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Full length article

A mixed method, phase 2 clinical evaluation of a novel device to treat postpartum haemorrhage

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ABSTRACT

Background: We evaluated the safety, efficacy, and acceptability of a new device designed to facilitate uterine compression in women with postpartum haemorrhage (PPH).

Methods: A prospective, phase two clinical device trial with concurrent qualitative study, conducted in a UK consultant obstetric unit. The device was used in addition to standard care in women unresponsive to initial oxytocin therapy. The primary effectiveness outcome was additional blood loss of over 1000mls, whilst safety was assessed through adverse events. Interviews assessed device feasibility and acceptability, and were analysed using framework analysis.

Results: We recruited 57 women with clinical PPH after vaginal birth; 67% were primiparous and 47% had undergone operative birth. All but two (96%) had atony as a cause of the haemorrhage; in addition, 30% also had bleeding from lacerations and 11% had retained tissue.

After device use, only one woman had additional blood loss over 1000mls, although 3 women (7%) needed a Bakri balloon and 14% received a blood transfusion. All but one clinician felt that the device was easy to use. Clinicians stated that the device assisted management in 85% of cases. All 56 women who responded stated that if they bled in a future birth they would want the device to be used again.

There were no serious adverse events related to the device. However, 3 events were judged as 'possibly' being caused by the device – 2 minor vaginal grazes and one postnatal episiotomy infection and breakdown. Lax vaginal tissue complicated the use of the device in three women. In 47 interviews, participants, birth partners, clinician users and attending midwives viewed the device positively. Clinicians found it useful as a way of stopping blood loss and as an aid to diagnose the source of bleeding.

Conclusions: The PPH Butterfly may provide a rapid, acceptable and effective treatment for postpartum haemorrhage. Clinical Trial Registration prospective with ISRCTN15452399 11/09/2017 (www.isrctn.com/ISRCTN15452399).

Introduction

It is estimated that 60,000 women die from postpartum haemorrhage (PPH) each year [1,2]. The initial treatment of uterine atony involves repeated uterotonic agents and then bimanual compression (BMC) [3,4]. BMC, however, is painful for the mother in the absence of an epidural

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analgesia, tiring to maintain for the clinician, and so is therefore generally used as a secondary measure. However, if uterine compression was less invasive, then it could be used as an effective first aid procedure to abruptly 'turn off the tap' of PPH [5] whilst other therapies are administered. Effective uterine compression could also help to diagnose the underlying cause, as if it does not stop the bleeding then the bleeding is likely to be from lacerations.

The PPH Butterfly (PPHB) is a simple intravaginal device that is inserted beneath the uterus in place of the fist, providing a platform against which the abdominal hand can apply pressure to the uterus (Fig. 1, Supplementary video sV1) [6]. This is the first clinical report of the device use, prior to approval for general use by the FDA or MHRA.

Materials and methods

The study was a prospective cohort study using mixed methods in a UK consultant obstetric unit. Our objective was to investigate the devices' efficacy, safety and acceptability. We hypothesized that clinicians could halt postpartum haemorrhage using the device, that it would be safe to use, and acceptable to both clinicians and women.

All recruiting doctors underwent training in consent and device use. Women at high risk of PPH could be recruited antenatally with advance informed consent sought in case of PPH. However, most participants were recruited at the time of their PPH, in a process developed by the Royal College of Obstetricians and Gynaecologists [7] and user groups. After initial uterotonic treatment, women were briefly informed about the device and verbal consent sought for its use. Women who declined or who were uncertain were not included.

All participants had a vaginal birth and received routine intramuscular oxytocin 10 IU as PPH prophylaxis. Those who had clinical PPH following placental delivery that persisted despite an additional dose of oxytocin +/- ergometrine were recruited. The device was used within 1 h of birth (or 15 min of manual placental removal). In view of the rapid consent process, only fluent English speakers and those over 16 years old were approached. Those with clotting disorders, stillbirth, or unreversed female genital mutilation were not approached.

Prior to the study, each recruiting obstetrician had 10 min of training on a custom-made mannequin with repeated insertions to ensure 'muscle memory'. The device was folded and slid longitudinally into the vagina (see Supplementary Online Video sV1). It was then unfolded and held in place whilst the uterus was compressed against it with the other hand through the abdominal wall. If the bleeding did not stop with compression, then the device was removed and the genital tract examined for lacerations. If the bleeding stopped, however, then pressure was maintained for 5 min. If the bleeding then returned when the pressure was released, the compression was restarted and maintained for a further 5 min. This continued for a maximum of 5 further cycles. If the bleeding still persisted after this, then the woman was transferred to theatre for examination under anaesthetic. During device use, medical therapies with uterotonic drugs and tranexamic acid were continued as per normal practice. Blood loss at time of insertion and at the end of the bleeding were estimated by clinicians using weighing of swabs and measuring of blood volume where available.

The day following the birth, a research midwife sought fully informed consent to continue study participation and collect outcome data including postnatal haemoglobin levels. Participants and treating clinicians evaluated their experience of the device using Likert scales.

An interim safety analysis was carried out after 15 recruits and the Independent Data and Safety Monitoring Committee (ISDMC) deemed the study safe to continue.

The prototype was made by Protolabs Ltd (Telford, UK) from computer aided designs by Astarcor (High Wycombe, UK) in collaboration with the University of Liverpool. The single use injection-moulded polypropylene prototypes (PPM H250) underwent ethylene oxide sterilization by Anderson Caledonian Ltd (Bellshill, UK).

Clinical outcomes were based on the PPH Core Outcome Set [8]. The primary outcome was blood loss of over 1000mls after first device use. Secondary outcomes included total blood loss, use of additional interventions and organ dysfunction [9]. All data were collected initially on paper, then double entered by two researchers independently into a REDCap database (Vanderbilt University, Tennessee, USA); discrepancies were resolved by ADW. All cases are reported, irrespective of whether the device was fully engaged.

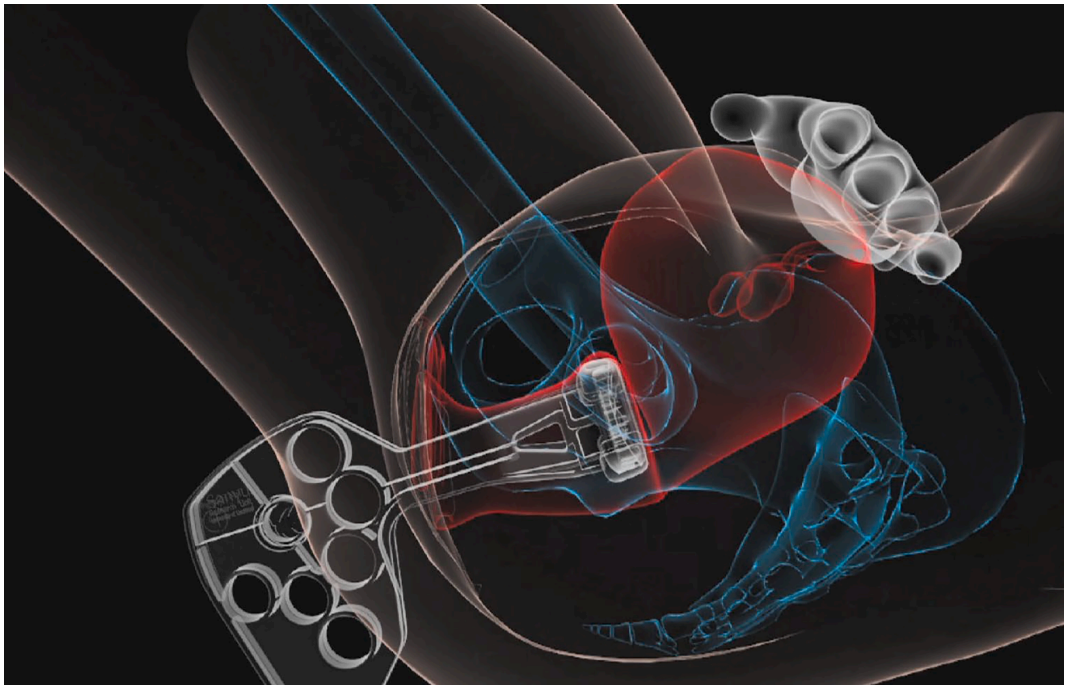

Fig. 1. Mechanism of action of the PPH Butterfly.

Qualitative assessment

Qualitative research using grounded theory [10] was undertaken to explore the experience, feasibility, usability and acceptability of the device for women, obstetricians, midwife observers and birth partners. Informed written consent was obtained postnatally from each participant; interviews continued until data saturation [11].

Face-to-face semi-structured interviews were conducted by a specialist research team within 3 weeks of recruitment; open-ended questions were digitally recorded and transcribed verbatim. Most interviews with women and birth partners were conducted in the home with clinical interviews in the hospital. Data were analysed using framework analysis [12,13]: data from each group were analysed separately before exploring the commonalities and diversity of views.

The clinical study was approved from the Health Research Authority (HRA) and the North West Liverpool Central Research Ethics Committee (Ref 17/NW/0373). The qualitative study was approved by the Office for Research Ethics Committees Northern Ireland (17/NI/0140). Both studies were sponsored by the University of Liverpool. A Public Engagement Panel (PEP) were consulted throughout the study: their coordinator (EH) was a member of the Trial Management Group (TMG).

Results

In total, 57 women were recruited from Jan-Dec 2018 (Fig. 2). The study had aimed to recruit 118 women over a 12-month period based on the comparison with historical controls (see Supplementary File). After 45 women had been recruited over 9 months, the Trial Steering Committee (TSC) and IDSMC reviewed the safety reports and interim outcomes for the participants. They considered that, as a Phase 2 study, the data generated was adequate and recommended that recruitment be stopped at the end of pre-planned 12 months of recruitment so as to allow progress to a definitive Phase 3 study.

Demographics and delivery characteristics are shown in Table 1. The median blood loss at the time of device insertion was 750mls (IQR: 550–1300, range: 400–2600). The device was used was for a median of five minutes (IQR: 4–8) and reinserted a second time in five women when bleeding restarted. Various uterotonics were used along with the device. An oxytocin infusion was used in 17 women (30 %), ergometrine 15 (26 %), carboprost 12 (21 %) and misoprostol 1 (2 %). TXA was given to 25 women (44 %).

Table 1
Demographics and delivery characteristics.

	PPHB cases (n = 57)
Maternal age at booking (years); mean (SD)	28.8 (5.9)
BMI at booking (kg/m^2); mean (SD)	26.4 (6.4)
PPH in a previous pregnancy	5 (9 %)
Details of the current birth	
Primiparous, n (%)*	38 (67 %)
Multiple Pregnancy, n (%)*	3 (5 %)
Induced birth, n (%)	38 (67 %)
Received oxytocin as treatment for slow labour, n (%)	7 (13 %)
Operative vaginal birth, n (%)*	27 (47 %)
Birth weight (g), mean (SD)	3482 (506)
Intact perineum / vagina [i.e. no episiotomy, vaginal or perineal lacerations], n (%)	7 (12 %)
Length of third stage (mins), median (IQR)	9.00 (6.00–16.00)
Cause of PPH†	55 (97 %)
Atony	6 (11 %)
Retained placenta or tissue	0 (0 %)
Coagulopathy	17 (30 %)
Lacerations	
Blood loss at time of device insertion (mls); median (IQR)	750 (550, 1300)

†multiple options possible.
SD = Standard Deviation.
IQR = Interquartile range.

Fifteen adverse events were reported for 13 women (Table 2). The 3 serious adverse events were all unrelated to the device. Of the 12 non-severe adverse events, 5 were assessed to be either possibly or almost certainly caused by the device. In 2 women, vaginal grazes were seen after use of the device (one required a single suture) but it was unclear whether these had been caused by use of the device. One woman had an episiotomy breakdown that required outpatient antibiotic treatment, and in 2 women lax vaginal tissue obstructed the use of the device. In one woman, tissue caught between the device handles as they were closed causing sudden pain, and the device was removed. In the other, it only hindered visualization as it was inserted.

Additional blood loss of over 1000mls occurred in only 1 of the 57 women treated with the PPHB (Table 3). She had the device inserted when blood loss reached 750mls after failed treatment with oxytocin, fundal massage and standard bimanual compression. Her final blood loss was 1955mls. Eight women (14 %) required a postnatal blood

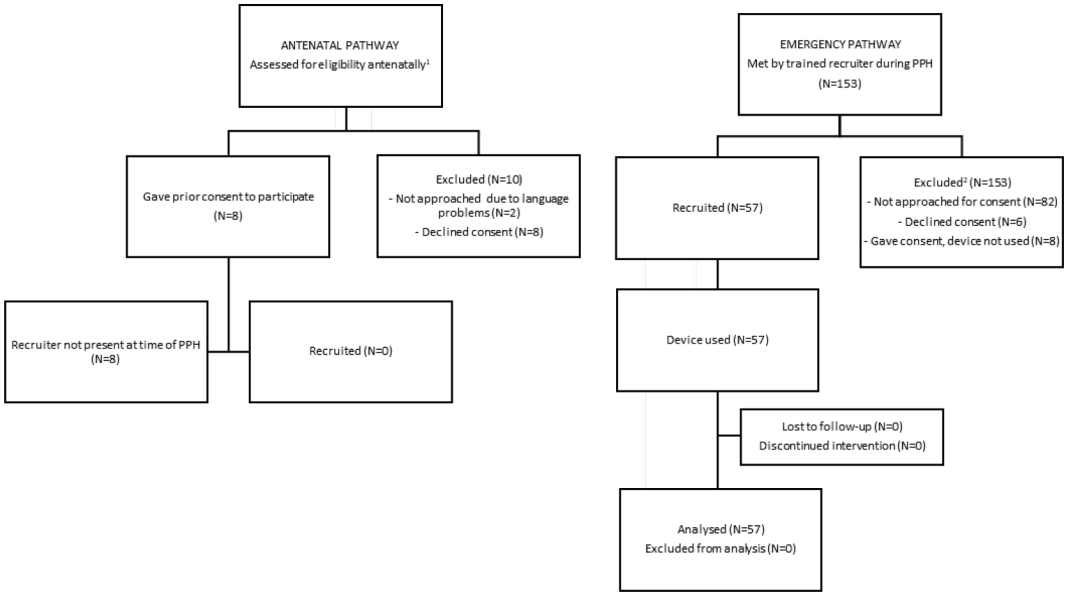

Fig. 2. CONSORT flowchart.

Table 2
Adverse Events and Serious Adverse Events.

	Description (Free-text)	CI assessment of severity	CI assessment of causality	Serious
1	Episiotomy, forceps delivery. Sutures in rectum removed and re-sutured. Treated as a 3rd degree tear (laxatives, antibiotics and follow up).	Mild	Unrelated	No
2	Noted something protruding from vagina, diagnosis of prolapse. Advised to do pelvic floor exercises.	Mild	Unrelated	No
3	Urticarial rash onset thought to be due to Fragmin. Not admitted, treated as outpatient.	Moderate	Unrelated	No
4	Had to be re-catheterised when catheter removed post-delivery.[1]	Mild	Unlikely	No
5	Broken down perineum.	Mild	Unlikely	No
6	Infected Episiotomy.	Mild	Unlikely	No
7	Patient attendance post discharge with perineal breakdown and infection.[2]	Moderate	Unlikely	No
8	Vaginal Graze.[2]	Mild	Possibly	No
9	Small right vaginal wall graze noted after examination under anaesthetic and removal of clots. Required 1 suture.	Mild	Possibly	No
10	Episiotomy breakdown/ infection P/N. Treated as outpatient, reviewed later and discharged from hospital care.[1]	Moderate	Possibly	No
11	Labia minora caught by the PPH Butterfly device causing pain.	Mild	Almost certainly	No
12	Labia minora caught on insertion of the PPH Butterfly.	Mild	Almost certainly	No
13	Attended hospital postnatally with heavy lochia and pelvic infection. Ultrasound revealed retained products and she underwent an uncomplicated uterine evacuation.	Moderate	Unrelated	Yes: Hospitalisation/ prolongation of existing hospitalisation
14	Post epidural dural tap requiring blood patch.	Severe	Unrelated	Yes: Hospitalisation/ prolongation of existing hospitalisation
15	Returned to hospital 12 days postnatally with pelvic infection. Admitted as an inpatient and treated with IV antibiotics.	Severe	Unlikely	Yes: Hospitalisation/ prolongation of existing hospitalisation

[1] AEs 4 and 10 relate to the same woman.
[2] AEs 7 and 8 relate to the same woman.

Table 3
Clinical outcomes.

	Index cases N = 57
PRIMARY OUTCOME	
Estimated additional blood loss after device insertion > 1000mls, N (%)	1 (2)
SECONDARY OUTCOMES	
Total estimated blood loss before and after device insertion, mls (median (IQR))	1110 (700, 1600)
Blood transfusion, N (%)	8 (14 %)
Number of units transfused	
1	4 (50 %)
2	3 (38 %)
3	1 (13 %)
Day 1 haemoglobin level in the 47 non-transfused women[1] (mean, SD)	97.02 (15.12)
Number of women transferred to a higher level of care, N (%)	24 (42 %)
Number of women examined under anaesthetic to investigate the cause of bleeding, N (%)	6 (11 %)
Number of women exclusively breastfeeding at time of hospital discharge, N (%)	26 (46 %)
Coagulopathy	0 (0 %)
Cardiovascular shock	0
Organ dysfunction (WHO criteria)	0
Hysterectomy	0
Maternal Death	0

[1] *12-36 h post birth or at discharge, whichever is soonest.*

transfusion, and 6 women (11 %) underwent examination under anaesthetic to determine the cause of the bleeding. After cessation of the bleeding, all but 2 women were judged to have an atonic uterus (97 %); 17 (30 %) also had blood loss from lacerations and 6 (11 %) also had retained tissue in the uterus. None went into clinical shock, had a hysterectomy or died. A comparison with matched historical controls is provided as a Supplementary File.

When questioned about pain during device use, 16 % reported pain on insertion and 34 % on uterine compression (Table 4). However, all women said that they would want the device to be used again if they bled after a future birth. In 98 % of cases, clinicians stated that it was easy to use; they said that it stopped the bleeding in 52 % of cases and assisted in making a diagnosis in 52 % of cases. In 86 % of cases it was thought that the device assisted with the management overall, and in 93 % of cases the doctor wanted it to be available in future for clinical use.

Qualitative findings

Fifty-one interviews were conducted with 12 recruited women, 12 birth partners, 16 users and 11 midwife observers. The interviews took place January - November 2018 and lasted from 7 – 61 minutes. Representative quotes are provided in Table 5 with more in Supplementary Table sT2.

The majority of the participants interviewed had some form of analgesia at the time of birth, primarily epidural. Most gave birth in lithotomy position; more than half were vacuum or forceps births on delivery suite. A small number who gave birth on the midwifery-led unit had the device used with minimal or no analgesia.

Women

Most of the women reported little or no pain with device use. Those who had already received BMC perceived the device to be more comfortable, whilst those who had not thought that BMC sounded more invasive and believed the PPHB would be preferable.

The perceived removal of the need to go to theatre was important to several women as it meant they could remain with their newborn and birth partner, and this played a part in consenting to device use.

Many were affected by exhaustion, blood loss, drugs, pain, or fear. However, they were also aware that the situation was serious and wanted this resolved. The requirement to stop the bleeding quickly was

Table 4
Clinician and Participant questionnaire results (n = 57).

Participant questionnaire	Completely disagree	Disagree	Neither agree nor disagree	Agree	Completely agree	Unobtainable
It was painful when the PPH Butterfly was inserted	10 (18 %)	18 (33 %)	18 (33 %)	9 (16 %)	0 (0 %)	2
It was painful when the PPH Butterfly was squeezing the womb	10 (18 %)	13 (24 %)	13 (24 %)	16 (29 %)	3 (5 %)	2
I was happy with the way that I was recruited to this study	0 (0 %)	2 (4 %)	4 (7 %)	33 (59 %)	17 (30 %)	1
If I bled after a future birth, I would want the PPH Butterfly to be used	0 (0 %)	0 (0 %)	0 (0 %)	35 (63 %)	21 (38 %)	1

Clinician questionnaire[1]	Definitely no	Possibly no	Undecided	Possibly yes	Definitely yes	Unobtainable
Was the PPH Butterfly easy to use?	0 (0 %)	0 (0 %)	1 (2 %)	10 (18 %)	45 (80 %)	1
Did the PPH Butterfly stop the bleeding?	5 (9 %)	4 (7 %)	18 (32 %)	20 (36 %)	9 (16 %)	1
Did the PPH Butterfly assist in making a diagnosis of the cause of the bleeding?	7 (13 %)	13 (23 %)	7 (13 %)	20 (36 %)	9 (16 %)	1
Did the PPH Butterfly device assist with the management of the PPH overall?	1 (2 %)	4 (7 %)	3 (5 %)	26 (46 %)	22 (39 %)	1
Would you like the PPH Butterfly to be available to use as a treatment for PPH?	0 (0 %)	0 (0 %)	4 (7 %)	18 (32 %)	34 (61 %)	1

1. Some clinicians used the device multiple times, and each response is added here.

their priority, and they were satisfied that the device had helped to stop or reduce the bleeding. Some were less aware of the urgency, but described that they would prefer not to know what was happening at the time. One indicated a preference for the health professionals to take control of the situation.

Obstetricians

All doctors interviewed had at least 3 years of training and the majority used BMC frequently.

The quality of the PPHB training was commended, especially the benefits of repeated mannequin insertions. The majority found the device easy to use and thought it more comfortable for the woman than BMC. They also believed it enabled better maintenance and sustenance of uterine compression. Some felt the device enabled better management of the emergency than BMC, as they could stand up whilst using it and have a better command of the room.

Ease of use was emphasised, but some had concerns about the risk of vaginal wall entrapment. Vaginal wall laxity was considered especially a problem due to the recruits being within 1 h of birth. A few queried whether the device could cause lacerations, especially if they had caught tissue themselves.

The majority were unable to say whether the device reduced bleeding because participants had also received standard PPH treatment. However, some believed it was a useful adjunct tool whilst waiting for the drugs to take effect and to diagnose the bleeding source. Several suggested that an RCT would be necessary to assess effectiveness.

Most would recommend the device, saw the experience as positive, thought it was a useful addition to standard treatment, and would be happy to use the device again.

Midwife observers

Most were busy providing care and so struggled to recall details of the device use. Furthermore, the haemostatic benefits of the device were unclear due to concurrent administration of uterotonic drugs. Despite this, they believed the device to be a positive addition to standard treatment, even though they struggled to see where it fitted into the PPH protocol.

It was generally believed that the device was less invasive, less painful, less traumatic, less aggressive and preferable to BMC, even by those who had been sceptical prior to use. Several midwives stated that they would prefer the device used on them to BMC if they personally experienced a PPH because it was less intimate and appeared less uncomfortable. They felt that effective BMC was usually difficult to perform due to both maternal discomfort and clinician effort, and the device would make the task less tiring and more effective.

Midwives were confident in the clinician's ability to use the device. A few stated that they would not have allowed the clinician to use the device if they were unsure as to their capabilities.

Birth partners

The quantity of blood, the number of people in the room and a rapidly changing situation left some partners feeling panic, fear and confusion. However, praise for the team caring for the woman was reiterated throughout interviews with birth partners citing confidence in the clinicians and the rapport that had already developed between clinician and the woman.

The majority of birth partners thought the device was a quick, effective, straightforward process that was better than the alternatives (BMC or surgical intervention). The comfort of their partner was also important to birth partners.

Overall, birth partners considered the device useful and were pleased that it was available. Several saw the device and remarked on its appearance. However, they accepted the device as a medical aid and did not feel it was unusual in the setting. They echoed the views of women that it was worth trying the device in order to resolve the emergency.

Discussion

The main message of this study is that the PPHB is both safe and acceptable in the hands of well-trained clinicians. Most clinicians felt that it provided a useful management tool, both to stop the bleeding and to determine the source of the blood loss, and virtually all would want to use it again.

The main strength of this study is the detailed mixed method assessment of the device use, giving a holistic view of the device from multiple perspectives. The use of the device in a normal practice setting also gives insight into how it might function in routine practice. However, both the cases and users may not be representative, and a randomised controlled trial (RCT) is needed to truly assess its efficacy.

The uterus was compressed for 5 min before release and checking for ongoing bleeding. The choice of a 5 min cycle was pragmatic, based

Table 5
Summary quotes from participants, birth partners, recruiting doctors and midwives.

Codes	Quote
Women	
Pain	*'They started talking to me about using this and then so when I said 'Yes, go for it', she went round that end of the table and put it in. And that was it. Definitely more comfortable with the device than the lady's hand.'* (W05)
Comparison with BMC	
Success in stopping bleeding	*'It does the job, I would recommend it. Er well I'm happy with the experience overall and it did the job and it wasn't er particularly painful'* (W07)
Depersonalization	*'It wasn't somebody with their hand inside of me, it was an ordained product that was going inside of me, doing its' job and then coming out.'* (W02)
Obstetricians	
Importance of training	*'It was very easy to use, 'cos you know, I know we've gone through the demonstrations and I have gone back to it and tried it again on the model, erm, it did feel quite natural, you know, the way that you do it.'* (O03)
Positive response	*'And the Butterfly's quite a good option erm so people find it, women find it more less distressing than a normal bimanual compression. Because they can't tolerate bimanual compression erm and having the Butterfly, I guess I presume it's been less difficult than a bimanual compression. It's er more able to carry on with compression for longer. I've not had a problem with it.''* (O15)
Well tolerated	
Ease of use	
Less tiring	
Constant pressure	*'There's more constant pressure with the device than bimanual compression so yeah I, I, I think certainly I was happy that it had stopped.'* (O16)
Ease of use	*'I think that any obstetric registrar would feel happy inserting it. Erm I think anyone used to doing vaginal examinations would feel happy inserting it. I think er I think junior er I think senior midwives would certainly be happy inserting it. Erm I'm not so sure that junior midwives would be happy inserting it.'* (O05)
Tissue entrapment	*'I opened the wings of the device that didn't reveal any further bleeding but there was limited view because the erm anterior vaginal wall blocked my view. It sort of came down into the device if you like…after 3 min, I started to remove the device and noticed that the anterior vaginal wall was still in the device, not allowing it to be removed easily. Erm, the patient was completely comfortable, at this point, she hadn't noticed, so I reduced the anterior vaginal wall with one hand while removing the Butterfly with the other hand erm and the patient was comfortable during this period.'* (O07)
Vaginal tissue	
Situational awareness	*'I felt as I could be aware of what was going on around the room a little bit more easily, it probably felt less intimate with the woman so you had a bit more maneuver but you were able to maintain eye contact a little bit better.'* (O02)
Intimacy	
Effect on blood loss	*'Erm yeah it's because you're giving those first line uterotonics first, you're never quite know what the impact has been. You know, and there's the question of, you know, would the bleeding have stopped anyway erm and the question I don't really know the answer to but what I would say is that I certainly didn't feel there was any significant discomfort or any I didn't have any concerns about using it and certainly would try it again.'* (O16)
Well tolerated	
Effect on blood loss	*'Certainly manages the bleeding whilst establishing iv access or waiting for drugs to work.'* (O06)
Diagnosis of PPH cause	*'I think as a diagnostic tool, the good thing was that I could feel the uterus hard against the platform and I could tell for definite that it was well contracted.'* (O01)
Diagnosis of PPH cause	*'Erm I provided pressure with the device, the er bleeding continued and erm and there was no decrease in the bleeding and therefore it was very obvious that it was actually coming from erm vaginal trauma…erm the midwife had already told me that she suspected that it em that it was from trauma because the uterus felt well contracted but this confirmed that that was the case erm therefore I removed the Butterfly. I didn't require to give any further uterotonics because we knew it was from trauma so gave tranexamic acid and completed the er suturing. Erm the woman was very happy with the device erm and it's erm helped to know definitely where the bleeding was coming from.'* (O11)
Positive response	*'I was quite impressed with the device. It was a positive experience. Worth using.'* (O12)
Midwife Observers	
Effect on blood loss	*'Erm the only thing about the Butterfly is you don't know whether it was the Butterfly or not if it was the drugs that actually stopped the bleeding. Erm but I mean the woman didn't look in discomfort and the partner didn't look erm he didn't look scared at all. It would be difficult to tell whether, when you're using the drugs you would normally use, if it's the drugs or the Butterfly or a combination of the two.'* (MW06)
Well tolerated	
Intimacy	*'I think an instrument is better than a hand. That's my impression. I think if it was me, and even for my husband, I think I think he'd be traumatized if he'd seen a male or female doctor with their hand right inside my private parts but with an instrument, it seems more, I don't know, legitimate, medicalized.'* (MW08)
Birth Partners	
Well tolerated	*'He [the clinician] couldn't believe that he was able to get done what he got done without any anesthetic…but she [woman] said the using of the device was pain free.'* (P01)
Trust in clinicians	*'But the fact that it was him, the fact that the rapport was there, I think, made a lot of difference.'* (P01)
Seeing the device	*'I was probably a bit more aware of the fact that she was bleeding because I could see sort of under the bed and I could see the device itself em so I think the thing is that if someone tells you that your wife's bleeding, you're not gonna say 'oh no, don't use that.' You know, you're always gonna say 'absolutely, let's give it a go.' Erm 'cos that's what you do in the hope that the bleeding should stop.'* (P06)
Agreeing to treatment	

partly on the normal bleeding time, and partly on the research teams experience of bimanual compression at CS where uterine stimulation itself causes uterine contraction that stops bleeding. An alternative protocol would be to provide prolonged compression, but the finding that bleeding stopped within 5 min in all but 5 women suggests that the use of a 5-minute cycle is appropriate. Given that this was the first use of the device in women who were actively bleeding, there would be room for adjustment based on clinical experience as time goes on and this will remain under review.

In future, once outside of a study setting, care will be needed to ensure that users are appropriately trained. This is especially important given the potential for entrapped tissue or vaginal wall grazes. Since this study, the PPHB has been modified to reduce the risk of both, but some risk remains, and monitoring will be needed when introduced into clinical practice.

Conclusions

This trial has demonstrated acceptability of the PPH Butterfly, as well as initial safety and efficacy. A randomised trial is required to demonstrate efficacy, but this initial Phase 2 study provides evidence of the required clinical equipoise, and gives confidence that recruitment would be ethical.

Availability of data and materials

Following publication of the main clinical and cost analysis articles, anonymized individual patient data will be available. Requests should be made via the trial sponsor (sponsor@liverpool.ac.uk). The anonymized data set will include clinical trial data from the study participants and historical controls. Transcripts of the interviews will not be published as we do not have participant permission to do this. However, relevant quotes will be available to researchers, on request to the corresponding author, to support qualitative evidence synthesis. Other

study documents (protocol, statistical analysis plan and patient information sheets) are freely available on request from the corresponding author.

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Declaration of Competing Interest

ADW and PW are co-inventors of the PPH Butterfly. The patent is held by the University of Liverpool, but ADW and PW could in future receive a share of any profits generated from commercialization.

The remaining authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2023.01.018.

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