Home telemonitoring versus hospital care in complicated pregnancies in the Netherlands: a randomised, controlled non-inferiority trial (HoTeL)

Mireille N Bekker, Maria P H Koster, Willem R Keusters, Wessel Ganzevoort, Jiska M de Haan-Jebbink, Koen L Deurloo, Laura Seeber, David P van der Ham, Nicolaas P A Zuithoff, Geert W J Frederix, Josephus F M van den Heuvel, Arie Franx

Summary

Background Women with complicated pregnancies often require hospital admission. Telemonitoring at home is a promising alternative that fulfils a worldwide need in obstetric health care. Moreover, the COVID-19 pandemic has accelerated the transformation to digital care. The aim of this study was to evaluate safety, clinical effectiveness, patient satisfaction, and costs of home telemonitoring against hospital care in complicated pregnancies.

Methods We did a multicentre, randomised, controlled, non-inferiority trial in six hospitals (four general teaching hospitals and two university hospitals) in the Netherlands (located in Utrecht, Amsterdam, and Groningen). Women aged 18 years and older with singleton pregnancies (>26 weeks gestation) requiring monitoring for pre-eclampsia, fetal growth restriction, fetal anomaly, preterm rupture of membranes, reduced fetal movements, or history of fetal death were included in the study. Participants were randomly assigned to either hospital admission or telemonitoring in (1:1), stratified for the six diagnoses for inclusion and the six centres of inclusion, using block randomisation (block sizes of four and six). When assigned to telemonitoring, participants went home with devices for cardiotocography and blood pressure measurements and had daily contact with their care providers after digitally sending their home measurements. When assigned to hospital admission, participants received care as usual on the ward until the postpartum period. The primary outcome was a composite of adverse perinatal outcomes assessed after delivery, including mortality; an Apgar score below 7 after 5 min or an umbilical arterial pH at birth below 7·05; maternal morbidity; admission of the newborn to the neonatal intensive care unit; and rate of caesarean section. The primary outcome was assessed in the intention-to-treat population. The non-inferiority margin for the primary outcome was a 10% absolute increase in composite primary endpoint based on baseline 20% incidence. The study was registered at the Dutch Trial Registration (NL5888) and is now closed to new participants.

Findings From Dec 1, 2016, to Nov 30, 2019, 201 pregnant women were randomly assigned to an intervention procedure. 101 women were allocated to the telemonitoring group and 100 to the hospital admission group. One participant in the telemonitoring group withdrew consent before the intervention was initiated, and 100 participants were analysed for the primary outcome. In the hospital admission group, four participants did not receive the allocated intervention because they did not accept hospital admission. 100 participants in each group were analysed for the primary outcome according to the intention-to-treat principal. No participants were lost to follow-up. The primary outcome occurred in 31 (31%) of 100 participants in the telemonitoring group and in 40 (40%) of 100 participants in the hospital admission group. Adjusted for centre of inclusion, diagnosis, and nulliparity, the risk difference in primary outcome between both groups was 10·3% (95% CI −22·4 to 2·2) lower in the telemonitoring group, below the pre-defined non-inferiority margin of 10% absolute increase. A similar distribution for each of the individual components within the composite primary outcome was seen between groups. Five serious adverse events were reported: one neonatal death in the hospital admission group, in addition to one intra-uterine fetal death, two neonatal deaths, and one case of eclampsia in the telemonitoring group, all unrelated to the study.

Interpretation This non-inferiority trial shows the first evidence that telemonitoring might be as safe as hospital admission for monitoring complicated pregnancies.

Funding Stichting Achmea Gezondheidszorg and ICT Healthcare Technology Solutions.

Lancet Digit Health 2023; 5: e116–24

See **Comment** page e103

Department of Obstetrics and Gynaecology (Prof M N Bekker PhD, J F M van den Heuvel PhD, Prof A Franx PhD)**; Department of Julius Center, Health Sciences** (W R Keusters MSc, N P A Zuithoff PhD, G W J Frederix PhD)**; University Medical Center Utrecht, Utrecht, Netherlands; Department of Obstetrics and Gynaecology, Erasmus Medical Centre, Rotterdam, Netherlands** (M P H Koster PhD, Prof A Franx)**; Department of Obstetrics and Gynaecology, Amsterdam University Medical Center, Amsterdam, Netherlands** (W Ganzevoort PhD)**; Department of Obstetrics and Gynaecology, Onze Lieve Vrouwe Gasthuis, Amsterdam, Netherlands** (J M de Haan-Jebbink PhD)**; Department of Obstetrics and Gynaecology, Diakonessenhuis, Utrecht, Netherlands** (K L Deurloo PhD)**; Department of Obstetrics and Gynaecology, Sint Antonius Hospital, Nieuwegein, Netherlands** (L Seeber PhD)**; Department of Obstetrics and Gynaecology, Martini Hospital, Groningen, Netherlands** (D P van der Ham PhD)

Correspondence to:
Prof M N Bekker, Department of Obstetrics and Gynaecology, University Medical Center Utrecht, 6 3584 EA Utrecht, Netherlands
m.n.bekker-3@umcutrecht.nl

Introduction

The aim of daily monitoring in complicated pregnancies is to assess fetal wellbeing using cardiotocography and maternal condition using registration of symptoms, blood pressure, and urinary and blood analysis. This increased surveillance leads to antenatal hospital admissions in up to 20% of pregnancies, mostly for hypertensive disorders including pre-eclampsia, fetal growth restriction, preterm rupture of membranes, imminent preterm birth, gestational diabetes, and fetal anomalies.[1–4] These hospital

Research in context

Evidence before this study

Pregnant women faced with complications of pregnancy are recommended increased surveillance of both maternal and fetal parameters. After diagnosis of preterm rupture of membranes, fetal growth restriction, fetal anomalies, and hypertensive disorders including pre-eclampsia, hospital admission is required to assess fetal and maternal wellbeing. These antenatal admissions can result in dissatisfaction with in-hospital stay and substantial costs and family burden. Recent technological innovations resulted in telemonitoring platforms allowing for home cardiotocography and blood pressure monitoring. At the start of this trial, no randomised studies had been done to assess safety of care of telemonitoring high-risk pregnant women. We searched PubMed for Articles in English from Jan 1, 2000, to June 1, 2017, using combinations of terms of "telemedicine", "pregnancy", "cardiotocography", and "remote monitoring". One review from 2017 reported on 14 studies, mostly using home monitoring of uterine activity and maternal glucose in high-risk pregnancy and concluded that telemonitoring can contribute to reductions in health-care costs and hospital visits and improved satisfaction when compared with control groups. However, telemonitoring of fetal parameters was not assessed in that review. After completion of the trial, the search was re-run (June 1, 2022). One retrospective study published in 2021 of 400 complicated pregnancies monitored with home cardiotocography showed no severe maternal complications and nine fetal or neonatal deaths, which were deemed attributable not to the home telemonitoring setting but to the complicated course of pregnancy. No other prospective or randomised studies were found.

Added value of this study

Our findings of the first randomised trial of home telemonitoring compared with hospital care in complicated pregnancy suggest that telemonitoring could be as safe as hospital admission in a heterogeneous study population with diverse complications of pregnancy requiring daily surveillance. Telemonitoring is non-inferior to hospital admission in both intention-to-treat and per-protocol analyses. A significant cost reduction in antenatal costs of 18% was found in favour of telemonitoring, with higher satisfaction scores as reported by telemonitoring participants.

Implications of all the available evidence

This first randomised trial using fetal cardiotocography and maternal monitoring suggests that telemonitoring is a safe alternative for monitoring selected high-risk singleton pregnancies. Combined with a reduction in costs and higher patient satisfaction, these results show the potential to change antenatal care strategies. As the health-care costs and staff shortages continue to increase worldwide, innovations reducing cost reduction without concessions to the quality of care are urgently required. Furthermore, the global challenges for health care during the COVID-19 pandemic emphasise the need for innovation of health-care delivery by digital health solutions allowing remote monitoring. Large-scale studies are needed to investigate safety of care in these pregnancies further and confirm these results.

admissions often last until delivery and are associated with patient dissatisfaction with the in-hospital stay, family burden, and substantial costs.[5,6]

Recent technological advancements in health care (eHealth) have resulted in remote monitoring platforms, mobile device-supported care, telemedicine, and tele-consultation.[7] eHealth has the potential to empower patients and create a better access to health care while reducing the necessity for hospital visits or admission. Pregnant women are frequent users of smartphones and the internet and are therefore already equipped with the hardware to perform self-measurements at home and the mindset to communicate these digitally with their prenatal care professional.[8] Telemonitoring in pregnancy is one of the most promising applications of eHealth in antenatal care.[9,10] Self-monitoring of maternal and fetal condition at home by blood pressure measurements and cardiotocography can considerably reduce the need for antenatal hospital admission and visits to outpatient clinics. Thus, telemonitoring might reduce costs and offer value to patients and society. Moreover, the COVID-19 pandemic has forced health-care professionals and health policy makers to speed up innovation and implementation of digital health-care solutions.

To our knowledge, there are no published clinical trials evaluating a digital health strategy with telemonitoring of self-recorded data against hospital admission in complicated pregnancies. Previous studies of pilots and retrospective data found favourable results for pregnancy telemonitoring regarding safety of care and patient experiences.[11,12] However, risks of implementation of digital innovations without evaluation beforehand include usability problems, issues regarding safety and costs, and adverse effects, resulting in disappointing adoption of digital procedures by end-users in clinical practice.

Given this lack of evidence, we did a multicentre, randomised controlled trial, the hospital care versus telemonitoring (HoTeL) study, in which complicated pregnancies requiring daily monitoring were randomly assigned to hospital care as usual or home telemonitoring. We aimed to evaluate safety and clinical effectiveness as well as patient satisfaction and cost-effectiveness of both strategies.

Methods

Study design and participants

We conducted a multicentre, randomised, controlled non-inferiority trial in six hospitals in the Netherlands

(Utrecht, Amsterdam, and Groningen), including four general teaching hospitals and two university hospitals. Women aged 18 years and older with a singleton pregnancy (>26+0 weeks gestational age) who required hospital admission for maternal or fetal surveillance, according to national guidelines, for one or more of the following reasons were eligible: (1) pre-eclampsia; (2) preterm pre-labor rupture of membranes without contractions; (3) fetal growth restriction; (4) recurrent reduced fetal movements; (5) fetal anomaly requiring daily monitoring; and (6) fetal death in a previous pregnancy. Exclusion criteria were: pregnancy complications requiring intravenous medication or expected need for obstetric intervention within 48 h of enrolment; current blood pressure higher than 160/110 mmHg; active antepartum haemorrhage or signs of placental abruption; cardiotocography registration with abnormalities indicating fetal distress or hypoxia; place of residence more than 30 min travel distance from a hospital; multiple pregnancy; and insufficient knowledge of Dutch or English or incapability to understand training or instructions of telemonitoring devices. All participants provided written informed consent. The trial protocol was approved by the Medical Research Ethics Committee of the University Medical Centre Utrecht (trial reference number 16-516) and has been previously published.[13]

Randomisation and masking

Participants were randomly assigned to either hospital admission or telemonitoring (1:1 ratio). Randomisation was done at each centre by trained research midwives or nurses through a secured web-based domain (Research Online, Julius Research Support, UMC Utrecht) and was stratified for the six diagnoses for inclusion and the six centres of inclusion. Balanced block randomisation with variable block sizes of four and six was used, including allocation concealment. Trial arm crossover was not permitted and considered a protocol violation. Due to the nature of the intervention, participants and health-care providers were not masked to group assignment.

Procedures

A detailed overview of the trial procedures, such as training of the telemonitoring protocol of obstetric care at each site, is provided in the trial protocol.[13] The process of telemonitoring is a result of more than 25 years of experience with home care for pregnant patients in the Netherlands and tested for feasibility, usability, and patient experiences aided with the involvement of admitted patients.[11] Participants randomised to telemonitoring were trained face-to-face to use the medical devices involved in the telemonitoring system (Sense4Baby cardiotocography system (ICT Healthcare Technology Solutions) and the Microlife WatchBP (Microlife). Each participant received an individual treatment plan according to national guidelines, including daily fetal monitoring by cardiotocography and, if needed, maternal blood pressure and temperature measurements. Patients were requested to perform cardiotocography monitoring once daily at a set time allowing for real-time assessment via the internet portal. Blood pressure was self-measured one to three times daily, depending on indication. The telemonitoring team, consisting of trained midwives in each participating centre, contacted all participants daily by regular phone call to discuss current symptoms and self-monitoring results. Examples of protocolled steps in the management were: expectant management, same-day clinical assessment (eg, in case of cardiotocography abnormalities, increase in blood pressure, or other symptoms) or, if necessary, clinical admission (eg, concerning cardiotocography results, hypertension, contractions, antenatal haemorrhage, signs of infection, maternal distress at home, or technical difficulties). Each participant assigned to the telemonitoring group visited the outpatient clinic at least once a week and, when indicated, ultrasound assessment and blood or urinary analyses were done. In case a woman allocated to the telemonitoring group was admitted to hospital, data collection continued throughout admission and, as per random assignment, when discharged antenatally from the ward (eg, after treatment optimisation for hypertension) she was allowed to return to telemonitoring until delivery.

When allocated to hospital admission, participants received standard obstetric care according to national guidelines, including state-of-the-art daily fetal monitoring and blood pressure measurements. In case hospital admission was no longer required, the patient was discharged and, when indicated, admitted to the ward again. Crossover to telemonitoring was not allowed.

Outcomes

The primary outcome was safety, expressed as a composite of the following adverse perinatal outcomes: perinatal mortality (maternal, fetal, or neonatal); an Apgar score below 7 after 5 min or an umbilical arterial pH at birth below 7·05, or both; maternal morbidity (eclampsia; haemolysis, elevated liver enzymes, and low platelets syndrome; and thromboembolic events); admission of the newborn to the neonatal intensive care unit; and rate of caesarean section. The components of the composite outcome were chosen for either the possibility to be affected by the new intervention (eg, a severe adverse event at a participant's home resulting in a newborn asphyxia) or the severity as a stand-alone adverse outcome (eg, a pre-labour emergency primary caesarean section for an admitted participant because of fetal distress in a growth-restricted fetus), or both. The primary outcome was assessed in the intention-to-treat population.

All separate components of the composite primary outcome were considered as secondary outcomes. Other secondary outcomes were patient satisfaction, quality of life, costs per patient, and budget impact. Patient wellbeing was assessed by the State Trait Anxiety

Inventory (STAI), Edinburgh Postnatal Depression Score (EPDS), and EuroQol 5D (EQ5D), questionnaires,[14–16] which were assessed at inclusion and 4 weeks after delivery. Patients' wellbeing was further assessed 4 weeks after delivery by a questionnaire including satisfaction score (developed by the authors and informed by focus group discussions; appendix pp 5–12).[11,13] In addition to the methods stated in the trial protocol, the Patient Participation and Satisfaction Questionnaire (PPSQ) was used.[17] For the STAI, EPDS, and PPSQ and satisfaction score, lower scores indicate better outcomes; for EQ5D score (inclusive of the Visual Analogue Scale which records the respondents self-rated health on a vertical, 20 cm scale), higher scores indicate better outcomes. Secondary outcomes were assessed in a modified intention-to-treat population (all patients with available data).

Health-care cost data regarding three time periods were collected (appendix pp 3, 18): antenatal costs consisted of all pregnancy-related health-care activities and interventions performed before delivery, delivery costs consisted of all interventions performed during delivery, and postpartum costs consisted of all admission days during and after delivery until discharge from the hospital. Unit costs were derived from literature or calculated using a bottom-up approach. All costs were converted to 2020 Euros using consumer price indices of Statistics Netherlands.[18] A budget impact analysis was done, assuming an incidence of adverse pregnancy outcomes of 20% in an annual number of 170 000 pregnancies in the Netherlands. Outcome assessors were not masked with respect to the allocated treatment.

Statistical analysis

The risk of the composite primary outcome in our study population was assumed to be 20% in either group.[13] The non-inferiority margin was set at a 10% adjusted absolute increase in risk difference of the primary outcome in the telemonitoring group compared with the hospital admission group. The trial group made a reasoned choice about the acceptable difference in adverse perinatal outcome and feasibility of the trial, since this is the first ongoing trial of telemonitoring in complicated pregnancies.[13] Considering a one-sided alpha of 0·05, a power of 0·80, and a loss to follow-up rate of 4%, a total of 416 patients were needed (ie, 208 in each arm). An interim analysis was performed after inclusion of 200 patients, after which it was decided to close the study.

As there were no missing data in the components needed to determine the primary endpoint, a complete case analysis was performed. Data analyses were primarily carried out according to the intention-to-treat principle. We also performed a pre-specified per protocol analysis for the primary outcome, for which we excluded participants in whom there was a clear deviation or suboptimal execution of the intended care. Examples include non-compliance of study agreements, crossover, or participants in the telemonitoring group with one or more hospital admissions accounting for more than half of their time in the study.

The primary outcome was analysed using logistic regression analysis by Firth's correction with the stratification factors (centre of inclusion and diagnosis) and parity as predefined covariates in the regression model. Because the non-inferiority limit was set as a risk

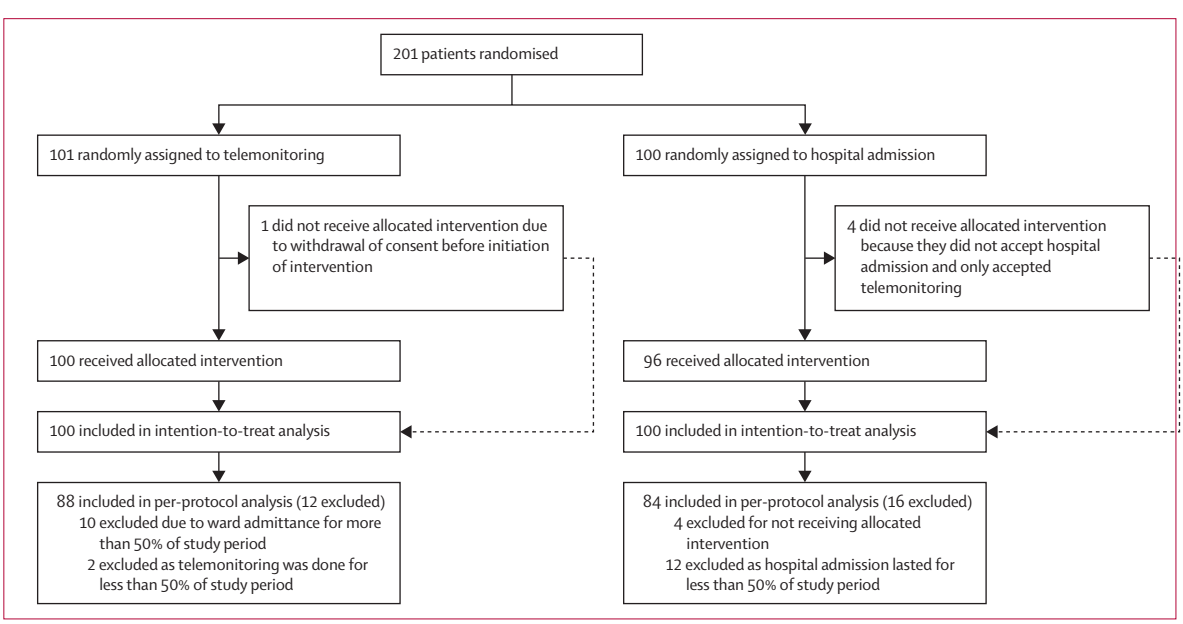

Figure: **Trial profile**
No participants were lost to follow-up in either group.

	Telemonitoring group (n=100)	Hospital admission group (n=100)
Age, years	33·2 (4·8)	33·4 (4·6)
BMI, kg/m²	25·4 (5·2)	24·6 (5·0)
Missing	1 (1%)	4 (4%)
Ethnicity		
Dutch	64 (64%)	72 (72%)
Other European	9 (9%)	2 (2%)
Mediterranean	9 (9%)	12 (12%)
Hindustani	6 (6%)	4 (4%)
Black	5 (5%)	6 (6%)
Asian	2 (2%)	2 (2%)
Unknown	5 (5%)	2 (2%)
Educational level (n, %)		
Low	8 (8%)	15 (15%)
Middle	23 (23%)	20 (20%)
High	35 (35%)	24 (24%)
Missing	34 (34%)	41 (41%)
Medical history		
Diabetes	2 (2%)	3 (3%)
Gestational diabetes	5 (5%)	7 (7%)
Pre-existent hypertension	7 (7%)	12 (12%)
Thrombophilia	1 (1%)	1 (1%)
Thyroid disease	4 (4%)	3 (3%)
Polycystic ovary syndrome	4 (4%)	6 (6%)
Missing	4 (4%)	2 (2%)
Current smoker	7 (7%)	11 (11%)
Missing	2 (2%)	4 (4%)
Alcohol use	0	0
Nulliparity	62 (62%)	66 (66%)
Centre of inclusion		
1	43 (43%)	46 (46%)
2	14 (14%)	17 (17%)
3	10 (10%)	9 (9%)
4	11 (11%)	9 (9%)
5	9 (9%)	8 (8%)
6	13 (13%)	11 (11%)
(Continued from previous column)		
Diagnosis and reason for inclusion in study		
Pre-eclampsia	34 (34%)	37 (37%)
Fetal growth restriction	18 (18%)	21 (21%)
Preterm rupture of membranes	36 (36%)	35 (35%)
Recurrent decreased fetal movement	8 (8%)	5 (5%)
Fetal anomaly requiring daily monitoring	3 (3%)	2 (2%)
Fetal death in obstetric history	1 (1%)	0
Gestational age at study entry, days (median [IQR])	241 (221–252)	238 (213–248)
Blood pressure at study entry, mmHg		
Systolic	124 (15)	126 (16)
Diastolic	78 (12)	78 (12)
Missing	1 (1%)	9 (9%)
Known fetal structural defects at study entry	8 (8%)	7 (7%)
Duration of inclusion in study from start to delivery, days (median [IQR])	11 (6–22)	12 (6–25)

Data are mean (SD), median (IQR), n (%), or n/N (%). Ethnicity and education level data were extracted from electronic health records.

Table 1: **Baseline characteristics**

difference, we applied the approach previously described by Austin[19] to determine risk differences from a logistic regression model. Details of the additional statistical plan and rationale, which deviate from the published statistical plan, are presented in the appendix (p 2).[13] For each individual component (secondary) outcome, absolute numbers and risk differences with accompanying 95% CIs were reported, without adjustment for covariates.

Patient wellbeing and satisfaction at 4 weeks after delivery were compared between groups using linear regression models adjusted for baseline scores, centre of inclusion, diagnosis, and parity, after assessment of normality, homogeneity, and linearity for quantitative predictors. Histograms and QQ-plots were constructed to assess normality, and a scatterplot of raw and studentised residuals against predicted values.

For the analysis of costs (appendix p 3), all health-care resources were transformed into cost estimates by multiplying the number of units of health-care use by standard unit prices (appendix p 18). In case of missing data, the mean of the population was used to impute these values. In order to assess outliers, costs per group were displayed as a distribution to visually inspect the measured cost differences. A sensitivity analysis using 10 000 bootstrapping samples was performed to assess variation between participants.

The trial was registered at the National Dutch Trial Registry (https://trialsearch.who.int/Trial2.aspx?TrialID=NTR6076, NL5888). To monitor the conduct of the trial and safeguard the interest of participants, an independent Data Safety Monitoring Board was installed. An independent monitor periodically visited participating centres, assessing quality of data and auditing trial conduct. Results are reported according to CONSORT guidelines, using the extension for non-inferiority trials (appendix p 21).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit for publication.

	Telemonitoring group (n=100)	Hospital admission group (n=100)	Risk difference (95% CI)
Primary outcomes			
Primary outcome	31 (31%)	40 (40%)	−0·103 (−0·224 to 0·022)*
Separate components of the primary outcome			
Caesarean section during labour	14 (14%)	15 (15%)	−0·010 (−0·108 to 0·088)
Maternal mortality	0	0	..
Fetal mortality	1 (1%)	0	0·010 (−0·010 to 0·030)
Neonatal mortality	2 (2%)	1 (1%)	0·010 (−0·024 to 0·044)
Deep venous thrombosis or pulmonary embolism	0	1 (1%)	−0·010 (−0·030 to 0·010)
Eclampsia	1 (1%)	2 (2%)	−0·010 (−0·044 to 0·024)
HELLP syndrome	0	2 (2%)	−0·020 (−0·047 to 0·007)
Low Apgar (<7 after 5 min) or arterial pH <7·05	8 (8%)	8 (8%)	0·000 (−0·075 to 0·075)
NICU admission	18 (18%)	20 (20%)	−0·020 (−0·129 to 0·089)
Additional secondary outcomes			
Gestational age at delivery, days	258 (239–261)	255 (243–260)	..
Preterm birth	56 (56%)	65 (65%)	−0·090 (−0·225 to 0·045)
Birth weight, g	2407 (751)	2270 (720)	..
Small for gestational age <p10	28 (28%)	27 (27%)	0·010 (−0·114 to 0·134)
Small for gestational age <p3	10 (10%)	13 (13%)	−0·030 (−0·118 to 0·058)
Congenital anomalies	7 (7%)	5 (5%)	0·020 (−0·046 to 0·086)
Time to delivery, days (median [IQR])	11 (6–22)	12 (6–25)	−0·010 (−0·050 to 0·030)

Data are n(%), median (IQR), or mean (SD). HELLP syndrome=haemolysis, elevated liver enzymes, low platelets syndrome. NICU=neonatal intensive care unit. p10=below the tenth percentile based on the Hadlock 3 fetal growth curve. p3=below the third percentile based on the Hadlock 3 fetal growth curve. *Primary outcome was adjusted for centre of inclusion, diagnosis, and nulliparity.

Table 2: **Intention-to-treat analysis of the primary and secondary adverse pregnancy outcomes**

	Telemonitoring group (n=100)	Hospital admission group (n=100)	Adjusted mean difference*
Wellbeing at inclusion			
Number of participants	72 (72%)	60 (60%)	..
STAI score	13·40 (1·90)	13·30 (2·10)	..
EPDS score	18·20 (4·70)	18·70 (4·50)	..
EQ5D score	0·77 (0·17)	0·80 (0·14)	..
VAS score within EQ5D	73·00 (17·00)	77·30 (13·70)	..
Wellbeing 4 weeks after delivery			
Number of participants	56 (56%)	42 (42%)	..
STAI score	14·00 (1·40)	13·80 (1·20)	0·33 (−0·31 to 0·98)
EPDS score	16·30 (4·40)	16·60 (3·50)	−0·56 (−2·54 to 1·43)
EQ5D score	0·84 (0·23)	0·86 (0·12)	−0·01 (−0·09 to 0·08)
VAS score within EQ5D	78·90 (15·60)	77·80 (16·20)	3·57 (−3·07 to 10·21)
Satisfaction 4 weeks after delivery			
Number of participants	56 (56%)	42 (42%)	..
PPSQ score	40·80 (12·20)	48·80 (16·50)	8·90 (−15·10 to −2·60)
Satisfaction score	1·60 (0·69)	1·95 (0·88)	−0·35 (−0·69 to 0·00)
Pregnancy care grading	8·34 (1·00)	7·68 (1·47)	0·68 (0·14 to 1·22)

Data are presented as mean (SD) or n (%). STAI=State Trait Anxiety Inventory. EPDS=Edinburgh Postnatal Depression Score. EQ5D=EuroQol 5D. VAS=Visual Analogue Scale. PPSQ=Patient Participation and Satisfaction Questionnaire. *Adjusted for centre of inclusion, diagnosis, nulliparity, and baseline scores.

Table 3: **Wellbeing and satisfaction of participants at inclusion and 4 weeks after delivery**

Results

From Dec 1, 2016, to Nov 30, 2019, a total of 201 pregnant women were randomly assigned to either telemonitoring or hospital admission. 101 women were allocated to the intervention group (telemonitoring) and 100 allocated to the control group (hospital admission). No participants were lost to follow-up. In the telemonitoring group, one participant withdrew consent before telemonitoring was initiated, and a total of 100 participants were analysed for the primary outcome. In the hospital admission group, four participants did not receive the allocated intervention because they did not accept hospital admission and wanted telemonitoring; however, according to the intention-to-treat principal, 100 participants were still analysed for the primary outcome (figure). The mean age of participants was 33 years and their mean BMI was 25 kg/m² (table 1). The most common indications for participants to be enrolled were pre-eclampsia (71 [36%] of 200), premature rupture of membranes (71 [36%] of 200), or intrauterine growth restriction (39 [20%] of 200). The mean gestational age at which participants were enrolled in the study was 34 weeks and the mean duration of inclusion in the study was 11–12 days. There were no obvious differences in characteristics between groups (table 1).

The composite primary outcome occurred in 31 (31%) of 100 participants in the telemonitoring group and 40 (40%) of 100 participants in the hospital admission group. In-labour caesarean sections (14% in the telemonitoring group and 15% in the hospital admission group) and admissions to the neonatal intensive care unit (18% in the telemonitoring group and 20% in the hospital admission group) accounted for most of the primary outcomes (table 2). The adjusted risk difference in primary outcome between both groups was 10·3% (95% CI −22·4 to 2·2) lower for telemonitoring, below the pre-defined non-inferiority margin of 10% absolute increase. A similar distribution for each of the individual components within the composite primary outcome was seen between groups (table 2). In total, five serious adverse events were reported (appendix p 13). One neonatal death (infection and prematurity) occurred in the hospital admission group. One intra-uterine fetal death (trisomy 21 and fetal growth restriction), two neonatal deaths (lung hypoplasia after immature rupture of membranes, and death after placental abruption), and one case of eclampsia occurred in the telemonitoring group. All adverse events were reported to the Medical Research Ethics Committee and the Data Safety Monitoring Board, and none of the adverse events were study related. The per-protocol analysis consisted of 88 participants in the telemonitoring group and 84 participants in the hospital admission group (figure); the adjusted risk difference in primary outcome between both groups was 11·8% (95% CI −25·8 to 2·4), suggesting the effectiveness of telemonitoring as well as hospital admission.

Upon inclusion in the study, 72 (72%) women in the intervention group and 60 (60%) women in the control group filled in patient wellbeing questionnaires. Participants in both groups scored high on average on mental and physical wellbeing (table 3). Longitudinal analysis of questionnaires showed similar results between groups (appendix p 20). 4 weeks after delivery, 56 (56%) participants in the intervention group and 42 (42%) participants in the control group filled in these questionnaires once more; compared with participants who did not respond to these questionnaires, responders were more often allocated to telemonitoring and were

	Telemonitoring group (n=100)			Hospital admission group (n=100)			Difference
	Mean costs	Median costs	Treated (%)	Mean costs	Median costs	Treated (%)	Mean costs
Antenatal							
Medication							
Anticonvulsants	€24	€0	13%	€37	€0	20%	€–13
Corticosteroids	€10	€0	44%	€9	€0	43%	€0
Intravenous antibiotic	€2	€0	8%	€2	€0	7%	€0
Intravenous antihypertensives	€5	€0	5%	€10	€0	11%	€–6
Diagnostic							
Blood samples	€71	€50	71%	€77	€50	79%	€–6
Ultrasounds	€146	€89	59%	€195	€89	70%	€–49
Outpatient							
Days of telemonitoring	€1549	€988	93%	€196	€0	4%	€1353
Emergency transport	€27	€0	4%	€0	€0	0	€27
Outpatient visits (scheduled)	€171	€98	58%	€0	€0	0	€171
Outpatient visits (unscheduled)	€65	€0	41%	€0	€0	0	€65
Inpatient							
Admission days	€995	€0	38%	€5184	€4270	95%	€–4189
Cardiotocography during admission*	€52	€0	38%	€179	€138	99%	€–127
Total antenatal	€3115	€1915	99%	€5889	€4692	100%	€–2774
Delivery							
Delivery							
Instrumental delivery	€155	€ 0	10%	€108	€0	7%	€46
Caesarean section	€1063	€ 0	46%	€785	€0	34%	€277
Vaginal delivery	€576	€ 0	44%	€772	€1309	59%	€–196
Pain medication							
Epidural	€50	€0	25%	€68	€0	34%	€–18
Pethidine	€0	€0	1%	€0	€0	0	€0
Remifentanil	€11	€0	7%	€12	€0	8%	€–2
Transfusions							
Blood transfusion	€48	€0	2%	€17	€0	3%	€31
Plasma transfusion	€24	€0	1%	€2	€0	1%	€22
Total delivery	€1926	€1747	100%	€1764	€1508	100%	€161
Inpatient post-partum (mother)							
Intensive care days	€186	€0	1%	€1904	€0	1%	€–1718
Medium care days	€13	€0	1%	€97	€0	4%	€–84
Admission days†	€1698	€1708	91%	€2092	€1708	93%	€–394
Total inpatient post-partum (mother)	€1898	€1708	92%	€4094	€1708	95%	€–2196
Inpatient postpartum (child)							
Intensive care days	€3310	€0	17%	€7142	€0	19%	€–3832
Medium care days†	€5348	€0	39%	€5346	€0	43%	€2
Admission days†	€3095	€854	55%	€1849	€854	56%	€1246
Total inpatient post-partum (child)	€11753	€3416	89%	€14337	€3507	95%	€–2584
Total	€18691	€11946	100	€26084	€15125	100%	€–7393

The % treated columns show the percentage of patients with at least one registered activity. Several cost differences do not add up due to rounding of numbers. €=Euro.
*Two missing values were imputed using the group mean. †One missing value was imputed using the population mean.

Table 4: **Overview of costs made during the antenatal period, delivery, and postpartum in the telemonitoring group versus the hospital admission group**

more highly educated (appendix pp 16–17). There were no significant differences between the intervention and control groups regarding mental and physical wellbeing, but participants in the intervention group reported significantly better PPSQ scores (adjusted mean difference –8·9 [95% CI –15·1 to –2·6]), better satisfaction scores (adjusted mean difference –0·35 [–0·69 to 0·00]), and higher pregnancy care grading (adjusted mean difference 0·68 [0·14 to 1·22]).

The mean total costs per participant in the intervention group were €18 691 versus €26 084 in the control group (table 4). Telemonitoring appeared to reduce the antenatal costs by a mean price of €2774. This difference was mainly caused by fewer antenatal admission days and was not strongly affected by telemonitoring costs. This effect was equally distributed among all participants, indicating a systemic cost reduction effect. After bootstrapping, the 95% CI of the antenatal cost reduction was between €1641 and €3933 (appendix p 15).

Discussion

This randomised trial, to our knowledge, is the first to suggest that home telemonitoring of complicated pregnancies requiring daily surveillance might be as safe as hospital admission and is associated with higher patient satisfaction and lower costs. The adjusted risk difference in primary outcome between both groups favoured telemonitoring, and was lower than the pre-defined non-inferiority margin. Additionally, we found no significant differences between groups for all individual maternal and fetal secondary outcomes. Similar scores were found for mental and physical wellbeing between groups. Participants in the telemonitoring group scored significantly higher on all constructs of satisfaction. A mean relative cost reduction of 18% per patient was calculated for the telemonitoring strategy, mainly due to a reduction in antenatal admission days and not strongly affected by the costs of telemonitoring.

Until now, evidence from randomised trials or cohort studies regarding the safety of home telemonitoring of complicated pregnancies was scarce. Published studies were retrospective cohort studies, mostly focusing on blood pressure management without daily fetal monitoring in low or medium risk patients instead of outpatient clinic visits.[12,20] Recent studies showed excellent compliance of patients allocated to telemonitoring of home measurements in pregnancy.[21] The HoTeL study focused on complicated pregnancies and telemonitoring as an alternative strategy to hospital admission. Furthermore, information regarding costs was necessary to solve reimbursement issues and build quality standards. Lack of payment structures is an important barrier for penetration of digital health solutions into the field in most countries.[22] Our results have the potential to change antenatal care strategies. As health-care costs and staff shortages continue to increase worldwide to unsustainable levels, innovations reducing cost without concessions to the quality of care are urgently needed. The cost analysis of our trial could have a potential annual budget impact of €56 million to €134 million per year, if telemonitoring becomes the preferred strategy for the surveillance of complicated pregnancies in the Netherlands. Moreover, the global challenges for health care during the COVID-19 pandemic underline the urgent need for innovation of health-care delivery by digital health solutions allowing remote monitoring.[23] Additionally, telemonitoring has the potential to improve patient empowerment by enhancing patient participation and commitment to treatment to improve autonomy and consequently health outcomes.[8]

Strengths of this trial are the randomised nature of the study, a heterogeneous population with diverse pregnancy complications requiring intensified maternal and fetal surveillance in hospital, and analysis by intention-to-treat as well as per-protocol. A limitation of the trial was that the sample size of 416 was not achieved. The execution of this trial within the planned timeframe turned out to be challenging. In the recruitment of participating centres, initially 15 Dutch hospitals supported the study. Once the study was funded, nine hospitals withdrew because they would miss revenues from admissions of patients randomly assigned for telemonitoring, without reimbursement. Hence, it showed once more that fee for service reimbursement is an obstacle for innovation of health care. In future innovation trials, health-care insurance companies might be able to assist with recruitment issues as a result of revenue loss. After interim analysis, a decision was made to end the study because the number of inclusions sufficiently demonstrated that telemonitoring was at least non-inferior to admission in monitoring complicated pregnancies. There were no a-priori criteria for ending the study. Another limitation is that the nature of the intervention does not allow for double-blind research, which could have resulted in treatment bias. Methodological limitations include the possibility of measurement bias in intention-to-treat estimates and possible selection bias in the per-protocol analyses. The measurement bias potentially led to overestimation of the true outcome due to the absence of blinded outcome assessors. The crossover to telemonitoring of four participants assigned to hospital admission could have led to selection bias because of the unblinded nature of the trial. Furthermore, responders to the wellbeing and satisfaction questionnaires were more often allocated to telemonitoring, more highly educated, and experienced the primary outcome less often. This could have biased the results of patient satisfaction both ways. Larger-scale studies are therefore needed to investigate this further and confirm the encouraging results of this trial. However, conducting larger-scale studies might be difficult given that components within our primary adverse outcome are rare events.

In conclusion, our findings suggest that home telemonitoring in pregnancy care is an acceptable alternative to monitoring selected pregnancies with complications, with a reduction in costs and higher patient satisfaction, and therefore has potential to reduce admissions and costs in obstetric care.

Contributors

MNB, MPHK, JFMvdH, and AF conceived and designed the trial. WG, JMdH-J, KLD, LS, DPvdH, and JFMvdH were responsible for data acquisition. JFMvdH, MNB, AF, WRK, and MPHK directly accessed and verified the raw data. MPHK, WRK, NPAZ, GWJF, and JFMvdH analysed the data. MNB, MPHK, JFMvdH, and AF interpreted the data. All authors vouch for the completeness and accuracy of the data. MNB and MPHK drafted the manuscript. All authors critically revised the manuscript. All authors saw and approved each revised manuscript including the final text. All authors confirm that they had full access to all the data in the study, and accept responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

De-identified participant data can be made available upon requests directed to the corresponding author. Proposals will be reviewed on the basis of scientific objective. A data use agreement will be required before the release of participant data and institutional review board approval. After approval of a proposal, data can be shared through a secure online platform.

Acknowledgments

The trial was funded by Stichting Achmea Gezondheidszorg (grant number Z659) and supported by ICT Healthcare Technology Solutions.

References

1 Broekhuijsen K, Groen H, van den Berg PP, Mol BWJ, Franssen MTM, Langenveld J. Gestational hypertension and advanced maternal age—authors' reply. *Lancet* 2015; **386:** 1628.

2 NICE. Hypertension in pregnancy: diagnosis and management. 2019. https://www.nice.org.uk/guidance/ng133 (accessed Nov 11, 2020).

3 Royal College of Obstetricians and Gynaecologists. Small-for-gestational-age fetus, investigation and management (green-top guideline no. 31). 2013. https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg31/ (accessed Nov 11, 2020).

4 NICE. Preterm labour and birth. 2015. https://www.nice.org.uk/guidance/ng25 (accessed Nov 11, 2020).

5 Gourounti C, Karpathiotaki N, Vaslamatzis G. Psychosocial stress in high risk pregnancy. *Int Arch Med* 2015; **8:** 1–9.

6 Huynh L, McCoy M, Law A, et al. Systematic literature review of the costs of pregnancy in the US. *Pharmacoeconomics* 2013; **31:** 1005–30.

7 WHO. mHealth: new horizons for health through mobile technologies: second global survey on eHealth. Geneva: World Health Organization, 2011.

8 van den Heuvel JF, Groenhof TK, Veerbeek JH, et al. eHealth as the next-generation perinatal care: an overview of the literature. *J Med Internet Res* 2018; **20:** e202.

9 van den Heuvel JFM, Lely AT, Huisman JJ, et al. SAFE@HOME: digital health platform facilitating a new care path for women at increased risk of preeclampsia—a case-control study. *Pregnancy Hypertens* 2020; **22:** 30–36.

10 Alves DS, Times VC, da Silva ÉMA, Melo PSA, Novaes MA. Advances in obstetric telemonitoring: a systematic review. *Int J Med Inform* 2020; **134:** 104004.

11 van den Heuvel JFM, Teunis CJ, Franx A. et al. Home-based telemonitoring versus hospital admission in high risk pregnancies: a qualitative study on women's experiences. *BMC Pregnancy Childbirth* 2020; **20:** 77.

12 Zizzo AR, Hvidman L, Salvig JD, Holst L, Kyng M, Petersen OB. Home management by remote self-monitoring in intermediate- and high-risk pregnancies: a retrospective study of 400 consecutive women. *Acta Obstet Gynecol Scand* 2022; **101:** 135–144.

13 van den Heuvel JFM, Ganzevoort W, De Haan-Jebbink JM, et al. HOspital care versus TELemonitoring in high-risk pregnancy (HOTEL): study protocol for a multicentre non-inferiority randomised controlled trial. *BMJ Open* 2019; **9:** e031700.

14 Marteau TM, Bekker H. The development of a six-item short-form of the state scale of the Spielberger State-Trait Anxiety Inventory (STAI). *Br J Clin Psychol* 1992; **31:** 301–06.

15 Bergink V, Kooistra L, Lambregtse-van den Berg MP, et al. Validation of the Edinburgh Depression Scale during pregnancy. J Psychosom Res 2011; **70:** 385–89.

16 Versteegh MM, Vermeulen KM, Evers SMAA, de Wit GA, Prenger R, Stolk EA. Dutch tariff for the five-level version of EQ-5D. *Value Health* 2016; **19:** 343–52.

17 Littlefield VM, Adams BN. Patient participation in alternative perinatal care: impact on satisfaction and health locus of control. *Res Nurs Health* 1987; **10:** 139–48.

18 CBS. Consumer prices; price index 2015=100. 2021. https://opendata.cbs.nl/statline/?dl=3F0E#/CBS/nl/dataset/83131NED/table (accessed Feb 2, 2021).

19 Austin PC. Absolute risk reductions, relative risks, relative risk reductions, and numbers needed to treat can be obtained from a logistic regression model. *J Clin Epidemiol* 2010; **63:** 2–6.

20 Lanssens D, Vandenberk T, Smeets CJ, et al. Remote monitoring of hypertension diseases in pregnancy: a pilot study. *JMIR mHealth uHealth* 2017; **5:** e25.

21 Tucker KL, Mort S, Yu L, et al. Effect of self-monitoring of blood pressure on diagnosis of hypertension during higher-risk pregnancy: the BUMP 1 randomized clinical trial. *JAMA* 2022; **327:** 1656–65.

22 Keesara S, Jonas A, Schulman K. COVID-19 and health care's digital revolution. *N Engl J Med* 2020; **382:** e82.

23 Shah BR, Schulman K. Do not let a good crisis go to waste: health care's path forward with virtual care. *NEJM Catal Innov Care Deliv* 2021; **23:** 2.