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A trial-based economic evaluation

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Title

Cost-effectiveness of incisional negative pressure wound therapy compared to standard care after caesarean section in obese women: A trial-based economic evaluation

Authors

Nana Hyldig,¹,²,³ Jan Stener Joergensen,² Chunsen Wu,² Camilla Bille,¹ Christina Anne Vinter,² Jens Ahm Sorensen,¹ Ole Mogensen,¹ Ronald Francis Lamont,²,⁵ Sören Möller,³,⁶ Marie Kruse⁷

Affiliations

¹ Department of Plastic Surgery, Odense University Hospital, Institute of Clinical Research, University of Southern Denmark, Odense, Denmark
² Department of Gynaecology and Obstetrics, Odense University Hospital, Institute of Clinical Research, University of Southern Denmark, Odense, Denmark
³ OPEN Odense Patient data Explorative Network, Odense University Hospital, Odense, Denmark
⁴ Division of Pelvic Cancer, Karolinska University Hospital, and the Karolinska Institute, Stockholm, Sweden
⁵ Division of Surgery, University College London, Northwick Park Institute of Medical Research Campus, London, UK
⁶ Department of Clinical Research, University of Southern Denmark, Odense, Denmark
⁷ Danish Centre for Health Economics (DaCHE), Department of Public Health, University of Southern Denmark, Odense, Denmark

Corresponding Author

Nana Hyldig, Odense University Hospital, J. B. Winsløwsvej 4, entrance 20, 1st floor, 5000 Odense C, Denmark, e-mail: nana.hyldig@rsyd.dk

Short title

Cost-effectiveness of prophylactic iNPWT after caesarean section

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ABSTRACT

OBJECTIVE
To evaluate the cost-effectiveness of incisional Negative Pressure Wound Therapy (iNPWT) in preventing surgical site infection in obese women after caesarean section

DESIGN
A cost-effectiveness analysis conducted alongside a clinical trial

SETTING
Five obstetric departments in Denmark

POPULATION
Women with a pre-gestational body mass index $\geq 30$ kg/m$^2$

METHOD
We used data from a randomised controlled trial of 876 obese women who underwent elective or emergency caesarean section and were subsequently treated with iNPWT (n=432) or a standard dressing (n=444). Costs were estimated using data from four Danish National Databases and analysed from a healthcare perspective with a time horizon of three months after birth.

MAIN OUTCOME MEASURES
Cost effectiveness based on incremental cost per surgical site infection avoided and per quality-adjusted life year (QALY) gained.

RESULTS
The total health care costs per woman were 5,793.60 for iNPWT and 5,840.89 for standard dressings. Incisional NPWT was the dominant strategy because it was both less expensive and more effective, however, no statistical significant difference was found for costs or QALYs. At a willingness to pay threshold of 30,000, the probability of the intervention being cost-effective was 92.8 percent. A subgroup analysis stratifying by BMI shows that the cost saving of the intervention was mainly driven by the benefit to patients with a pre-pregnancy BMI $\geq 35$ kg/m$^2$.

CONCLUSION
Incisional NPWT appears to be cost saving compared to standard dressings but this finding is not statistically significant. The cost savings were primarily found in patients with a pre-pregnancy BMI $\geq 35$ kg/m$^2$.

FUNDING
No funding was obtained for this economic evaluation. The randomised controlled trial (RCT) was funded by grants from the University of Southern Denmark, Odense University Hospital, the Region of Southern Denmark, Lundbeckfonden, and Smith&Nephew.
KEYWORDS
Caesarean Section, Cost-Effectiveness, Economic Evaluation, incisional Negative Pressure Wound Therapy, Obesity, Quality-Adjusted Life-Years, Surgical Site Infection

TWEETABLE ABSTRACT
Prophylactic incisional NPWT reduces the risk of SSI after caesarean section and is probably dominant compared to standard dressings #healtheconomics

Introduction
Surgical site infections (SSI) are a substantial burden on healthcare through prolonged inpatient stays, readmissions, re-operations, and increased costs.1–4 Furthermore, SSIs can delay recovery, cause pain and discomfort, and reduce patients’ quality of life.5,6 Caesarean section (CS) is a surgical procedure, which is often associated with SSI,7–8 and obese women have higher risk compared to non-obese women.9,10

Prophylactic use of incisional Negative Pressure Wound Therapy (iNPWT) on closed surgical incisions is a relatively new strategy to reduce the risk of SSI and other surgical wound complications.11–13 We recently carried out a multicentre randomised controlled trial (RCT) that evaluated the effectiveness of prophylactic iNPWT in obese women (body mass index; BMI ≥30 kg/m²) delivering by caesarean section.14 This study demonstrated that prophylactic iNPWT statistically significantly halved the risk of SSI compared with standard postoperative dressings after CS (RR 0.50, 95% CI 0.30–0.84; P=0.007). Some decision-analytic modelling studies of iNPWT used on abdominal surgical incisions suggests that iNPWT may lower hospital or healthcare costs in obese patients at high risk of SSI.15,16 The objective of this paper is to evaluate the cost-effectiveness of prophylactic iNPWT after CS by performing a trial-based economic evaluation, comparing iNPWT to standard postoperative dressings. We hypothesize that the use of iNPWT dressing can reduce healthcare costs.

Methods
We used individual patient level data from a multicentre RCT (ClinicalTrials.gov identifier NCT01890720) to conduct an incremental cost-effectiveness analysis of iNPWT compared to standard postoperative dressings for prevention of SSI after CS. Details of the RCT have been reported elsewhere.14 In brief, the trial was performed in two tertiary, and three teaching hospitals in Denmark from 2013 to 2016. Overall, 876 women with a pre-pregnancy BMI of ≥30 kg/m² who had an emergency or planned CS were randomised to iNPWT (n=432) or a standard postoperative dressing (n=444) and followed for 30 days post-CS. The cost of implementing iNPWT was derived from a Danish healthcare perspective. Health care costs in the two groups were assessed per month up to one year, and no differences in costs between the groups were detected after three months. Therefore, three-months costs were used for the cost assessment. For quality-adjusted life years
(QALYs), the time horizon was assumed to be one year. Discounting was not necessary due to the short time frame of treatment and benefits.\textsuperscript{17}

Measurement of effectiveness

The two outcome measures selected for the cost-effectiveness analysis were SSI and QALYs. Surgical site infection, defined as an infection at the surgical site requiring antibiotic treatment within the first 30 days after CS, was identified in 20/432 women (4.6\%) in the intervention group and 41/444 women (9.2\%) in the control group.

Data on QALYs were collected using the generic health-related quality of life instrument EuroQol EQ-5D-5L,\textsuperscript{18} which was sent to all participants 30 days post-CS. In total, 827 women (94.4\%) responded to the questionnaire. The QALY differences between the intervention and control groups were calculated as the mean difference in the EQ-5D index value: intervention, 0.863 (95\% CI 0.852–0.873); control, 0.855 (95\% CI 0.845–0.866) (Table S1). The QALY gain was measured at one month but expanded to one year due to the notion that an intervention should aim at improving health-related quality of life for a period longer than 30 days. The Danish crosswalk value sets were used to derive preference based index values.\textsuperscript{19, 20}

No core outcome set was used, and no patients were involved when designing the cost-effectiveness analysis.

Estimation of costs

We used a micro-costing approach, using cost data at individual level for all participants. The total costs consisted of four cost components: i) hospital costs (inpatient stays and outpatient care), ii) contact with GPs, iii) antibiotic treatment, and iv) the cost of the postoperative dressing (either iNPWT or standard dressing). To identify contacts within healthcare and dispensed antibiotic prescriptions, data were extracted from four Danish National Databases. Danish citizens have a unique Social Security number (CPR-number) that functions as a key identifier in the National Health and Social Care Registers. This enabled us to analyse healthcare outcomes per patient, we used the following CPR-linked registers: i) the Danish National Patient Register\textsuperscript{21} that comprises all hospital admissions and outpatient visits; ii) the Cost Database\textsuperscript{22} that contains detailed information on cost components during admission; iii) the Danish National Health Service Register\textsuperscript{23} with information about the activities of primary health care; and iv) the Danish National Prescription Registry\textsuperscript{24} that provides individual data (including costs) on all dispensed prescription pharmaceuticals sold in Danish community pharmacies. Details of the specific registers and their cost components are summarized in Appendix S1. Overall, the accuracy of the population-based databases (on which costs were collected) is high, as there is a financial incentive for providers to register services. Due to different registration practices, it was not possible to disentangle the costs of the CS from other costs of the admission such as those who developed a SSI. Accordingly, we divided hospital costs into the caesarean admission, subsequent hospital admissions, and outpatient visits. For practical reasons, some cost data were only available up to and including year 2016. As the last participant was enrolled at the beginning of October 2016, the time horizon was set at three months, which we considered sufficient to capture most long-term costs of a SSI. Any difference in the average healthcare costs between the intervention and control groups was interpreted as attributable to the intervention as all
other cost factors were assumed to be identical in the two groups due to randomisation. The cost of the iNPWT dressing (PICO™, Smith & Nephew, Hull, United Kingdom) was 151.40. This cost included the price of the device itself (147) and the additional time costs for its application. The iNPWT dressing took on average 8 minutes longer to apply than the standard dressing, which amounted to an additional cost of 4.40. The average purchase price for standard dressings was 0.67, which was assumed to be included in the caesarean admission cost. Costs were obtained in DKK and converted to EUROS at year 2015 value, (1= DKK 7.46, and US$ 1.11).

Costs are presented as average hospital costs (i.e. caesarean admission, subsequent hospital admissions, and outpatient visits), primary health care costs, pharmaceutical costs, and as average total healthcare cost per patient. The total healthcare costs are subsequently presented as average total costs for women with and without SSI, and for women with a pre-pregnancy BMI under or over 35 kg/m², as women with a BMI ≥35 kg/m² have an increased risk of SSI compared to women with a BMI between 30 and 35 kg/m².

Missing data

The Cost Database had an estimated coverage ratio of 86% in 2013 to 91% in 2016 for hospital admissions and 79% to 84% for outpatient contacts. Accordingly, some missing data was expected for the variable hospital costs. We assumed that the missing data occurred at random due to an error by the Health Data Board, not patient or hospital-related. In total, 39 of the 876 participating women (4.5%) had missing data for the cost components “surgical procedure” and/or “anaesthesia” in the Cost database. Women with missing hospital cost data were excluded from the base case analysis. To address missing cost, the median costs per hospital per year were imputed in a scenario analysis. In addition, 27/444 (6.1%) non-responders to the study questionnaire in the control group and 22/432 (5.1%) non-responders in the intervention group missed the EQ-5D index value (used to calculate QALYs). Non-response is likely to be related to patient characteristics and therefore assumed not to be randomly missing. Accordingly, we chose not to impute missing EQ-5D index values, but addressed the issue in a scenario analysis. Cost data from the Health Service Register, the Danish National Prescription Register, and data on SSIs were available for all 876 women in the study.

Outlier

One woman had total hospital costs higher than 55,000, which was almost three times as high as the second most costly caesarean admission. This outlier was a woman in the intervention group with a pre-pregnancy BMI of 41.9 kg/m² who had prolonged hospitalization and outpatient care because of deep SSI that required repeated surgery and conservative wound healing. Her patient trajectory was atypical and contributed an additional 122 to the mean hospital cost in the intervention group. This outlier was included in the base case analysis but excluded in a scenario analysis in order to test the impact of including these costs.
Cost-effectiveness analysis

Average healthcare costs were summarised per group as total costs across all trajectories and divided by the total number of women in each group. The incremental cost-effectiveness ratio (ICER) for SSI and for QALY was calculated by dividing the mean cost difference between the groups by the difference in SSI incidence and in mean QALYs between the groups. The ICER reflects the costs needed to avoid one case of SSI, and to gain one additional QALY. Dominance in the results exists if one strategy is found to be both cheaper and more effective.

To determine if the intervention was cost-effective, the cost-effectiveness ratio for a QALY was assessed against a threshold of “willingness-to-pay”. As the real value of the “willingness-to-pay” for a QALY is unknown, the threshold was set at 30,000, corresponding to a conservative estimate of known thresholds in Europe. An intervention is deemed cost-effective if the ICER is less than what the decision maker is willing to pay per QALY gained.

Additional analyses

A probabilistic sensitivity analysis using Monte Carlo simulation and assuming a \( \gamma \)-distribution for costs and a \( \beta \)-distribution for QALY was carried out to investigate the uncertainty in the estimated ICER. The cost and QALY were sampled 1,000 times and a cost-effectiveness acceptability curve as well as a plot of the cost-effectiveness plane were produced, and a 95% credibility interval for ICER was determined.

Furthermore, to establish the robustness of the base case analysis, two “one-way” deterministic sensitivity analyses were conducted to permit determination of possible uncertainty in the ICER that would result from a change in a single parameter in the analysis. In the first deterministic sensitivity analysis, costs were expanded to a time horizon of 12 months to capture healthcare costs occurring beyond three months after CS. Women included in year 2016 were excluded (n=299) because one-year follow-up was not accessible. In the second deterministic sensitivity analysis, we extrapolated the QALY gain to five years and discounted at an annual rate of 3%.

Furthermore, three scenario analyses were undertaken to evaluate the impact of missing cost and QALY data, and the influence of one outlier (with hospital cost > 55,000) on the incremental cost-effectiveness ratios. In the first analysis, we repeated the base case analysis, but excluded the outlier. In the second analysis, the median costs per hospital per year were used to impute missing costs for the costs components “surgical procedure” and “anaesthesia” (Table S2). In the third analysis, women with data on cost but missing QALY data were excluded.

Finally, in a subgroup analysis, the base case analysis was stratified by BMI 30-34.9 kg/m\(^2\) and \( \geq 35 \) kg/m\(^2\) on the rationale that extremely obese women have an increased risk of SSI. Net Monetary Benefit (NMB) was calculated in cases where the mean ICER was non-negative. The NMB is computed as the incremental QALY gain multiplied by the societal threshold for willingness-to-pay for a QALY, minus the incremental costs. The interpretation of NMB is the societal saving when there is a positive willingness-to-pay for a QALY gain (the threshold value) and this value exceeds the incremental cost per QALY. Here a societal willingness-to-pay of 30,000 per QALY gained was assumed, and thus a QALY gained for less than 30,000 represents a societal saving. In a graphical presentation we applied societal thresholds from 0 to 50,000 for estimating the NMB with 95 percent confidence intervals; computed by bootstrapping.
All statistical analyses were performed in Stata, version 15.1 (StataCorp, College Station, TX, USA).

**Results**

Table 1 shows the number of women with healthcare contacts and dispensed antibiotic prescriptions, along with the associated average costs, during the first three months after CS, and the total healthcare costs per patient, stratified by SSI and BMI. The average length of stay for a caesarean admission did not differ by group (data not shown). No overall difference in total healthcare costs per patient between the intervention and control groups was detected (5793.60 vs. 5840.89, p=0.81). Breaking down the costs, we found that superficial SSI on average triggered an additional cost of 20.07 compared to no SSI (p=0.96) whereas deep SSI’s were significantly costlier with an additional cost of 9065.70 (p<0.001). These findings were unrelated to group allocation. Pre-pregnancy BMI ≥35 kg/m² rendered higher health care costs than did a lower BMI (intervention 321.30, p=0.28; control 815.44, p=0.001).

Incisional NPWT was associated with an absolute reduction in SSI of 4.6% (4.6% vs. 9.2%) and a difference in QALY of 0.008 (0.863 vs. 0.855) compared to standard dressings. These measures were 4.7 % (4.4 % vs. 9.1 %) and 0.007 (0.863 vs. 0.856), respectively, for the base case analysis where patients with missing cost data were excluded. Using the mean cost difference of 47.29, the results show that prophylactic iNPWT was the dominant strategy compared to standard dressings as it was both less expensive and more effective (Table 2).

The probabilistic sensitivity analysis (Figure 1) resulted in a large proportion of the scenarios leading to improved QALY with limited or no additional cost, corresponding to a probability of being cost-effective of approximately 65.4% at a willingness to pay threshold of 0, and almost 92.8% at a threshold of 30,000 as illustrated by the cost-effectiveness acceptability curve (Figure 2). The intervention remained dominant in the two one-way sensitivity analyses expanding the time horizon to one year for costs and five years for QALY and in the scenario analysis that excluded the outlier. However, the scenario analysis imputing missing hospital costs changed the incremental costs from -47.29 to 13.39. Two women with deep SSI in the intervention group caused the change in direction of the ICER, and these were left out of the base case analysis. Similar results were found in the analysis excluding 46 women with costs data, but missing data on QALYs in the base case analysis. In this case, two women with deep SSI from the control group were left out of the analysis because of missing QALYs (Table 2).

In the subgroup analysis it appeared that the cost savings were primarily found in patients with a pre-pregnancy BMI ≥35 kg/m². In patients with BMI 30-35 kg/m², the ICER per QALY gained was 29,005, corresponding to a NMB of 5 (95% CI: -716 - 726) at a willingness-to-pay threshold of 30,000 per QALY. The NMB at different thresholds for this subgroup is displayed in Figure S1. Generally the NMB’s are close to zero, reflecting a very small QALY gain in this subgroup.
Discussion

Main findings

To our knowledge, this is the first full economic evaluation of iNPWT within a RCT. The results from the RCT showed that iNPWT significantly reduced the risk of SSI in a population of obese women delivering by CS and that the risk of SSI increased with increasing pre-pregnancy BMI. This trial-based economic evaluation furthermore demonstrates that the iNPWT intervention is the dominant strategy per SSI avoided and QALY gained, respectively, in the base case analysis. The results proved robust when subjected to sensitivity analyses.

The three scenario analyses show that deep SSI requiring surgery is particularly costly and that the inclusion or exclusion of a few women with this condition affects the corresponding ICERs. Because cost data are usually skewed to the right, it is not uncommon, in clinical trials, to have a small number of cases with very high costs, that have a large effect on the mean costs. In our study, the outlier demonstrated that a SSI requiring further surgery can be very costly. However, we believe it is a coincidence that this outlier was in the intervention group, because the prophylactic treatment with iNPWT affects the risk of infection but not the severity. The high cost of the outlier was due to the severity of the infection.

When stratifying the base case analysis by BMI, it appears that the cost saving of the intervention is mainly driven by the benefit to patients with a pre-pregnancy BMI ≥35 kg/m². This finding can probably be explained by the association between increasing BMI and risk of SSI. Overall, the analyses revealed an uncertainty in the ICER estimates due to high variation in costs, and little variation in effects. However, the calculated ICERs are mostly negative and close to zero, which means that the intervention is likely to be dominant and in all analyses are far less than the assumed societal threshold of 30,000 per QALY gained.

Strengths and limitations

The greatest strength of this economic evaluation is that it is based on a large-scale RCT and uses individual patient level cost data. The RCT design, combined with the richness of Danish registry data, strengthens the validity and precision of the results. In addition, the pragmatic nature of the trial strengthens the external validity of the study. Since most costs are related to the actual birth, results are easily transferable to other countries. The study has some limitations, as it was not powered to find a statistically significant difference in costs or in QALY. Therefore, we only have indications of cost-effectiveness in terms of QALY’s. The absence of a cost difference between the intervention and control groups has several possible explanations: i) the additional cost of the iNPWT dressing cancelled out the additional healthcare costs in the control group caused by a higher SSI rate; ii) the study participants were generally young and healthy and had relatively little contact with the healthcare system; iii) costs related to healthcare consumption after CS, as well as antibiotic treatment, are relatively low from a Danish healthcare perspective; iv) although costs were considerably higher in women treated for SSI or who required re-operation because of this, SSI was a rare event. The small (and statistically non-significant) difference between the intervention and control groups in QALYs gained was probably due to the reduced health-related quality of life among patients with SSI, which was more common in the control group. However, SSI was a rare event, and a larger sample size would be needed to demonstrate any statistically significant difference in QALYs gained.
We did not record hospital costs related to time spent on wound care such as removing the standard dressing, wound care after removal of the dressing or troubleshooting related to the iNPWT dressing, because these cost components are generally insignificant. In addition, some costs were expected in the iNPWT group after discharge because removal of the dressing may require GP or hospital involvement. An additional visit to the GP would cost approximately $19, but for 60% of the women, the incision was closed with staples requiring an extra visit to the outpatient clinic or GP for removal of staples anyway. Alternatively, the woman could easily remove the dressing herself.

Interpretation

Several decision-analytic modelling studies have examined the economic benefit of iNPWT compared with standard dressing on closed incisions.\(^15\)\(^,\)\(^16\)\(^,\)\(^33\)\(^,\)\(^34\) The decision-analytic models were conducted using previously published data, where complication rates, QALY gains, and cost data were obtained from various literature sources and national DRG codes. Furthermore, the model-based approach required several assumptions. A study of iNPWT for hip and knee replacement\(^35\) suggested that iNPWT has a probability of being cost-effective of 91% at a threshold of $27,400 (£20,000 at year 2015 value). Two Australian studies of iNPWT after CS showed that iNPWT was cost-effective at an additional cost of $27,924 (Australian$ 42,340 at year 2015 value)\(^33\) and $9893\(^34\) per QALY gained, respectively, and at $888 per SSI avoided\(^33\). Other decision models of iNPWT versus standard dressings after CS or surgery for gynaecological cancer operations, concluded that iNPWT was potentially cost-saving for patients with infection risk greater than 14%,\(^15\) if the infection risk was reduced by at least 33% in an obese population,\(^16\) or if the price of the iNPWT device was less than $177 (US$ 192).\(^15\) In our study, the iNPWT device was priced at $147, corresponding to the list price of the iNPWT dressing used in the RCT (PICO™, Smith & Nephew, Hull, United Kingdom). This price may vary locally or between providers, just as clinical practice and availability of healthcare resources are likely to differ across settings and influence the total costs of healthcare.

Conclusion

In conclusion, this trial-based economic evaluation indicates that the intervention is the dominant strategy because it is both less expensive and more effective, however, no statistical significant difference was found in either costs or QALYs. From a health economic perspective, prophylactic iNPWT is the preferred strategy in obese women with a pre-pregnancy BMI >35 kg/m\(^2\) giving birth by CS compared to standard postoperative dressing. For women with a BMI between 30-35 kg/m\(^2\) prophylactic iNPWT is cost-effective due to the improved effectiveness.

Disclosure of interests

NH, JAS and CB have received funding or honorariums from the company Smith & Nephew. All other authors have nothing to disclose. Completed disclosure of interest forms are available to view online as supporting information.
Contribution to authorship

NH wrote the first draft of the manuscript. NH, MK, CW and SM contributed to the analysis of the data. NH, JSJ, CW, CB, CAV, JAS, OM, RFL, SM, and MK have critically revised the first draft, and approved the final version for publication. NH is guarantor for the trial report.

Details of ethics approval

The study was approved by the Regional Scientific Ethical Committees for Southern Denmark on April 9, 2013 (S-20130010) and the Danish Data Protection Agency on March 13, 2013 (2008-58-0035) and was registered at ClinicalTrials.gov (NCT 01890720).

Funding

The RCT was funded by grants from the University of Southern Denmark, Odense University Hospital, the Region of Southern Denmark, Lundbeckfonden, and an unrestricted grant from the iNPWT device manufacturer Smith&Nephew. None of these sources of funds had influence on study design, data collection, data analyses, interpretation of results, or in the writing of the report.

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Figure Legends

**Figure 1**: Scatterplot of incremental cost and quality-adjusted life-years (QALYs) based on Monte Carlo simulations for incisional Negative Pressure Wound Therapy (iNPWT) and standard postoperative dressings. Q1: iNPWT strategy more costly, less effective. Q2: iNPWT strategy more costly, more effective. Q3: iNPWT strategy less costly, more effective. Q4: iNPWT strategy less costly, less effective. The line shows the willingness-to-pay for a QALY at a threshold of 30,000.

**Figure 2**: Cost-effectiveness acceptability curve for incisional Negative Pressure Wound Therapy. The curve shows the probability that the treatment is cost-effective across a range of willingness-to-pay thresholds, using probabilistic sensitivity analysis.

Table Legends

**Table 1**: Contacts with the healthcare system and antibiotic prescriptions in the 35 days after caesarean section, and average costs per patient, for women with complete available hospital data, treated with incisional Negative Pressure Wound Therapy or standard postoperative dressing; overall, and stratified by surgical site infection (SSI) and body mass index (BMI).

**Table 2**: Incremental cost-effectiveness ratios (ICER) for surgical site infection (SSI) and quality-adjusted life years (QALY) for women treated with incisional Negative Pressure Wound Therapy versus standard postoperative dressing. Results from the base case, sensitivity, scenario, and subgroup analyses.

Supplemental Files

**Figure S1**: Presentation of net monetary benefit (NMB) for women with a pre-pregnancy BMI between 30 and 35 kg/m², together with its sampling uncertainty, as a function of the willingness-to-pay threshold. QALY, quality-adjusted life-years; ICER, incremental cost-effectiveness ratio; CI, confidence interval.

**Table S1**: Self-reported health-related quality of life assessed by EQ-5D-5L for 827 responders to the questionnaire (response rate 94.4%) 30 days after caesarean section, treated with incisional Negative Pressure Wound Therapy or standard postoperative dressing; overall and with surgical site infection (SSI).

**Table S2**: Summary statistic per hospital per year for the costs components ‘surgical procedure’ and ‘anaesthesia in the Cost database.'
Appendix S1: Cost for postpartum care in Denmark, data sources and description of cost components.

Table 1: Types of contacts with the healthcare system and antibiotic prescriptions within 3 months after caesarean section, and average costs per patient, for women with complete available hospital data, treated with incisional Negative Pressure Wound Therapy or standard postoperative dressing; overall, and stratified by surgical site infection (SSI) and body mass index (BMI).

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
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<tbody>
<tr>
<td></td>
<td>N contacts /</td>
<td>N contacts /</td>
</tr>
<tr>
<td></td>
<td>mean contacts</td>
<td>mean contacts</td>
</tr>
<tr>
<td></td>
<td>(95% CI)</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>Caesarean admission</td>
<td>409 (5182.52–5754.83)</td>
<td>428 (5365.03–5745.03)</td>
</tr>
<tr>
<td>Rehospitalisation*</td>
<td>35 / 1.2 (1.0–1.3)</td>
<td>39 / 1.3 (1.0–1.6)</td>
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<tr>
<td>Outpatient visits</td>
<td>347 / 2.0 (1.8–2.2)</td>
<td>324 / 2.1 (1.9–2.3)</td>
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<td>General practitioners</td>
<td>395 / 2.1 (2.0–2.2)</td>
<td>417 / 2.2 (2.1–2.3)</td>
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<tr>
<td>Prescriptions of antibiotic**</td>
<td>112 / 2.1 (1.1–1.3)</td>
<td>111 / 2.1 (1.1–1.2)</td>
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<tr>
<td>Postoperative dressing</td>
<td>409 151.34***</td>
<td>428 0.67****</td>
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</table>

Average total healthcare costs per patient

<table>
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<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
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<tr>
<td>Overall</td>
<td>409 5793.60 (5503.71–6083.49)</td>
<td>428 5840.77 (5597.38–6084.16)</td>
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<tr>
<td>No SSI</td>
<td>391 5626.13 (5465.28–5786.98)</td>
<td>389 5664.92 (5466.63–5863.20)</td>
</tr>
<tr>
<td>Superficial SSI</td>
<td>12 5608.31 (4331.15–6885.46)</td>
<td>30 5928.25 (5108.68–6747.82)</td>
</tr>
<tr>
<td>SSI requiring surgery</td>
<td>6 17,077.48 (519.37–33,635.59)</td>
<td>9 13,150.03 (6786.85–19,513.2)</td>
</tr>
</tbody>
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| BMI < 35 kg/m² | 208 | 5635.70 | 239 | 5480.59 |
|               |     | (5403.88–5867.52) |     | (5285.74–5675.44) |
| BMI ≥ 35 kg/m²| 201 | 5956.99 | 189 | 6296.24 |
|               |     | (5417.19–6496.80) |     | (5809.16–6783.31) |

N, number of women with at least one contact/prescription and mean contacts/prescriptions per woman; CI, confidence interval; * any subsequent hospital admissions regardless of cause; ** all prescriptions regardless of the indication for antibiotic treatment; *** this cost includes the price of the device itself (147.0) and the time costs for its application; *** this cost is included in the cost of caesarean admission

Table 2: Incremental cost-effectiveness ratios (ICER) for surgical site infection (SSI) and quality-adjusted life years (QALYs) for women treated with incisional Negative Pressure Wound Therapy versus standard postoperative dressing. Results from the base case, sensitivity, scenario, and subgroup analyses.

<table>
<thead>
<tr>
<th></th>
<th>Average costs</th>
<th>Risk of SSI (%)</th>
<th>Average QALYs</th>
<th>ICER per SSI avoided</th>
<th>ICER per QALY gained</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base case analysis</strong> (costs 3 months, QALY 1 year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n=409)</td>
<td>5793.60</td>
<td>4.40</td>
<td>0.863</td>
<td>Dominant</td>
<td>Dominant</td>
</tr>
<tr>
<td>Control (n=428)</td>
<td>5840.89</td>
<td>9.11</td>
<td>0.856</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>-47.29</td>
<td>4.71</td>
<td>0.007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(               )</td>
<td>(-424.51–329.93)</td>
<td>(1.34–8.10)</td>
<td>(-0.008–0.022)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Probabilistic sensitivity analysis</strong> (costs 3 months, QALY 1 year)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n=409)</td>
<td>5793.88</td>
<td>NA</td>
<td>0.868</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (n=428)</td>
<td>5839.64</td>
<td>NA</td>
<td>0.861</td>
<td>NA</td>
<td>Dominant</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>-45.76</td>
<td>NA</td>
<td>0.007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(               )</td>
<td>(-124.45–220.52)</td>
<td>NA</td>
<td>(-0.005, 0.017)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sensitivity analysis I</strong> (costs 12 months, QALY 1 year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n=272)</td>
<td>6388.41</td>
<td>4.41</td>
<td>0.863</td>
<td>Dominant</td>
<td>Dominant</td>
</tr>
<tr>
<td>Control (n=280)</td>
<td>6634.75</td>
<td>12.50</td>
<td>0.855</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>-246.34</td>
<td>8.09</td>
<td>0.008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(               )</td>
<td>(-711.78–219.10)</td>
<td>(3.51–12.67)</td>
<td>(-0.010–0.027)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sensitivity analysis II</strong> (costs 12 months, QALY 5 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n=272)</td>
<td>6388.41</td>
<td>NA</td>
<td>4.071</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (n=280)</td>
<td>6634.75</td>
<td>NA</td>
<td>4.032</td>
<td>NA</td>
<td>Dominant</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>-246.34</td>
<td>NA</td>
<td>0.039</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(               )</td>
<td>(-711.78–219.10)</td>
<td>NA</td>
<td>(-0.049–0.129)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Scenario analysis I (base case analysis, excluding one woman with hospital costs > 55,000)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Intervention (n=408)</th>
<th>Control (n=428)</th>
<th>Difference (95% CI)</th>
<th>Dominant</th>
<th>Dominant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5671.39</td>
<td>5840.89</td>
<td>-169.50 (-465.35–126.35)</td>
<td>0.864</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Scenario analysis II (imputation of missing hospital cost; cost 3 months, QALY 1 year)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Intervention (n=432)</th>
<th>Control (n=444)</th>
<th>Difference (95% CI)</th>
<th>Dominant</th>
<th>Dominant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5839.69</td>
<td>5826.30</td>
<td>13.40 (-351.49–378.29)</td>
<td>0.862</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Scenario analysis III (excluding women with missing QALY data; cost 3 months, QALY 1 year)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Intervention (n=389)</th>
<th>Control (n=402)</th>
<th>Difference (95% CI)</th>
<th>Dominant</th>
<th>Dominant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5794.61</td>
<td>5756.64</td>
<td>37.97 (-321.37–397.30)</td>
<td>0.863</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Subgroup analysis (base case analysis for women with BMI < 35 kg/m²)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Intervention (n=208)</th>
<th>Control (n=239)</th>
<th>Difference (95% CI)</th>
<th>Dominant</th>
<th>Dominant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5635.70</td>
<td>5480.80</td>
<td>-154.90 (-145.74–455.54)</td>
<td>0.860</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Subgroup analysis (base case analysis for women with BMI ≥35 kg/m²)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Intervention (n=201)</th>
<th>Control (n=189)</th>
<th>Difference (95% CI)</th>
<th>Dominant</th>
<th>Dominant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5956.99</td>
<td>6296.24</td>
<td>-339.24 (-1069.3–390.82)</td>
<td>0.867</td>
<td>0.008</td>
</tr>
</tbody>
</table>

* The probability distributions of cost and QALY were sampled 1000 times (with 2000 patients in each, 1000 in each group) and presented as median and 95% credibility interval; BMI, body mass index; NA, not applicable