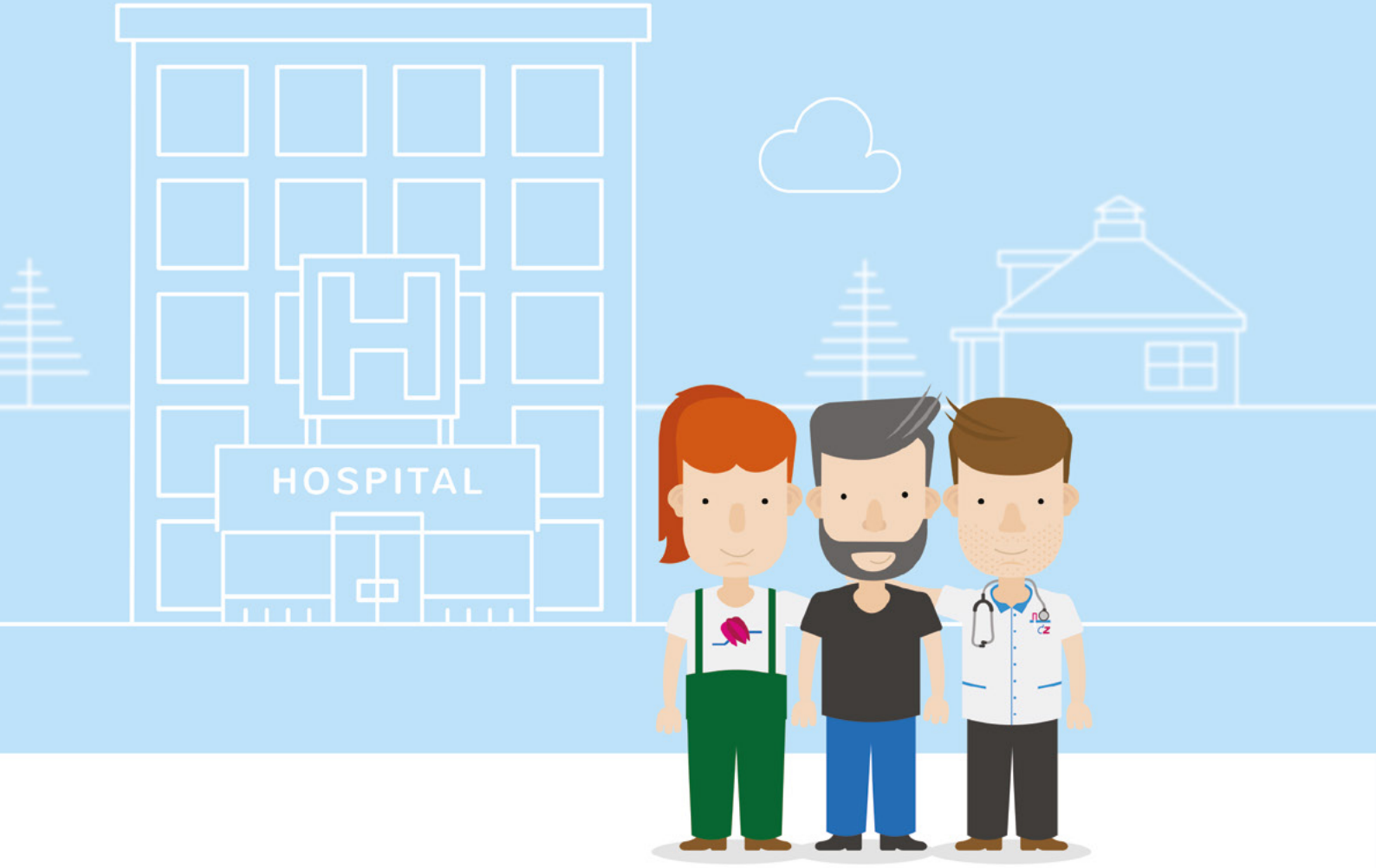
Getting a grip on drug residues in our waters

Final report



A collaborative project from

Groot Salland
UW WATERSCHAP

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16 December 2015

Credits

Getting a grip on drug residues in our waters
A report on a source-oriented approach to drug residues in our waters
Zwolle, Water Authority Groot Salland, 2015

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Getting a grip on drug residues in our waters

Final report

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Preface

Prevention is better than cure. If medicine residues do not end up in waste water then they do not need to be removed. We thus investigated whether medicine users would be willing to cut their contribution to medicine residues in our water, and how this behavioural change would impact upon the waste water itself.

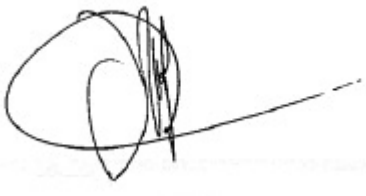
A previous project by Water Authority Groot Salland had shown that advanced techniques could be employed to remove medicine residues from waste water. The technical complexity and the corresponding investment costs for this solution were the motivation for considering an approach that focuses on the source of the problem, i.e. the person. The water board thus created a cooperative partnership with Deventer Hospital. The fact that the hospital wanted to substantiate their goals with respect to sustainability meant that this approach was a logical step for them too.

This required both organisations to cooperate on the boundaries of our core tasks. With support from Wageningen UR, the social study was set up and executed in the Radiology department in Deventer Hospital.

We are both very enthusiastic about the results and the collaboration. Mutual appreciation has been expressed regarding the positive attitude, flexibility and commitment that were clear throughout the project. In line with this, we would also like to thank the patients, research staff and other relevant members of staff in Deventer Hospital and Water Authority Groot Salland for their efforts. Thanks to them, we can look back on a successful collaboration and some great research results. We would like to invite you to read this report on how we approached the research, the results and conclusions, what we have learned as a result and how we now wish to proceed. This project is a first step in a sustainable future with even cleaner water.

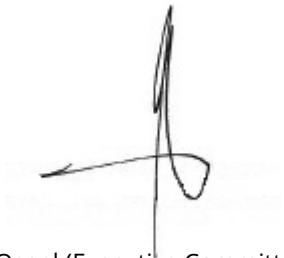
We hope you enjoy reading our report.

On behalf of Deventer Hospital,



Jeroen Kleinjan (Board of Directors)

On behalf of Water Authority Groot Salland,



Jan Oggel (Executive Committee)

Summary

Medicine usage in the Netherlands rose by almost 3% in 2014 and will continue to increase in the coming years due to the ageing population. Medicines end up in the sewerage system and surface water via urine and faeces. The current waste water treatment plants are inadequate in terms of removing this type of micropollutant. The impact of this form of micropollutant on the ecological water quality and the mixtures that are formed with other substances in the water are currently unknown. Nevertheless, the measured concentrations and effects that have so far been identified are ringing alarm bells in the Netherlands and the rest of Europe. The Dutch government is arguing for a strategy across the entire medication chain. The problem with medicine residues in surface water is not just a problem for the water managers and must be tackled chain-wide. The European Commission is expected to have drafted a strategic approach by 2016 and a package of measures two years later. Within Europe, various studies are taking place in order to provide building blocks for this strategic approach and policy development. The results of the ' Getting a grip on drug residues in our waters' project that are elaborated in this report, could also provide an important contribution.

Research set up

In the project 'Getting a grip on drug residues in our waters', the focus lies on the beginning of the medicine chain. The aim was to investigate the extent to which patients are willing to contribute towards reducing medicine residues in water. The structure chosen was a study whereby CT-scan patients were asked to change their toilet behaviour. These patients were administered x-ray contrast agent prior to their scan. In ordinary circumstances, that would have been excreted via urine within 24 hours and would thus end up in the surface water. The patients were approached by a research assistant after their scan, however, and asked if they would collect their urine in urine bags for 24 hours. The patients could dispose of these bags with their 'grey' household waste and they would then be incinerated by the waste processing company. Measurements took place at the waste water treatment plant in Deventer to measure the effect of the study on the quantities of x-ray contrast agent in the waste water.

Results

During the research period, 1,224 patients were asked to complete a questionnaire. 68% of them returned it. Of these respondents, 85% said that they had used one or more urine bags. Respondents were overwhelmingly positive with respect to experiences with the urine bag and their intention to use the urine bag in the future. The project partners were pleasantly surprised by these findings. Important success factors in the research structure include the personal approach to patients by research assistants,

the fact that the research was carried out in a hospital setting and the fact that the period covered was just 24 hours. Simultaneously, theoretical calculations suggest that the load at WWTP Deventer in the trial period reduced by one quarter. As a result of complicated factors, that came to light during the trial period, it was not possible to support the calculations with impact measurements and a full mass balance.

Recommendations

The findings from this study lead to recommendations for both the care and water sectors. These recommendations are:

- Hospitals that are working or wish to work with the 'Milieuthermometer Zorg' (Healthcare Environmental Thermometer) can include the findings in improvements for the environmental aspect 'waste water'.
- Water managers are advised, with respect to similar measurement studies, to investigate whether a full mass balance can be set up prior to the study.
- Water managers and hospitals should work together in subsequent studies into the practicality of urine bags, in order to reduce medicine residues in water.

Glossary

Flow
The flow is the average quantity of water that passes a specific point per time unit, expressed in cubic metres per second (m^3/s).

Influent
Waste water that is supplied for processing at a waste water treatment plant. This waste water comes from households, businesses and also from rainwater and is supplied to the purification installation via the sewers. After purification the water is referred to as effluent.

Iodixanol
Iodixanol is an x-ray contrast agent that contains iodine; it is given to the patient so that specific parts of the body are visible on an x-ray or scan.

Micropollutant
Pollution that is of a limited quantity but is undesirable due to its hazardous properties. It is a collective name for a large group of substances with various applications and diverse chemical characteristics. It concerns, for example, medication, hormones, softeners, fire-retardants, pesticides, UV filters and microplastics

Non-respondents
Persons who do not respond to a survey.

Baseline situation
In scenario studies, this refers to the current situation, i.e. the situation without further interventions. It is also called a zero/baseline measurement, to which later measurements can be related.

Polyclinic patients
Polyclinic patients are out-patients who may go home after a treatment or intervention and are not, therefore, admitted to hospital.

Respondents
Persons who do respond to a written survey.

Waste water treatment plant

In a waste water treatment plant (WWTP), the waste water from sewers is treated before it ends up in the surface water. The incoming dirty water (see influent) is treatedvia a number of processes that take place in the installation. One after the other, contaminants are removed via a grille or separation well to remove large particles, then settlement tanks to remove smaller particles and finally the soluble substances are removed using specific bacteria.

WWTP

See waste water treatment plant.

Load

The quantity of a substance in grams.

1 Introduction

1 Introduction

1.1 Background and context

1.1.1 Increasing medicine usage

Medicines have been developed so that they can have an effect on man and animals at relatively low concentrations. In the Netherlands, at the moment, there are almost 22,000 trading permits for human medicines, involving around 1,000 different active substances (B. Klijn, personal communication, 10 October 2014; Nefarma, 2013; RIWA/RIZA 2001). Of these active substances, using the available measurement methods, around 200 have been identified in the environment[1], some of which are regularly found in the water chain (Derksen and Ter Laak, 2013). Medicine usage has risen substantially over the past few years and is expected to keep on increasing. This is primarily due to the fact that the population is ageing. Between 1 January 2014 and 1 January 2015, the number of people aged over 65 rose by 3% and medicine usage rose by 2.9%. According to population forecasts by the CBS, the ageing process will reach a climax in 2040, with the share of people aged over 65 reaching 26.4% The impact of this is clear from the pharmacies. Public pharmacies hand out three times as many medicines to those over 65 as they do to the average Dutch person, usually for chronic disorders (SFK, 2015).

1.1.2 Medicine residues in water

Once they have taken effect, medicines must then be excreted. Excretion via the urine (± 80%) and/or faeces (± 20%) leads to the original medicine, together with the corresponding metabolites, and via residential sewers, ending up in waste water treatment plants (referred to hereafter as: WWTP's) (Derksen and Ter Laak, 2013). Despite the fact that the current WWTP's are not set up to remove micropollutants such as medicines, this does occur to a lesser or greater extent (metformin ± 90% and carbamazepine ± 9% - average 65%[2]). It all depends on the physical-chemical properties of the medicine and the specifications of the water treatment (STOWA 2011a). The rest of the medicine residues are discharged into surface water via effluent. Surface water concentrations of medicine residues usually lie between a few nanograms and a few micrograms per litre. In general the highest concentrations are found in smaller waters and in waters with a high level of WWTP-effluent (Grontmij, 2008; STOWA, 2011b; Derksen and Ter Laak, 2013; Laak et al., 2013; BIO Intelligence Service, 2013). Legal frameworks are lacking and there is currently (still) no policy for tackling this form of micro-contamination. A few medicines have been placed on the so-called European Watchlist and, for this reason, are being widely monitored (European parliament, 2013).

1 Newer measurement methods can now measure >1,000 substances (Wode et al., 2015)

2 This 65% removal rate is based on measurements at eight treatment plants for 27 medicines that are detected above the reporting limit (STOWA, 2011a)

In some cases, it has been shown that medicines in very low concentrations have a detrimental impact on water organisms in surface water. In addition, water organisms are continuously exposed, over their lifetimes, to a mixture of multiple (decomposition products) medicines (and other substances) (Derksen and Ter Laak, 2013). Consideration must also be made of the possible accumulation in organisms, mixture toxicity and the creation of (active) decomposition products (STOWA, 2014). Man is also exposed to medicine residues that can be regularly detected in our drinking water, despite the advanced purification techniques that drinking water companies use to turn their sources (sometimes surface water) into drinking water. The concentrations of individual medicines in Dutch drinking water are so low (a few ng/L) that health risks are very unlikely (Schriks et al., 2010; Derksen and Ter Laak, 2013; Houtman et al., 2014). Given the effects of continuous exposure to (mixtures of) low concentrations of medicine residues are unknown, however, the possible risks must not dismissed out of hand. The perception of the user must also be considered: we don't want substances like that in our water.

1.1.3 Central government and the EU - forming a vision

The fact that medicine residues have been shown in Dutch waterways since the end of the 1990's was the provocation for the Health Council[3] (Gezondheidsraad) to issue a recommendation which asks for attention to be paid to the presence and risks of medicine residues in water (Gezondheidsraad, 2001) A working group '(animal) medicines in the environment' was then created, various exploratory (monitoring) studies took place and this topic was discussed at length in the House of Representatives (House of Representatives, 2007; House of Representatives, 2009; House of Representatives, 2012; House of Representatives, 2013; House of Representatives, 2014a&b&c; House of Representatives, 2015a&b). Annex 1 provides comprehensive descriptions of the policy developments (European and national) over the past few years. The government is now applying a chain-approach whereby a source-based method at the beginning of the medicine chain (see §1.1.4) is encouraged, supplemented with measures at the end of the chain. Former Secretary of State Mansveld has taken steps to stimulate a source-focussed approach among hospitals, pharmacies, the pharmaceutical industry and the water sector (House of Representatives, 2014b&c).

Given the ambitions and complexity of the water quality policy, Minister Schultz van Haegen requested advice on this topic from the Dutch Water Advice Committee (AcW) in 2015. According to the AcW, it is necessary to first create agreement between all parties about the degree of urgency and collectively recognise the problems (AcW, 2015). This requires a national approach with greater direction. The Minister, in a letter to the House of Representatives, then indicated that he would provide direction and that the definitive

3 The Health Council has been an advisory body since 1902 and is tasked with 'providing information on the scientific situation with respect to issues relating to public health' to the government and parliament(art. 21 Health Act) (Health Council, 2001)

advice from the AcW (end 2015) would be used to further substantiate and execute the water quality policy (House of Representatives, 2015b)

An interdepartmental working group, set up by and under the directorship of the Ministry of Infrastructure and Environment (I&M) is currently working on the development of an action plan for medicine residues in the chain. This is expected to be presented to the Minister at the beginning of 2016 (C. Blom, personal communication, 17 August 2015).

The above developments connect into the coverage that this topic has had at a European level in the context of the Water framework directive. This directive has been in force since the end of 2000, with the aim that good chemical and ecological surface water quality will be achieved by 2027 (European Parliament, 2000). The latest amended directive (Directive 2013/39/EU), also states that the European Commission will deliver a strategic approach for medicine contamination in water by September 2015 (has been delayed; dated October 2015 and not yet issued). In addition, the European Commission, in the context of this strategic approach and if appropriate, must draw up a proposal for a package of measures in 2017 (European Parliament, 2013).

1.1.4 A chain problem

Medicines can be a threat to aquatic life. This is a chain-wide problem, not only one for the water managers. That is why every chain player must make a contribution to the solution to this collective problem. The National Institute for Public Health and the Environment (RIVM) has set out the points at which the medicines are getting into the environment (figure 1). These are also the points at which measures could be taken. In annex 2, these intervention points (A to O) and the corresponding possible measures have been further detailed (RIVM, 2015).

There are currently many studies going on into the various solution areas for the different components of the chain. The pharmaceutical industry is principally focussing on points A and E. The EFPIA (European umbrella organisation for innovative pharmaceutical industry) has developed an Eco Pharmaco Stewardship (EPS), a platform for discussions about medicine residues in the environment (Ministry of Infrastructure and the Environment, 2015) An important element of this EPS is the proposal to monitor the environmental impact of medicine residues over a longer period. Some of the information about the environmental impact will also be improved. The EFPIA has also announced a publicity campaign with the title 'Don't flush drugs', whereby consumers will be encouraged to dispose of medicines they do not need responsibly instead of putting them down the drain or toilet.

The healthcare sector is focussing on point D. The Ministry of Health, Welfare and Sport (VWS) started the programming 'Waste in Healthcare' in 2013. Within this programme, around fourteen organisations are working on a range of activities. These are focussed

on topics such as unnecessary left-over medicines, the re-issuing of medicines and treatment tailored to and with the patient (House of Representatives, 2015a).

The UMC Utrecht and University of Utrecht are also working on the options for environmental labelling of medicines. This would allow medicines with a similar effect but a different environmental impact to be given a different label. This targets point C in the chain. In Sweden, there is a similar environmental classification system (SECIS[4]).

Several hospitals, water boards and drinking water companies are also focussing on measures in relation to points I and O. This concerns the (decentralised) purification of medicine residues from water (UvW and Vewin, 2014). One of the examples of decentralised purification is the Pharmafilter concept that has already been implemented in the Reinier de Graaf Hospital in Delft and will soon also be introduced to a hospital in Terneuzen and two in Rotterdam (Pharmafilter, 2012). This is an integrated concept for improving healthcare and waste processing in hospitals, nursing homes and other healthcare centres. In this context, these institutions have a local waste water purification plant. This water purification system removes medicine residues from water.

Another example of decentralised purification is the trial installation in the Antonius Hospital in Sneek. A five-year pilot has been running here since spring 2014; this enables techniques to be tested for purifying waste water from the hospitals. Prior to

Figure 1:

Medicine chain. How do medicines end up in the environment? (RIVM, 2015).

- **A.** Development and production;
- **B.** Access to the market;
- **C.** Purchasing and sales by pharmacies;
- **D.** Prescription and use;
- **E.** Disposal with household waste;
- **F.** Disposal via sewerage system;
- **G.** Collection of unused medicines;
- **H.** Collection of household waste;
- **I.** Treatment of sewerage water;
- **J.** Dump for household waste;
- **K.** Incineration of household waste and sludge;
- **L.** Sewage sludge used in agriculture (not in NL);
- **M.** Treated waste water is discharged into surface water;
- **N.** Small chemical waste is incinerated;
- **O.** Drinking water companies supply water.

4 Swedish Environmental Classification and Information System for pharmaceuticals – www.fass.se (currently only available in Swedish)

this, Water Authority Groot Salland carried out the European PILLS[5] project between 2008 and 2012, in collaboration with bodies such as the Isala klinieken (hospital in Zwolle, The Netherlands) and Vitens. A compact and innovative waste water purification system has been built at the water board site to specifically focus on more effecitvely removing medicine residues from the waste water from the neighbouring Isala clinics. Other European initiatives such as TAPES[6], DEMEAU[7] and SOLUTIONS[8] focus on technical measures and the design of instruments to support decision-making.

A European initiative that has focussed on the user/patient (D - after administration - to F) is the follow-up to PILLS, called noPILLS. This European project concentrates on source reduction and awareness. Project partners were two German water boards, universities from Limoges (France) and Glasgow (Scotland), a scientific and technological research body from Luxembourg and the Dutch RIVM. In the period between 2012 and 2015, public campaigns (D-E) were carried out in France, Germany and Scotland to increase societal awareness of the consumption and removal of medicines (noPILLS, 2015). It was thus concluded that the ordinary citizen as patient and employees from the care sector are receptive to the idea of helping to reduce the impact of medicine residues on the environment. Everyone has a clear opinion on the (over) consumption of medicines and they would like clear, accessible and consistent information about correct usage and disposal. There is also a willingness among the public at large to 'do the right thing'.

noPILLS also carried out a two-week urine separation campaign with urine bags (F) in two hospitals (Germany and Luxembourg). The conclusion is that it is possible to introduce procedures for separated urine into radiology departments (requires five to ten minutes extra per patient) and that the active involvement of the medical personnel is the key for efficiency. There is also a clear need for information for medical personnel regarding the impact of medicine residues on the environment.

The most effective approach to medicine residues in our water is expected to be a combination of measures at the beginning and end of the chain, or management across the entire chain (see figure 1). Local and regional studies can make a significant contribution towards the development of this all-in approach. Research can further develop expertise in this area, provide insights into which measures can be taken and where and also how effective they are. As a result, possible relevant building blocks will be created for the development of an integrated approach with measures focused on both the beginning and end of the chain. The project 'Getting a grip on drug residues' provides a building block via an intervention in the chain by the medicine user themselves (F). The options and bottlenecks with regard to an approach at the end of the chain are thus explored.

5 Pharmaceutical Inputs and eLimination from Local Sources. European project in which the removal of medicine residues from waste water was the central point, focussing on so-called 'end-of-pipe measures'.

6 Transnational Action Program on Emerging Substances - http://www.tapes-interreg.eu/

7 Demonstration of promising technologies to address emerging pollutants in water and waste water - http://demeau-fp7.eu/

8 Solutions for present and future emerging pollutants in land and water resources management http://www.solutions-project.eu/

1.2 Provocation and problem outline

The direct provocation for 'Getting a grip on drug residues in our waters' was the PILLS project outlined above. The technical complexity and the necessary investment costs linked to the separate purification of hospital water were the provocation for considering an approach that focuses on the source of the problem, i.e. the person. Water Authority Groot Salland thus explored the options for cooperation with Deventer Hospital. This hospital is very enthusiastic about the source approach and would like to actively substantiate its social role in this context. The project is not part of the European noPILLS project but does connect into the corresponding goals and method. If it transpires that the approach of the underlying research is successful, these results could also contribute towards the reduction of emissions of other micropollutants into surface water.

1.3 Reading guide

The research structure will be elaborated in chapter 2. In §2.1, the main questions will be formulated and the corresponding objective and hypothesis will be set out. §2.2 will cover delineation, detailing which choices were made and how this came about. Finally, §2.3 explains the ultimate working method which was actually used prior to and during the research period.

Chapter 3 presents the results. This chapter comprises two sections: the results of the study of CT patients in Deventer Hospital and the result of the study into the impact on waste water quality by WWTP Deventer.

Chapter 4 concludes the results as set out in chapter 3, sets out learning points from this research and makes connections to the future; where do we go from here? This chapter provides the plans for the two cooperative partnerships in this project and outlines the recommendations for hospitals and water managers regarding how this research could be significant to them. A number of possible follow-up studies are also elaborated.

The annexes contain supplementary information about policy development regarding water quality in the Netherlands and Europe (annex 1), possible action points for measures in the medicine chain according to the RIVM (annex 2), the working instruction for Deventer Hospital research assistants (annex 3), information about the Chronbach's alpha test used to analyse results (annex 4) and a map of the sewerage systems in Deventer (annex 5).

2
Research

2 Research

2.1 Goal

The project 'Getting a grip on drug residues in our waters' studies the following central question:

> *Are patients prepared to make a contribution to prevent or reduce medicine residues in waste water?*

The aim is to investigate where an intervention can be made in the chain and if end-of-pipe measures transpire to be insufficient or are limited in terms of resolving the problem of medicine residues in waste water. Research also covered the extent to which the impact of this intervention can be measured in the waste water (influent).

For the purposes of the central questions, a decision was made to approach polyclinic patients who were to undergo a CT scan in Deventer Hospital and were therefore given x-ray contrast agent. They were asked to collect their urine in a urine bag for a period of 24 hours and then dispose of them with the 'grey' waste for incineration. Little is known about the environmental load that corresponds to this process but, as a result of conversations with environmental and waste processing experts, it is estimated that this waste route is less environmentally damaging than draining x-ray contrast agent into surface water. The hypothesis is that the research will result in an effective method for behavioural change and awareness-raising. We also hope, on the basis of results, to be able to make a statement on the scalability of this method(s) to other substance groups and/or medicine users, e.g. cytostatic drugs (for cancer prevention) or chronic medicine users, such as those with diabetes.

During the study, the focus lay on this social aspect. Wageningen UR provided sociological expertise and support with respect to the structure and working method of the research. The study's secondary aim was to measure the effect of intervention in waste water.

2.2 Research set-up and delineation

The method of approaching patients within a hospital was chosen because it is relatively easy to control the environment compared to approaching medicine users in residential areas. Despite the fact that the highest loading of medicines comes from residential areas (Le Corre et al., 2012: Hermann et al., 2015), the distribution of medicine users is greater there and it would be more difficult to approach them. With a small-scale study on an individual level, the success factor of the hospital-based approach is greater.

2.2.1 X-ray contrast agent as medicine group

In the study, x-ray contrast agent was used as the medicine group due to the high loads and concentrations observed in the water environment. Although this group of substances is less relevant in terms of toxicity compared to medicines such as cytostatic drugs, the load of x-ray contrast agents that end up in the WWTP every year is as high as all other medicines put together (Grontmij, 2011).

The patients who were asked to participate in the study are polyclinic patients at Deventer Hospital who had been given the x-ray contrast agent iodixanol prior to a CT scan. The contrast agent iodixanol is the most frequently used agent for CT scans at Deventer Hospital. The agent is also primarily excreted via urine (97% within 24 hours), meaning that it can be almost entirely collected in the urine bags. The maximum concentration in the urine is reached within one hour. Clinical patients are not approached as these patients are generally bed-bound and need assistance to go to the toilet. As a result, the willingness of the patient is not being tested and the load is placed on the hospital staff.

2.2.2 Urine bags as aids

A urine bag was selected for urine collection (figure 2). It is available in both male and female versions. The urine bag contains gel beads that absorb urine so that it does not leak out. The bags can be disposed of with household waste and then incinerated by the waste processing company with the rest of the waste. These urine bag have also been used in similar research that was carried out as part of noPILLS (see §1.1.4 and §1.2). Other methods to keep medicine residues out of the water system are also under development. This concerns, for example, mobile toilets for the home for cytostatic drug users (Pharmafilter, 2012) and toilet blocks or toilet paper containing active carbon which absorbs the medicine residues (adhesion). Urine bags were chosen for the project because they are suitable for the patient and do not correspond to any risks.

Figure 2:

Urine bags used for this study

A. Male version

B. Female version

In order to research whether the use of urine bags impacted upon the quality of waste water, the incoming waste water (influent) at the RZWI Deventer was measured. Deventer Hospital is the most relevant source of iodixanol in the WWTP Deventer's sewerage area. Iodixanol is also used in a nearby radiotherapy centre. These quantities, however, are negligible (± 5%). It is also possible that patients who have been given iodixanol by another hospital have used the toilet within this sewerage system. This percentage is unknown but is also regarded as negligible.

A decision was made to run measurements alongside the regular sampling programme. This involves an alternating pattern, only on weekdays. A condition was that the postcodes of the polyclinic patients and the details of the iodixanol administered within Deventer Hospital were known during the trial period. These details were used to investigate whether a mass balance could be used to ascertain whether the use of urine bags had impacted upon the concentration of iodixanol in the incoming waste water at WWTP Deventer.

The study did not concentrate on the objectives outside the water authority's direct sphere of influence, such as reducing medicine consumption or influencing the production of medicine. Neither did this project focus on the development of end-of-pipe technology by the water authority, as was the focus in the PILLS project.

2.3 Working method

On 12 December 2014 a pilot study of eighteen CT scan patients was carried out to check whether the selected approach method (request for cooperation, time, place and method of address by research assistant[9], instruction for patients via written or audio-visual material) was feasible in practice. The response-friendliness of the questionnaire was also examined during the pilot. At the location, the participant completed a short questionnaire asking about gender, age, postcode, if any assistance is required to pass urine and contact details for a telephone call if there are unclear or missing details. The patients were then given a long questionnaire to take home and complete and then send back in the envelope provided, in order to find out:

- whether and how many urine bags had been used;
- the experiences of the patient with the urine bags;
- whether the willingness to use the urine bags corresponded to environmental concerns;
- how the patients felt about the approach used by the study;
- how patients felt about the issue of medicine residues in our water;

Patients who had chosen not to use the urine bags were also asked to complete the questionnaire. This was to demonstrate why patients had not been willing to

9 Specially selected and trained volunteers from Deventer Hospital.

participate. The analysis of the answers on the questionnaire form the most important element of the results.

On the basis of this pilot, the questionnaires were modified and the materials (use of urine bag) were chosen. The protocol for the research assistants was also drawn up (see annex 3) so that all patients would receive the same personalised approach. A personal approach to patients was selected because this was expected to produce a better response than simply handing out or sending a questionnaire. In addition, the topic (urinating) and the setting (the hospital, in which the results of a CT scan could drastically change somebody's life) lent themselves to the personal approach.

Data collection began on 26 January 2015, in Deventer Hospital. Polyclinic patients (see §2.2) who underwent a CT scan with the contrast agent iodixanol were informed by the CT technician that they would be approached in the waiting room by a research assistant regarding an ongoing study. Patients that have had a CT scan usually spend a little time in the waiting room afterwards due to possible side-effects from the contrast agent.

After the scan, the patients were approached by research assistants from the hospital with three requests:

1. completing a short questionnaire;
2. using a urine bag for 24 hours after the examination;
3. completing a longer questionnaire (regardless of whether they had used the urine bags).

The short questionnaire was completed in the waiting room and handed back to the research assistant. Patients were also given a bag containing information on the study, seven urine bags, the long questionnaire, a bottle of antibacterial hand gel, a ticket for a cup of coffee in the hospital restaurant and also a booklet for children on the subject of medicines in our water.

In the waiting room, from 13 February 2015, an animation[10] about medicine residues in waterways was played on the television. This short film was interchanged with a series of films about the hospital and CT/MRI scans. The number of patients who actually saw this animation is unknown[11].

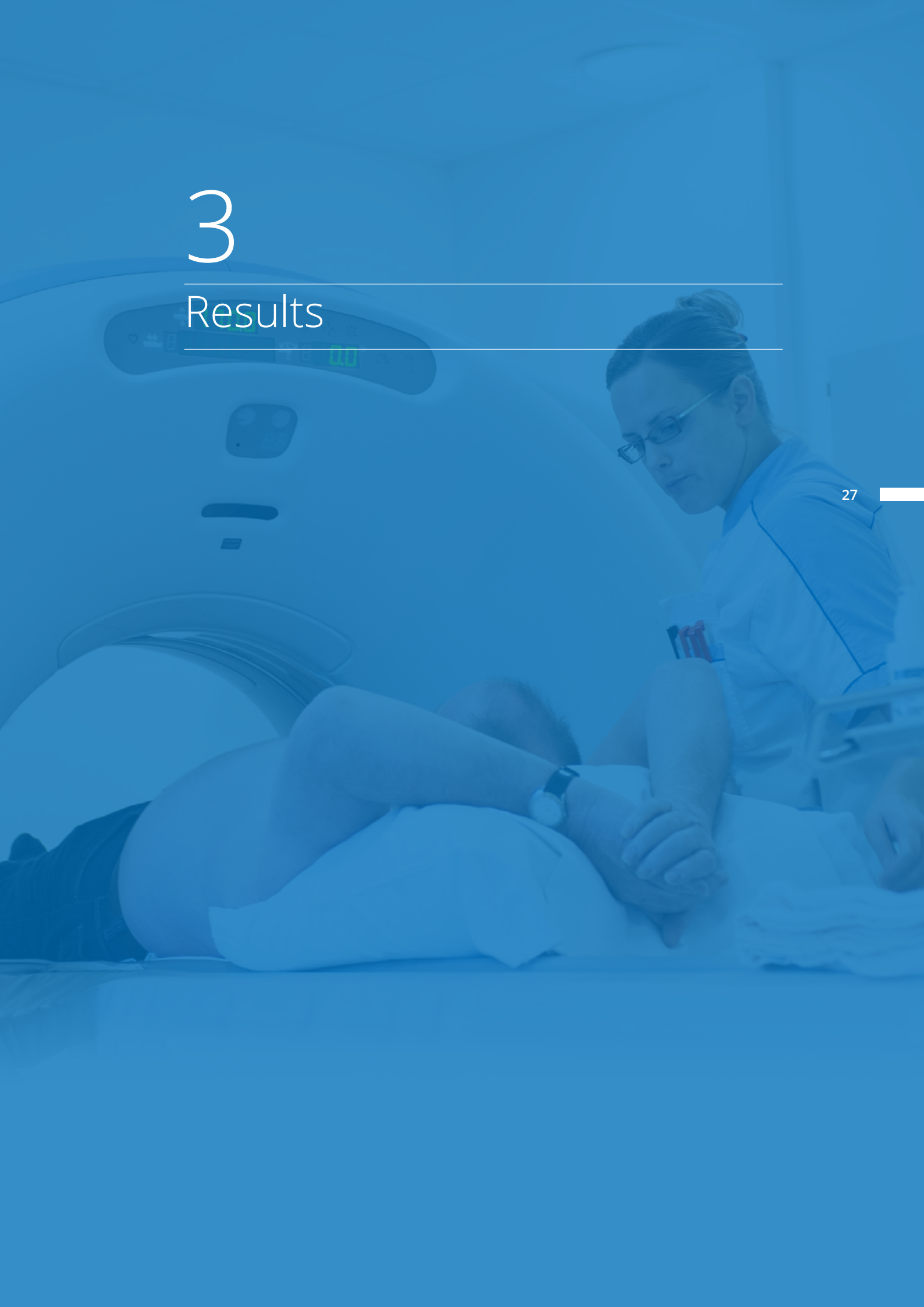
Patients who had not returned the long questionnaire a week after their CT scan and for whom a telephone number had been noted (from the short questionnaire) were called by a research assistant from the hospital. The protocol for this telephone component was to ask if they had used the urine bags (if so, how many; if not, why not), whether they were going to send the questionnaire back (if not, why not) and their response to the statement: 'Medicine users are asked to use urine bags too frequently'.

10 http://www.wgs.nl/schoon-water/grip-medicijnresten-0/achtergrond/grip-medicijnresten/

11 As a result of the setting of the waiting room (it was unclear which patients had seen the film or could see the film) and the limited space on the questionnaire, it was impossible to measure the impact of the film on the willingness to use urine bags.

In order to ascertain the extent to which behavioural change could be measured in the water, measurements were taken in the incoming waste water at WWTP Deventer. Samples were taken from this waste water (influent) for 24 hours; they were then analysed by the Aqualysis laboratory for the level of iodixanol. With the registered supply flow, the supplied loading in grams per day was calculated. For organisational and technical reasons, the influent quality was not sampled every day. A alternating pattern is followed which covers all working days at around the same ratio. In order to create a comprehensive mass balance, it was therefore important to be able to make reliable assumptions regarding influent quality on the days when no measurements were taken.

3
Results



3. Results

In this chapter the results are presented for both the research in Deventer Hospital among polyclinic CT patients (§3.1), and the effect measurements at WWTP Deventer (§3.2). The significance of this research for a source-focussed approach to medicine residues in waste water is further elaborated in chapter 4.

3.1 Are patients willing to do their part?

A CT scan that used iodixanol was carried out, on average, on around ten to fifteen polyclinic patients per day. On other days during the week, PET scans were also done using iodixanol. The frequency of these and numbers of patients varied per week. Research assistants were given an overview each day of all of the patients that were eligible for the research. For practical/organisational reasons (availability of research assistants, scans that were carried out simultaneously in different rooms), it was not possible to approach all patients for the study. In addition, some of the patients attended in the evening or at the weekend to be treated urgently and there were some who did not want to participate right from the start.

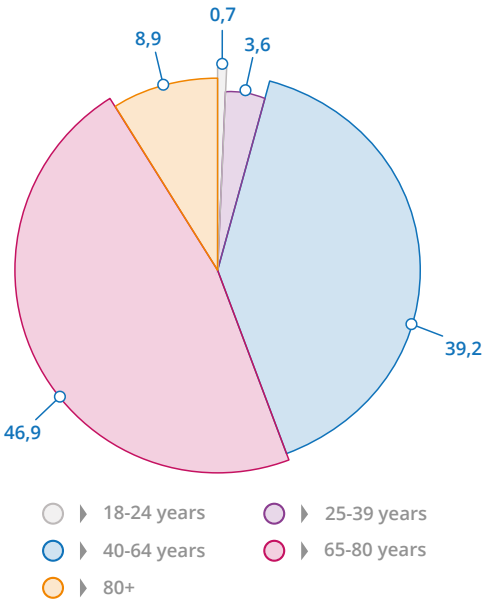


Figure 3:
Patient age groups

A total of 1,224 patients completed the short questionnaire. 831 patients filled out the long questionnaire as well as the short questionnaire (referred to hereafter as 'respondents'). This total figure includes the 193 patients that only sent the questionnaire back once they had been called by a research assistant from the hospital. This subsequent telephone contact turned out to be very effective: 47% (193 of the 411[12] patients who were contacted by phone) then returned the long questionnaire.

Not all respondents completed all of the questions. The results are based on the answers given. Missing answers were omitted per answer. Of the 831 people who completed the long questionnaire, 56% were male and 44% female. The age division among respondents is shown in figure 3.

12 478 telephone follow-ups, of which 67 involved 'no contact' being made.

3.1.1 Use of urine bags and experiences

Reported use

Of the 831 respondents that completed the long questionnaire, 708 respondents (85%) indicated that they had used one or more bags. During the subsequent telephone call follow-up, it was found that 105 patients who had sent the questionnaire back had used one or more urine bags.

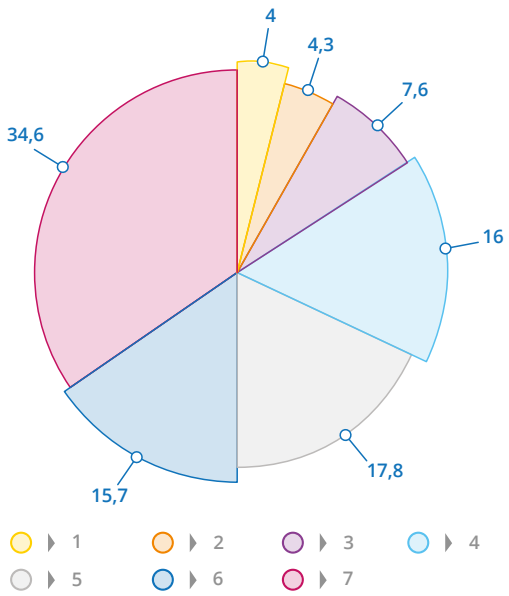


Figure 4:
Number of urine bags used

Of all of the respondents, 99% indicated that they had not needed any assistance when using the urine bags. Of the 24 respondents that indicated in the short questionnaire that they needed assistance in order to pass water, seven also completed the long questionnaire. Of these seven respondents, three (two male and one female, between the ages of 65-80) indicated that they had not been able to use the urine bag without assistance. In addition, seven respondents (five male and two female aged between 40 and 80+) who had indicated that they had not needed assistance to pass water, said that they had required assistance to use the urine bag.

Of the 708 respondents that had used the urine bags, 35% used all seven urine bags (figure 4). 49% used four to six urine bags and 16% used up to three urine bags. 87% of the males and 84% of the females used one or more urine bags. 3% of the males and 12% of the females used one urine bag and 30% of the males and 41% of the females used all seven urine bags.

In total 14% of the respondents did not use the urine bags. Of these 33% were under the age of 24, 17% fall into the age range 25-40, 10% were between 41 and 64 years old, 14% are between the age of 65 and 80 years and 21% were older than 80.

In the questionnaire, respondents were able to provide several answers as to why they used no or less than seven urine bags. 63% of the respondents indicated that they used no or less than seven urine bags because they didn't need them in the 24 hours

after the scan. 20% of the respondents used less than seven urine bags because they found it too inconvenient (figure 5a).

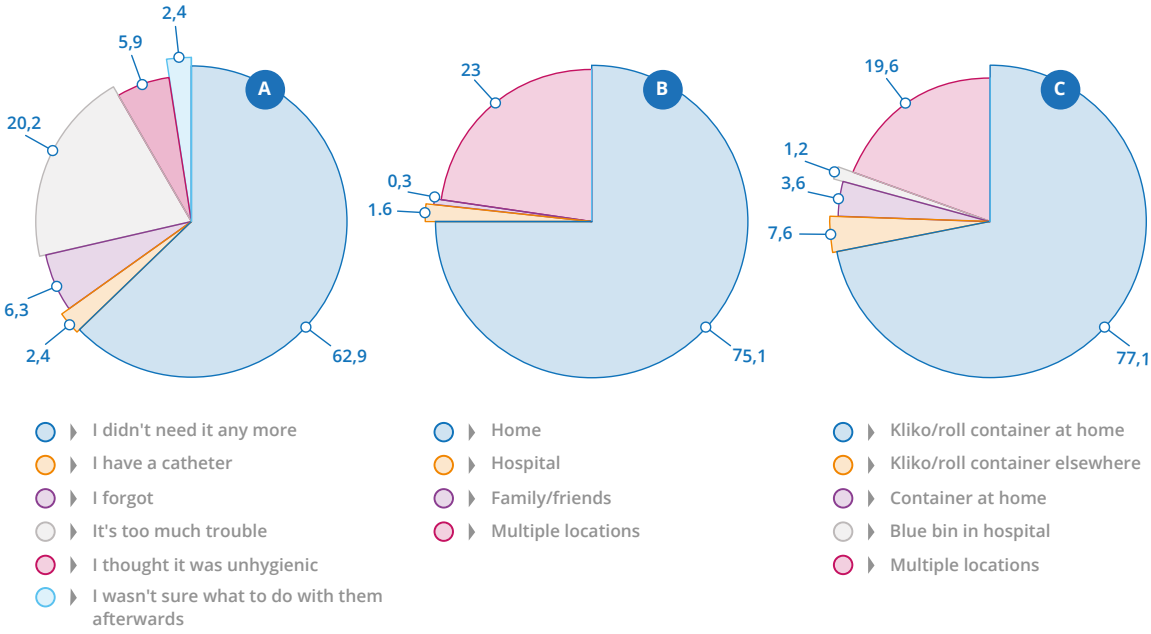


Figure 5: Use of urine bags
A: Reason for using less than seven urine bags
B: Location of use
C: Location of disposal point

Other reasons the respondents gave were: forgot (6%), found it unhygienic (6%); did not know where to put them (2%); had a catheter (2%). 98% of the respondents used and disposed of the urine bags at home. Of these respondents 23% used the bags at multiple locations and 20% disposed of them at different locations (figures 5b&c).

Experience with the use of urine bags

Of the respondents, 91% of the respondents like the format and 94% liked the opening of the urine bag (figures 6a and 6b). 69% of the respondents found the instructions to be clear and 24% of the respondents found the instructions to be 'neutral' (figure 6c). The answer categories for this last question deviate from the other two questions in terms of experiences with the use of the urine bag. This could explain the difference between the over 90% of the respondents who found the format and opening or the urine bag to be satisfactory and the 'just' 69% of the respondents who found the instructions to be clear.

Opinions on the use of urine bags

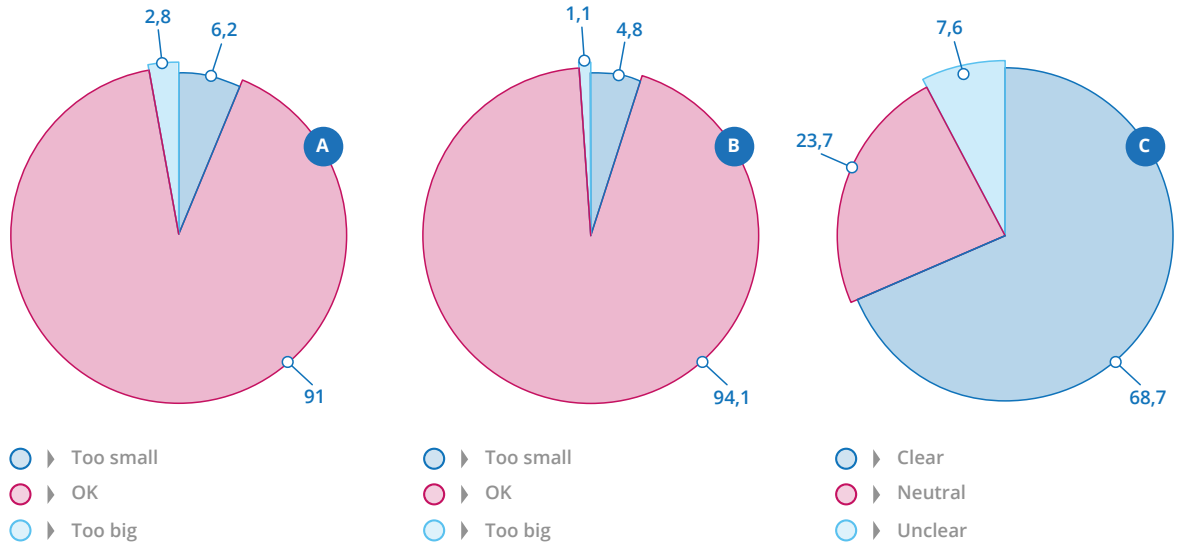


Figure 6: Experience of urine bag use
A: Experience with format
B: Experience with opening
C: Experience with instructions

Almost 90% of the respondents agreed with the statement 'I found it easy to urinate using the urine bag'. In addition, 90% of the respondents found the urine bag easy to dispose of. 100% of females and 31% of males found urinating in a urine bag less hygienic than urinating in the toilet. 9% of the respondents indicated that their current health situation had made it difficult to use the urine bag. Relatively more of those aged over 80 indicated that their current health situation had made it difficult to use the urine bag. Around half of the respondents agreed with the statement that they would rather nobody knew about them using a urine bag. Graph 1 visualises the statement about use of the urine bag.

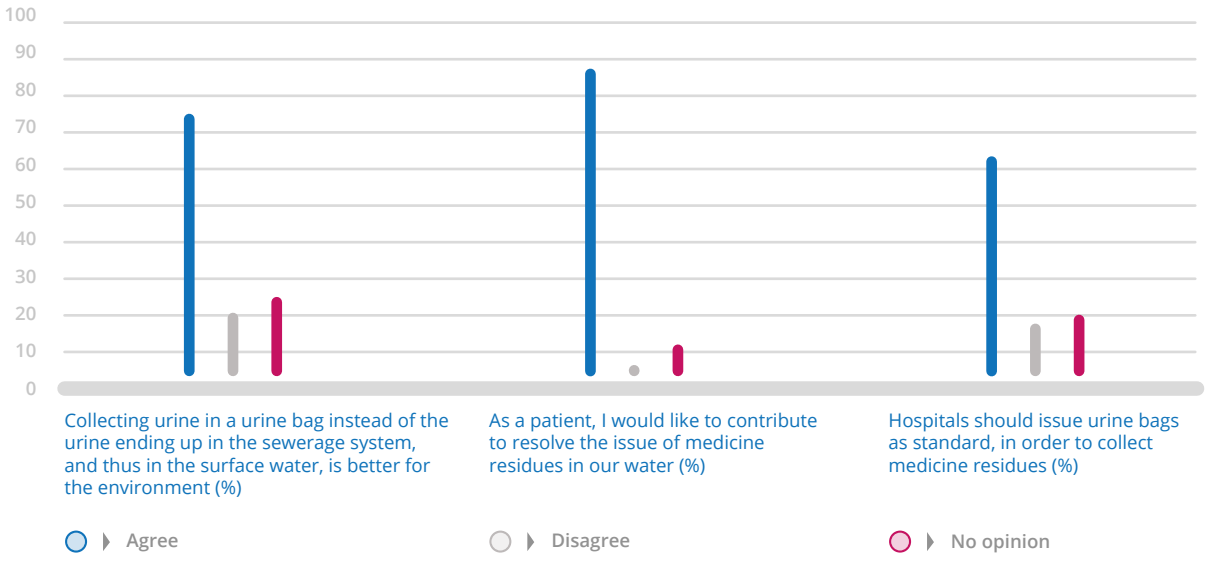
Graph 1: Opinions on the use of urine bags

3.1.2 Intention to use urine bag or not

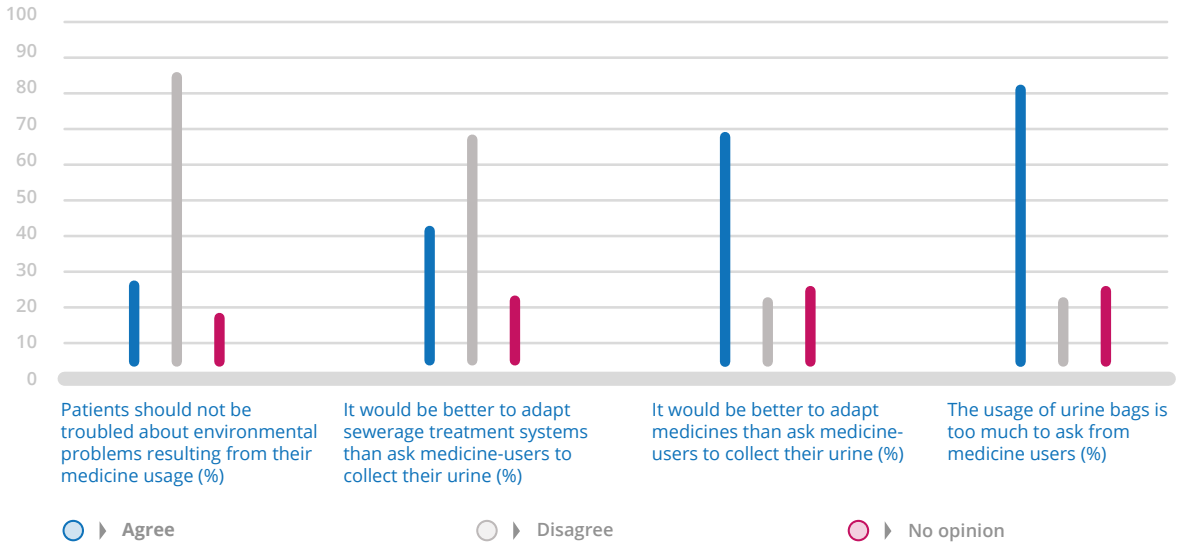
Future use

When it comes to future use, 44% of the respondents indicated that they would use the urine bag if there was no nearby toilet; 48% if the doctor prescribed them and 55% to contribute towards a better environment. 37% of the respondents ticked multiple answers for this question. The opinions of males and females did not vary significantly with respect to future use of the urine bag. Contrary to the norm in attitude research, this study asked about behavioural intentions among respondents that had already been made aware of and had gained experience with the desired behavioural change (i.e. use of urine bag).

To statements regarding the intention to use the urine bag (graph 2a), the most positive response was given to the question of whether respondents, as patients, wanted to contribute towards solutions to the problem of medicine residues in our water (86% agreed). Just 3% of the respondents disagreed with this statement. The two other statements that relate to the environment score relatively positively. 75% of the respondents agreed with the statement 'Collecting urine in a urine bag instead of the urine ending up in the sewerage system, and thus in the surface water, is better for the environment'. 64% of the respondents agreed with the statement 'Hospitals must hand out urine bags as standard in order to collect medicine residues'. Furthermore, 62% of the respondents indicated that medicine users were not asked to use urine bags overly frequently. 66% of the respondents agreed with the statement that patients should not be troubled about environmental issues as a result of their medicine usage. 38% of the respondents agreed with the statement 'urine bags are unsuitable for user for longer than 24 hours', compared to 29% who agreed with this and 33% who had no opinion.



Graph 2a: Opinions on the environment and responsibilities in the waste water chain



Graph 2b: Opinions on the environment and responsibilities in the waste water chain

Intention to use urine bags in relation to environment concepts

There was a check on whether the above environmental statements (graph 2b) are cohesive. In other words, whether they could form one scale due to sufficient internal consistency. This is not the case (see the Cronbach's alpha test, annex 4). This means that we are unable to collate the results of the environmental statement in order to seek correlations with, for example, age or gender, or with the answers to other questions and statements.

The following findings relate to the respondents that indicated they would use a urine bag in the future if this meant they would be contributing to a better environment (86% of the total). These findings are therefore not included in graphs 2a and 2b. A large majority of these (89%) stated that collecting the urine in a urine bag was better for the environment than the urine ending up in surface water. 81% of the same group of respondents agreed with the statement that urine bags should be issued as standard in order to collect medicine residues. Just 10% of these respondents thought that patients should not be troubled about environmental issues due to medicine usage. 78% agreed with the statement and 12% had no opinion. Medicine users are not asked too frequently to use urine bags according to 80% of the respondents. When it comes to who should take measures in the medicine/water chain, 16% of the respondents believed that it was better to modify the waste water treatment plant than ask users to collect their urine. 70% agreed with the statement and 14% had no opinion. 41% of these respondents said that it was better to make medicines more environmentally-friendly than ask patients to collect their urine. 37% agreed with the statement and 22% had no opinion.

3.2 Effect in waste water at WWTP Deventer

3.2.1 Theoretical effect

Figure 7 is a schematic representation of the routes taken by and quantities (percentage) of iodixanol from Deventer Hospital that end up at an WWTP. The diagram shows that around half of the quantities of iodixanol administered ultimately end up at WWTP Deventer. The rest ends up in another WWTP because almost two-thirds of the patients treated in polyclinics live outside the sewerage catchment area of Deventer (see annex 5 for the map of Deventer's system).The extent to which the iodixanol occurs in Deventer's waste water can be ascertained on the basis of the questionnaires filled in. The following details are important in this context:

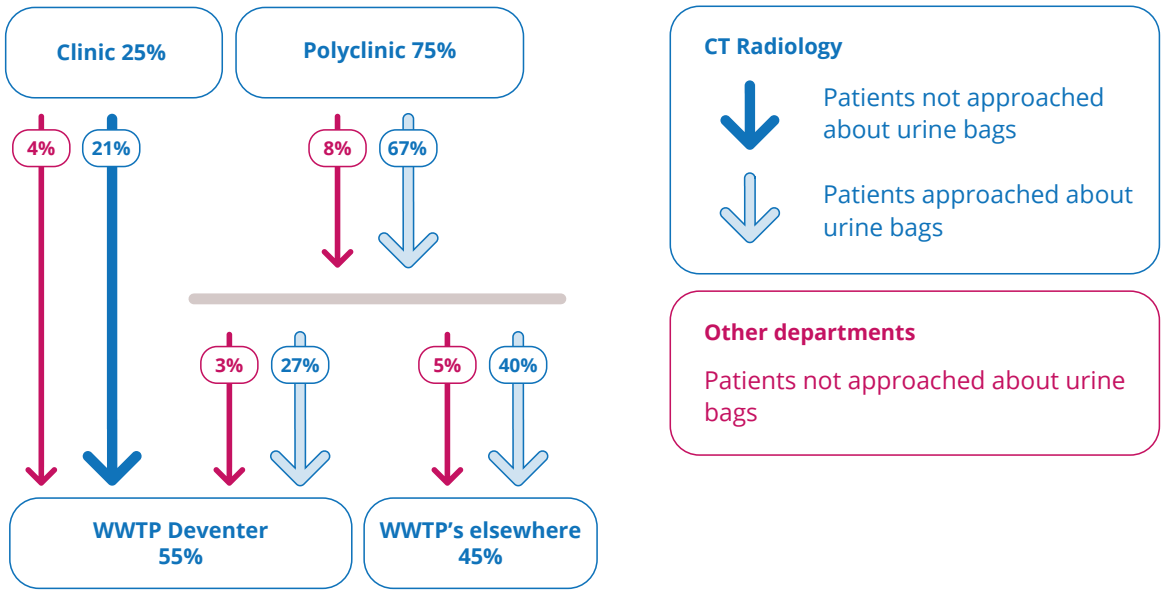


Figure 7: Loading and routes of iodixanol from Deventer Hospital to WWTP's in normal situation

- The questionnaires show that 85% of the 831 respondents used one or more urine bags.
- Of the non-respondents, around half did use urine bags (information from telephone follow-up).
- About 40% of the polyclinic patients live within the area that is connected to the WWTP Deventer.
- The Radiology department at Deventer Hospital recorded how much iodixanol was administered to each patient.
- Just under 30% of the polyclinic patients were not approached to use urine bags (see §3.1).

A calculation using the above figures shows that the total quantity of iodixanol that was used in the polyclinic's CT department was collected within the urine bags. The

clinical department is also responsible for some of the iodixanol that ends up at the WWTP Deventer. The clinical patients were not offered a urine bag (see §2.2.1). This equates to around a quarter of the total iodixanol that is administered via the hospital. Around 8% of the iodixanol is administered in other departments. These patients were also not offered urine bags.

The result is that a third of the total amount of iodixanol administered by Deventer Hospital, was collected. If we focus on the WWTP Deventer, the load on the WWTP during the trial period reduced by a quarter according to the modelled mass balance. This is further illustrated in figure 8.

3.2.2 Measured effect

During the research, checks were made on whether the quality improvements (§3.2.1)

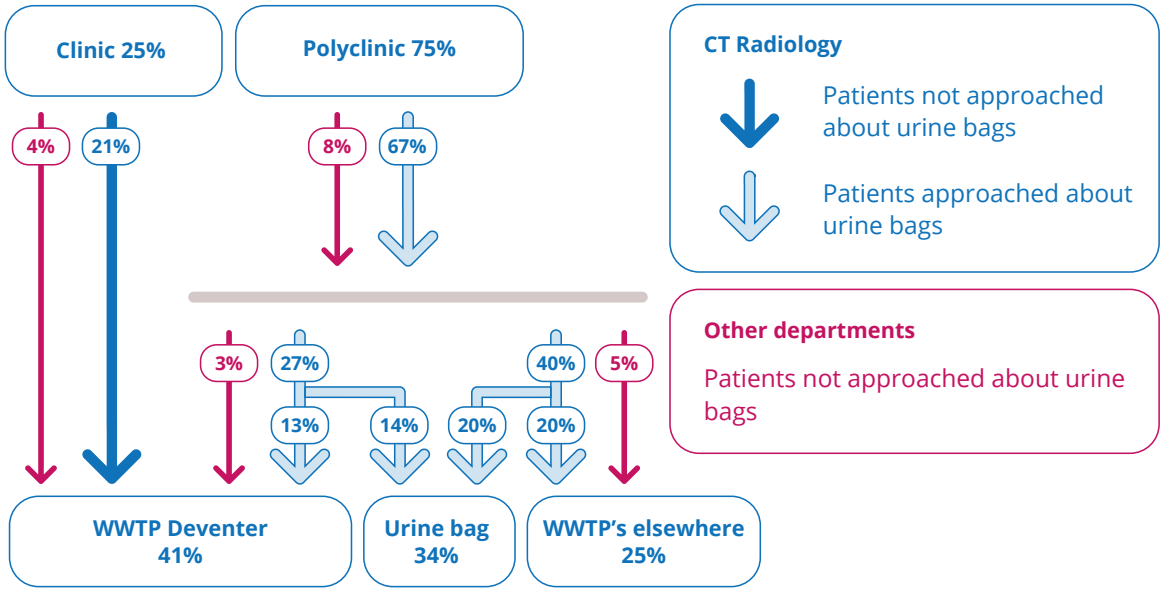


Figure 8: Loading and routes of iodixanol from Deventer Hospital to WWTP's and collection in urine bags during trial period

in the waste water, derived from modelling, were also clear in practice on the basis of measurements of the waste water at the WWTP Deventer. The quantities of iodixanol (loading) that is administered on a daily basis, after correction for the part that was collected in urine bags, was compared with the loading that ended up at the WWTP Deventer. The aim was to establish whether the use of urine bags was measurable, by creating a comprehensive mass balance. As a result of various factors, that became clear during the measurement period, it was not actually possible to demonstrate

the realised water quality improvement using the measurement method proposed in advance. The scope of the individual error sources and the sum thereof was difficult to quantify. We were unable to gain an insight into the largest of these error sources and it could not be quantified in advance. At a later stage of the research, it therefore transpired that the current measurement method was inadequate for measuring the effects of this intervention on waste water quality. The measurement research provided great insights that are briefly elaborated in chapter 4[12].

12 Measurements and the combination of patient details, administration details and details about the quality and flow of waste water have been evaluated. This led to a number of recommendations that are not all covered by this report. These can be provided to anyone who is interested. You can contact Water Authority Groot Salland for this purpose.

4

What has this study shown?

4. What has this study shown?

4.1 Conclusions

4.1.1 Willingness to use urine bags among CT patients is high

In general, the level of willingness to use urine bags among CT patients is high and this does not depend on age or gender. Respondents were overwhelmingly positive with respect to questions about their experiences with the urine bag and their intention to use the urine bag in the future. Respondents who used fewer than seven urine bags provided various reasons why they had not used all seven bags. This was generally due to practical reasons, such as not requiring the full seven bags, being outside the home, and unexpectedly having to go to the toilet, or having diarrhoea after the scan and not being able to use them. It is worth noting that most of the respondents did not stop using the bags because of the urine bags themselves. This applied to around 30% of the respondents, who found it less hygienic to urinate in the urine bag than in the toilet. By far most of the respondents found the design of the urine bag to be good, the instructions clear and they found urinating into the urine bag to be easy. Respondents largely used the urine bags at home and did not have any difficulty disposing of the full bags in the waste container.

A few indicated that they were only cooperating because it was a research project and that urinating into the toilet is more pleasant or hygienic. Other respondents indicated that they found the urine bags handy for use out of the home or if the toilet was not clean.

A result worth noting is that a relatively high number of males think the urine bags are unsuitable for females whereas females found them to be suitable. One reason for this could be that men are not familiar with the female version of the urine bag.

A (more) positive score from respondents regarding the statement about the environment did not impact upon the actual use of urine bags. This is even less relevant for experiences with the urine bags or the intention to use them in the future. One reason for this could be that the majority of the respondents score positively on the (future) use of urine bags and the experiences with them, anyway. Sub-groups cannot be distinguished because the response to all items is overwhelmingly positive. In other words, if greater diversity had been found in the answers to the statements, this diversity could have been correlated to the variables age, gender or others. Given that all of these categories of patient provided similar responses, it can be concluded that age category[13] or gender has little impact on the willingness to use urine bags.

13 Younger patients (under the age of 40) are not really represented in this study. The conclusion applies to the age range above 40

4.1.2 Personal approach and hospital setting explain greater willingness to take part in study

A large majority of the CT patients were willing to contribute towards preventing medicines ending up in surface water by using urine bags. It is worth noting that a small majority of these people believe that medicines should be manufactured to be more environmentally-friendly rather than patients having to use urine bags. Just a minority believe that it would be better if the sewerage purification process could be adapted to resolve the problem rather than patients having to collect their urine. This gives an overview of how patients position themselves in the waste water chain when it comes to medicines in waste water. In the first instance, this is regarded as an issue for the pharmaceutical industry, then for the consumer and, finally, for the water boards.

A possible additional explanation for the high and positive response is, firstly, the personal approach to patients by research assistants. This type of intensive approach can be expected to increase response levels. Patients that did not send the questionnaire back within one week were also called by one of the research assistants. This process was very effective (47% of the patients returned the questionnaire after they had received a call).

The second possible explanation for the high response is the fact that the study took place in a (for most people, out-of-the-ordinary) hospital setting. If hospital staff distribute a medical survey in their own waiting room, the response is expected to be higher than for a survey that is sent out by post. In addition, the extraordinary situation of having to have a CT scan also equates to the patient being more accepting of other non-ordinary practices, such as urinating into a urine bag.

A possible explanation for the high degree of willingness to use urine bags is that the effort required only covers a time-span of 24 hours.

4.1.3 In theory, load of iodixanol at WWTP Deventer decreased by a quarter during trial period

Calculations can be used to conclude that the iodixanol load at WWTP Deventer decreased by one quarter during the trial period.
As a result of complicating factors, such as various missing details in the administration phase and drainage phase (toilet and urine bag usage), uncertainties in the transport phase (sewerage system) and margins of error in the measurement phase, it was impossible to support the calculations with impact measurements and a comprehensive mass balance.
It would seem advisable, prior to the research, to carry out a baseline measurement

for a reasonable period in order to check whether a mass balance can be created. It can then be established whether measurements involving the influent quality are of added value.

4.2 Lessons learned

4.2.1 Good collaboration with Water Authority Groot Salland and Deventer Hospital

The collaboration between Water Authority Groot Salland and Deventer Hospital was new, as was the project. A similar project, as set out in chapter 1, had taken place within the European noPILLS project, but the results had not been published prior to the start of this study and the scope of noPILLS was limited (two-week approach).

The cooperation was found to be satisfactory by both sides. Both parties mentioned the other party's enthusiastic attitude, flexibility and hard work, as strong points. The parties listened to one another and sought solutions together. This provided new insights even within the individual organisations. Both parties also expressed appreciation for the enthusiastic, voluntary efforts made by the research assistants who had approached the patients. Their hard work was one of the most important success factors within this research.

4.2.2 Better preparation for employees and project leader in Deventer Hospital

Several areas for improvement were noted with respect to the work-floor. First of all, this concerns improved preparation with regard to the approach method, and providing information to and preparing the research assistants. The impact of and information requirements of the CT laboratory assistants was also underestimated. They should have been involved and kept informed right from the start. The sociological expertise of Wageningen UR could have been put to better use in both contexts.
Areas for improvement according to both cooperative partners included having a project leader in the department in which the research was taking place (in our case, the Radiology department) and creating a more private area where patients could be approached, to provide a sense of privacy (the public CT/MRI waiting room was used).

4.2.3 Volunteer research assistant is most important key factor

What was most noteworthy from the social research was the high degree of accessibility, positive reactions and willingness of patients to cooperate. Prior to the study, this was estimated to be lower. There was only a small group that was not willing to meet the research assistant. A relatively high percentage of patients made the effort to complete the questionnaire and send it back; the majority of these were also willing to use the urine bags. The efforts of volunteer research assistants and the referrals to them by the CT laboratory assistants were a significant key factor in the study.

4.2.4 Include more background variables in survey

The questionnaires could have been improved by including more background variables (example: see §4.3.3), so that sub-groups could be distinguished. The results could then have been related back to the research strategy for specific target groups. It also transpired that volunteers and lab assistants could sometimes unwittingly influence patients with their enthusiasm. Better instructions and guides provided in advance could have helped.

4.2.5 Setting up a mass balance prior to the research is vital

Within this project, a great deal of knowledge was gained regarding measuring the impact of an intervention in waste water. The most important learning point is that, prior to the trial period, it should be established whether a comprehensive mass balance can be created. If this is possible, the effect of an intervention can be quantified. This also requires a longer period of measurement of the waste water in advance of the intervention so that a representative baseline situation can be established against which the data from the trial period can be compared. In order to realise an effective mass balance, measurements must be taken continuously (seven days per week). This is due to the high fluctuations in administration quantities in combination with the large variations in travelling time of iodixanol to the WWTP. Other learning points relating to the use of measurements can be explained in person.

Other uncertainties that impacted upon the creation of a mass balance, could possibly have been accommodated via modifications to the patient approach. This includes outlining the importance of the first (two) urination(s) being collected and/or a more concrete question about (the location of) the first urination being included in the survey. Ultimately, however, not all error sources are easy to identify and minimise. This refers, for example, to the (unknown) error in the debit flow measurement for one of the waste water pipes that discharge into the WWTP Deventer.

4.3 Next steps

4.3.1 Planning for project partners

The project at Deventer Hospital taught us that patients are aware of the environmental impact that corresponds with medication. Patients are genuinely willing to contribute to reducing this environmental load, despite their health problems. The project also raised awareness and willingness to cooperate among those providing care at the hospital. This realisation reinforces the belief that Deventer Hospital has a social task to help resolve environmental issues. The fact that urine bags are not suitable for every type of medicine, means that Deventer Hospital believes that additional research should focus on the medication itself. Research must take place, with the pharmaceutical industry, into how medication can be made less damaging to the environment.

As a result of this project, Water Authority Groot Salland is aware that it is possible to reduce specific medicine residues in waste water before the water flows into the WWTP. The project flagged up the importance of cooperating with parties that are in direct contact with the user of a problematic substance (in this case, medication). By taking collective responsibility, Water Authority Groot Salland and Deventer Hospital, enabled the discharge of this problematic substance to be reduced. A positive side-effect of this project is that the collaboration with Deventer Hospital also raised awareness about the contamination of waste water with medicines within the hospital as a whole. The water board will include this fact in its efforts to realise its vision of being connected into its surroundings.

Both Water Authority Groot Salland and Deventer Hospital were pleasantly surprised by the fact that a majority of CT patients were willing to contribute towards preventing medicine residues ending up in the water. This provides an impetus for further research. It is, for example, still unclear as to whether CT scan patients would be similarly willing to contribute if urine bags were part of the routine (and there was no personal approach by a research assistant) or if they were asked to use them for longer than a 24-hour period, and also whether the urine bag could be effective for other patients too. That is why both Water Authority Groot Salland and Deventer Hospital, in collaboration with other parties, would like to cooperate in the realisation of follow-up research in order to provide insights into these uncertainties.

4.3.2 Recommendations for the future

The research results are valuable for hospitals that would like certification with respect to sustainability via the Environmental Care Thermometer (Milieuthermometer Zorg) from the Environmental Care Platform (Vereniging Milieu Platform Zorg/MPZ) and Environmental Inspection Association (Stichting Milieukeur/SMK), the development of which was encouraged by Secretary of State Mansveld (see annex 1). The environmental aspect of 'waste water' encompasses requirements regarding the drainage of chemicals and medication into waste water. Preventing the contrast agents that are administered to patients ending up in the sewerage systems, is specifically mentioned in the certification programme.

In addition, the information from this research is valuable for water managers. As stated previously, the loading of x-ray contrast agents is the same as the loading of all other medicines put together (§2.2). Given that the patients do not regard the use of urine bags as particularly onerous, it would be wise to further investigate the use of urine bags for the elimination of medicine residues. If this is successful, the effect could be expanded by tackling this across the entire 'flow'.

Experiences with effect measurements within this research are also very valuable for water managers. They provide an insight into measuring effects on the basis

of a mass balance and the complications that play a role in this context. The most important recommendation is first to create a mass balance in the baseline scenario, prior to this mass balance being used for the purposes of effect measurements. Other recommendations are included in a note that can be requested from Water Authority Groot Salland.

4.3.3 Follow-up research

Any follow-up research could deliver far-reaching insights into the practical usage of urine bags. Research could focus on:

1. variations in the effectiveness of urine bags between specific sub-groups of patients;
2. the successful use of urine bags in other, perhaps less intensive, settings;
3. the successful use of urine bags among medicine-users for a longer period.

The results of this type of follow-up research could lead to a second step being taken towards large-scale implementation of a source-focussed approach to reducing medicine residues in waste water.

1. **Research among patients that are having a CT scan, when more background variables are measured.**
   The current research was not able to distinguish any sub-groups as there was too little differentiation with respect to background variables and, to a large extent, unambiguous answers were given in response to questions and statements. No significant differences were therefore shown between willingness, use and intentions on one side, and gender or age on the other. Background variables, such as educational level, residential situation, household composition, health and illness details, could be correlated with user experiences and opinions regarding urine bag usage and the role of patients in the chain. More sub-groups could then be distinguished, as could specific target-groups for the further (customised) introduction of a urine bag strategy to prevent medicine residues ending up in waste water.
2. **Research into the willingness and use of urine bags among CT patients with another, less intensive, approach method to patients.**
   The approach method using research assistants within a hospital setting led to an unprecedented response rate that was much higher than the norm for this type of survey. This is certainly the case when you also consider that not all questionnaires were completed and returned but also that behavioural changes were actually made. The question is what degree of response, willingness and behavioural change would be achieved with a simple, paper instruction or a short explanation by the CT laboratory assistant. This is important in terms of an affordable, source-focussed strategy that could be applied in practice on a much larger scale.

3. **Research into urine bag user experiences and willingness among patient groups that would have to collect medicine residues via their urine for a longer, but limited, time-frame, e.g. during antibiotic treatment or chemotherapy.**
   This research showed that almost 40% of patients did not rule out using urine bags for longer than 24 hours. Follow-up research could identify whether patients are also prepared to use the urine bags for a week or longer or if there are limits to the patients' willingness to cooperate in this context. A variant on this theme is follow-up research among medicine-users but with another (mobile) device, i.e. not a urine bag, being used to collect urine.

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Annex 1: Developments in water quality policy in Europe and the Netherlands

Europe

The European Water framework directive (KRW) has been in force since the end of 2000 (European Parliament, 2000). This directive aims to realise good chemical and ecological surface water quality by 2027 at the latest. The assessment is based on standards in the Priority Substance list that was added to the directive in 2008 and which originally contained 33 substances (European Parliament, 2008). The standards from this list were established in the Netherlands via the Environment and Planning Act - Monitoring Order (BKMW) in the Ministerial Regulation Monitoring Water Framework Directive (MR). This list, however, does not contain (standards for) medicines. In 2013, 12 new substances were added to the list (European Parliament, 2013). The painkiller diclofenac and two hormones (pilhormone and natural oestrogen) were also proposed for the list but were not included. This was mainly due to the (very) low concept norms and the corresponding large-scale investments in additional purification steps at WWTP's. There will, however, be comprehensive monitoring in the planning period 2016-2021 as a result of inclusion on the European Watch list.

This latest modified directive (Directive 2013/39/EU), also states that the European Commission will deliver a strategic approach for medicine contamination in water in 2015 . In addition, the European Commission, in the context of this strategic approach and if appropriate, must draw up a proposal for a package of measures in 2017 (European Parliament, 2013).

International cooperation between European countries on (waste) water quality is taking place via bodies such as the European federation EUREAU. Dutch water boards and drinking-water companies are represented within this federation via the Union and Water boards and Vewin. EUREAU has provided a collective standpoint on 'emerging substances' and 'source control', whereby the focus lies on tackling the issue at the source. There is also collaboration on this problem at flow area level (Rhine[14] and Maas).

In December 2013, a report was published on behalf of the Executive Agency for Health and Consumers on the risk of medicine residues in the environment (BIO Intelligence Service, 2013). This elaborated on topics such as the routes, behaviour, risks for water-based life and human health, influencing factors and possible solutions.

14 International Commission for the Protection of the Rhine (ICBR)

The Netherlands

Medicine residues have been identified in Dutch waterways since the end of the 1990s. This was the provocation for an informative recommendation from the Dutch Health Council (Gezondheidsraad)[15] in 2001, which demanded policy-related attention be paid to the presence and risk of medicine residues in water (Health Council, 2001). A working group '(animal) medicines in the environment' was then created, various exploratory (monitoring) studies took place and this topic was discussed at length in the House of Representatives (House of Representatives, 2007; House of Representatives, 2009; House of Representatives, 2012).

During the revision of the Dutch list of specific contaminating and drinking-water related substances, under the Water framework directive 2012, three medicines and one x-ray contrast agent were placed on the 'Dutch Watch list'[16] (Smits & Wuijts, 2012). These are being more thoroughly monitored and were evaluated at the beginning of 2015. Findings regarding the risks for the Netherlands would seem to be quite positive (STOWA, 2015). Draft norms were created by the RIVM for these three medicines (Moermond, 2014).

In June 2013, former Secretary of State Mansveld (Ministry of Infrastructure and Environment) sent a letter to the House of Representatives, on behalf of the Ministry of Health, Welfare and Sport (VWS) and Economic Affairs (EZ). This letter once again stresses the importance of reducing medicine residues and other micropollutants in surface water, and also proposes the following:

1. A source-focussed approach, targeting the first steps in the medicine chain.
2. Raising awareness and creating a sense of urgency in consultation with the parties concerned and, on this basis, exploring the options with respect to specific measures that focus on medicine residues and other micropollutants in the waste phase.
3. On the basis of this exploration, making agreements with the parties concerned about the period of time and location of additional measures for the purification of medicines.
4. Requesting coverage of these measures in international commissions for various catchment areas and within the European Union.

In January 2014, a round-table meeting was held by the permanent commission for Infrastructure and Environment with participants from the medicines sector (pharmacists, pharmaceutical industry and hospitals), water chain parties (water boards, drinking-water sector and sewerage) and representatives from the fields

15 The Dutch Health Council has been an advisory body since 1902 and is tasked with 'providing information on the scientific situation with respect to issues relating to public health' to the Dutch government and parliament (art. 21 Health Act) (Health Council, 2001)

16 Medicines carbamazepine, metformin and metoprolol and x-ray contrast agent amidotrizoic acid

of science, research and innovation (House of Representatives, 2014a). The parties involved endorsed a chain-approach whereby a source-focussed method at the beginning of the chain is encouraged, supplemented with measures at the end of the chain. This approach will then be monitored by the government, and former Secretary of State Mansveld has now taken steps to stimulate a source-focussed approach within care organisations, pharmacies, the pharmaceutical industry and the water sector (House of Representatives, 2014b&c).

Former Secretary of State Mansveld has also take steps with regard to stimulating a source-focussed approach (House of Representatives, 2014b).

- Care establishments: Development of the Environmental Thermometer, (a certifiable environmental management system that stimulates and guarantees sustainable operations) and the creation of the Green Deal (the importance of sustainable operations in care collectively implemented by the parties concerned) in collaboration with Economic Affairs (EZ), Public Health, Welfare and Sport (VWS), and Foreign Affairs (BZK).

- Pharmaceutical industry: Discussions held and follow-up talks planned with delegation from the pharmaceutical industry for exploring possible contribution to the social task (specifically solutions within hospitals).

- Pharmacies: In consultation between the Minister for Public Health, Welfare and Sport and the Dutch society that represents pharmacists (Koninklijke Nederlandse Maatschappij ter bevordering der Pharmacie/KNMP), map out examples of agreements between municipalities, pharmacists and waste collection firms, and bring these to the attention of other parties. The aim is to remove barriers to pharmacies accepting unused or old medicines.

- Water sector: Conversations with water boards and drinking-water companies about developing an action plan for their contribution to the social task.

The Union of Water Boards and Association of drinking water companies in the Netherlands (Vewin) presented an action plan to the Secretary of State, on behalf of the water sector, in November 2014 (uvW and Vewin, 2014). This proposes a three-pronged policy with a separate branch for communicating the results. The three branches are:

1. Problem definition: ecological and human health effects
2. Source approach
3. Approach within the water chain.

The combination of existing and ongoing research, pilot projects, policy initiatives and other relevant informations from all chain parties also forms an important component.

The approach to medicine residues in surface water was set out in the National Water Plan 2016-2021, which was presented in 2014. This approach contained the same principles as outlined above.
Given the ambitions and complexity of the water quality policy, Minister Schultz van Haegen requested advice on this topic from the Advisory Commission Water (AcW). This commission, in the first part of its recommendation, indicated that it was concerned about developments in water quality and the speed at which measured were being taken (Advisory Commission Water, 2015). According to the AcW, the Netherlands is lagging behind in its approach to new substances in the Rhine catchment area. Various participants have been working on the problem definition for fifteen years but there is a lack of coordination. The chain parties are scared to take responsibility due to the corresponding costs. The implementation of measures and formulation of policy is therefore delayed. In addition, the various frameworks (water quality, monitoring, acceptance of substances, etc) must be harmonised more effectively. There is also still a substantial lack of expertise on the effects of substances on man and the environment and the corresponding measures. It takes a great deal of time to acquire this knowledge, but on the basis of the precautionary principle, this does not necessarily have to be a barrier to (considering) implementing measures. According to the AcW, it is necessary to first create agreement between all parties about urgency and also collectively recognise the problems. This requires a national approach with greater direction. Subsequently, the Minister, in a letter to the House of Representatives, indicated that he would provide direction and that the definitive advice from the AcW (end 2015) would be used to further substantiate and execute the water quality policy (House of Representatives, 2015b)

An interdepartmental working group, set up by and under the directorship of the Ministry of Infrastructure and Environment (I&M) is currently working on the development of an action plan for medicine residues in the chain. This is expected to be presented to the Minister at the beginning of 2016 (C. Blom, personal communication, 17 August 2015).

Annex 2: Possible intervention points for measures in the medication chain according to RIVM

Figure 1:

Medicine chain. How do medicines end up in the environment? (RIVM, 2015).

- **A.** Development and production;
- **B.** Access to the market;
- **C.** Purchasing and sales by pharmacies;
- **D.** Prescription and use;
- **E.** Disposal with household waste;
- **F.** Disposal via sewerage system;
- **G.** Collection of unused medicines;
- **H.** Collection of household waste;
- **I.** Treatment of sewerage water;
- **J.** Dump for household waste;
- **K.** Incineration of household waste and sludge;
- **L.** Sewerage sludge used in agriculture (not in NL);
- **M.** Treated waste water is discharged into surface water;
- **N.** Small chemical waste is incinerated;
- **O.** Drinking water companies supply water.

According to the RIVM, the possible measures for the various points in the medicine chain are as follows:

A: Development of medicines with more favourable environmental properties and making the environmental data for medicine more readily available. This could impact upon raising the awareness of citizens and thus increase social demand thereafter

B: Including environmental impact in decisions with regard to admitting medicines to the market and/or allowing them to be sold freely by drug stores/supermarkets. Information about the environment included in the instruction leaflet or as an environmental seal of approval on the packaging.

C: Include consequences of medicine usage in the training of pharmacists and doctors. Oblige insurers to include not only price, but also environmental aspects when making decisions regarding the medicine reimbursement system.

D: Patients could modify lifestyle or diet in some cases. Environmental aspects included when developing guidelines for doctors. Optimisation of quantities of medicines per patient. Information about environmental aspects and method of returning excess medicines provided to patients by pharmacies.

E: Encourage patients to return medicines that have passed use-by dates to the pharmacy or collection point for small chemical waste. Develop laws with respect to the collection of waste that contains medicines.

F: Patients could use urine bags or special toilets after medicine usage in order to limit known environmental effects.

G: Remove the financial barriers that prevent pharmacies accepting returned medicines. Conduct research into the extent to which it is possible to re-issue unused medicines. Ensure a good, accessible collection system for small chemical waste by municipalities.

I: WWTP's could add in treatment steps and develop more advanced purification methods. Reduce leaks and overflows via better management and design of sewerage system. Decentralised purification of hospital waste water.

O: Drinking water companies could invest in methods for purifying drinking water (RIVM, 2015).

Annex 3: Work instruction for Deventer Hospital research assistants for Grip

1. Optional: leave your bag/jacket in the locker in the hall (behind taxi point)
2. You can hang your jacket up in the changing room in the department, behind the large sliding door. Do not leave any valuables unattended. This room contains a stock of bags, empty forms, pens, clipboards, etc; these must be left here. Please shut the sliding door at the end of the day (rotating knob on inside) and then leave by the by the back exit.
3. You may take your own telephone with you and use it in the department. If you must call Inge, Yolanda or a colleague, you can do this free of charge at the reception in the hall.
4. Put your personnel pass and name badge on.
5. Walk round the back (via the door with a card reader) to the back of the desk (45); the second set of desks is the Radiology Planning section. Ask for the daily plan. All of the people who have been administered contrast agent (not a drink or anything else) will be approached.
6. Take a stock of everything with you to the CT/MRI waiting room or the seating area in the PET-CT corridor. Make sure you have two types of bag: female (green/pink) and male (blue).
7. Take a seat on the bench to the right (opposite the doors to the CT changing cubicles) or the seat by the PET-CT. You can then see who is going in and out. Only approach people who are on their way out. Please use the script for this purpose.
8. Who you can approach: polyclinic patients for a CT or PET-CT scan.
9. Who you cannot approach: clinical patients, patients who have not had contrast agent, small children (cross these off on your plan).
10. After the survey, people are asked to remain in the waiting room for around 15 minutes and drink a glass of water (to see if there is any reaction to the injected contrast agent). If people have been before, and know they are not allergic to the substance, they will leave immediately. Try to speak to them too, and follow the script.
11. Patients that are on the plan twice, will be undergoing multiple examinations in one go but they will only come out once. You can write any notes on the plan, e.g. people who did not turn up, who you missed or who did not have any contrast agent, or any other details.
12. Let people fill out the short questionnaire themselves and check they they have completed it in full. If they ask for help, you may help but it is better if they do it themselves. People may fill out their phone number if they do not wish to give their email address (or the other way around). This will be used to call them at a later date if they have not returned the longer questionnaire or it is returned

incomplete. It will not be used for any other purpose. NB: You do not need to fill in the amount of contrast agent!

13. On the plan, note the number of the questionnaire after the name of the patient to which you gave it.
14. If people would rather not take a bag, please ask them to fill in the short questionnaire. Note the reason why the patient did not want to cooperate on the short questionnaire. Add the long questionnaire to the short questionnaire so that the numbering is correct.
15. If patients do not wish to complete the short questionnaire, please complete a short questionnaire yourself (date, scan, gender). Write on the questionnaire 'COMPLETED BY VOLUNTEER'. Note the reason why the patient did not want to cooperate on the short questionnaire. If patients do not give a reason, just note 'reason unknown'.
16. It is just as valuable, for the study, if people who do not wish to cooperate, fill in the long questionnaire. Always try to ask people to complete the long questionnaire even if they do not want to cooperate in the study (do not complete with the patient!). Give them the long questionnaire plus the reply-envelope and also the coffee voucher ('perhaps you could fill it in while enjoying a cup of coffee'). NB: Make sure you do not offer this as a 'way out'. In other words, don't say to someone who looks like they may take part 'oh you could just fill in the questionnaire'. You may only ask this if you are certain that the patient does not want to take part!
17. If someone is unsure whether they wish to take part, suggest that they go home and have a think about it and, if they decide to take part, fill in and return the questionnaire (then we know why they did not want to take part).
18. If patients indicate that they have participated already, because they already had a CT scan, they do not need to take part again. If a patient is unhappy with this approach, please given them urine bags anyway. These patients should not be given a number. Note on the plan that the patient had already participated and was issued with urine bags.
19. If you are unexpectedly unable to approach patients, for whatever reason, write on the plan 'not approached' and the reason why.
20. Place the long questionnaire (that has the same number as the short questionnaire) in the bag. Always keep the short questionnaire yourself. Check once again that the number on the completed short questionnaire is the same as the number on the long questionnaire that you place in the bag.
21. Show the patient the things that are in the bag and explain briefly what they are for. Now, you can check that you have the right urine bags (male/female). There

are 7 urine bags in the bag. The disposable bags could be used if the person concerned is out of the house or not near a waste bin.

22. If anyone indicates that they need to go to the toilet immediately, point them to the disabled toilet (right, around the corner in the hallway). Please place the urine bag in the bin that is in the toilet cubicle. PET-CT: there is a toilet opposite the waiting room where patients sit.
23. If there is a programme on at PET-CT, you will be given 2 lists (at the bottom of the page, you will see CT 1 - this is the large waiting room - or N8 - that is the small waiting room). If you have time and there are a few patients one after the other, you could pop over to the other waiting room. If anyone is hard of hearing, you could sit with them on the bench at the front.
24. At the end of the day, hand the plan and the completed short questionnaires to the Radiology office; they will collate the lists (and plans) and send them in at the end of the week. The rest of the items must be put back in the changing room and close the door.
25. Plan you own break on the basis of the plan. You can take your break in the coffee room in the radiology department or in the personnel canteen on the 1st floor. You can use the vending machines there that provide free coffee and tea.
26. Sometimes there is a great deal of time between the last few patients, you do not need to wait for 1 or 2 patients, if there is more than an hour in between appointments.
27. If you run out of bags, please inform the department: Inge Vreeswijk, head of Radiology department or Yolanda.
28. Keep to the script as far as possible and the text that is given on the 'question and answer' form. If you do not know the answer, just say you don't know. Keep explanations brief and try not to go into too much detail about environmental aspects as this could impact too much on the research.
29. Be aware that most of the people will be quite stressed when waiting so do your work quietly and adapt the level of your voice. Maintain the sense of calm in the waiting room as much as you can.
30. The research is not anonymous (because you are taking telephone numbers and/ or email addresses) but the details will be treated in confidence.
31. In the waiting room, an information film from the Water board will be shown and the laboratory assistants will also tell the patients about your presence. For more information, you can refer people to Water Authority Groot Salland's website: wgs. nl./grip or provide their phone number: 038 455 74 34.

Annex 4: Cronbach's alpha

The reliability of a scale that contains various items can be analysed using Cronbach's alpha. This is a measure of the scale's internal consistency. Cronbach's alpha is a method of establishing whether multiple items together form a scale (underlying structure). This is checked on the basis of the correlation between the various items. Values between .70 and .90 demonstrate high internal consistency.

The concept of 'thinking in environmental solutions' encompasses the following statements:

Cronbach's Alpha 0.562; N of items 4	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
In the future, I will use a urine bag in order to make an environmental contribution.	,296	,598
Collecting urine in a urine bag instead of the urine ending up in the sewerage system, and thus in the surface water, is better for the environment.	,435	,407
As a patient, I would like to do my bit to resolve the issue of medicine residues in our water.	,448	,400
Hospitals should issue urine bags as standard, in order to collect medicine residues..	,378	,481

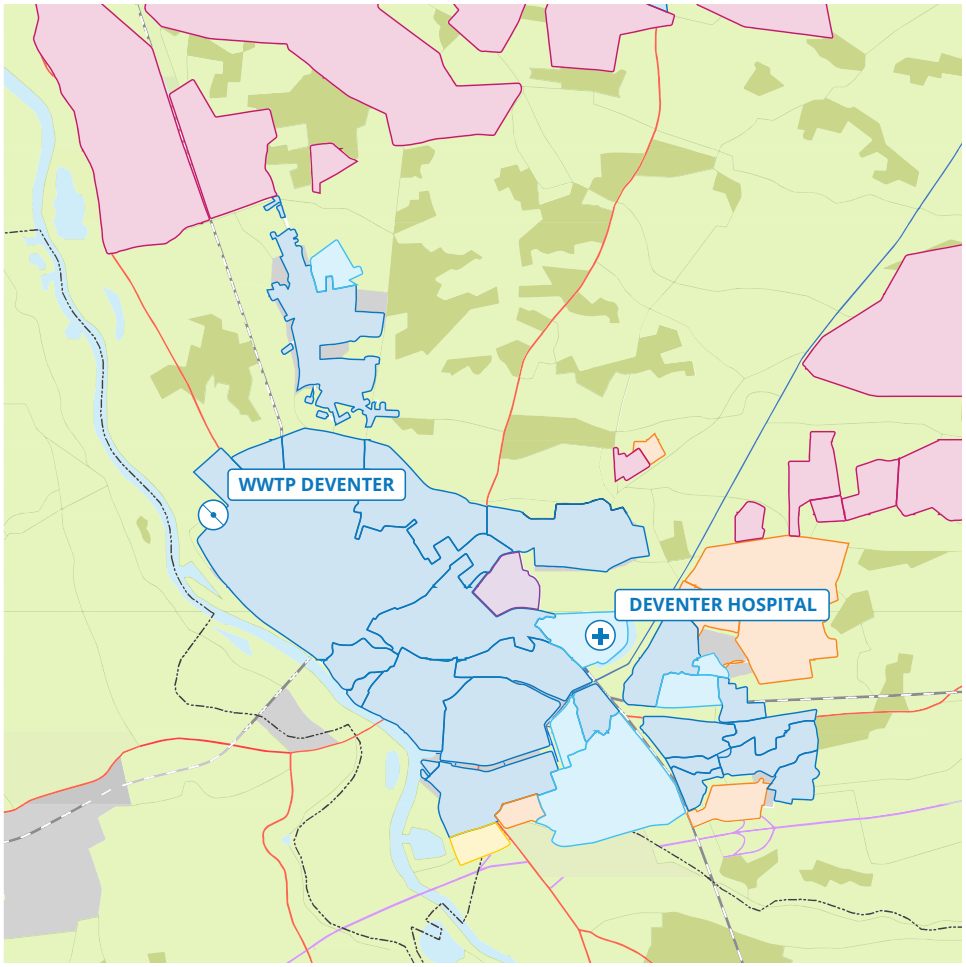
The reliability of a scale that contains various items can be analysed using Cronbach's alpha. This is a measure of the scale's internal consistency. Cronbach's alpha is a method of establishing whether multiple items together form a scale (underlying structure). This is checked on the basis of the correlation between the various items. Values between .70 and .90 demonstrate high internal consistency.

The concept of 'thinking in environmental solutions' encompasses the following statements:

Cronbach's Alpha 0.614; N of items 4	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
It would be better to adapt sewerage treatment systems than ask medicine-users to collect their urine.	,454	,503
It would be better to adapt medicines than ask medicine-users to collect their urine.	,432	,515
Patients should not be trouble about environmental problems resulting from their medicine usage.	,309	,613
Medicine users are asked to use urine bags too frequently.	,395	,543

Alpha Cronbach's scores 0.614.on the 'environmental solutions' scale. This is insufficiently high to construct a 'thinking in alternatives' scale.

Annex 5: Map of sewerage catchment area Deventer



Legenda

10 cm

- Sewerage area (dirty water sewer, centrally drained)
- Sewerage area (Improved separation system, rainwater)
- Sewerage area (pressure sewerage system)
- Sewerage area (mixed system)
- Sewerage area (separated system)
- Sewerage area (improved separation system)

RWZI