

Cost-effectiveness of an app-based treatment for urinary incontinence in comparison to care as usual in general practice: A pragmatic randomised controlled trial over 12 months

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Abstract

Objective: Long-term cost-effectiveness of app-based treatment for female stress, urgency, or mixed urinary incontinence (UI) compared to care-as-usual in primary care. **Design:** A pragmatic, randomised controlled, superiority trial. **Setting:** Primary care in the Netherlands from 2015 to 2018, follow-up at 12 months. **Population:** Women with ≥ 2 UI-episodes per week, access to mobile apps, wanting treatment. 262 women randomised equally to app or care-as-usual; 89 (68%) and 83 (63%) attended follow-up. **Methods:** The standalone app included conservative management for UI with motivation aids (e.g., reminders). Care-as-usual delivered according to the Dutch GP guideline for UI. **Main outcome measures:** Effectiveness assessed by the change in symptom severity score (ICIQ-UI-SF) and the change in quality of life (ICIQ-LUTS-QoL, EQ-5D-5L) on superiority with linear regression on an intention-to-treat basis. Cost-effectiveness and -utility from a societal perspective, based on Incontinence Impact Adjusted Life Years (IIALYs) and Quality Adjusted Life years (QALYs). **Results:** Clinically relevant improvement of UI severity for both app (-2.17 ± 2.81) and care-as-usual (-3.43 ± 3.6), with a non-significant mean difference of 0.903 (-0.66 to 1.871). Costs were lower for app-based treatment with $\text{euro}-161$ (95%CI: -180 to -151) per year. Cost-effectiveness showed small mean differences in effect for IIALY (0.04) and QALY (-0.03) and thus larger ICER ($-3,696$) and ICUR ($\text{euro}6,379$). **Conclusion:** App-based treatment is a viable alternative to care-as-usual for UI in primary care in terms of long-term cost-effectiveness. **Funding:** Dutch Organisation for Health Research and Development (ZonMw: 837001508), sub-funding P.W. Boer Foundation Dutch Trial Register identifier: Trial NL4948 (www.trialregister.nl/trial/4948).

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Running title: Cost-effectiveness app-based treatment female urinary incontinence

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Tweetable abstract: App-treatment for female urinary incontinence cost-effective compared to care-as-usual in general practice after 12 months.

Keywords: App, eHealth, self-management, urinary incontinence, general practice, primary care, cost-effectiveness, long-term, pragmatic

Trial registration: Dutch Trial Register identifier: Trial NL4948 (www.trialregister.nl/trial/4948). The trial was registered before participant inclusion started.

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Introduction

Urinary incontinence (UI) affects one in three women and causes a loss of quality of life. This is compounded by the fact that many women experience barriers to seeking help¹ and often receive suboptimal care when they seek care from a general practitioner (GP).^{2,3} These factors can lead both to avoidable suffering if symptoms persist and to unnecessarily high costs for society when inadequate treatment results in limited benefit.

An eHealth application for the treatment of incontinence may not only improve care but also reduce costs by offering an accessible and effective standalone strategy. For this reason, we have developed an app to

guide the treatment of women with stress, urgency, and mixed UI. Although digital content and care-as-usual are delivered differently, the content of the app has been carefully designed to reflect that of relevant Dutch and International guidelines for pelvic floor muscle training (PFMT) and bladder training.^{4,5} In a qualitative study, we showed that this digital approach to content delivery and treatment was appreciated by women who reported that they expected it to help lower barriers to seeking help, increase self-awareness, and provide support with treatment adherence.⁶ Subsequently, in a pragmatic randomised controlled trial, we also confirmed the short-term effectiveness of app-based treatment compared to care-as-usual for treating UI in general practice over 4 months.⁷ In that research, app-based treatment was not inferior to care-as-usual and both treatments produced clinically significant decreases in the severity of incontinence, consistent with the results of two Swedish trials showing the effectiveness of an internet-based programme and mobile app for treating stress UI.^{8,9} These also reported on the cost-effectiveness of their approach for stress UI compared to postponed treatment or a postal-based programme.^{10,11}

The long-term effectiveness and cost-effectiveness of an eHealth application for all common types of UI have not been compared to care-as-usual. However, such a comparison is important if we are to decide whether large-scale implementation is worthwhile from a societal perspective. In the current study, we therefore aimed to assess the long-term effectiveness, costs, and cost-effectiveness of our app-based treatment compared to care-as-usual by GPs.

Methods

Study design

We performed a pragmatic, parallel arm, randomised controlled trial of patients with stress, urgency, or mixed UI to compare app-based treatment and care-as-usual in a general practice setting. The study design, recruitment challenges, and the primary outcome (non-inferiority of treatment after 4 months) have been published in detail elsewhere.^{7,12,13} In this report, we perform a secondary superiority analysis with a focus on the cost-effectiveness after 12 months.

We recruited adult Dutch women with stress, urgency or mixed UI via general practices, the lay press, and social media from July 2015 through July 2018. The full inclusion and exclusion criteria are presented in Appendix A. A baseline assessment was performed by a researcher/GP trainee (AMML and NJW), with participants asked to complete web-based questionnaires and a 3-day frequency-volume chart. Women then underwent a physical and urogynecological examination.¹⁴ The questionnaires and frequency-volume chart were repeated after 4 and 12 months.

Randomization and blinding

A researcher/GP trainee confirmed eligibility, gained signed informed consent, collected baseline data, and enrolled the participant in the study. Randomization was performed using the computer program ALEA, which allowed full concealment of group allocation.²³ Participants were randomised with 1:1 allocation and random block sizes stratified at the GP level.¹² The study design meant that we could not blind participants or care providers to treatment allocation.

Interventions

The details of the interventions are outlined in Appendix A. Women in the intervention group gained access to the URinControl App, the content of which was based on relevant Dutch GP and international guidelines for treating UI.^{4,5} Women in the care-as-usual group were referred to their own GP to discuss treatment options. GPs were advised to follow the Dutch GP guideline on UI, without limitations on the type and mode of treatment.⁴

Outcomes

Treatment effectiveness after 12 months was assessed by the change in incontinence symptom severity scores, measured by the International Consultation on Incontinence Modular Questionnaire Urinary Incontinence Short Form (ICIQ-UI-SF), the condition-specific quality of life (ICIQ-LUTSqol), and the five-level version of

the EuroQol health status measure (EQ-5D-5L).¹⁵⁻¹⁷ The minimum important differences for the change of score within the treatment groups have been established at 2.52 (SD2.56) for the ICIQ-UI-SF and 3.71 (SD 4.69) for the ICIQ-LUTSqol.¹⁸ A minimum important difference for the EQ-5D-5L was previously established at 0.04 amongst adults with type 2 diabetes.¹⁹

Costs were measured at a patient level at both 4 and 12 months based on enquiries about medical and non-medical consumption and productivity over the past 4 months. We used the adapted iMCQ and iPCQ questionnaires from the institute of Medical Technology Assessment and included the costs of app development and maintenance. We doubled the costs measured at 12 months to estimate costs between 4 and 12 months. We rated cost components collected during the trial based on the standard Dutch guideline for economic evaluations composed by the Dutch National Health Care Institute.²¹ The sum of costs was recorded as the total societal cost. All costs are presented in euros based on the 2017 year-end prices (2014 prices indexed to inflation by 2.414%). Yearly costs for app development and maintenance were based on the actual costs. A scenario of 30,000 users was used, derived as a conservative estimate from the number of users of freely available apps for UI and on the number of downloads of the Swedish Tåt app.²²

For the cost analysis, effectiveness was measured with the Incontinence Impact Adjusted Life Years (IIALY) score derived from the ICIQ-UI-SF symptom score.²⁰ The IIALY score reflects disease-specific quality of life weighted from the patient's perspective with a score from 0 (severe impact of UI on quality of life) to 1 (no impact of UI on quality of life). Utility was based on the EQ-5D-5L, with valuations generated using the Dutch tariff for the EQ-5D.¹⁷ The EQ-5D questionnaire is a generic quality of life questionnaire that generates preference-based scores from -0.33 (severe problems on all five dimensions) to 1 (best possible health state). Areas under the receiver operating characteristic curve were used to calculate the IIALYs and QALYs gained for each individual during the 12-month follow-up period: to gain one IIALY or one QALY at a population level (i.e. to add one additional life year in perfect health), the calculated amount (in euros) would need to be invested.

Statistical methods

We assessed treatment effect for superiority between groups by linear regression on an intention to treat basis, with results considered statistically significant if the p-value was <0.05. We compared baseline characteristics of the final cohort with those of the group lost to follow-up with linear regression and non-parametric tests. Data were analysed with IBM SPSS version 26.0 (IBM Corp., Armonk, NY) and R Studio version 1.2.5033.

The economic evaluation was conducted from a societal perspective, including direct and indirect medical and non-medical costs over 12 months. Incremental costs per IIALY gained were expressed as an Incremental Cost-Effectiveness Ratio (ICER). The balance between costs and QALYs were expressed as an Incremental Cost-Utility Ratio (ICUR).²¹ Costs and effects were recorded and calculated on an individual basis, then the mean differences between the two study groups were calculated. The ICER and ICUR represent the average incremental cost needed to be invested to achieve 1 additional unit of the measure of effect and were computed by dividing the differences in mean effects and mean costs (as shown in Appendix A). By performing 5,000 bootstrap replications of the trial data, alternative confidence intervals were calculated based on the 2.5th and 97.5th centiles. Cost-effectiveness planes visualise the uncertainty surrounding the ICER and ICUR. If the app-based treatment saved costs and differences in effects to be minimal, we would not construct an acceptability curve to assess the probability of cost-effectiveness, as this would already imply accurate cost-effectiveness based on the difference in costs.

Additionally, we performed a sensitivity analysis for a scenario with higher costs for app maintenance and extra costs for annual development. Data robustness was assessed by using the mean of the follow-up data at 4 and 12 months to estimate costs between 4 and 12 months. Finally, we performed subgroup analyses with the type of recruitment or type of UI.

Results

In total, 262 eligible women were randomly allocated to app-based treatment (n = 131) or care-as-usual (n

= 131) (Figure 1). The mean age of the included women was 54 years (range 23–86 years) and most (66%, $n = 114$) had moderate UI.¹⁵ Stress UI and more severe UI were more common in the care-as-usual group, despite randomization (Table 1). The 12-month follow-up period ended on 23 September, 2019, by which point 89 women (68%) from the app-based treatment group and 83 (63%) from the care-as-usual group were available for the intention to treat analysis.

Treatment groups

Supplemental table S1 shows the interventions received by both treatment groups. Loss to follow-up in both treatment groups was associated with younger age and higher body mass index, we found no other significant differences between the groups (Supplemental table S2). We chose not to impute any values because the group with follow-up data was representative and few data were missing.

Effectiveness

Both app-based treatment and care-as-usual showed improvements of all symptom scores after 12 months (Supplemental table S3). Severity of incontinence improved with respectively -2.17 (SD 2.8) versus -3.43 (SD 3.6) points, the change in condition-specific quality of life improved with respectively -4.66 (SD 5.1) versus -4.34 (SD 5.7) and generic quality of life improved with respectively 0.021 (SD 0.17) versus 0.0008 (SD 0.14) points. However, there were no statistically significant differences in the change in symptom scores between treatment groups (Supplemental table S4). After 12 months, women gained an average 0.71 IALYs in the intervention group and 0.66 IALYs in the care-as-usual group (Table 2). In addition, women gained an average of 0.89 QALYs in the app-based treatment group and 0.91 QALYs in the care-as-usual group, equating to respective gains of 0.89 and 0.91 years in perfect (incontinence-specific) health.

Costs

The mean direct and indirect cost per participant in the app-based treatment group was €1,520 (95% CI: 1,512–1,532), including indirect cost per participant in the care-as-usual group was 192–195) for UI-specific costs (Supplemental table S5). For both the app-based treatment and care-as-usual groups, incontinence material drove much of the UI-specific costs (€62 and €80, respectively). Compared with app-based treatment, care-as-usual was associated with higher costs for physical therapy, medication, and other treatments for UI, equating to mean differences of €82, €9, and €8 per patient per year, respectively. The cost of app-usage was €1.10 per patient per year based on the scenario of 30,000 users.

Cost-effectiveness and cost-utility analyses

The cost-effectiveness analysis showed that the mean difference in effect gained per IALY was 0.043 more for app-based treatment than for care-as-usual. The mean difference in costs was €161 less (95% CI: -180 to -151) in the app-based treatment group, giving an ICER of -€3,696 (95% CI: -6,716 to 12,712). The cost-utility analysis revealed that there was a mean difference of -0.025 QALYs (i.e. fewer) for app-based treatment compared with care-as-usual, with an ICUR of

In total, 65.6% of the 5,000 replications in the bootstrap simulation were in the lower half of the plane, indicating lower costs for app-based treatment (Figure 2). Moreover, any effects and utilities gained were comparable, with minimal differences between the groups in either IALY (0.043) or QALY (-0.025).

Sensitivity and subgroup analyses

App-based treatment remained cost-effective when assessed with fewer app users, extra developmental and higher maintenance costs (Supplemental table S6). Sensitivity analysis using the mean costs at 4 and 12 months' follow-up revealed comparable results, demonstrating the robustness of the cost calculation.

Subgroup analysis revealed differences in effects and costs by UI type and recruitment type (Supplemental table S7). App-based treatment for urgency UI resulted in higher IALYs gained (0.74) compared with care-as-usual (0.60). The costs for UI-specific treatment were also approximately €60 higher for urgency UI compared with stress UI mainly due to the cost of incontinence material. Subgroup analysis by recruitment

type showed that, for care-as-usual, the group recruited through (social) media had lower costs (\euro131) and a lower treatment effect (IIALY 0.64) than the group recruited by a GP (\euro235, IIALY 0.68). These cost differences were mainly based on lower use of physical therapy (\euro56 versus \euro122) and other treatments (e.g. pessary or tension-free vaginal tape) (\euro2 versus

Discussion

Main Findings

App-based treatment for female stress, urgency, and mixed UI appears to be a cost-effective alternative to care-as-usual in general practice. After 12 months, both treatments produced clinically relevant changes in the main outcome measures that were larger than after 4 months. Indeed, UI symptoms and quality of life measures continued to improve. However, there was no significant difference in change between the two study groups. App-based treatment was less expensive than care-as-usual, with mean differences of \euro161 and \euro87 per patient per year in total and UI-specific costs, respectively. The gained effects and utilities were comparable between groups after 1 year, with only small mean differences in the IIALY (0.043) and the QALY(-0.025). This resulted in an ICER of -\euro3,696 and an ICUR of \euro6,379. These results were robust and remained valid in a scenario that included higher app development costs.

Strengths and limitations

The main strength of this study is that we compared app-based treatment with care-as-usual. The pragmatic design is considered the gold standard for economic evaluations in health care.²⁴ Other strengths are the inclusion of all common UI types, the use of patient-centred and validated outcome measures, the 12-month follow-up period, and the inclusion of sensitivity analyses to confirm the robustness of our data.

The cost and effect analyses were sufficient to make valid conclusions about cost-effectiveness. Although the ICER and ICUR are typically used to represent costs associated with 1 unit of health gain, we set the difference to focus on cost rather than health gains given that the latter was comparable between the groups. Consideration of this health gain would be confusing, as the minimal differences result in high ratios of ICER and ICUR.

Limitations that must be considered are power and loss to follow-up. Often, cost-effectiveness studies are underpowered because their power depends on the primary outcome measure of a trial. This trial was powered on non-inferiority of effectiveness after 4 months. In this secondary analysis, 172 women (65.6%) were available for follow-up and power was lower. By performing a bootstrap analysis, this issue does not affect the results of the cost-effectiveness analysis. However, the lower power must be considered in our effectiveness and subgroup analyses. Loss to follow-up was associated with higher body mass index. Participation of these women could have further improved effects and lowered costs for both treatment groups, as weight loss is effective for UI and a cheap intervention.

Interpretation (in light of other evidence)

Our study findings are consistent with those from two other studies concluding that app- or internet-based treatment is a cost-effective alternative when managing UI.^{10,11} These studies compared an app-based approach with either a postal-based programme or postponed treatment and assessed their cost-effectiveness for stress UI in superiority trials. However, in any such evaluation, it is recommended to use a pragmatic design with a control group that reflects usual care.²⁴ Ours is the first study to conduct such a comparison, with the results indicating that app-based treatment is a cost-effective alternative for women with UI who present to general practice.

The UI-specific follow-up costs over 12 months in our data were comparable to other studies, while our total costs were higher for both app-based treatment and care-as-usual (\euro1520 and \euro1680, respectively) compared with the data provided by Sjöström et al. (\euro547 and \euro482, respectively) and Vermeulen et al. (\euro417 and \euro87, respectively).^{11, 20} Although all three studies used a societal perspective, we

took into consideration a broader range of costs unrelated to UI, for example loss of productivity, to conduct the societal perspective as thorough as possible.

We consider that women recruited to our trial via (social) media represent a cohort that experience barriers to seeking help from a GP. Subgroup analysis showed that for care-as-usual, the effects and costs were lower for women recruited through (social) media. These women did visit their GP to discuss treatment options just as often, but received PFMT less often (31% compared to 50%). This leads us to question if women who experience barriers to seeking help also experience barriers to accepting help when it is offered. It is conceivable that women in this cohort prefer treatment without professional involvement, which would bring the role of app-based treatment and the importance of access via (social) media to the fore.

Our subgroup analysis showed that app-based treatment for urgency UI had higher treatment effects on the impact of incontinence on daily life (0.74 IIALYs) than did care-as-usual for urgency UI (0.60 IIALYs). This may result from the accessibility of the app, which helps women to distract from feelings of urgency and to monitor the bladder training (e.g. the pee button). The treatment of urgency UI with an eHealth approach has not been studied before, precluding meaningful comparison.

Conclusion

Practical recommendations

With these results, we believe App-based treatment can be recommended as a viable alternative to care-as-usual in general practice. Furthermore, we expect that its implementation will lower barriers to seeking and receiving help for UI because it can be used either as a standalone option or as a tool in blended care (supporting care-as-usual). Although GPs or pelvic physical therapists can offer the app to women who seek help for UI, there is scope for it to be promoted through (social) media and offered online, allowing it to reach cohorts that may not otherwise seek care.

Research recommendations

It will be important to identify the factors associated with treatment success and failure if we are to ensure successful implementation and treatment efficacy. Indeed, clarifying these factors could help to improve the app's content and to ensure that it targets the most appropriate populations. Mixed-methods research could be of benefit,²⁵ and as such, we are currently preparing a report that combines our quantitative and qualitative results. Additionally, it will be important to evaluate and improve the implementation process continuously by collecting user feedback and evaluating log data.

We conclude that the app-based treatment for stress, urgency, and mixed female UI is a cost-effective alternative to care-as-usual in general practice after 12 months. App-based treatment can therefore be recommended as a viable alternative to care-as-usual in general practice.

No competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and report no conflict of interest.

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Contributors and guarantor information

AMML collected the data, did the analysis, and wrote the paper. HvdW assisted with the analysis and contributed to the writing of the paper. NJW collected the data and contributed to writing the paper. JHD designed the study, acquired the funding, and contributed to writing the paper. MCStH contributed to the study design, the app's content, and the writing. MYB assisted in the study design and contributed to writing the paper. K MV assisted with the analysis and contributed to writing the paper. MHB designed the study, acquired the funding, was project leader, contributed to the analysis, contributed to writing the paper, and is the guarantor. The corresponding author attests that all listed authors meet the authorship criteria and that no others meeting the criteria have been omitted.

Ethical approval

The Medical Ethical Review Board of the University Medical Center Groningen, Netherlands, approved this study on 12-05-2015 (METc-number: 2014/574). All participants gave written informed consent.

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Table and figure caption list

Figure 1. CONSORT Flow diagram of participant recruitment

Abbreviations: POPQ= Pelvic Organ Prolapse Quantification; UI = Urinary incontinence

Figure 2. Incremental cost-effectiveness planes per outcome parameter.

Abbreviations: CAU = care-as-usual; IIALY= Incontinence Impact Adjusted Life Years ; QALY = Quality Adjusted Life Years

Table 1. Baseline characteristics of women with complete follow up data shown by treatment group

Table 2. Cost-effectiveness of app-based treatment for urinary incontinence for women in general practice

Supplemental tables

Supplemental Table S1. Comparison of groups by interventions received at both follow-up assessments

Supplemental Table S2: Comparison of baseline characteristics between patients followed up and patients lost to follow up at 12 months

Supplemental Table S3. Questionnaire scores at baseline and follow up comparing app-based treatment and care-as-usual

Supplemental Table S4. Change in questionnaire scores from baseline to 12 months by treatment group, including the adjusted difference between groups

Supplemental table S5. Mean costs per participant for app-based treatment and care-as-usual for women with urinary incontinence

Supplemental table S6. Sensitivity analyses of the Incremental cost-effectiveness ratios

Supplemental table S7. Subgroup analyses of the Incremental cost-effectiveness ratios, including UI-specific costs

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Tables manuscript

Table 1. Baseline characteristics of women with complete follow up data shown by treatment group

Characteristics

Age, (years)

Higher educational level

Body mass index (kg/m²)

Duration of UI (years)

Type of UI

Stress

Mixed, stress predominant

Urgency

Mixed, urgency predominant

Incontinence severity

ICIQ-UI SF score

ICIQ-LUTSqol score

Generic quality of life score (EQ-5D-5L)

Makes use of incontinence products, yes

If yes, mean number of products per day

Previous treatment for UI

None

Pessary

Physical therapist

N varied because of missing data of one baseline assessment and three baseline questionnaires. Values are means \pm standard deviation

Table 2. Cost-effectiveness of app-based treatment for urinary incontinence for women in general practice

	Treatment Group	Treatment Group	Mean difference	
	Treatment Group	Treatment Group	Mean difference	
	App-based N = 87	Care-as-usual N = 82		ICER (95% CI)
IIALYs gained	0.71 ± 0.215	0.66 ± 0.250	0.043	\euro-3,696 (CI -6,716 to 12,712)
Costs	1,520 ± 3,425	1,680 ± 3,357	-161	
				ICUR (95% CI)
QALYs gained	0.89 ± 0.165	0.91 ± 0.145	-0.025	\euro6,379 (CI -4,128 to 12,769)
Costs	1,520 ± 3,425	1,680 ± 3,357	-161	

		Treatment Group	Treatment Group		Mean difference		
IHALYs, Inconti- nence Impact Adjusted Life Years; ICER, In- cremental Cost Ef- fectiveness Ratio; QALYs, Quality Adjusted Life Years; ICUR, In- cremental Cost Utility Ratio. * Three cases were excluded from the analyses because a large influence on the data due to outliers in costs.	IHALYs, Inconti- nence Impact Adjusted Life Years; ICER, In- cremental Cost Ef- fectiveness Ratio; QALYs, Quality Adjusted Life Years; ICUR, In- cremental Cost Utility Ratio. * Three cases were excluded from the analyses because a large influence on the data due to outliers in costs.	IHALYs, Inconti- nence Impact Adjusted Life Years; ICER, In- cremental Cost Ef- fectiveness Ratio; QALYs, Quality Adjusted Life Years; ICUR, In- cremental Cost Utility Ratio. * Three cases were excluded from the analyses because a large influence on the data due to outliers in costs.	IHALYs, Inconti- nence Impact Adjusted Life Years; ICER, In- cremental Cost Ef- fectiveness Ratio; QALYs, Quality Adjusted Life Years; ICUR, In- cremental Cost Utility Ratio. * Three cases were excluded from the analyses because a large influence on the data due to outliers in costs.	IHALYs, Inconti- nence Impact Adjusted Life Years; ICER, In- cremental Cost Ef- fectiveness Ratio; QALYs, Quality Adjusted Life Years; ICUR, In- cremental Cost Utility Ratio. * Three cases were excluded from the analyses because a large influence on the data due to outliers in costs.	IHALYs, Inconti- nence Impact Adjusted Life Years; ICER, In- cremental Cost Ef- fectiveness Ratio; QALYs, Quality Adjusted Life Years; ICUR, In- cremental Cost Utility Ratio. * Three cases were excluded from the analyses because a large influence on the data due to outliers in costs.	IHALYs, Inconti- nence Impact Adjusted Life Years; ICER, In- cremental Cost Ef- fectiveness Ratio; QALYs, Quality Adjusted Life Years; ICUR, In- cremental Cost Utility Ratio. * Three cases were excluded from the analyses because a large influence on the data due to outliers in costs.	IHALYs, Inconti- nence Impact Adjusted Life Years; ICER, In- cremental Cost Ef- fectiveness Ratio; QALYs, Quality Adjusted Life Years; ICUR, In- cremental Cost Utility Ratio. * Three cases were excluded from the analyses because a large influence on the data due to outliers in costs.

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