into the water distribution network through a cross-connection between these pipelines. This waste water effluent had gone through the whole waste water treatment process. Although this process substantially reduces the microbial load, the treated effluent still contains relatively high amounts of faecal microbes (Pradhan, Kauppinen et al. 2013).

The waste water plant processes the whole town's output, including discharges from households, hospital and industry. This mechanism enabled large quantities of human faecal matter to enter the drinking water system, the level of contamination being thus extensive. Sewage backflow has been reported as a technical cause of one drinking water-associated outbreak in Denmark (Vestergaard, Olsen et al. 2007) and two in France (Beaudeau, de Valk et al. 2008). In the Danish outbreak, 43% of the

population in the contaminated area fell ill with gastroenteritis. As in the Nokia case, a human error played a role in the incident.

6.3 Microbiological findings

Seven pathogens were detected in clinical patient samples during the epidemic and six of them were proved to be waterborne, being found also in network samples. *Campylobacter* was the most prominent bacterial pathogen, as has been the case in most Finnish drinking water-associated outbreaks (Miettinen, Zacheus et al. 2001; Zacheus and Miettinen 2011). *C. difficile* was for the first time suggested to be a possible water-related pathogen (Kotila, Pitkanen et al. 2013). Furthermore, the Nokia epidemic was the first in which a protozoan pathogen caused a drinking water-associated outbreak in Finland, although these pathogens are frequently associated with waterborne outbreaks elsewhere (Rimhanen-Finne, Hänninen et al. 2010).

Norovirus was tested in only a few clinical specimens; however, later studies of preserved faecal samples as well as observations of person-to-person spread have shown a major role of norovirus in this epidemic (Maunula, Klemola et al. 2009). Other enteric viruses have also been detected in a subsequent study (Rasanen, Lappalainen et al. 2010).

The spectrum of pathogens found in this epidemic was exceptionally wide compared to other Finnish waterborne outbreaks. This was also the case in the Danish outbreak, where several bacterial, two viral and one protozoan pathogen were detected (Vestergaard, Olsen et al. 2007). The large number of pathogens probably reflects the common mechanism of contamination in these outbreaks; waste water is a mixture of faeces of thousands of people. It is not surprising that when large amounts of waste water (although fully treated) is discharged into the household water network, a number of pathogens are distributed in quantities sufficient to cause infection.

6.4 The burden of gastroenteritis

Taking the whole town together, 8453 people fell ill with gastroenteritis during the epidemic period, 6500 of these being excess cases in comparison to the control population. The highest morbidity, 53% of the population, was observed in the contaminated area, but in comparison to the control population it was also found to be higher in the uncontaminated part of the town. The latter finding is probably due to visits to the contaminated part of the town and consumption of water there as well as possibly person-to-person spread of viral pathogens.

These figures make the Nokia epidemic the largest drinking water-associated epidemic in Finland. The proportion of the population falling ill was found to be even higher (63%) in a North-Karelian outbreak (Kuusi, Nuorti et al. 2004), but the

methods used in that study (internet survey) may be considered experimental at the time of the investigation and vulnerable to selection bias.

The proportion of sufferers in Nokia epidemic was comparable to that in other major drinking water-associated epidemics in industrialized countries. Although comparison with Walkerton and Milwaukee epidemics is difficult as the size of exposed populations, microbiological agents involved and clinical consequences were different, roughly a half of the affected population fell ill in all of these three epidemics.

The high attack rate observed in these epidemics highlights the importance of thorough maintenance and quality surveillance of household water distribution systems. As one waterworks may serve thousands or even hundreds of thousands of inhabitants, pathogens are effectively distributed widely if contamination takes place. In Finland, the Nokia incident acted as an awakening of the potential hazards of water distribution systems. As a result, the risks associated with these systems will presumably receive more attention in the future.

6.5 The burden of joint symptoms

The frequency of new joint symptoms within eight weeks from exposure was nine-fold in the contaminated group in comparison to the control group (13.9% vs. 1.5%). For arthritis-like symptoms, the frequency was 13-fold compared to that in the control group (6.7% vs. 0.5%). As with gastroenteritis, excess prevalence of joint symptoms was also observed in the uncontaminated group in comparison to the control group.

Register-based studies concerning ReA after an episode of *Campylobacter* infection have observed a frequency of 7% in Finland (Hannu, Mattila et al. 2002) and 16% in Denmark (Locht and Krogfelt 2002). According to a telephone survey in the USA, 13% of subjects with bacterial gastroenteritis of mixed etiologies (*Campylobacter, E. coli* O157, *Salmonella* and *Shigella)* had joint symptoms within 8 weeks of positive stool culture (Townes, Deodhar et al. 2008). These studies, however, involved only cases with positive stool cultures and infections of various origins.

Joint symptom studies after a point-source outbreak are also usually made by observing only cases with positive stool cultures or only the section of the exposed population who fell ill with gastroenteritis. The study of arthritis risk after the Walkerton outbreak was, in contrast, population-based and controlled. In that study, 21.6% of subjects with severe gastroenteritis and 17.6% with moderate symptoms reported having received a diagnosis of arthritis, while the frequency was 15.7% among the controls (Garg, Pope et al. 2008). However, the control group in that study consisted of the same town's residents who did not fall ill during the outbreak. A substantial proportion of them may have had symptomless infection, which may have influenced the findings. In fact, the adjusted relative risk of ReA against the control group was only 1.19 (95% CI 0.99-1.43) in the moderate gastroenteritis group and

1.33 (1.07-1.66) in the severe gastroenteritis group, suggesting that there may also have been excess morbidity of ReA among asymptomatic subjects.

In our study, residence in the contaminated area seemed to increase the probability of joint symptoms even in the absence of gastrointestinal illness. This raises the suspicion that asymptomatic infections may have been common among the exposed population and these have triggered joint symptoms. Such a phenomenon may explain the lack of a clear difference in ReA risk between the study groups in the Walkerton study.

Every gastrointestinal symptom and fever predicted joint symptoms, diarrhoea and blood in faeces being the clearest indicators. This observation seems plausible, as diarrhoea is the main symptom of bacterial gastroenteritis and blood in faeces may also be observed. Surprisingly, the association was stronger in the uncontaminated than in contaminated group. This observation is difficult to explain. However, in this analysis subjects with a specific gastrointestinal symptom were compared to subjects without that symptom within the same group. As there is a possibility that there were a substantial number of asymptomatic bacterial infections in the contaminated group, these subjects with asymptomatic infection were in that analysis handled as "unaffected". If also asymptomatic bacterial infections would in some cases trigger joint symptoms, this would weaken the association between gastrointestinal and joint symptoms in the contaminated group.

As over 8000 inhabitants fell ill in Nokia and 27% of bacterial stool specimens revealed *Campylobacter,* a large number of ReA-cases was expected. However, only 21 verified cases were noted in the study by *Uotila* and colleagues (Uotila, Antonen et al. 2011). Extrapolating the proportions of the present questionnaire study, over 2000 inhabitants in Nokia experienced joint symptoms and over 1000 arthritis-like symptoms. Taking these two studies together, it seems that milder forms of joint complaints after a gastroenteritis outbreak are clearly more common than confirmed ReA. They also suggest that studying ReA occurrence after an outbreak using only a questionnaire without clinical verification may significantly overestimate the burden of post-outbreak ReA.

6.6 Water use and joint symptoms

Large amounts (>6 glasses/day) of tap water used for drinking were significantly associated with the probability of joint symptoms and back pain at rest and almost significantly for arthritis-like symptoms, compared to consumption of only small amounts. Moderate amounts (3-6 glasses per day), instead were not associated with increased probability.

Previously in drinking water-associated outbreaks the association between the amount of water ingested and the risk of developing gastroenteritis has been

demonstrated in several studies (Kuusi, Klemets et al. 2004; Kuusi, Nuorti et al. 2005; Gallay, De Valk et al. 2006; O'Reilly, Bowen et al. 2007).

In this study, those who ingested moderate or large amounts of tap water were compared to those who ingested fewer than three glasses daily. As tap water is widely used for drinking in Finland, comparison against non-users is not possible. As the water was heavily contaminated, small amounts of tap water may have sufficed to cause illness. Thus no correlation with increasing amounts of tap water ingested and joint symptoms can be seen among those using moderate amounts of water.

On the other hand, those ingesting large amounts (more than 6 glasses daily) may have been exposed heavily enough to show an increased risk. In addition, the concentration in water of some microbes seen less in this epidemic (for example Salmonella) may have been lower and larger amounts ingested would be needed to contract the infection. Those who ingested large amounts of contaminated water may thus have been infected with more arthritogenic pathogens and possibly had mixed infections.

6.7 Persistence of gastrointestinal symptoms within 15 months (III)

According to the findings in the follow-up study, 42.7% of those who had experienced gastroenteritis during the epidemic suffered from prolonged IBS-like symptoms: loose stools and abdominal pain or distension. This proportion diminished promptly during the first months but remained thereafter practically stable until the end of the follow-up. At 15 months, little more than every tenth were still having IBS-like symptoms.

This study did not utilize any common criteria for IBS. However, this combination is reasonable close to the Rome I and Manning criteria for IBS (Hillila and Farkkila 2004). The remaining symptoms at 15 months from the epidemic may therefore reflect the presence of PI-IBS after bacterial gastroenteritis. However, the proportion of adult patients with residual symptoms (11.5%) is close to the prevalence of IBS (11.2%) in general adult population according to a meta-analysis of IBS studies (Lovell and Ford 2012). It is thus questionable, whether there was an excess frequency of IBS symptoms left at all at the end of the follow-up time.

The natural course of postinfectious IBS-like symptoms in this study was in line with the findings of *Mearin* and group (Mearin, Perez-Oliveras et al. 2005). They observed an IBS prevalence of 13.4% at 12 months after a *Salmonella* outbreak. On the other hand, the prevalence of IBS-like symptoms in this study was lower than the observed frequency of PI-IBS after two major drinking water-associated epidemics. The Walkerton researchers found a PI-IBS prevalence of 28% at 2-3 years and 15% at 8 years among subjects who had had gastroenteritis during the outbreak of *Campylobacter* and *E. coli* O157:H7 (Marshall, Thabane et al. 2006; Marshall, Thabane et al. 2010). In a study of IBS-prevalence 3 years after the Bergen *Giardia*-

outbreak, a very high prevalence (46%) of IBS was found among exposed subjects (Wensaas, Langeland et al. 2012). In that study however, the prevalence among the unexposed was also high (14%) which, in light of the literature, suggests that there may be methodological aspects partially explaining the high prevalence.

There are few data on the frequency of PI-IBS among children. In this study, the prevalence of IBS-like symptoms among persons under 16 years of age was 8.9%, a slightly lower figure than among adults. In a study by the Walkerton group, the cumulative incidence of IBS was 10.5% among exposed children, which suggests a considerably lower frequency of PI-IBS among children than adults (Thabane, Simunovic et al. 2010).

6.8 Persistence of arthritis-like symptoms within 15 months (III)

A total of 31.8% (55/174) of subjects in the contaminated group who had experienced gastroenteritis during the epidemic reported arthritis-like symptoms after the acute gastroenteritis. This figure is substantially higher than the proportion of subjects with arthritis-like symptoms (6.7%) observed in the contaminated group in Q1. This difference can be explained by two factors. First, in Q2 only those with gastroenteritis during the epidemic were followed, while in Q1 the prevalence was counted from the whole group. Secondly, a selection bias of respondents in Q2 was noted towards those who reported joint symptoms in Q1.

The prevalence declined moderately for three months, thereafter slowly but continuously. At the end of the follow-up, 19% were still experiencing arthritis-like symptoms.

The previous literature on the duration of joint symptoms after an episode of gastroenteritis focuses on the duration of ReA. This is usually 3-5 months and duration over 6 months has been considered a sign of a chronic state (Leirisalo-Repo 2005; Carter 2006). However, studies have suggested that less than half of the patients recover fully when followed even for several years (Hannu, Inman et al. 2006). The long-term risk of arthritis after the Walkerton outbreak was studied by the WHS group *(Garg, Pope et al. 2008)*. They found that the risk of new arthritis was increased up to 4 years after the outbreak. This study did not, however, report the duration of symptoms.

According to a follow-up study of 21 ReA patients after the Nokia outbreak, 33% of cases were still on antirheumatic medication and over half were taking analgesics at one year after the diagnosis of ReA (Uotila, Antonen et al. 2013). The observed proportion of symptomatic cases at one year is reasonably well in line with the observation in the present study. Again, the suggested number of subjects with arthritis-like symptoms in the affected population according to Q2 is greater than the number of clinically followed patients. Our study, together with the studies by the

ReA group, point that joint complaints after a waterborne gastroenteritis outbreak can be longstanding in a substantial proportion of cases.

A significant association between prolonged gastrointestinal and arthritis-like symptoms was observed in this study. A similar association has been observed in at least two studies of reactive joint symptoms after *Salmonella* outbreaks (Locht, Molbak et al. 2002; Lee, Hall et al. 2005). As the pathogenesis of both conditions remains to be clarified, the mechanism underlying this association cannot be defined. There may be common pathogenetic or genetic mechanisms behind these observations.

6.9 Health-economic costs

Assessment of the costs of an outbreak is a difficult task. Large epidemics affect a community in many ways, and costs may arise in many different fields. Epidemics incur expenses directly in health-care and water supply plants. Indirect costs such as sick leaves, diminished economic activity, arrangement of compensatory water distribution and reduced confidence in authorities may be much more significant than direct costs.

In this study, direct health-economic costs due to excess use of public health care were counted. Total excess health care costs amounted to 354 496 EUR. Treatment provided at the municipal health centre constituted the most significant portion (44%), followed by treatment at TAUH (42%). Despite the large number of stools samples examined, laboratory costs made up only 10.2% of expenses, due to the low unit cost of these tests.

Most cases suffered from self-limiting gastroenteritis and needed no hospital care, except for children who were commonly referred to TAUH. None needed intensive care. Had it been otherwise, the combined costs in TAUH could have been substantially higher. In the Walkerton outbreak, STEC caused 27 cases of haemolytic-uremic syndrome needing haemodialysis (Anonymous 2000a). If STEC had been involved in the Nokia epidemic, some 19 persons would have needed acute haemodialysis (cost 1 000 EUR per session), probably several times. There may also have been individuals developing a chronic need for dialysis and possibly kidney transplantation.

The health-economic costs counted in this study are probably a minimum estimate. Care provided by the private sector and occupational health care was not included, nor was the use of medicines. The costs of the use of private and occupational health care were likely minimal, as in Finland most of the health care is provided by public sector. According to the register data of THL and the Finnish Social Insurance Institution (Kela), 75% of the health care in Nokia is provided by the public sector and the proportion was probably higher during the epidemic (Kela 2013; THL 2013). Illnesses were mostly mild or moderate cases of gastroenteritis and therefore medicine costs were probably not of great significance.

Furthermore, this analysis did not cover cases treated as outpatients in the health centres of other municipalities. As the town of Nokia is an industrial locus, workers also commute from neighbouring municipalities and they may have been exposed during their workday.

Another study has focused on the costs of lost workdays due to the Nokia epidemic (Halonen, Kivimaki et al. 2012). The authors found that the prevalence of sick leaves was 3.5 times higher during the first epidemic week compared to a reference period in the contaminated area of the town. The estimated costs of lost workdays were counted to be 1.2 – 2.1 million EUR. The indirect costs of this epidemic were thus far greater than the direct costs.

6.10 Strengths and limitations of the study

The major strength of this study was the epidemic itself. Such a large point-source epidemic caused by extensively contaminated drinking water is rare in developed countries. The microbiological aetiology was extensively studied in the water. Although only a portion of those affected were examined by stool cultures, a reliable picture of microbiological agents involved in this epidemic was obtained. Comprehensive data on health care visits were also available from the municipal health centre. Data concerning children taken care of in TAUH were also of good quality. In contrast, data on adult patients in TAUH were incomplete, but as the number of adult patients was low, clinicians' impressions of the situation can be regarded as fairly reliable.

Although the incident was a severe crisis for the community, it offers an opportunity to study a waterborne gastroenteritis outbreak and its consequences in a systematic manner. Thorough assessment of the contaminated area made it possible to define the population who became exposed. As the population register of Finland holds coordinates of place of residence, the cohort of people living in the affected area could be defined, and a reliable population-based design for the analytic epidemiological studies could be created.

The use of a control group was a strength of this study. As gastroenteritis is a common disease even without outbreak the lack of a control group may lead to overestimation of disease burden (Hunter and Syed 2001). On the other hand, counting only contacts with health-care misses mild cases, which in turn leads to underestimation of the disease burden.

The residents were agreeable to participate in the study and the response rates in the first questionnaire study were good enough to conclude that the population samples were representative. For the second questionnaire, some selection bias towards those who had experienced gastroenteritis and joint symptoms took place. However, as the aim of the follow-up study was to assess the persistence of symptoms, this selection bias does not seriously hamper the conclusions.

In a study using questionnaires, subjective impressions of matters asked are gathered. Some caution should be exercised when interpreting results. For example, although a combination of symptoms suggesting ReA (arthritis-like symptoms) was used, the observed frequency of arthritis-like symptoms was substantially higher than the clinically verified cases of ReA observed in the ReA study (Uotila, Antonen et al. 2011). Self-reporting describes the symptoms participants experience, not clinical syndromes.

The first questionnaire study was conducted two and the second 15 months after the incident. Recall bias of some degree is therefore unavoidable. The concordance of reporting gastroenteritis during the epidemic was, however, good between Q1 and Q2. The epidemic was a disturbing incident raising a great deal of concern and anger and it was widely discussed in the media. People were informed regarding possible consequences of outbreak-related gastroenteritis, for example ReA and advised to seek medical care in such circumstances. Furthermore, claims for compensation were made by many persons falling ill and the incident became a subject of criminal investigation and a trial. All these circumstances may have influenced study participants' perceptions.

As stool cultures were taken only from selected cases, mostly from those with severe symptoms, we do not know the specific pathogen involved in the majority of the cases. In consequence, only a handful of cases with known microbiology were included in the study groups. This proportion was too small to draw microbe-specific conclusions as to the nature and course of disease by combining microbiological data and the data from questionnaire studies.

Appointments at private and occupational health-care providers were not included in the data. As indicated above, these constitute approximately 25% of the health-care services for inhabitants in Nokia. As these data are missing, estimates of the primary care load and costs are somewhat underrated. However, the busiest days of the epidemic fell on a weekend and the health centre focused on managing epidemic victims. It is therefore reasonable to assume that the use of private providers was at least not greater during the epidemic than in normal circumstances.

7 Summary and conclusions

The main findings in this study were:

1. Approximately 8453 Nokia residents had gastroenteritis during the epidemic; 6500 of these were caused by the water contamination. The attack rate in the contaminated area of Nokia was 53.0% and 15.6% in the uncontaminated area.

2. The spectrum of microbial agents was exceptionally wide. Seven pathogens were found in patient samples and six of these were also detected in network samples.

3. 13.9% of residents in the contaminated area and 4.3% in the uncontaminated area experienced joint symptoms within eight weeks. Arthritis-like symptoms were reported by 6.7% and 2.1%, respectively. Joint symptoms and arthritis-like symptoms were significantly more common in both areas in comparison to the control population.

4. The risk of having joint complaints was significantly associated with gastrointestinal symptoms and fever in both study areas of Nokia. Furthermore, residence in the contaminated area was associated with joint symptoms even without gastroenteritis.

5. In the contaminated area, 10.9% of those who had gastroenteritis during the epidemic reported continued gastrointestinal symptoms at 15 months after the epidemic. Arthritis-like symptoms were reported by 19% at the end of the follow-up.

6. The direct health-economic costs of the epidemic were 354 496 EUR. This figure is probably a minimum estimate.

The drinking water-associated epidemic of gastroenteritis in Nokia at the end of 2007 was the largest published drinking water-associated epidemic in Finland to date. The mode of contamination was unparalleled in Finnish outbreaks and a rare even elsewhere. The large spectrum of microbial findings reflects the substantial magnitude of the contamination. This diversity of pathogens also differentiates the Nokia epidemic from other Finnish waterborne outbreaks.

It is important to use a control population when studying outbreaks. A comparison against a control population enables assessment of the true excess burden when the disease involved is a common one.

A substantial proportion of exposed subjects experienced joint symptoms and arthritis-like symptoms. Milder forms of joint complaints may be substantially more common than ReA. A notable portion of these symptoms seem to persist at least 15 months.

Given the circumstances of the incident, the results of this study give the picture of a relatively favourable outcome. If the pathogens involved had been more dangerous, for example STEC, the impression would be quite different. This study, however, did not include a follow-up of individual cases. It has been observed from clinical sources and studies by the ReA group that despite the overall favourable outcome of the epidemic, some persons are left with long-lasting or permanent, severe consequences.

The epidemic in Nokia was a potentially dangerous situation. Pathogens became effectively distributed to the population and an extensive epidemic ensued. The safety of drinking water and water supply systems must be a high priority.

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10 Appendix

(00000) *2007n2* 1

ERKKI ESIMERKKI
OTOSKATU 1
99999 DEMOLA

(Kansanterveyslaitos täyttää)

Osoitelähde:
Väestötietojärjestelmä
Väestörekisterikeskus
PL 70
00581 HELSINKI

Kyselylomake - Vesiepidemia Nokialla marras-joulukuussa 2007

Arvoisa ERKKI ESIMERKKI,
tämän kyselyn tarkoituksena on kerätä tietoja, jotka auttavat Nokialla marras-joulukuussa 2007 todetun vatsatautiepidemian laajuuden ja sen aiheuttaman haitan selvittämisessä. Selvitystyön tekevät yhteistyössä Nokian kaupunki, Pirkanmaan sairaanhoitopiiri, Tampereen yliopisto ja Kansanterveyslaitos. Henkilöt, joille kysely lähetetään, on valittu satunnaisesti siten, että he edustavat kaikkia nokialaisia sekä puhtaana säilyneeltä että likaantuneelta alueelta. Lisäksi kysely lähetetään osalle Kangasalan asukkaista, jotta voidaan verrata vatsatautien esiintymistä väestössä ilman vesiepidemiaa. Osallistuminen kyselyyn on vapaaehtoista. Vaikka ette olisikaan itse sairastunut on apunne epidemian selvittämisessä erittäin tärkeää. Kaikki tiedot käsitellään luottamuksellisina eikä yksittäisen vastaajan tietoja esitetä tuloksissa.

Täyttöohjeet: Lomakkeen kysymykset koskevat sitä henkilöä, jolle kysely on lähetetty, vaikka perheestänne muutkin olisivat sairastuneet. On hyvin tärkeää, että vastaatte lomakkeen kaikkiin kysymyksiin huolellisesti, vaikka osa kysymyksistä sopisi huonosti omaan tilanteeseenne. **Pyydämme palauttamaan lomakkeen mahdollisimman pian, mutta viimeistään 6.2.2008 mennessä oheisessa palautuskuoressa.**

Kiitos avustanne!
Lisätietoja: Kansanterveyslaitokselta ma-pe klo 8-16 numerosta 050 5984789

Eila Kujansuu
Ylilääkäri

Petri Ruutu
Tutkimusprofessori

Jukka Lumio
Osastonylilääkäri

NOKIAN kaupunki

Kansanterveyslaitos
Folkhälsoinstitutet
National Public Health Institute

PIRKANMAAN SAIRAANHOITOPIIRI
Yhdessä terveyttä

Ohje: ympyröikää tai rastittakaa sopiva vaihtoehto.

0. Täyttöpäivämäärä: _____ . _____ . 2008_____

Lomakkeen täyttäjä:
1 Henkilö, jolle lomake on osoitettu
2 Hänen omaisensa tai huoltajansa

Kysymykset 1 - 37 koskevat henkilöä (ERKKI ESIMERKKI), jolle lomake on osoitettu

1. Sukupuoli:
1 Mies
2 Nainen

Ikä: _____ vuotta

2. Siviilisääty
1 Naimisissa tai avoliitossa
2 Eronnut tai asumuserossa
3 Leski
4 Naimaton

3. Mikä seuraavista vaihtoehdoista kuvaa parhaiten pääasiallista toimintaanne 28.11.2007 - 20.1.2008 välisenä aikana? (Valitkaa vain yksi vaihtoehto.)
1 Kokopäivätyö
2 Osa-aikatyö tai osa-aikaeläke
3 Opiskelija tai koululainen
4 Eläkkeellä
5 Työtön tai lomautettu
6 Hoitamassa omaa kotitaloutta tai perheenjäsentä
7 Varusmies- tai siviilipalvelu
8 Alle kouluikäinen lapsi
9 Muu

4. Kuinka monta vuotta olette yhteensä käynyt koulua ja opiskellut päätoimisesti? (Kansa- ja peruskoulu lasketaan mukaan.): _____ vuotta

5. Ammattinne: _____

Työpaikka / koulu / päivähoitopaikka: _____

6. Onko teillä yksityinen sairausvakuutus?
1 Ei
2 Kyllä

7. Oletteko sairastanut vatsataudin viime vuoden tammi - lokakuussa (1.1. - 31.10.2007 välisenä aikana) eli ennen Nokian kaupungin vesiongelmaa?
1 Ei
2 Kyllä, _____ kertaa

Kysymykset 8 - 37 koskevat ajanjaksoa 28.11.2007 - 20.1.2008. (Suosittelemme käyttämään almanakkaa täyttämisen tukena)

8. Sairastuitteko vatsatautiin 28.11.2007 - 20.1.2008 välisenä aikana?
1 Ei, siirtykää kysymykseen 12
2 Kyllä

Merkitkää rastilla ne oireet, joita teillä on ollut, ja arvioikaa oireiden alkupäivämäärä ja kesto. Merkitkää oire, vaikka ette muistaisi tarkkaa alkupäivämäärää tai oireiden kestoa.

	Kyllä	Oireiden alkupäivämäärä (esim. 29.11.2007)	Oireiden kesto (päivää)	Jatkuu edelleen
Oksentelu	☐	_____ . _____ . 200_____	_____	☐
Ripuli (yli 3 ulostuskertaa/vrk)	☐	_____ . _____ . 200_____	_____	☐
Näkyvää verta ulosteessa	☐	_____ . _____ . 200_____	_____	☐
Vatsakivut	☐	_____ . _____ . 200_____	_____	☐
Pahoinvointi	☐	_____ . _____ . 200_____	_____	☐
Vatsan turvotus	☐	_____ . _____ . 200_____	_____	☐
Ummetus	☐	_____ . _____ . 200_____	_____	☐
Kuume (mitattu yli 38°C)	☐	_____ . _____ . 200_____	_____	☐

9. Sairastuitteko **uudelleen** vatsatautiin ensimmäisten vatsatautioireiden parannuttua?
1 Ei, siirtykää kysymykseen 10
2 Kyllä

Merkitkää rastilla vain **uudet**, toiseen vatsatautijaksoon liittyneet oireet, joita teillä on ollut, ja arvioikaa **uusien** oireiden alkupäivämäärä ja kesto.

	Kyllä	Oireiden alkupäivämäärä (esim. 29.11.2007)	Oireiden kesto (päivää)	Jatkuu edelleen
Oksentelu	☐	_____ . _____ . 200_____	_____	☐
Ripuli (yli 3 ulostuskertaa/vrk)	☐	_____ . _____ . 200_____	_____	☐
Näkyvää verta ulosteessa	☐	_____ . _____ . 200_____	_____	☐
Vatsakivut	☐	_____ . _____ . 200_____	_____	☐
Pahoinvointi	☐	_____ . _____ . 200_____	_____	☐
Vatsan turvotus	☐	_____ . _____ . 200_____	_____	☐
Ummetus	☐	_____ . _____ . 200_____	_____	☐
Kuume (mitattu yli 38°C)	☐	_____ . _____ . 200_____	_____	☐

10. Määräsikö lääkäri teille 28.11.2007 - 20.1.2008 välisenä aikana vatsataudin hoitoon reseptilääkkeitä?
1 Ei
2 Kyllä, lääkkeen nimi: _____

11. Käytittekö käsikauppalääkkeitä 28.11.2007 - 20.1.2008 välisenä aikana **vatsataudin hoitoon**?
1 Ei
2 Kyllä, kuinka monena päivänä? _____ päivänä
lääkkeiden nimet: _____

12. Ilmaantuiko teille 28.11.2007 - 20.1.2008 välisenä aikana **uutena oireena** joitakin seuraavista oireista? Merkitkää oire vaikka ette muistaisi tarkkaa alkupäivämäärää tai kestoa. Älkää merkitkö pitkäkestoisia oireita, jotka ovat alkaneet ennen 28.11.2007.

	Kyllä	Oireiden alkupäivämäärä	Oireiden kesto (päivää)	Jatkuu edelleen
Nivelsärkyä	☐	____ . ____ . 200____	____	☐
Kipuja niveliä liikuteltaessa	☐	____ . ____ . 200____	____	☐
Nivelturvotusta	☐	____ . ____ . 200____	____	☐
Nivelkuumotusta/punoitusta	☐	____ . ____ . 200____	____	☐
Kipua tai kirvelyä virtsatessa	☐	____ . ____ . 200____	____	☐
Silmien punoitusta ja rähmimistä	☐	____ . ____ . 200____	____	☐
Selkäkipuja nukkuessa	☐	____ . ____ . 200____	____	☐

Missä nivelissä oireet olivat: _____

13. Käytittekö särkylääkkeitä 28.11.2007 - 20.1.2008 välisenä aikana ilmaantuneiden **uusien niveloireiden hoitoon**?

1 Ei

2 Kyllä, kuinka monena päivänä? ____ päivänä

14. Kävittekö lääkärissä 28.11.2007-20.1.2008 välisenä aikana?

1 Ei, siirtykää kysymykseen 15

2 Kyllä, yhteensä: ____ kertaa

Merkitkää taulukkoon käyntikerrat eri syistä.

	Vatsataudin takia	Niveloireiden takia	Muun sairauden / oireen takia
Käynti terveyskeskuslääkärin vastaanotolla	____ kertaa	____ kertaa	____ kertaa
Käynti sairaalan poliklinikalla (TAYS, Valkeakosken sairaala)	____ kertaa	____ kertaa	____ kertaa
Käynti yksityislääkärin vastaanotolla	____ kertaa	____ kertaa	____ kertaa
Käynti työterveyslääkärin vastaanotolla	____ kertaa	____ kertaa	____ kertaa
Suonensisäisessä nestehoidossa (tiputuksessa) terveyskeskuksen ensiavussa	____ kertaa	____ kertaa	____ kertaa
Lääkärin kotikäynti	____ kertaa	____ kertaa	____ kertaa

15. Kävittekö terveydenhoitajan vastaanotolla 28.11.2007-20.1.2008 välisenä aikana?

1 Ei, siirtykää kysymykseen 16

2 Kyllä, yhteensä: ____ kertaa

Merkitkää taulukkoon käyntikerrat eri syistä.

	Vatsataudin takia	Niveloireiden takia	Muun sairauden / oireen takia
Käynti terveydenhoitajan vastaanotolla	____ kertaa	____ kertaa	____ kertaa
Käynti työterveyshoitajan vastaanotolla	____ kertaa	____ kertaa	____ kertaa
Käynti yksityisen terveydenhoitajan vastaanotolla	____ kertaa	____ kertaa	____ kertaa

16. Olitteko puhelimitse yhteydessä terveydenhuoltoon 28.11.2007-20.1.2008 välisenä aikana?

1 Ei, siirtykää kysymykseen 17

2 Kyllä, yhteensä: _____ kertaa

Merkitkää taulukkoon yhteydenottokerrat eri syistä.

	Vatsataudin takia	Niveloireiden takia	Muun sairauden / oireen takia
Yhteydenotto puhelimitse terveyskeskukseen	_____ kertaa	_____ kertaa	_____ kertaa
Soitto TAYS:n neuvovaan puhelimeen (03-31169350)	_____ kertaa	_____ kertaa	_____ kertaa

17. Olitteko sairaalahoidossa 28.11.2007-20.1.2008 välisenä aikana?

1 Ei, siirtykää kysymykseen 18

2 Kyllä, yhteensä: _____ päivää

Merkitkää päivien lukumäärä kunkin sairauden / oireen kohdalle.

	Vatsataudin takia	Niveloireiden takia	Muun sairauden / oireen takia
Hoidossa Nokian terveyskeskuksen vuodeosastolla tai Nokian sairaalassa	_____ päivää	_____ päivää	_____ päivää
Hoidossa Tampereen Yliopistollisessa sairaalassa (TAYS) tai Valkeakosken aluesairaalassa	_____ päivää	_____ päivää	_____ päivää
Hoidossa Kangasalan terveyskeskuksen vuodeosastolla	_____ päivää	_____ päivää	_____ päivää

18. Otettiinko teiltä 28.11.2007-20.1.2008 välisenä aikana **ulostenäyte** (mainitkaa montako kertaa)

☐ Ei otettu lainkaan

☐ Terveyskeskuksessa, _____ kertaa

☐ Työterveyshuollossa, _____ kertaa

☐ Yksityisellä lääkäriasemalla, _____ kertaa

☐ Sairaalassa, _____ kertaa

19. Otettiinko teiltä 28.11.2007-20.1.2008 välisenä aikana **verinäyte** (mainitkaa montako kertaa)

☐ Ei otettu lainkaan

☐ Terveyskeskuksessa, _____ kertaa

☐ Työterveyshuollossa, _____ kertaa

☐ Yksityisellä lääkäriasemalla, _____ kertaa

☐ Sairaalassa, _____ kertaa

20. Millä kuljitte matkan lääkäriin, terveydenhoitajan luo, sairaalaan tai laboratorioon? (Merkitkää kuinka moneen yhdensuuntaiseen matkaan käytitte kutakin kulkuneuvoa)

Jalan	_____ matkaa
Polkupyörällä	_____ matkaa
Henkilöautolla	_____ matkaa
Julkisilla kulkuvälineillä	_____ matkaa
Taksilla	_____ matkaa
Ambulanssilla	_____ matkaa

21. Olitteko poissa töistä / koulusta / päivähoidosta 28.11.2007 - 20.1.2008 välisenä aikana?

	Kyllä	Päivien lukumäärä
Oman sairautenne takia	☐	_____ päivää
Jonkun muun perheenjäsenen sairauden takia	☐	_____ päivää
Oman tai lapsenne päivähoitopaikan tai koulun sulkemisen takia (ei koske koulun loma-aikoja)	☐	_____ päivää

22. Oliko **joku muu perheenjäsen** poissa töistä tai koulusta 28.11.2007 - 20.1.2008 välisenä aikana?

	Kyllä	Päivien lukumäärä
Teidän sairautenne takia	☐	_____ päivää
Teidän päivähoitopaikkanne tai koulunne sulkemisen takia (ei koske koulun loma-aikoja)	☐	_____ päivää

23. Kuinka monta lasillista keittämätöntä vesijohtovettä (sellaisenaan tai mehuun sekoitettuna)

	Määrä
Juotte yleensä päivittäin?	_____ lasillista/päivä
Joitte 28.11.2007 jälkeen päivässä, ennenkuin saitte tiedon veden likaantumisesta?	_____ lasillista/päivä

24. Seuraava kysymys koskee oleskelua ja käyntiä Nokian kaupungin likaantuneen vesijohtoveden alueella. Vastatkaa kysymykseen riippumatta siitä missä kunnassa itse asutte.
Olitteko likaantuneen veden alueella?

	En lainkaan	Kyllä, 28.11.2007 - 30.11.2007	Kyllä, 1.12.2007 - 20.1.2008
Kotona	☐	☐	☐
Työssä, koulussa tai päivähoidossa	☐	☐	☐
Kylässä, harrastuksissa tai asioilla	☐	☐	☐
Joitteko keittämätöntä vesijohtovettä	☐	☐	☐

25. Olitteko läheisessä kanssakäymisessä 28.11.2007 - 20.1.2008 välisenä aikana vatsatautia sairastaneiden Nokian kaupungin asukkaiden kanssa?

2 Useita kertoja
1 Muutaman kerran
0 En lainkaan

Seuraavaksi toivomme teidän vastaavan kysymyksiin, jotka koskevat elämänlaatuanne ja mielialaanne. Mikäli henkilö, jolle lomake on osoitettu on alle 12-vuotias, siirtykää kysymykseen 38.

26. Oletteko viime aikoina pystynyt keskittymään töihinne?
- 0 Paremmin kuin tavallisesti
- 1 Yhtä hyvin kuin tavallisesti
- 2 Huonommin kuin tavallisesti
- 3 Paljon huonommin kuin tavallisesti

27. Oletteko viime aikoina valvonut paljon huolien vuoksi?
- 0 En ollenkaan
- 1 En enempää kuin tavallisesti
- 2 Jonkin verran enemmän kuin tavallisesti
- 3 Paljon enemmän kuin tavallisesti

28. Onko teistä viime aikoina tuntunut siltä, että mukana olonne asioiden hoidossa on...
- 0 Tavallista hyödyllisempää
- 1 Yhtä hyödyllistä kuin tavallisesti
- 2 Vähemmän hyödyllistä kuin tavallisesti
- 3 Paljon vähemmän hyödyllistä kuin tavallisesti

29. Oletteko viime aikoina tuntenut kykenevänne päättämään asioista
- 0 Paremmin kuin tavallisesti
- 1 Yhtä hyvin kuin tavallisesti
- 2 Huonommin kuin tavallisesti
- 3 Paljon huonommin kuin tavallisesti

30. Oletteko viime aikoina tuntenut olevanne jatkuvasti rasituksen alaisena?
- 0 En ollenkaan
- 1 En enempää kuin tavallisesti
- 2 Jonkin verran enemmän kuin tavallisesti
- 3 Paljon enemmän kuin tavallisesti

31. Onko teistä viime aikoina tuntunut siltä, ettette voisi selviytyä vaikeuksistanne?
- 0 Ei ollenkaan
- 1 Ei enempää kuin tavallisesti
- 2 Jonkin verran enemmän kuin tavallisesti
- 3 Paljon enemmän kuin tavallisesti

32. Oletteko viime aikoina kyennyt nauttimaan tavallisista päivittäisistä toimistanne?
- 0 Enemmän kuin tavallisesti
- 1 Yhtä paljon kuin tavallisesti
- 2 Vähemmän kuin tavallisesti
- 3 Paljon vähemmän kuin tavallisesti

33. Oletteko viime aikoina kyennyt kohtaamaan vaikeutenne
- 0 Paremmin kuin tavallisesti
- 1 Yhtä hyvin kuin tavallisesti
- 2 Huonommin kuin tavallisesti
- 3 Paljon huonommin kuin tavallisesti

34. Oletteko viime aikoina tuntenut itsenne onnettomaksi ja masentuneeksi?
- 0 En ollenkaan
- 1 En enempää kuin tavallisesti
- 2 Jonkin verran enemmän kuin tavallisesti
- 3 Paljon enemmän kuin tavallisesti

35. Oletteko viime aikoina kadottanut itseluottamuksenne?
0 En ollenkaan
1 En enempää kuin tavallisesti
2 Jonkin verran enemmän kuin tavallisesti
3 Paljon enemmän kuin tavallisesti

36. Oletteko viime aikoina tuntenut itsenne ihmisenä arvottomaksi?
0 En ollenkaan
1 En enempää kuin tavallisesti
2 Jonkin verran enemmän kuin tavallisesti
3 Paljon enemmän kuin tavallisesti

37. Oletteko viime aikoina tuntenut itsenne kaiken kaikkiaan kohtalaisen onnelliseksi?
0 Enemmän kuin tavallisesti
1 Yhtä paljon kuin tavallisesti
2 Vähemmän kuin tavallisesti
3 Paljon vähemmän kuin tavallisesti

Seuraavat kysymykset nro 38 - 44 koskevat koko talouttanne / perhettänne ajanjaksolla 28.11.2007 - 20.1.2008

38. Kuinka monta henkilöä yhteensä kuului perheeseenne / kotitalouteenne 28.11.2007 - 20.1.2008 välisenä aikana? (itsenne mukaan lukien): _____ henkilöä

joista alle 7v. _____ henkilöä

7 - 17v. _____ henkilöä

18 - 64v. _____ henkilöä

yli 64v. _____ henkilöä

39. Merkitkää tähän muiden 28.11.2007 tai sen jälkeen **vatsatautiin sairastuneiden** perheenjäsentenne tiedot riippumatta siitä tarvitsivatko he terveydenhoitopalveluja.
(terveenä pysyneiden perheenjäsenten tietoja ei tarvitse merkitä)

Ikä	Mies	Nainen	Ensimmäinen sairastumispäivämäärä	Kävi lääkäris-sä	Tervey-denhoi-tajan vas-taanot-olla	Sairaa-lahoi-dossa
_____ vuotta	1	2	_____ . _____ . 200_____	☐	☐	☐
_____ vuotta	1	2	_____ . _____ . 200_____	☐	☐	☐
_____ vuotta	1	2	_____ . _____ . 200_____	☐	☐	☐
_____ vuotta	1	2	_____ . _____ . 200_____	☐	☐	☐
_____ vuotta	1	2	_____ . _____ . 200_____	☐	☐	☐
_____ vuotta	1	2	_____ . _____ . 200_____	☐	☐	☐

40. Milloin perheenne sai ensimmäistä kertaa tiedon Nokian kaupungin talousveden saastumisesta?

_____ . _____ . 200_____

Mistä saitte tiedon ensimmäisenä?

1 Megafoniautosta
2 Terveyskeskuksesta
3 Televisiosta, myös teksti-TV
4 Radiosta
5 Lehdestä
6 Internetistä
7 Naapurilta / tuttavalta / sukulaiselta
8 Kiertävältä vedenjakajalta
9 Koteihin jaetusta lehtisestä
10 Muualta, mistä: _____

Olitteko huomannut vedessä poikkeavaa hajua, makua tai väriä ennen kuin saitte tiedon?

1 Ei
2 Kyllä, Ilmoititteko asiasta viranomaisille?
  1 Ei
  2 Kyllä, minne: _____

41. Asutteko likaantuneen veden alueella Nokialla

1 Ei
2 Kyllä

42. Tuliko juomavetenne 28.11.2007

1 Kunnan vesijohtoverkosta
2 Omasta kaivosta
3 Muualta, mistä: _____

43. Teittekö jotain seuraavista muutoksista vesiongelman takia?:

	Kyllä, en jatka enää	Kyllä, jatkan yhä
Muutitte ruokailutottumuksia	1	2
Pesitte pyykkinne muualla kuin kotona	1	2
Kävitte pesulla muualla kuin kotona	1	2
Haitte itse vettä vedenjakelupisteestä	1	2
Ostitte pullovettä	1	2
Muutitte käsienpesutottumuksianne	1	2
Aloitte käsien desinfiointiaineen käytön	1	2
Luovuitte kyläilystä tai vieraiden kutsumisesta kotiinne	1	2
Luovuitte joukkotilaisuuteen osallistumisesta	1	2
Peruitte suunnittelemanne joukkotilaisuuden	1	2
Peruitte loman tai muun matkan	1	2
Matkustitte itse tai lähettitte perheenjäsenen toiselle paikkakunnalle	1	2
Palkkasitte ulkopuolisen hoitajan lapsellenne tai muulle lähiomaiselle	1	2
Muutitte työtehtäviänne	1	2

44. Oletteko:

- ☐ Saanut korvausta vesiongelman aiheuttamista kuluista
- ☐ Hakenut korvausta vesiongelman aiheuttamista kuluista
- ☐ Ajatellut hakea korvausta vesiongelman aiheuttamista kuluista
- ☐ Korvausasia ei koske teitä

Kiitos avustanne!

45. Voimmeko ottaa teihin myöhemmin yhteyttä jos on tarvetta?

1 Ei
2 Kyllä

Puhelin: _____

Lisätietoja: _____

Questionnaire form for Q2

(Terveyden ja hyvinvoinnin laitos täyttää)

Osoitelähde:
Väestötietojärjestelmä
Väestorekisterikeskus
PL 70
00581 HELSINKI

Tiedote - Vesiepidemia Nokialla marras-joulukuussa 2007

Arvoisa ,

Osallistuitte keväällä 2008 toteutettuun kyselytutkimukseen, jolla selvitettiin Nokian vesiepidemian laajuutta ja vaikutuksia. Tutkimuksen avulla saatiin arvokasta tietoa laajan vesiepidemian ominaispiirteistä. Tämä tieto auttaa osaltaan ehkäisemään vastaavanlaisia tapahtumia vastaisuudessa ja toisaalta opastaa viranomaisia toimimaan parhaalla mahdollisella tavalla, mikäli kohdataan uusi epidemia.
Kiitos teille panoksestanne selvitystyölle!
Nokian vesiepidemiasta on kulunut yli vuosi, ja on aika selvittää mahdollisia myöhäisvaikutuksia. Tämän vuoksi pyydämme apuanne vielä uudelleen. Pyydämme Teitä täyttämään tämän lomakkeen, ja palauttamaan sen täytettynä Terveyden ja hyvinvoinnin laitokseen (THL). THL on uusi valtion tutkimuslaitos, joka syntyi Kansanterveyslaitoksen ja Stakesin yhdistyttyä vuodenvaihteessa.
Kyselytutkimus toteutetaan Nokian kaupungin, Pirkanmaan sairaanhoitopiirin, Tampereen yliopiston ja THL:n yhteistyönä. Kyselyyn vastaaminen on vapaaehtoista. Toivomme mahdollisimman laajaa osallistumista, jotta tutkimuksen tulokset olisivat luotettavia. Nokialaisten lisäksi lomakkeita lähetetään myös Kangasalan asukkaille. Useimpia heistä Nokian vesiepidemia ei koskenut. Kangasalaisten osallistuminen kyselyyn on tärkeää, jotta nokialaisten antamia vastauksia voidaan vertailla väestöön, joka ei kokenut vesiepidemiaa.
Antamanne vastaukset käsitellään luottamuksellisesti. Tuloksia julkistetaan pelkästään koko ryhmää koskevina. Teitä ei voida julkistettavista tuloksista yksilönä tunnistaa.

Täyttöohjeet: Lomakkeen kysymykset koskevat sitä henkilöä, jolle kysely on lähetetty, vaikka perheestänne muutkin olisivat sairastuneet. On hyvin tärkeää, että vastaatte lomakkeen kaikkiin kysymyksiin huolellisesti, vaikka osa kysymyksistä sopisi huonosti omaan tilanteeseenne.
Pyydämme palauttamaan lomakkeen ja allekirjoitetun suostumuksen mahdollisimman pian, mutta viimeistään 23.2.2009 mennessä oheisessa palautuskuoressa.

Kiitos avustanne!
Lisätietoja: Terveyden ja hyvinvoinnin laitoksesta ma-pe klo 8-16 numerosta 020 610

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Ylilääkäri	Tutkimusprofessori	Osastonylilääkäri
Nokian kaupunki	Terveyden ja hyvinvoinnin laitos	Pirkanmaan sairaanhoitopiiri

NOKIAN kaupunki

TERVEYDEN JA HYVINVOINNIN LAITOS

PIRKANMAAN SAIRAANHOITOPIIRI
Yhdessä terveyttä

Kyselylomake

Ohje: ympyröikää tai rastittakaa sopiva vaihtoehto.

0. Täyttöpäivämäärä: _____ . _____ . 2009

Lomakkeen täyttäjä:
1 Henkilö, jolle lomake on osoitettu
2 Hänen omaisensa tai huoltajansa

1. Sukupuoli:
1 Mies
2 Nainen

Ikä: _____ vuotta

2. Siviilisääty
1 Naimisissa tai avoliitossa
2 Eronnut tai asumuserossa
3 Leski
4 Naimaton

3. Mikä seuraavista vaihtoehdoista kuvaa parhaiten pääasiallista toimintaanne **tällä hetkellä**? Valitkaa vain yksi vaihtoehto.
1 Kokopäivätyö
2 Osa-aikatyö tai osa-aikaeläke
3 Opiskelija tai koululainen
4 Eläkkeellä
5 Työtön tai lomautettu
6 Hoitamassa omaa kotitaloutta tai perheenjäsentä
7 Varusmies- tai siviilipalvelu
8 Alle kouluikäinen lapsi
9 Muu

4. Kuultuanne Nokian vesiepidemiasta, muutitteko tottumuksianne? Valitkaa kaikki vaihtoehdot.

	En	Kyllä, jonkin aikaa	Kyllä, jatkan yhä
Muutitte ruokailutottumuksianne	☐	☐	☐
Lisäsitte pulloveden kulutusta	☐	☐	☐
Lisäsitte käsidesinfiointiaineen käyttöä	☐	☐	☐
Vähensitte vesijohtoveden kulutusta	☐	☐	☐
Harkitsitte muuttoa toiselle paikkakunnalle	☐	☐	☐

5. Sairastuitteko vatsatautiin, johon kuuluu oksentelua tai ripulointia (vähintään 3 kertaa vuorokaudessa), **joulukuussa 2007**?
1 Ei
2 Kyllä

6. Oliko teillä vatsatautinne jälkeen jotain alla mainituista oireista? Kauanko ne jatkuivat? Merkitkää kesto viikkoina tai kuukausina.

	Kyllä	Kesto		Jatkuu yhä
Tavallisuudesta poikkeavaa vatsan löysyyttä	☐	_____ vk	_____ kk	☐
Vatsakipua	☐	_____ vk	_____ kk	☐
Näkyvää verta ulosteessa	☐	_____ vk	_____ kk	☐
Pahoinvointia	☐	_____ vk	_____ kk	☐
Vatsan turvotusta	☐	_____ vk	_____ kk	☐
Ummetusta	☐	_____ vk	_____ kk	☐
Kipuja niveliä liikuteltaessa	☐	_____ vk	_____ kk	☐
Nivelturvotusta, -kuumotusta, tai -punoitusta	☐	_____ vk	_____ kk	☐
Selkäkipuja levossa	☐	_____ vk	_____ kk	☐
Käyttänyt kipulääkkeitä selkä- tai nivelkipujen vuoksi	☐	_____ vk	_____ kk	☐

7. Esiintyikö teillä vuoden 2008 aikana seuraavia oireita? Rastittakaa kaikki ne kuukaudet, jolloin muistatte oireita esiintyneen. Merkitkää viimeiseen sarakkeeseen, mikäli oireenne jatkuvat yhä. Merkitää kaikki oireet riippumatta siitä, ovatko ne uusia, viime vuoden aikana ilmaantuneita, tai vanhempia.

	Ta	He	Ma	Hu	To	Ke	He	El	Sy	Lo	Ma	Jo	jatkuu
Päänsärky/migreeni	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Huimaus	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Muistihäiriö	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Jännitys- tai pelkotila	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Rintakipu	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	Ta	He	Ma	Hu	To	Ke	He	El	Sy	Lo	Ma	Jo	jatkuu
Väsymys	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ihottuma	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Hengenahdistus	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Yskä tai nuha	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Silmätulehdus	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	Ta	He	Ma	Hu	To	Ke	He	El	Sy	Lo	Ma	Jo	jatkuu
Närästys tai mahakatarri	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ripuli tai ummetus	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Virtsaamisvaiva	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Virtsatietulehdus	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Niska- tai hartiavaiva	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

7. (jatkuu)

	Ta	He	Ma	Hu	To	Ke	He	El	Sy	Lo	Ma	Jo	jatkuu
Selkävaiva	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Painon nousu	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Painon lasku	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Univaikeus	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Seksuaalisen kanssakäynnin ongelmia	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

8. Mitä muuta terveydentilaanne liittyvää haluatte tässä sanoa: _____

_____

_____

Seuraavaksi toivomme teidän vastaavan kysymyksiin, jotka koskevat elämänlaatuanne ja mielialaanne. Mikäli henkilö, jolle lomake on osoitettu on alle 12-vuotias, siirtykää kysymykseen 21.

9. Oletteko viime aikoina pystynyt keskittymään töihinne?
- 0 Paremmin kuin tavallisesti
- 1 Yhtä hyvin kuin tavallisesti
- 2 Huonommin kuin tavallisesti
- 3 Paljon huonommin kuin tavallisesti

10. Oletteko viime aikoina valvonut paljon huolien vuoksi?
- 0 En ollenkaan
- 1 En enempää kuin tavallisesti
- 2 Jonkin verran enemmän kuin tavallisesti
- 3 Paljon enemmän kuin tavallisesti

11. Onko teistä viime aikoina tuntunut siltä, että mukana olonne asioiden hoidossa on...
- 0 Tavallista hyödyllisempää
- 1 Yhtä hyödyllistä kuin tavallisesti
- 2 Vähemmän hyödyllistä kuin tavallisesti
- 3 Paljon vähemmän hyödyllistä kuin tavallisesti

12. Oletteko viime aikoina tuntenut kykenevänne päättämään asioista
- 0 Paremmin kuin tavallisesti
- 1 Yhtä hyvin kuin tavallisesti
- 2 Huonommin kuin tavallisesti
- 3 Paljon huonommin kuin tavallisesti

13. Oletteko viime aikoina tuntenut olevanne jatkuvasti rasituksen alaisena?
- 0 En ollenkaan
- 1 En enempää kuin tavallisesti
- 2 Jonkin verran enemmän kuin tavallisesti
- 3 Paljon enemmän kuin tavallisesti

14. Onko teistä viime aikoina tuntunut siltä, ettette voisi selviytyä vaikeuksistanne?
- 0 Ei ollenkaan
- 1 Ei enempää kuin tavallisesti
- 2 Jonkin verran enemmän kuin tavallisesti
- 3 Paljon enemmän kuin tavallisesti

15. Oletteko viime aikoina kyennyt nauttimaan tavallisista päivittäisistä toimistanne?
0 Enemmän kuin tavallisesti
1 Yhtä paljon kuin tavallisesti
2 Vähemmän kuin tavallisesti
3 Paljon vähemmän kuin tavallisesti

16. Oletteko viime aikoina kyennyt kohtaamaan vaikeutenne
0 Paremmin kuin tavallisesti
1 Yhtä hyvin kuin tavallisesti
2 Huonommin kuin tavallisesti
3 Paljon huonommin kuin tavallisesti

17. Oletteko viime aikoina tuntenut itsenne onnettomaksi ja masentuneeksi?
0 En ollenkaan
1 En enempää kuin tavallisesti
2 Jonkin verran enemmän kuin tavallisesti
3 Paljon enemmän kuin tavallisesti

18. Oletteko viime aikoina kadottanut itseluottamuksenne?
0 En ollenkaan
1 En enempää kuin tavallisesti
2 Jonkin verran enemmän kuin tavallisesti
3 Paljon enemmän kuin tavallisesti

19. Oletteko viime aikoina tuntenut itsenne ihmisenä arvottomaksi?
0 En ollenkaan
1 En enempää kuin tavallisesti
2 Jonkin verran enemmän kuin tavallisesti
3 Paljon enemmän kuin tavallisesti

20. Oletteko viime aikoina tuntenut itsenne kaiken kaikkiaan kohtalaisen onnelliseksi?
0 Enemmän kuin tavallisesti
1 Yhtä paljon kuin tavallisesti
2 Vähemmän kuin tavallisesti
3 Paljon vähemmän kuin tavallisesti

Seuraavat kysymykset nro 21 ja 22 koskevat koko talouttanne / perhettänne

21. Asutteko **tällä hetkellä** likaantuneen veden alueella Nokialla
1 Ei
2 Kyllä

22. Oletteko te tai perheenne, Nokian vesiongelman takia: (valitkaa kaikki sopivat vaihtoehdot)

	Ei	Kunnalta tai valtiolta	Yksityisestä sairasvakuutuksesta	Muualta
Hakenut korvausta	☐	☐	☐	☐
Hakenut korvausta, muttette **vielä** saanut	☐	☐	☐	☐
Hakenut korvausta, mutta hakemus hylätty	☐	☐	☐	☐
Saanut korvausta	☐	☐	☐	☐

Kiitos avustanne!

23. Voimmeko ottaa teihin myöhemmin yhteyttä jos on tarvetta?

1 Ei
2 Kyllä

Puhelin: _____

Lisätietoja: _____

THL:n kappale – palautetaan

Vesiepidemia Nokialla vuonna 2007
– kyselytytkimus myöhäisten ja pitkäkestoisten seurausten selvittämiseksi

Olen saanut kirjallista tietoa Nokian vesiepidemian seurauksia selvittävästä kyselytutkimuksesta. Tutkimusta koskevia kysymyksiä voin esittää puhelimitse tiedotteessa ilmoitettuun puhelinnumeroon.

Ymmärrän, että tutkimukseen osallistuminen on vapaaehtoista ja että minulla on oikeus kieltäytyä siitä milloin tahansa syytä ilmoittamatta. Ymmärrän myös, että tiedot käsitellään luottamuksellisesti.

Jos kyselylomakkeen saaja on alle 18-vuotias, kyselylomake tulee näyttää myös huoltajalle. Alle 18-vuotiaan saaman lomakkeen allekirjoittaa sekä huoltaja että alaikäinen lomakkeen vastaanottaja, jos hän on ikänsä puolesta siihen kykenevä.

Suostun osallistumaan tutkimukseen:

Nokialla/Kangasalla . .2009

Vastaajan allekirjoitus

Nimenselvennys

Alle 18-vuotiaan vastaajan huoltajan allekirjoitus

Nimenselvennys

Oma kappale – revi irti

Vesiepidemia Nokialla vuonna 2007
– kyselytytkimus myöhäisten ja pitkäkestoisten seurausten selvittämiseksi

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