VIBRANT: Early Prediction of Life-Threatening Uterine Atony Using Maternal Heart Rate

Kimberly K. Trout
kimberly.trout@villanova.edu
Villanova University
Villanova, Pennsylvania, USA

Stefanie Modri
modris@nursing.upenn.edu
University of Pennsylvania
Philadelphia, Pennsylvania, USA

Amanda Watson
aawatson@virginia.edu
University of Virginia
Charlottesville, Virginia, USA

Insup Lee
lee@cis.upenn.edu
University of Pennsylvania
Philadelphia, Pennsylvania, USA

Harish Sehdev
hsehdev2@pennmedicine.upenn.edu
University of Pennsylvania
Philadelphia, Pennsylvania, USA

James Weimer*
james.weimer@vanderbilt.edu
Vanderbilt University
Nashville, Tennessee, USA

Abstract

Uterine atony accounts for a vast majority of all postpartum hemorrhages (PPH), the leading cause of maternal mortality worldwide. Uterine atony occurs when the uterine muscle (called the myometrium) does not sufficiently contract to arrest parturient bleeding after delivery. While there exist treatments for uterine atony, delays in intervention reduce their effectiveness. To improve time-to-intervention, postpartum hemorrhage risk prediction tools have been integrated into the standard-of-care for obstetrics. Unfortunately, these tools miss almost half of all PPHs. This paper presents VIBRANT as a clinical decision support tool providing early prediction of potentially life-threatening uterine atony. VIBRANT is physiologically inspired and designed to identify signals of myometrial fatigue argued to be present in streaming maternal heart rate data. Evaluations of the system indicate that VIBRANT , at a clinically actionable specificity, identifies over 80% of potentially life-threatening uterine atony missed by current gold-standard risk prediction tools. Moreover, the system provides between 2 and 8 hours advance warning to care teams prior to delivery for parturients at high-risk, providing ample time for preparation and timely intervention. VIBRANT has been licensed to a commercial partner and is in preparation for a clinical trial to support a regulatory submission and pre-market approval.

CCS Concepts

• **Applied computing** → **Health informatics**; *Health care information systems*; *Consumer health.*

Keywords

Postpartum Hemorrhage, Uterine Atony, Prediction, Myometrial Fatigue

ACM Reference Format:
Kimberly K. Trout, Stefanie Modri, Amanda Watson, Insup Lee, Harish Sehdev, and James Weimer. 2025. VIBRANT: Early Prediction of Life-Threatening Uterine Atony Using Maternal Heart Rate. In *ACM/IEEE International Conference on Connected Health: Applications, Systems and Engineering Technologies (CHASE '25), June 24–26, 2025, New York, NY, USA.* ACM, New York, NY, USA, 12 pages. https://doi.org/10.1145/3721201.3721379

*corresponding author

CHASE '25, June 24–26, 2025, New York, NY, USA

ACM ISBN 979-8-4007-1539-6/2025/06
https://doi.org/10.1145/3721201.3721379

1 Introduction

Postpartum hemorrhage (PPH) – excessive bleeding after delivery – is the leading cause of maternal mortality worldwide, affecting between 1% to 5% of all deliveries and resulting in over 70 thousands deaths, annually [46, 47]. Moreover, PPH disproportionately affects women-of-color, regardless of education level or socioeconomic status [20]. The vast majority (80%) of PPHs are due to uterine atony [19], which occurs when the uterine muscle fibers do not arrest parturient bleeding at the site of placental detachment during delivery – resulting in PPH [11]. Consequently, most uterine atony (and resulting PPH) occur within a few minutes of delivery and requires quick intervention.

Treatments exist. There are safe and effective treatments for uterine atony to arrest bleeding and prevent PPH, including medications (*e.g.,* uterotonics), mechanical intervention, blood transfusions, and (in extreme scenarios) surgical procedures such as hysterectomy. However, the effectiveness of these treatments diminishes with time-to-intervention. Unfortunately, economic and resource constraints facing birthing facilities prevents having these life-saving treatments prepped and nearby for all deliveries. Worse, since uterine atony (and the corresponding PPH) often occurs shortly after delivery, there is little (often no) time to prepare treatments post-delivery. The combination of these factors contributes to an increase in time-to-intervention for uterine atony and ultimately PPH rates.

State-of-the-art. To help clinical teams better prepare for potential PPHs (and uterine atony), state-of-the-art risk screening tools that identify parturients[1] at elevated risk of PPH have been integrated into clinical workflow and planning. These tools aim to provide a safe and effective way to predict a PPH prior to delivery, so care teams can be proactive (as opposed to reactive) and adequately prepare for a timely intervention before a high-risk parturient delivers. However, a significant and ongoing shortcoming of these gold-standard tools is that more than 40% of hemorrhages occur in patients designated as low risk [18]. In light of these poor predictive values, researchers are actively exploring a number of

[1] A parturient is defined as someone who is in labor.

approaches to improving the existing models of risk assessment, including the incorporation of intrapartum factors or non-obstetric risk factors [1, 17, 41, 53].

Our approach. In this work, we take a novel and fundamentally different approach. We postulate that myometrial[2] fatigue precedes uterine atony. While not directly measurable in laboring patients, myometrial fatigue has been shown to shift muscle cell metabolism from aerobic to anaerobic, resulting in accumulation of lactic acid in both myocytes and amniotic fluid [49]. We posit that another marker of myometrial fatigue can be seen with specific trends in maternal heart rate during active labor contractions. This is based on the physiological fact that during contractions, blood is forced from the uterus and into the maternal circulatory system, resulting in an autotransfusion that increases maternal cardiac output and changes maternal heart rate [34]. We combined these facts to develop a new physiological biomarker for myometrial fatigue that is observable through maternal heart rate data. To develop and evaluate a risk prediction tool based on the above rationale, we employ a model-based systems engineering approach.

First, leveraging the clinical literature, we develop a first-of-its-kind physiologically-inspired biomarker that relates myometrial fatigue to cardiac output (which combines maternal heart rate and blood volume). We call this biomarker the *Myometrial Fatigue Index*. Unfortunately, cardiac output is difficult to practically measure in real-time, so we derive a surrogate statistic that only requires maternal heart rate data, but retains equivalence as a statistic for testing myometrial fatigue. To ensure robustness, we also identify a set of confounding factors that affect maternal heart rate dynamics and identify a set of nuisance transformations over maternal heart rate telemetry that cover the effect of confounding factors.

Second, leveraging the minimal model, we develop a test for myometrial fatigue that is provably maximally invariant to the identified nuisance transformations. Maximally invariant statistics, originally developed for radar signal processing, have recently been utilized in multiple medical applications. In this application, we employ the statistics to design a detector that tests for non-linear ranked relationships invariant to confounding factors that contain elements of the surrogate myometrial fatigue index statistic discriminating the presence and absence of myometrial fatigue. To instantiate the test, we present an implementable version suitable for real-world deployment, called VIBRANT (and illustrated in Figure 1) .

Third, we evaluate VIBRANT on a dataset collected during labor and delivery that demonstrates clinically-significant performance. At a clinically acceptable specificity of over 90%, the system achieves over 80% sensitivity at predicting PPH associated with uterine atony. Clinically, this can be interpreted as the proposed system identifying the 10% of parturients that contain over 80% of potential life-threatening uterine atony currently missed by the standard-of-care risk predictors.

In summary, the major contributions of this work are as follows:

(1) **Develop a biomarker for myometrial fatigue.** We develop the *myometrial fatigue index* as a new biomarker that relates myometrial fatigue to cardiac output. To facilitate real-world utilization, we also identify an equivalent surrogate implementation using only maternal heart rate telemetry and describe the corresponding confounding factors.
(2) **Introduce VIBRANT as a robust test for the biomarker.** We develop VIBRANT as a test that is maximally invariant to the confounding factors and leverages maternal heart rate to discriminate the presence/absence of intrapartum myometrial fatigue – as a surrogate for predicting risk of life-threatening uterine atony. We also present a clinical decision support system architecture that describes a commercially-viable implementation of the risk predictor.
(3) **Evaluate VIBRANT on real-world data against a gold-standard alternative**. We evaluate VIBRANT on a dataset collected during labor and delivery that demonstrates clinically-significant performance – catching hours ahead of delivery over 80% of potential life-threatening uterine atony currently missed by the standard-of-care.

The remainder of this paper is structured as follows. Section 2 summarizes the work related to our research. In Section 3, we describe requirements and a problem statement to satisfy these requirements. Section 4 derives the Myometrial Fatigue Index, presents a statistic that is equivalent for testing, and formally models corresponding confounding factors. Section 5 presents VIBRANT as an implementation-friendly surrogate for life-threatening uterine atony risk prediction. Section 6 presents an evaluation of VIBRANT in the context of current state-of-the-art standard-of-care. Section 7 presents on-going work on obtaining regulatory pre-market approval. Finally, we conclude the paper in Section 8.

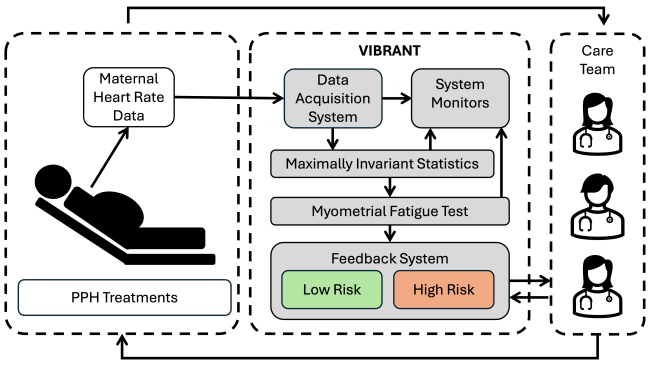

Figure 1: VIBRANT System Architecture

2 Related Work

In this section we overview the related work. Specifically, we describe the causes of uterine atony, present the treatment landscape, and briefly overview the state-of-the-art for improving maternal outcomes associated with uterine atony (and PPH).

2.1 Causes of Uterine Atony

The vast majority (80%) of PPHs[3] are caused by problems with Tone (clinically known as uterine atony) [19]. The physiological

[2]The myometrium is the thick muscular middle layer of the uterus wall.

[3]The other causes of PPH are associated with trauma (*e.g.*, laceration), tissue (*e.g.*, retained placenta), or thrombin (*e.g.*, problems with clotting) [5].

relationship between uterine atony and PPH is well understood. The figure-of-eight muscle fibers of the uterus are wrapped around blood vessels at the former intrauterine site of the placenta. As the placenta delivers, these muscle fibers must contract around the open vessels at the site of placental detachment. When these muscle fibers fail to contract, resulting in uterine atony, a parturient can bleed profusely, resulting in PPH which is defined by the American College of Obstetricians and Gynecologists (ACOG) as ≥ 1000 mL blood loss [44]. However, the cause of uterine atony is far less clear, where several underlying risk factors have been shown to be associated with excessive bleeding and PPH, including (but not limited to) uterine overdistention, certain medications/anesthesia, prolonged/fast labor, high body mass index, uterine fibroids, chorioamnionitis, and placenta disorders [10].

Of particular interest to this work, is the fact that fast/prolonged labor is known to correlate with – but not cause – uterine atony. Towards understanding uterine atony causation, it is known that the thick uterine wall muscle (*i.e.,* myometrium) can experience fatigue in cases of both prolonged or quick delivery [31]. From studying athletes, it is well known that a shift in muscle cell metabolism from aerobic to anaerobic can occur in both prolonged and quick intense periods of exertion, resulting in an accumulation of lactic acid that can impair muscle function (*i.e.,* fatigue) [8]. Similarly, myometrial fatigue in parturients has been shown to shift muscle cell metabolism from aerobic to anaerobic, resulting in accumulation of lactic acid in both myocytes and amniotic fluid [49]. Consequently, it has been postulated in the clinical community that parturient myometrial fatigue is a significant precursor of uterine atony [31]. However, continuously and directly measuring levels of myometrial fatigue in human subjects during active labor remains an open challenge.

2.2 Treatments for Uterine Atony

While safe and effective treatments for uterine atony (and PPH) exist, their effectiveness is complicated by availability, timely diagnosis/intervention, and implicit bias. The first line treatment for suspected uterine atony is to administer uterotonic drugs, often in rapid succession until the uterus is firm and the bleeding subsides [22]. However, often these medications are not positioned nearby in birthing scenarios, increasing the time-to-intervention and reducing intervention effectiveness. When uterine atony is suspected, clinicians often perform physical treatments (*e.g.,* bimanual uterine compression) or invoke mechanical means to arrest bleeding [23, 50]. Ultimately, in severe and delayed-intervention cases, uterotonics and physical treatment may not work and more aggressive treatments are employed, including surgeries such as uterine artery embolization or hysterectomy [23]. Rapid transfusions of blood products are frequently needed to replace lost blood in order to save a patient's life – but in some areas, blood products are not always readily available.

Healthcare providers often rely on visual estimation of blood loss or patient behavior, resulting in inaccurate outcome diagnoses. This leads to underestimated blood loss or missed atony/PPH cases, resulting in increased morbidity and mortality. The accessibility and efficacy of interventions vary worldwide, with challenges in transporting and storing essential drugs like oxytocin and carboprost tromethamine, which requires refrigeration. Racial and economic disparities further compound the issue with implicit bias often underpinning these disparities [20]. Implicit bias has been shown to affect treatment administration (and corresponding clinical care outcomes) and maternal care providers are not immune to this bias [38].

The factors above combine to contribute to the over 60 thousand annual deaths from uterine atony. Of these subjects, a majority experienced PPH due to uterine atony shortly after delivery while under the observation of the clinical care team. Most troubling, research suggests that up to 93% of PPH deaths are preventable [7], where delays in diagnosis and treatment significantly contributes to preventable pregnancy-related deaths and extreme morbidity [15].

2.3 State-of-the-Art: Improving Outcomes

Given the prevalence and severity of PPH and uterine atony, there are many ongoing efforts to improve maternal outcomes. Multiple recent surveys have been published on the state-of-the-art clinical, technological, economical, and human factor solutions to reduce PPH rates (often associated with uterine atony) [18, 54]. Consequently, in this subsection, we restrict our review to technological techniques for postpartum detection and intrapartum prediction.

2.3.1 Postpartum Detection Techniques. Diagnosis of excessive bleeding is usually based on visual estimation of blood loss, quantitative blood loss, vital sign changes and patient report of symptoms [22, 48]. Healthcare providers' establishment of a diagnosis based on visual assessment of blood loss or patient reporting of symptoms tends to be inaccurate. Some cases are underestimated or missed completely, which significantly increases morbidity and mortality [2]. Gravimetric methods to measure blood loss quantitatively have less error than visual estimation techniques [3] and are experiencing increased adoption; however, the process remains manual and burdensome. In response to these challenges, multiple approaches to detect excessive blood loss have been explored including optical quantitative blood loss (*e.g.,* [58]), non-invasive hemoglobin monitoring (*e.g.,* [26]), and monitoring of vital sign trends (*e.g.,* [40]) – and have shown promise in improving delayed PPH outcomes. While detection of delayed PPH is an important endeavor, the vast majority of all PPH and uterine atony occur within minutes of delivery while clinical care teams are present and observing the parturient – which limits the effectiveness and impact of postpartum detection systems in practice [16].

2.3.2 Intrapartum Prediction Techniques. Recognizing the shortcomings of postpartum (after delivery) detection techniques, intrapartum (during labor and delivery) prediction techniques are considered standard-of-care [11, 18]. Early versions of these risk prediction tools relied on expert-designed risk factors and stratifications [18], and though validation studies [17, 24, 53, 67] and subsequent revisions to the tools themselves have evolved to incorporate evidence-driven measures. Consistent shortcomings of these screening tools are their low-to-moderate specificity and sensitivity; positive predictive values of <10%, and more than 40% of hemorrhages occurring in patients designated as low risk [18]. To add, the standard-of-care surveys are performed at static times during the labor process and do not incorporate any patient biometric data. In

light of these poor predictive values, researchers are actively exploring a number of approaches to improving the existing models of risk assessment, including the incorporation of intrapartum factors or non-obstetric risk factors [1, 17, 41, 53]. While some of these approaches have seen limited utilization, none have been widely adopted and do not represent the current standard-of-care. Notably, a major challenge with adoption of these emerging systems is that they are not turnkey solutions. Each healthcare system has different devices and data streams integrated at varying fidelities and utilize different methods of manually recording observed patient data – which significantly increases integration efforts and system tuning prior to utilization. Also, these systems typically are designed (often using machine learning) to correlate with patient outcomes and are not designed to identify a cause of PPH – which introduces both technological risks (*e.g.,* distribution shifts) and regulatory risks.

3 Problem Formulation

In this section, we motivate and present the performance requirements for a commercially-viable risk predictor of life-threatening uterine atony. To begin, we note that the definition of *life-threatening* PPH (and uterine atony) in the clinical literature typically refers to scenarios with observed blood loss far exceeding the definition of a PPH [39]. Since this work focuses on risk prediction prior to delivery (and not detecting life-threatening PPH events), we introduce a definition of *potentially* life-threatening uterine atony to be PPH with associated uterine atony and requiring clinical intervention.

Definition 1 (Potentially Life-Threatening Uterine Atony). *A potentially life-threatening uterine atony is uterine atony resulting in PPH (blood loss greater than 1000 mL) and requiring clinical intervention.*

In the remainder of this work, and solely for readability purposes, we refer to potentially life-threatening uterine atony as just uterine atony where convenient. We now introduce the problem considered in this work.

Problem Statement (Early Prediction of Uterine Atony). *Develop a test that predicts uterine atony and satisfies the performance and implementation requirements (described below).*

Performance Requirements. The performance requirements of an uterine atony risk predictor are well informed by the clinical literature. To facilitate clinical adoption of a uterine atony risk predictor – and leveraging the multiple validation studies and reviews on existing standard-of-care intrapartum PPH risk prediction tools [17, 18, 24, 53, 67] – performance requirements can be stated as follows:

- ***Sensitivity (≥ 80%).*** A major shortcoming of existing standard-of-care risk prediction tools is that more than 40% of hemorrhages occur in patients identified as low-risk (*i.e.,* 60% sensitivity) [18]. To demonstrate potential for clinically significant impact, we aim to reduce the number of missed uterine atony by half. Consequently, we aim to achieve a sensitivity greater than 80% on (potentially life-threatening) uterine atony predictions.
- ***Specificity (≥ 90%).*** When tuned to achieve 60% sensitivity, current standard-of-care risk prediction tools achieve specificity less than 90% [18]. At this specificity, the risk predictions are deemed clinically actionable. Consequently, to ensure actionable alerts, we aim to achieve a specificity greater than 90%.
- ***High-Risk Timing (≥ 30 minutes before delivery).*** Predicting a parturient to be at high-risk for uterine atony too close to delivery makes clinical action much more difficult. While care teams often must respond quickly to a developing unpredicted PPH, these teams and corresponding treatments are far more effective with sufficient time (up to 30 minutes) to maximally prepare for PPH intervention. Consequently, we aim to predict patients at high-risk for uterine atony at least 30 minutes hour prior to delivery.
- ***High-Risk Frequency (once per parturient max).*** Once a subject is predicted as high-risk for uterine atony, clinical care teams will begin preparing for a potential PPH. These preparations may include (but are not limited to) assigning additional personnel, adjusting resources, preparing medications, executing blood typing and crossmatch, and relocating equipment. Consequently, to avoid clinical decision support whip-lash (similar to alarm fatigue), all parturients predicted to be high-risk shall remain at high-risk for the remaining duration of their labor and delivery.

Implementation Requirements To have impact on real-world clinical outcomes will require implementation into clinical care, where clinical outcome predictors are subject to regulation – especially in the U.S.. Additionally, the cost of executing a regulatory-grade pivotal clinical trial requires commercial viability to raise the necessary funding from outside investors (*e.g.,* private equity, venture capital, and/or government). While enumerating all the specific implementation requirements necessary for commercialization and clinical adoption are beyond the scope of this work, at this stage we seek to identify necessary (but not sufficient) implementation requirements to reduce future commercialization risk. Specifically, we motivate and consider the following implementation requirements:

- ***Regulatory.*** To reduce regulatory risk and expedite adoption, the implementation must be adjunctive (*i.e.,* complementary) to existing standard-of-care. This means that any implementation must not supersede or replace the current standard-of-care (*i.e.,* static risk assessments), but rather be used in coordination. Consequently, when static risk assessments identify parturients at high-risk, the subject must be considered high-risk regardless of our implementation's assessment.
- ***Integration.*** A full-function low-cost turn-key implementation that can scale with minimal clinical integration effort should be feasible. The minimal-integration turn-key implementation would enable piloting/adoption of the solution by care facilities prior to requiring upfront integration costs. Ideally, the implementation would utilize data that can be collected from existing regulator-approved hardware common to all care facilities, such that the turn-key solution can be easily transitioned into an electronic health record based solution (if desired) to lower hardware costs.
- ***Usability.*** Recognizing that the usability and acceptability of the turn-key implementation is paramount to its market penetration and adoption, it must be engineered to maximize

patient comfort and ease of setup/use for nursing staff. The implementation should alert at most once per patient (the first time a subject transitions from nominal-risk to high-risk) to avoid overburdening clinical staff or causing alarm fatigue. Additionally, the implementation should have no patient-facing auditory or tactile alarms to eliminate patient distraction while sleeping/resting (as is common during early stages of labor or with epidural anesthesia).

4 Modeling Myometrial Fatigue

Muscle fatigue is defined as the reduction in the muscle's maximal capacity to generate force [64]. While there are several ways to measure intrauterine pressure (*e.g.,* intrauterine pressure catheter and electrohysterogram) [29], to directly calculate myometrial force requires multiplying intrauterine pressure by the internal surface area of the uterus (*i.e.,* force = pressure × area). Since labor contractions progressively shrink the uterus, it follows that a requirement to measure myometrial force using intrauterine pressure is the availability of a real-time measurement for uterine area during labor contractions. Although ultrasound and MRI techniques can be used to statically calculate uterine area pre-labor [9], there are no commercial systems that can provide a real-time measurement of uterine area during labor. Since myometrial force (and by correlation fatigue) cannot be directly measured, we aim to relate the observable impact of myometrial fatigue on measurable signals (using current technology).

Specifically, in this section, we seek to develop a new biomarker, the Myometrial Fatigue Index, that can relate nominal/increased myometrial fatigue to maternal heart rate as a surrogate for cardiac output. The aim is to capture, crudely, observable trends in maternal heart rate that are physiologically motivated to be driven by myometrial fatigue. Similar techniques have been successfully employed in multiple hard-to-measure clinical applications including artificial pancreases [6, 12], pacemakers [25], and stroke detection [37]. Often referred to as minimal models, their aim is to capture *useful* relationships for a target application, not be the most accurate dynamical physiological model. Consequently, when leveraging minimal models in real-world clinical applications, it is necessary to identify how confounding factors affect the modeled dynamics such that systems built using minimal models are robust.

4.1 Myometrial Fatigue Index

Myometrium dynamics are approximately bi-modal. Crudely, the myometrium acts as a bi-modal system during labor with two states: contracted and relaxed. Once in active labor, the myometrium generally enters the contracted state every 2 to 5 minutes (usually with increasing frequency as labor progresses) and generally stays in this state for between 45 and 90 seconds. After a contraction ends, the myometrium re-enters the resting state and the cyclic process continues throughout labor. The length and duration of contractions – monitored by tocodynamometry, intrauterine pressure catheter, or electrohysterogram [29] – vary during labor.

Each cycle, contractions increase cardiac output. While the combined maternal-fetal pre-delivery blood volume is effectively constant, the myometrium state affects myometrium blood volume and cardiac output, where cardiac output is clinically defined as the amount of blood the heart pumps in one minute [28]. When in the relaxed state, the myometrium blood volume normalizes to a steady-state blood volume and steady-state cardiac output, although the true steady-state value can be different for each contraction [55]. When the myometrium contracts, the blood vessels within the uterus are squeezed causing between 300mL to 500mL of blood to be pushed back into the maternal circulation (known as an autotransfusion) which results in an increase in cardiac output [13, 30, 51, 61–63]. Physiologically, the increase in cardiac output due to uterine contraction autotransfusion is largely attributed to the increase in cardiac preload [33] associated with isotonic and isometric muscle contractions [36, 60]. At the end of each contraction, the myometrium relaxes, the uterine blood volume normalizes, and cardiac output returns to a (potentially new) relaxed steady-state until the next contraction.

Myometrial fatigue affects the increase in cardiac output. In general, the amount of autotransfusion during muscle contractions is proportional to cardiac output [35]. Stated differently, contraction autotransfusion increases with cardiac output – regardless of myometrial fatigue. This is due to multiple physiological effects including: blood flow distribution, muscle vasodilation, vascular resistance, and heightened demand for oxygen in working muscles. Conditioned on resting cardiac output, the amount and rate of autotransfusion during muscle contractions is known to be dependent on muscle fatigue [36, 45] – where fatigued muscles have smaller autotransfusions during contraction than their non-fatigued state [42]. Consequently, as the myometrium fatigues, there will be less change in cardiac output between relaxed and contracted states. Leveraging the above, we define the myometrial fatigue index (MFI) as follows:

Definition 2 (Myometrial Fatigue Index (MFI)). The *myometrial fatigue index* (MFI) is the change in cardiac output between contracted ($co_c[k]$) and resting ($co_r[k]$) states normalized by the resting cardiac output:

$$MFI[k] = \frac{co_c[k] - co_r[k]}{co_r[k]} \tag{1}$$

where k denotes the k-th contraction cycle from the end of contraction $k-1$ to the end of contraction k.

The MFI provides an insightful statistic by which to test for myometrial fatigue in parturients. Namely, parturient's MFI decreasing over multiple contractions (*i.e.,* $MFI[k] \geq MFI[k-1] \geq \dots$) suggests the presence of myometrial fatigue. We will formalize a test for myometrial fatigue using MFI in Section 5. While the MFI is physiologically motivated, we note that MFI has two significant limitations. ***Limitations of MFI:***

- Calculating the MFI requires determining cardiac output, which is non-trivial. (See Section 4.2)
- Parturient cardiac output is affected by other confounding factors – not just myometrial fatigue (See Section 4.3)

These limitations will be addressed in the following subsections.

4.2 Measuring Myometrial Fatigue

Determining the MFI requires measuring cardiac output. Cardiac output is determined at any instance as heart rate (hr) times stroke

volume (sv) – *i.e.,* $co = hr \times sv$ [28]. Heart rate can be measured non-invasively by many common sensors and devices, but measuring stroke volume requires specialized equipment (*e.g.,* echocardiography, doppler techniques). In this subsection, we present a surrogate measure for MFI, and show that under reasonable assumptions decreasing surrogate values occur if and only if MFI is also decreasing.

When fatigue is unlikely, stroke volume increases and maternal heart rate decreases during contractions. During active labor, cardiac output *always* increases during contractions. However, in the latent (early) phase of stage 1 labor, the increase in cardiac output during contractions often materializes as increased stroke volume – due to cardiac preload – and a corresponding decrease in maternal heart rate [63]. The decrease in heart rate is a result of the body's autonomic response to maintain hemodynamic stability during periods of increased stroke volume [30, 61]. For completeness, we point out that this effect is consistent with the previous subsection (Section 4.1) since during early labor, the increase in stroke volume during contractions is substantially greater than the corresponding decrease in maternal heart rate, such that cardiac output still increases during contractions [30, 61]. Moreover, it is generally assumed that myometrial fatigue occurs as labor progresses (late stage 1 and stage 2) and is unlikely to occur early in pre-labor and stage 1 labor when maternal heart rate decreases with labor contractions [31].

When fatigue is likely, both stroke volume and maternal heart rate increase during contractions. As labor progresses – and usually while still in the latent phase of stage 1 labor – both stroke volume and heart rate begin to increase during contractions. At this point, the relative increase in maternal heart rate during contractions is roughly proportional to the relative increase in stroke volume [31, 32]. Most importantly, the likelihood of myometrial fatigue increases as labor progresses [31].

We formalize how we measure MFI in real-world scenarios by introducing a surrogate MFI measurement:

Definition 3 (Surrogate Myometrial Fatigue Index (sMFI)). The *surrogate myometrial fatigue index* (sMFI) is the change in maternal heart rate between contracted ($hr_c[k]$) and resting ($hr_r[k]$) states normalized by the maternal heart rate:

$$sMFI[k] = \frac{hr_c[k] - hr_r[k]}{hr_r[k]} \tag{2}$$

where k denotes the k-th contraction cycle from the end of contraction $k-1$ to the end of contraction k.

We note that $sMFI[k]$ is calculated using exclusively maternal heart rate and is measurable using common sensors (*e.g.,* pulse oximeters, electrocardiogram monitors, heart rate monitors). Additionally, we introduce the temporary variable:

$$\sigma[k] = \frac{sv_c[k] - sv_r[k]}{sv_r[k]} \tag{3}$$

to denote the stroke volume during contraction cycle k. Although $\sigma[k]$ is not easily measurable, we leverage the relationship between stroke volume and maternal heart rate when maternal heart rate increases during contractions and make the following reasonable real-world assumption.

Assumption 1 (Maternal Heart Rate and Stroke Volume).

$$\forall k,\ 0 \le sMFI[k] \le sMFI[k-1] \longleftrightarrow \sigma[k] \le \sigma[k-1] \tag{4}$$

In words, Assumption 1 formalizes that changes between contractions of maternal heart rate and stroke volume (normalized to their respective resting state) are directionally equivalent. In other words, if normalized maternal heart rate increases then normalized stroke volume also increases, and vice versa. We also note that the assumption is only assumed to be true when maternal heart rate increases during contractions (*i.e.,* $0 \le sMFI[k] \le sMFI[k-1]$). Under this assumption, it follows that directional changes in normalized maternal heart rate (*i.e.,* sMFI) can be used as an equivalent surrogate for observing directional changes in MFI, formally stated as:

Proposition 1 (Conditional Equivalence of sMFI and MFI). Given Assumption 1:

$$\forall k,\ 0 \le sMFI[k] \le sMFI[k-1] \longleftrightarrow MFI[k] \le MFI[k-1] \tag{5}$$

Proof. Proof provided in appendix. □

The importance of this proposition is that monitoring changes in a surrogate measure based exclusively on maternal heart rate (which can be obtained easily) provides equivalent information as calculating MFI (which is very challenging). We stress that sMFI does not equate to MFI – sMFI only provides the same directional information as MFI (*i.e.,* increasing vs. decreasing). In this sense, when maternal heart rate increases during contractions, we can effectively bypass calculating MFI and provide equivalent information for testing myometrial fatigue using just sMFI. Thus, we have negated the first limitation of MFI presented at the end of Section 4.1 by introducing a surrogate measure, sMFI, to obtain the same testing information for myometrial fatigue without needing to calculate cardiac output (and correspondingly stroke volume).

4.3 Modeling Confounding Factors

The MFI and sMFI are vulnerable to confounding factors associated with other physiological processes – not just myometrial fatigue. We present our approach for addressing confounding factors in terms of sMFI (not MFI) since sMFI is measurable. We note that this is not a limitation of our approach since sMFI will be utilized for testing myometrial fatigue, not MFI. Moreover, we do not immediately address challenges of measurement noise – which will be addressed statistically in the testing approach in Section 5. Consequently, in this subsection, we discuss *confounding physiological factors* (not measurement noise) for maternal heart rate telemetry and present a mathematical formulation capturing the corresponding impacts on sMFI.

During labor, maternal heart rate is affected by physiological processes that are confounding for testing myometrial fatigue using sMFI. Maternal heart rate is known to naturally increase with labor due, in part, to exertion requiring increased cardiac output [51]. Additionally, maternal heart rate during contractions increases as pain increases, the Valsalva maneuver, and anxiety (among others) [14, 63].

To capture these confounding factors on maternal heart rate, we define a corresponding nuisance set of endomorphisms capturing their effect on maternal heart rate telemetry [56]. While not originating in medical applications, representing confounding factors as

transformations of the data has been successfully applied to other medical applications where measurements are known to vary with other physiological processes or parameters [37, 52, 65]. The benefit of capturing nuisance transformations formally is that it allows for their provably complete removal/attenuation [56]. We define the nuisance set capturing the maternal heart rate nuisance factors described above in the following, where $\mathbb{R}_+$ is the set of positive reals and $\mathbb{1}_x$ is an indicator function and equates to 1 when x is true and 0 otherwise.

Definition 4 (Heart Rate Nuisance Set).

$$\mathcal{G}_{hr} = \left\{ g : \mathbb{R}_+ \to \mathbb{R}_+ \;\middle|\; g(a;b) = a + c\mathbb{1}_{(a>b)},\ c \in \mathbb{R}_+ \right\} \tag{6}$$

Each function contained in $\mathcal{G}_{hr}$ represents a potential nuisance that could be imposed on maternal heart rate – and there are an infinite number of functions in $\mathcal{G}_{hr}$.

Recall that calculating sMFI requires maternal heart rate measurements during contracted and relaxed states – both of which are subject to maternal heart rate confounding factors. Consequently, we can extend the effect of $\mathcal{G}_{hr}$ on maternal heart rate to a set of nuisance transformations affecting sMFI , namely:

Definition 5 (sMFI Nuisance Set).

$$\mathcal{G}_{sMFI} = \left\{ g : \mathbb{R}_+^2 \to \mathbb{R}_+^2 \;|g = (g_c, g_r),\quad g_c, g_r \in \mathcal{G}_{hr} \;\right\} \tag{7}$$

In words, each function contained in $\mathcal{G}_{sMFI}$ represents a potential nuisance transformation that could be imposed on sMFI, generated by applying all the heart rate nuisance set transformations to the hr_c and hr_v variables. To resolve the second limitation of MFI presented at the end of Section 4.1, in the following section we will prove a candidate statistic for testing myometrial fatigue is maximally invariant to the confounding factors captured in the sMFI nuisance set (*i.e.,* $\mathcal{G}_{sMFI}$).

5 Predicting Life-Threatening Uterine Atony

In this section, we present a test for myometrial fatigue as a predictor for (potentially life-threatening) uterine atony. At a high-level, our approach to developing the test involves two steps. First, we leverage the sMFI nuisance set developed in the previous section to introduce a maximally invariant statistic to the corresponding nuisance transformations. Next, and leveraging the maximally invariant statistic, we develop a test for evaluating myometrial fatigue. Finally, we present VIBRANT which provides a real-world implementation of the test for myometrial fatigue.

5.1 Maximally Invariant Statistic

In this subsection, we seek to remove the effect of confounding factors through the design of maximally invariant statistics. For a set of (possibly infinite) nuisance transformations, a maximally invariant statistic removes the effect of the nuisance transformations – and only their effect. Mathematically, a maximally invariant is traditionally defined as:

Definition 6 (Maximally Invariant Statistic [56]**).** A statistic, $t(x;y)$, is maximally invariant to set of transformations, $\mathcal{G}$, if:

$$\begin{aligned} &\text{invariant} \;:\; \forall g \in \mathcal{G},\ t(g(x;y)) = t(x;y) \\ &\text{maximal} \;:\; \forall x, x',\ t(x;y) = t(x';y') \to \exists g \in \mathcal{G},\ x = g(x') \end{aligned} \tag{8}$$

Before introducing a candidate maximally invariant statistic, we formalize the necessary maternal heart rate measurement space as

$$y[k] = [hr_c[k],\ hr_r[k],]^\top \in \mathbb{R}_+^2. \tag{9}$$

Leveraging the confounding factors in the previous section, the measurement space is subject to the sMFI nuisance set, $\mathcal{G}_{sMFI}$. Consequently, we present the following statistic as a candidate for a maximally invariant statistic to $\mathcal{G}_{sMFI}$:

$$t\left(y[k]; y[k-1]\right) = \begin{bmatrix} \mathbb{1}_{hr_c[k] \le hr_c[k-1]} hr_c[k] \\ \mathbb{1}_{hr_r[k] \le hr_r[k-1]} hr_r[k] \end{bmatrix} \in \mathbb{R}_+^2 \tag{10}$$

where t is a function of the maternal heart rate measurement for contraction cycle k parameterized by the maternal heart rate measurement during the $k-1$ contraction cycle, namely $y[k-1]$. Leveraging t, we now prove it to be maximally invariant.

Proposition 2. The statistic t is maximally invariant to $\mathcal{G}_{sMFI}$

Proof. Proof provided in Appendix. □

In words, the statistic t contains precisely all the information in the measurement y that is not confounded by the nuisance set for sMFI. Stated more simply, t removes the confounding factors – and only the confounding factors. We note that when maternal heart rate during uterine contractions is increasing (*i.e.,* $hr_c[k] > hr_c[k-1]$) then the first element of t is zero. Similarly, when the maternal heart rate during relaxed periods between contractions is increasing (*i.e.,* $hr_r[k] > hr_r[k-1]$) the second element of t is also zero. Lastly, when maternal heart rate is decreasing during both contracted and relaxed periods, the maximally invariant statistic (*i.e.,* $t(y[k]; y[k-1])$) is equivalent to the original measurement (*i.e.,* $y[k]$).

5.2 Testing for Myometrial Fatigue

In this subsection, we leverage the maximally invariant statistic from the previous subsection to test for myometrial fatigue as a predictor for uterine atony. We observe that sMFI can only be calculated using the maximally invariant statistic, t, when maternal heart rate is decreasing during periods of contraction and relaxation, namely $hr_c[k] \le hr_c[k-1]$, and $hr_r[k] \le hr_r[k-1]$. For notational simplicity in the following, we write

$$\phi[k] = hr_c[k] \le hr_c[k-1] \;\wedge\; hr_r[k] \le hr_r[k-1] \tag{11}$$

to be a logical test of decreasing maternal heart rate corresponding to uterine contractions and relaxations. Leveraging ϕ, a robust test for myometrial fatigued using sMFI can be formulated:

Definition 7 (Testing Myometrial Fatigue using sMFI). Myometrial fatigue exists if the sMFI has decreased.

$$\mathcal{H}_W[k] : \begin{cases} H_F : sMFI[n] \le sMFI[n-1] \wedge \phi[n], & \forall n \in \mathcal{K}_W[k] \\ H_N : \text{otherwise} \end{cases}$$

where H_F and H_N correspond to the *fatigued* and *nominal* hypotheses, and $\mathcal{K}_W[k] = \{k, \ldots, k-W\}$ and $W \in \mathbb{N}^+$ is a parameter representing the duration in the UFI to signify fatigue.

Since the robust test for myometrial fatigue is based on a maximally invariant statistic it follows that it is also invariant to the confounding factors. The robust test is parameterized by a window W, which effectively controls the significance of the test. The window size

determines how many consecutive contraction cycles are needed to alert for uterine fatigue.

Muscle fatigue is non-linear. It is worth noting that muscle fatigue is non-linear, with initially there being very little observable fatigue, followed by a period of marked and increasing fatigue which eventually resolves to a steady-state fatigue level [27]. Consequently, the test for myometrial fatigue will only be sensitive during periods of marked and increasing fatigue – not prior to fatigue nor after steady-state fatigue is achieved. This process makes the selection W important. Selecting W too small and the test will be noisy, and conversely, selecting W too large and the test will not be sensitive to uterine fatigue. The selection of W will be addressed in the next subsection.

5.3 VIBRANT Implementation

In this subsection we describe our implementation of the robust test for myometrial fatigue as a predictor of uterine atony (and PPH). There are two main challenges with implementing $\mathcal{H}_W$ (as presented in Definition 7). First, the strict requirements on monotonicity of maternal heart rate and sMFI may be violated in the presence of myometrial fatigue due to noisy maternal heart rate telemetry measurements (*e.g.,* due to motion artifact). Second, calculating maternal heart rate during contractions and rest requires identifying contractions – which is challenging. In this subsection, we discuss relaxations of the strict monotonicity testing based on maternal heart rate and present an approach for overcoming challenges with identifying maternal heart rate during contractions and rest. This subsection concludes by stating the VIBRANT algorithm.

Overcoming strict monotonicity testing. Practically speaking, maternal heart rate telemetry (and by extension sMFI) are noisy. Consequently, in the real-world, requiring strict assessments of noisy measurements as tests leads to reduced utility and performance. Recognizing that the intuition behind $\mathcal{H}_W[k]$ is myometrial fatigue corresponds to maternal heart rate telemetry that is decreasing (both during contractions and rest) and sMFI is decreasing, we opt for a statistical test (rather than absolute test) that captures these general trends. One classical approach that captures monotonic trends is data is the spearman's rank correlation coefficient [57], traditionally denoted as

$$(c, p) = \rho\,(\text{set of 1-D input data}) \tag{12}$$

where, c and p are the correlation coefficient and p-value, respectively. For testing myometrial fatigue, the spearman's rank correlation coefficient provides some useful features. First, it is non-parametric, which makes it accurate for data with unknown distributions. This is important since the distribution of maternal heart rate is different for each parturient and changes over the course of labor. Secondly, by thresholding the corresponding $p - value$, the test can be effectively tuned to achieve different desired performance levels.

Overcoming identification of contractions. While identifying contractions is commonly done via tocodynamometry, intrauterine pressure catheter, or electrohysterogram [29], extracting contractions from maternal heart rate remains an open-challenge [59]. We recall that contractions during active labor occur at least every 10 minutes and only last up to approximately 90 seconds. Observing that robustly testing for myometrial fatigue targets labor stages where maternal heart rate increases due to contractions, we introduce the following heuristic for calculating maternal heart rate during rest and contraction. Let $\mathcal{Y}[k]$ represent the k-th set of heart rate measurements corresponding to non-overlapping periods 10 minutes (such that at least one contraction is contained in $\mathcal{Y}[k]$) we write:

$$\begin{aligned} \overline{hr}_c[k] &= \text{median (largest 5\% of } \mathcal{Y}[k]) \\ \overline{hr}_r[k] &= \text{median } (\mathcal{Y}[k]) \\ \overline{sMFI}[k] &= \frac{\overline{hr}_c[k] - \overline{hr}_r[k]}{\overline{hr}_r[k]} \end{aligned} \tag{13}$$

In words, $\overline{hr}_r[k]$ is chosen to be the median of all data in the period (to mitigate the effects of outliers associated with contractions). Our definition of $\overline{hr}_c[k]$ targets the median of the top 5% of the data which *should* occur during myometrial contractions – assuming maternal heart rate increases with the contractions and the progression of labor. Note, when the maternal heart rate decreases, we will observe that $\overline{hr}_c[k]$ and $\overline{hr}_r[k]$ will be much closer than during periods where maternal heart rate increases and result in a smaller $\overline{sMFI}[k]$ – possibly within the measurement noise profile. Consequently, it is unlikely that $\overline{sMFI}[k]$ will exhibit monotonicity during early labor when myometrial fatigue is unlikely.

We now introduce the VIBRANT test at period K. For thresholds, η_c and η_p on the rank correlation coefficient and corresponding p-value, respectively, and given a set of windows $\mathcal{W}$, we present the VIBRANT test for myometrial fatigue at period K in the following algorithm. A feature of the $VIBRANT$ test is that it satisfies the implementation requirements in Section 3 for alarm frequency. If at period K VIBRANT determines a parturient to be *High Risk*, then for all future periods $K' > K$ VIBRANT will also determine that parturient to be *High Risk*. This is consistent with the physiological reasoning that if the myometrium becomes fatigued, it will remain fatigued through delivery. For completeness, the VIBRANT test should only be used prior to delivery and begin monitoring during active labor. Since parturients are assumed to be experiencing contractions, the VIBRANT test should not be used on planned cesarean births – and is only indicated for vaginal and non-planned cesarean births. Lastly, the VIBRANT test is not indicated to work in subjects not in labor.

Algorithm 1 VIBRANT Test for Myometrial Fatigue at Period K

```
Initialize output as Low Risk
for Every k ≤ K do
    Calculate hr̄_c[k], hr̄_r[k], and sMFI̅[k]
    for Every W ∈ 𝒲 do
        Calculate (c_c, p_c) = ρ(hr̄_c[k], ..., hr̄_c[k − W])
        Calculate (c_r, p_r) = ρ(hr̄_r[k], ..., hr̄_r[k − W])
        Calculate (c_f, p_f) = ρ(sMFI̅[k], ..., sMFI̅[k − W])
        if max(c_c, c_r, c_f) ≤ η_c and max(p_c, p_r, p_f) ≤ η_p then
            Change output to be High Risk
        end if
    end for
end for
```

6 Evaluation

In this section, we evaluate VIBRANT against a current standard-of-care admission PPH risk score. In the following, we first introduce the dataset used for evaluation then present the results.

6.1 Evaluation DataSet

We performed a primary, prospective, observational study collecting maternal heart rate data from patients admitted to the Pennsylvania Hospital to validate the VIBRANT test (IRB #848588). Participants wore a commercially available Samsung Galaxy Watch Active and the Raproto application [21] was used to collect to collect photoplethsymgraphy (PPG) data. From the PPG data, maternal heart rate was generated at a rate of 1 Hz using standard techniques [66]. To ensure conditions were representative of real-world practice, no instructions to change clinical procedures were given while the parturient was monitored. No collected data was revealed to parturients or their clinical care team, thus there was no opportunity to influence the patient care setting during the observational study. At the institution where the study was conducted, quantitative blood loss (QBL) is not consistently performed as part of routine clinical care (and is typically only done in severe cases), consequently visual estimated blood loss (EBL) was utilized to determine PPH.

A total of 525 parturients were recruited from the corresponding obstetric and midwifery practices at the study hospital. Parturients 18 years of age or older were eligible to enter the study if admitted to give birth to a term ($\geq$ 37 weeks gestation) live, singleton infant. In this study, parturients were excluded if they were preterm (<37 weeks gestation), had a fetal demise, or were pregnant with multiples (twins, triplets, etc.). An admission PPH risk score – based on the Association of Women's Health, Obstetrics and Neonatal Nurses (AWHONN) criteria – was recorded for each subject as a baseline [4]. Parturients with the following characteristics were omitted from the analysis herein:

- withdrawn from the study;
- missing chart data critical for analysis;
- scheduled cesarean births;
- prior history of postpartum hemorrhage.

To motive the exclusion criteria for this analysis, and as discussed at the end of the Section 5, the VIBRANT test is not designed to work on scheduled cesarean births where parturients do not experience uterine contractions. Additionally, we remove parturients with a known prior history of PPH since these subjects automatically receive elevated care – patients with known prior PPH are 3x more likely to have a PPH than the general population [43]. Consequently, providing a prediction of uterine atony provides limited actionable information since the care team is already prepared. The resulting study population contained 380 parturients. In the study population, 11 experienced a potentially life-threatening PPH (2.9%) – which is consistent with known PPH rates between 1% and 5%.

To identify subjects experiencing uterine atony, clinical notes for the parturient in the chart data were examined for documentation and discussion of uterine atony-related diagnosis and intervention (*e.g.,* uterine atony, boggy, lacking firmness). Of the 11 subjects experiencing a PPH 6 parturients had documented uterine atony (1.6% of total population, 55% of PPH). This rate is slightly lower than anticipated (uterine atony accounts for approximately 80% of PPH), likely due a lack of clinical notes on some subjects. Consequently, in this evaluation we also omit the 5 parturients who experienced PPH but did not have documented uterine atony, resulting in a study population of 375 parturients.

6.2 Prediction Performance and Analysis

We evaluate VIBRANT on the dataset against the gold-standard AWHONN PPH admission risk scoring system [4], the performance results are provided in Table 1. We note that the VIBRANT satisfies the performance requirements specified in Section 3.

Table 1: Prediction Results

	VIBRANT	AWHONN [4]
Sensitivity	83%	0% (see discussion)
Specificity	90%	90%
Positive Predictive Value	13%	0% (see discussion)
Negative Predictive Value	99%	97%
High-risk prediction before delivery (in hours) median ± interquartile range	4.0 ± [1.7, 7.9]	8.5 ± [3.9, 14]

Why does AWHONN have 0% sensitivity and 0% positive predictive value? The answer is because the AWHONN system – being standard-of-care – was implemented during our data collection (as ethics requires). Consequently, clinicians had access to the AWHONN predictions during delivery. This is not a limitation of our approach or analysis. It stands to reason that AWHONN did not predict any of the potentially life-threatening uterine atony cases because clinicians – given sufficient warning – were able to mitigate a PPH. Stated simply, when AWHONN identified a parturient as high-risk, clinicians used that information effectively. This is consistent with the clinical literature that asserts 93% of all PPH can be avoided with sufficient planning and resources [7]. Consequently, the evaluation of VIBRANT was performed in a realistic scenario – since VIBRANT is adjunctive to clinical care.

Analysis of VIBRANT 's sensitivity and positive predictive value.. The real-world results indicate that VIBRANT predicts over 80% of the potentially life-threatening uterine atony currently missed by standard-of-care admission risk scoring. This represents a significant improvement and could significantly decrease PPH rates once integrated into clinical care – assuming clinicians are as effective at responding to the VIBRANT high-risk predictions as they are at responding to AWHONN high-risk predictions. We note that a 13% positive predictive value may appear low, but this is because only 2% of the population experienced potentially life-threatening uterine atony in our study. Impressively, this means that the parturients VIBRANT predicts as high-risk are over 5x more likely to experience uterine atony than the rest of the population. This is significantly better than a current gold-standard benchmark – recalling from our dataset discussion – that subjects with prior PPH automatically receive elevated care (which only has a 3x more likely chance of PPH). Additionally, the VIBRANT performance criteria satisfies the minimum requirements specified in Section 3.

Comparative analysis of specificity and negative predictive value. The results demonstrate, comparatively, no clinically significant difference in performance in terms of specificity and negative predictive value – with VIBRANT having a slight advantage in negative predictive value. The fact that VIBRANT has similar performance to AWHONN is promising for its real-world use. Recognizing a 90% specificity equates to a 10% false positive rate, it is worth noting that a 10% false alarm rate is considered clinically actionable (see AWHONN performance). At the 90% specificity operating point, clinical care teams are highly likely to respond to VIBRANT high-risk predictions, as evidenced by the fact that care teams continue to respond to AWHONN (which also has a 90% specificity). Clinically, this can be interpreted as VIBRANT is capable of identifying the 10% of parturients that contain over 80% potentially life-threatening uterine atony currently current missed by the standard-of-care risk predictors – a clinically significant achievement.

Analysis of high-risk prediction timing. To be clinically actionable, high-risk predictions must occur with enough time to prepare prior to delivery. In Table 1 we report the median and interquartile range of high-risk predictions (prior to delivery) and a cumulative distribution of high-risk prediction times (also prior to delivery) are provided in Figure 2. We stress that AWHONN makes predictions at admission time and prior to when maternal heart rate monitoring commences. Consequently, AWHONN should always predict earlier than VIBRANT . The distribution of VIBRANT suggests that alarms occur sufficiently prior to delivery during active labor to allow for ample time for care teams to respond. This gives promise to the VIBRANT as a viable system to complement current risk prediction techniques (*e.g.,* AWHONN) to significantly reduce PPH associated with uterine atony.

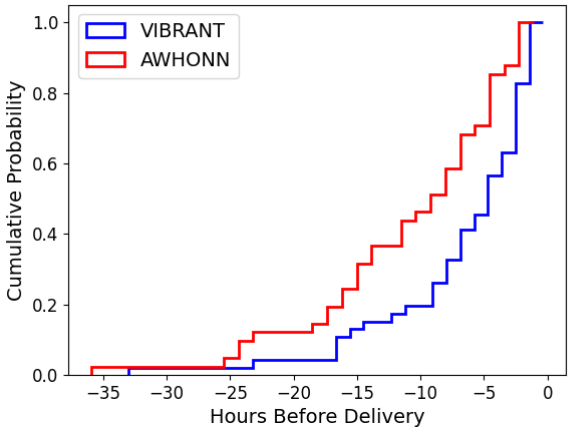

Figure 2: High-risk prediction timing. AWHONN prediction occurs at admission, while VIBRANT prediction occurs based on monitoring.

7 Regulatory Considerations

In this section, we briefly overview ongoing regulatory efforts and considerations. VIBRANT is a clinical decision support system that evaluates maternal heart rate data and provides actionable feedback on a patient's risk of PPH. Ongoing work focuses on system integration of VIBRANT for a pivotal clinical trial and eventual regulatory approval and commercialization. Given the cost of executing a clinical trial, the VIBRANT has been licensed to a commercial partner for build-out and integration in clinical environments. Prior to widespread integration into clinical care, the integrated VIBRANT system will be subject to regulatory oversight as a clinical decision support system. Consequently, we have presented the system to the U.S. Food and Drug Administration (FDA) through the 510(k) pre-submission process. The meeting with the FDA indicated that VIBRANT will likely be regulated in the U.S. as a class II de novo software-as-a-medical device. Critical to being granted regulatory pre-market approval will be the successful completion of a clinical trial to establish safety and efficacy on observable clinical outcomes. To de-risk the impending high-cost clinical trial, the VIBRANT is in preparation to be evaluated in a closed-loop pilot study as an investigational device. The results of the pilot study will inform the effect size of the device on reducing PPH rates which will be utilized to perform a power analysis to determine the regulatory-grade clinical trial size.

8 Conclusions

This paper introduced VIBRANT as a clinical decision support tool providing early prediction of life-threatening uterine atony. VIBRANT is physiologically motivated and designed to identify signals corresponding to myometrial fatigue in maternal heart rate data. Evaluations of the system indicate that VIBRANT has high accuracy and provides between 2 to 8 hours advance warning prior to delivery for parturients at high-risk of experiencing life-threatening uterine atony postpartum. Accurate advanced warning is critical to reducing PPH rates as it allows for preparation and planning by clinical care teams. Uterine atony represents 80% of all PPH which is the leading cause of maternal mortality world-wide. While VIBRANT has the potential to address a large portion of PPH missed by current tools, it is one (of potentially many tools/techniques) that will be needed to solve the world-wide PPH problem. Consequently, predicting maternal outcomes remains an open research area with substantial opportunity for innovation.

Disclosures

Modri, Sehdev, and Weimer have equity in a company named Vasowatch, which has licensed VIBRANT as described in this paper. Additionally, Trout has been a paid consultant for Vasowatch. The remaining authors have no disclosures to report.

Acknowledgments

This material is based upon work supported by the National Science Foundation under Award No. 2339637. Research reported in this publication was supported by National Heart, Lung, and Blood Institute of the National Institutes of Health under award number 1R41HL164191. Support provided by the University of Pennsylvania School of Nursing Innovation Accelerator.

References

[1] Diana Abbas, Michelle J Wang, Lindsey Claus, Megan Alexander, Akanksha Srivastava, Sara Young, Swetha Tummala, Ronald Iverson, Christina Yarrington, and Ashley Comfort. 2022. Intrapartum Risk Factors and Prediction of Obstetric Hemorrhage–Related Morbidity. *American Journal of Perinatology* (2022).

[2] Nasreen B Aflaifel, Nomita Chandhiok, Bukola Fawole, Stacie E Geller, and Andrew D Weeks. 2019. Use of histograms to assess the efficacy of uterotonic treatment for post-partum haemorrhage: a feasibility study. *Best Practice & Research Clinical Obstetrics & Gynaecology* 61 (2019), 15–27.

[3] Hanan MF Al Kadri, Bedayah K Al Anazi, and Hani M Tamim. 2011. Visual estimation versus gravimetric measurement of postpartum blood loss: a prospective cohort study. *Archives of gynecology and obstetrics* 283 (2011), 1207–1213.

[4] Obstetric Association of Women's Health and Neonatal Nurses (AWHONN). 2017. Postpartum hemorrhage project: A multi-hospital quality improvement program.

[5] Melanie Basso, Cynthia Chan, Kirsten Duckitt, Ryan Lett, et al. 2022. Guideline No. 431: postpartum hemorrhage and hemorrhagic shock. *Journal of Obstetrics and Gynaecology Canada* 44, 12 (2022), 1293–1310.

[6] Richard N Bergman, Y Ziya Ider, Charles R Bowden, and Claudio Cobelli. 1979. Quantitative estimation of insulin sensitivity. *American Journal of Physiology-Endocrinology And Metabolism* 236, 6 (1979), E667.

[7] Debra Bingham and Reneé Jones. 2012. Maternal death from obstetric hemorrhage. *Journal of Obstetric, Gynecologic & Neonatal Nursing* 41, 4 (2012), 531–539.

[8] Simeon P Cairns. 2006. Lactic acid and exercise performance: culprit or friend? *Sports medicine* 36 (2006), 279–291.

[9] Ishwari Casikar, Max Mongelli, Shannon Reid, and George Condous. 2015. Estimation of uterine volume: A comparison between Viewpoint and 3D ultrasound estimation in women undergoing laparoscopic hysterectomy. *Australasian Journal of Ultrasound in Medicine* 18, 1 (2015), 27–32.

[10] Cleveland Clinic. [n.d.]. Uterine Atony. https://my.clevelandclinic.org/health/diseases/24010-uterine-atony. Accessed: 2024-12-19.

[11] California Maternal Quality Care Collaborative (CMQCC). [n.d.]. OB hemorrhage toolkit v3.0 errata 7.18.22. https://www.cmqcc.org/resources-tool-kits/toolkits/ob-hemorrhage-toolkit. Accessed: 2024-12-17.

[12] Claudio Cobelli, Chiara Dalla Man, Giovanni Sparacino, Lalo Magni, Giuseppe De Nicolao, and Boris P Kovatchev. 2009. Diabetes: models, signals, and control. *IEEE reviews in biomedical engineering* 2 (2009), 54–96.

[13] Sanjay Datta, Bhavani Shankar Kodali, Scott Segal, Sanjay Datta, Bhavani Shankar Kodali, and Scott Segal. 2010. Maternal physiological changes during pregnancy, labor, and the postpartum period. *Obstetric Anesthesia Handbook: Fifth Edition* (2010), 1–14.

[14] Elias J Dayoub and Anupam B Jena. 2015. Does pain lead to tachycardia? Revisiting the association between self-reported pain and heart rate in a national sample of urgent emergency department visits. In *Mayo Clinic Proceedings*, Vol. 90. Elsevier, 1165–1166.

[15] Micaela Della Torre, Sarah J Kilpatrick, Judith U Hibbard, Louise Simonson, Shirley Scott, Abby Koch, Deborah Schy, and Stacie E Geller. 2011. Assessing preventability for obstetric hemorrhage. *American journal of perinatology* 28, 10 (2011), 753–760.

[16] Virginia Diaz, Edgardo Abalos, and Guillermo Carroli. 2018. Methods for blood loss estimation after vaginal birth. *Cochrane Database of Systematic Reviews* 9 (2018).

[17] Andrew J Dilla, Jonathan H Waters, and Mark H Yazer. 2013. Clinical validation of risk stratification criteria for peripartum hemorrhage. *Obstetrics & Gynecology* 122, 1 (2013), 120–126.

[18] Holly B Ende and Alexander J Butwick. 2021. Current state and future direction of postpartum hemorrhage risk assessment. *Obstetrics & Gynecology* 138, 6 (2021), 924–930.

[19] Steven G Gabbe, Jennifer R Niebyl, Joe Leigh Simpson, Mark B Landon, Henry L Galan, Eric RM Jauniaux, Deborah A Driscoll, Vincenzo Berghella, and William A Grobman. 2016. *Obstetrics: normal and problem pregnancies e-book*. Elsevier Health Sciences.

[20] Cynthia Gyamfi-Bannerman, Sindhu K Srinivas, Jason D Wright, Dena Goffman, Zainab Siddiq, Mary E D'Alton, and Alexander M Friedman. 2018. Postpartum hemorrhage outcomes and race. *American journal of obstetrics and gynecology* 219, 2 (2018), 185–e1.

[21] Tarek Hamid, Kimberly Helm, Hyonyoung Choi, Jean Park, Claire Kendell, Stephanie Cummings, Steve Messe, Stefanie Modri, Insup Lee, James Weimer, et al. 2024. Raproto: An Open-Source Platform for Rapid Prototyping with Wearable Devices. In *2024 IEEE 20th International Conference on Body Sensor Networks (BSN)*. IEEE, 1–4.

[22] Angela Hancock, Andrew D Weeks, and Lavender Dame Tina. 2019. Assessing blood loss in clinical practice. *Best Practice & Research Clinical Obstetrics & Gynaecology* 61 (2019), 28–40.

[23] G Justus Hofmeyr and Zahida Qureshi. 2016. Preventing deaths due to haemorrhage. *Best Practice & Research Clinical Obstetrics & Gynaecology* 36 (2016), 68–82.

[24] S Ahmed Hussain, Carla B Guarini, Colleen Blosser, and Aaron T Poole. 2019. Obstetric hemorrhage outcomes by intrapartum risk stratification at a single tertiary care center. *Cureus* 11, 12 (2019).

[25] Zhihao Jiang and Rahul Mangharam. 2011. Modeling cardiac pacemaker malfunctions with the virtual heart model. In *2011 Annual International Conference of the IEEE Engineering in Medicine and Biology Society*. IEEE, 263–266.

[26] Bellal Joseph, Ansab Haider, and Peter Rhee. 2016. Non-invasive hemoglobin monitoring. *International Journal of Surgery* 33, PB (2016), 254–257.

[27] PA Karthick, Diptasree Maitra Ghosh, and S Ramakrishnan. 2018. Surface electromyography based muscle fatigue detection using high-resolution time-frequency methods and machine learning algorithms. *Computer methods and programs in biomedicine* 154 (2018), 45–56.

[28] Jordan King and David R Lowery. 2017. Physiology, cardiac output. (2017).

[29] Katherine J Kissler, Nancy K Lowe, and Teri L Hernandez. 2020. An integrated review of uterine activity monitoring for evaluating labor dystocia. *Journal of midwifery & women's health* 65, 3 (2020), 323–334.

[30] Richard Klabunde. 2011. *Cardiovascular physiology concepts*. Lippincott Williams & Wilkins.

[31] Antonios Koutras, Zacharias Fasoulakis, Athanasios Syllaios, Nikolaos Garmpis, Michail Diakosavvas, Athanasios Pagkalos, Thomas Ntounis, and Emmanuel N Kontomanolis. 2021. Physiology and Pathology of Contractility of the Myometrium. *in vivo* 35, 3 (2021), 1401–1408.

[32] Wesley Lee, Roxann Rokey, Joanna Miller, and David B Cotton. 1989. Maternal hemodynamic effects of uterine contractions by M-mode and pulsed-Doppler echocardiography. *American Journal of Obstetrics and Gynecology* 161, 4 (1989), 974–977.

[33] Robert C Little and William C Little. 1982. Cardiac preload, afterload, and heart failure. *Archives of internal medicine* 142, 4 (1982), 819–822.

[34] NILS-OLOV LUNELL and LARS NYLUND. 1992. Uteroplacental blood flow. *Clinical obstetrics and gynecology* 35, 1 (1992), 108–118.

[35] S Magder. 2016. Volume and its relationship to cardiac output and venous return. *Critical care* 20 (2016), 1–11.

[36] Chris J McNeil, Matti D Allen, Eric Olympico, J Kevin Shoemaker, and Charles L Rice. 2015. Blood flow and muscle oxygenation during low, moderate, and maximal sustained isometric contractions. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 309, 5 (2015), R475–R481.

[37] Steven R Messé, Scott E Kasner, Brett L Cucchiara, Michael L McGarvey, Stephanie Cummings, Michael A Acker, Nimesh Desai, Pavan Atluri, Grace J Wang, Benjamin M Jackson, et al. 2023. Derivation and validation of an algorithm to detect stroke using arm Accelerometry data. *Journal of the American Heart Association* 12, 3 (2023), e028819.

[38] Amanda Millatt, Kimberly K Trout, Rachel Ledyard, Susan E Brunk, Dominique G Ruggieri, Lesley Bates, Anne M Mullin, and Heather H Burris. 2024. Giving Birth With a Midwife in Attendance: Associations of Race and Insurance Status With Continuity of Midwifery Care in Philadelphia. *Journal of Midwifery & Women's Health* (2024).

[39] Manuel Muñoz, Jakob Stensballe, Anne-Sophie Ducloy-Bouthors, Marie-Pierre Bonnet, Edoardo De Robertis, Ino Fornet, François Goffinet, Stefan Hofer, Wolfgang Holzgreve, Susana Manrique, et al. 2019. Patient blood management in obstetrics: prevention and treatment of postpartum haemorrhage. A NATA consensus statement. *Blood Transfusion* 17, 2 (2019), 112.

[40] HL Nathan, A El Ayadi, NL Hezelgrave, P Seed, E Butrick, S Miller, A Briley, S Bewley, and AH Shennan. 2015. Shock index: an effective predictor of outcome in postpartum haemorrhage? *BJOG: An International Journal of Obstetrics & Gynaecology* 122, 2 (2015), 268–275.

[41] Charlotte Neary, Sanobar Naheed, DJ McLernon, and Mairead Black. 2021. Predicting risk of postpartum haemorrhage: a systematic review. *BJOG: An International Journal of Obstetrics & Gynaecology* 128, 1 (2021), 46–53.

[42] Marta Nocella, Barbara Colombini, Giulia Benelli, Giovanni Cecchi, M Angela Bagni, and Joseph Bruton. 2011. Force decline during fatigue is due to both a decrease in the force per individual cross-bridge and the number of cross-bridges. *The Journal of physiology* 589, 13 (2011), 3371–3381.

[43] Anna Sara Oberg, Sonia Hernandez-Diaz, Kristin Palmsten, Catarina Almqvist, and Brian T Bateman. 2014. Patterns of recurrence of postpartum hemorrhage in a large population-based cohort. *American journal of obstetrics and gynecology* 210, 3 (2014), 229–e1.

[44] American College of Obstetricians and Gynecologists. 2017. Postpartum Hemorrhage. Practice Bulletin #183. *Obstetrics and Gynecology* 130, 4 (2017), e168–e186.

[45] Fumiko Ohmori, Shizuyo Shimizu, and Atsuko Kagaya. 2007. Exercise-induced blood flow in relation to muscle relaxation period. *Dynamic Medicine* 6 (2007), 1–6.

[46] World Health Organization. [n.d.]. Maternal mortality fact sheet. https://www.who.int/news-room/fact-sheets/detail/maternal-mortality. Accessed: 2024-12-17.

[47] World Health Organization. 2023. *A roadmap to combat postpartum haemorrhage between 2023 and 2030*. World Health Organization.

[48] Rodolfo Carvalho Pacagnella and Anderson Borovac-Pinheiro. 2019. Assessing and managing hypovolemic shock in puerperal women. *Best Practice & Research*

Clinical Obstetrics & Gynaecology 61 (2019), 89–105.
[49] Kinga Pospiech and Krzysztof Czajkowski. 2020. Amniotic fluid lactate level as a diagnostic tool for prolonged labour. *Journal of Mother and Child* 24, 3 (2020), 3–7.
[50] Cochrane Pregnancy, Childbirth Group, Frances J Kellie, Julius N Wandabwa, Hatem A Mousa, and Andrew D Weeks. 1996. Mechanical and surgical interventions for treating primary postpartum haemorrhage. *Cochrane Database of Systematic Reviews* 2020, 7 (1996).
[51] SC Robson, W Dunlop, RJ Boys, and S Hunter. 1987. Cardiac output during labour. *Br Med J (Clin Res Ed)* 295, 6607 (1987), 1169–1172.
[52] Alexander Roederer, James Weimer, Joseph DiMartino, Jacob Gutsche, and Insup Lee. 2015. Robust monitoring of hypovolemia in intensive care patients using photoplethysmogram signals. In *2015 37th Annual International Conference of the Ieee Engineering in Medicine and Biology Society (Embc)*. IEEE, 1504–1507.
[53] Halley Ruppel, Vincent X Liu, Neeru R Gupta, Lauren Soltesz, and Gabriel J Escobar. 2021. Validation of postpartum hemorrhage admission risk factor stratification in a large obstetrics population. *American journal of perinatology* 38, 11 (2021), 1192–1200.
[54] Oluwatosin D Sadiku, Susan A Aina, Chinonso C Odoemene, Temiloluwa E Ogunmoyin, Victor O Adedara, Omolara Olasimbo, Faridah A Ashir, Stephennie C Adili, Azeez O Kuteyi, Opeyemi O Fakayode, et al. 2024. Approaches to the Prevention and Treatment of Postpartum Hemorrhage: A Systematic Review of Past Advances, Recent Developments, and Best Practices. *Cureus* 16, 7 (2024), e65096.
[55] Monika Sanghavi and John D Rutherford. 2014. Cardiovascular physiology of pregnancy. *Circulation* 130, 12 (2014), 1003–1008.
[56] Louis L Scharf and Cédric Demeure. 1991. Statistical signal processing: detection, estimation, and time series analysis. *(No Title)* (1991).
[57] Patrick Schober, Christa Boer, and Lothar A Schwarte. 2018. Correlation coefficients: appropriate use and interpretation. *Anesthesia & analgesia* 126, 5 (2018), 1763–1768.
[58] Behnam Sharareh, Spencer Woolwine, Siddarth Satish, Peter Abraham, and Ran Schwarzkopf. 2015. Real time intraoperative monitoring of blood loss with a novel tablet application. *The open orthopaedics journal* 9 (2015), 422.
[59] Dan J Sherman, Eugenia Frenkel, Yaffa Kurzweil, Anna Padua, Shlomo Arieli, and Murat Bahar. 2002. Characteristics of maternal heart rate patterns during labor and delivery. *Obstetrics & Gynecology* 99, 4 (2002), 542–547.
[60] Nina Soehnchen, Katarina Melzer, B Martinez de Tejada, Nicole Jastrow-Meyer, Véronique Othenin-Girard, Olivier Irion, Michel Boulvain, and Bengt Kayser. 2011. Maternal heart rate changes during labour. *European journal of obstetrics & gynecology and reproductive biology* 158, 2 (2011), 173–178.
[61] Priya Soma-Pillay, Catherine Nelson-Piercy, Heli Tolppanen, and Alexandre Mebazaa. 2016. Physiological changes in pregnancy: review articles. *Cardiovascular journal of Africa* 27, 2 (2016), 89–94.
[62] Kent Ueland and John M Hansen. 1969. Maternal cardiovascular dynamics: II. Posture and uterine contractions. *American Journal of Obstetrics and Gynecology* 103, 1 (1969), 1–7.
[63] Teelkien R Van Veen, Michael A Belfort, and Shalece Kofford. 2012. Maternal heart rate patterns in the first and second stages of labor. *Acta obstetricia et gynecologica scandinavica* 91, 5 (2012), 598–604.
[64] Nina K Vøllestad. 1997. Measurement of human muscle fatigue. *Journal of neuroscience methods* 74, 2 (1997), 219–227.
[65] James Weimer, Sanjian Chen, Amy Peleckis, Michael R Rickels, and Insup Lee. 2016. Physiology-invariant meal detection for type 1 diabetes. *Diabetes technology & therapeutics* 18, 10 (2016), 616–624.
[66] Marek Wójcikowski and Bogdan Pankiewicz. 2020. Photoplethysmographic time-domain heart rate measurement algorithm for resource-constrained wearable devices and its implementation. *Sensors* 20, 6 (2020), 1783.
[67] Erica Wu, Jennifer A Jolley, Brooke A Hargrove, Aaron B Caughey, and Judith H Chung. 2015. Implementation of an obstetric hemorrhage risk assessment: validation and evaluation of its impact on pretransfusion testing and hemorrhage outcomes. *The Journal of Maternal-Fetal & Neonatal Medicine* 28, 1 (2015), 71–76.

A Proofs

A.1 Proof of Proposition 1

Proof. We begin by recalling from Assumption 1 that (under our monitoring conditions) when $0 \leq sMFI[k] \leq sMFI[k-1]$ it holds that $\sigma[k] \leq \sigma[k-1]$. Next, we write:

$$\begin{aligned} & sMFI[k] \leq sMFI[k-1] \\ \leftrightarrow & \frac{hr_c[k] - hr_r[k]}{hr_r[k]} \leq \frac{hr_c[k-1] - hr_r[k-1]}{hr_r[k-1]} \\ \leftrightarrow & \frac{hr_c[k]}{hr_r[k]} \leq \frac{hr_c[k-1]}{hr_r[k-1]} \end{aligned} \tag{14}$$

and

$$\begin{aligned} & \sigma[k] \leq \sigma[k-1] \\ \leftrightarrow & \frac{sv_c[k] - sv_r[k]}{sv_r[k]} \leq \frac{sv_c[k-1] - sv_r[k-1]}{sv_r[k-1]} \\ \leftrightarrow & \frac{sv_c[k]}{sv_r[k]} \leq \frac{sv_c[k-1]}{sv_r[k-1]} \end{aligned} \tag{15}$$

Combining Equation 14 and Equation 15 above, we write

$$\begin{aligned} & sMFI[k] \leq sMFI[k-1] \quad \text{and} \quad \sigma[k] \leq \sigma[k-1] \\ \leftrightarrow & \frac{sv_c[k]}{sv_r[k]} \frac{hr_c[k]}{hr_r[k]} \leq \frac{sv_c[k-1]}{sv_r[k-1]} \frac{hr_c[k-1]}{hr_r[k-1]} \\ \leftrightarrow & \frac{co_c[k]}{co_r[k]} \leq \frac{co_c[k-1]}{co_r[k-1]} \\ \leftrightarrow & \frac{co_c[k] - co_r[k]}{co_r[k]} \leq \frac{co_c[k-1] - co_r[k-1]}{co_r[k-1]} \\ \leftrightarrow & MFI[k] \leq MFI[k-1] \end{aligned}$$

□

A.2 Proof of Proposition 2

Proof. **For invariance**: Consider the case where $hr_c[k] \leq hr_c[k-1]$ and $hr_r[k] \leq hr_r[k-1]$. We note that in all other cases $t(g(y)) = 0 = t(y)$ since one of the indicators functions in t evaluate to zero. Then:

$$\begin{aligned} & t(g(y[k]; y[k-1])) \\ = & \begin{bmatrix} \mathbb{1}_{hr_c[k] + c_c \mathbb{1}_{hr_c[k] > hr_c[k-1]} \leq hr_c[k-1]} \left(hr_c[k] + c_c \mathbb{1}_{hr_c[k] > hr_c[k-1]} \right) \\ \mathbb{1}_{hr_r[k] + c_r \mathbb{1}_{hr_r[k] > hr_r[k-1]} \leq hr_r[k-1]} \left(hr_r[k] + c_r \mathbb{1}_{hr_r[k] > hr_r[k-1]} \right) \end{bmatrix} \\ = & \begin{bmatrix} \mathbb{1}_{hr_c[k] \leq hr_c[k-1]} hr_c[k] \\ \mathbb{1}_{hr_r[k] \leq hr_r[k-1]} hr_r[k] \end{bmatrix} \\ = & t(y[k]; y[k-1]) \end{aligned}$$

For maximality: Consider the condition where: $hr_c[k] \leq hr_c[k-1]$, $hr_r[k] \leq hr_r[k-1]$, $hr'_c[k] \geq hr_c[k]$ and $hr'_r[k] \geq hr_r[k]$, then:

$$\begin{aligned} & t(y[k]; y[k-1]) = t(y'[k]; y'[k-1]) \\ \rightarrow & \begin{bmatrix} \mathbb{1}_{hr_c[k] \leq hr_c[k-1]} hr_c[k] \\ \mathbb{1}_{hr_r[k] \leq hr_r[k-1]} hr_r[k] \end{bmatrix} = \begin{bmatrix} \mathbb{1}_{hr'_c[k] \leq hr'_c[k-1]} hr'_c[k] \\ \mathbb{1}_{hr'_r[k] \leq hr'_r[k-1]} hr'_r[k] \end{bmatrix} \\ \rightarrow & \begin{bmatrix} hr_c[k] \\ hr_r[k] \end{bmatrix} = \begin{bmatrix} hr'_c[k] \\ hr'_r[k] \end{bmatrix} \\ \rightarrow & \begin{bmatrix} hr_c[k] \\ hr_r[k] \end{bmatrix} = \begin{bmatrix} hr_c[k] + \left(hr'_c[k] - hr_c[k-1] \right) \\ hr_r[k] + \left(hr'_r[k] - hr_r[k-1] \right) \end{bmatrix} \\ \rightarrow & \begin{bmatrix} hr_c[k] \\ hr_r[k] \end{bmatrix} = \begin{bmatrix} hr_c[k] + c_c \mathbb{1}_{(hr'_c[k] > hr_c[k-1])}, \ \exists c_c \in \mathbb{R}_+ \\ hr_r[k] + c_r \mathbb{1}_{(hr'_r[k] > hr_r[k-1])}, \ \exists c_r \in \mathbb{R}_+ \end{bmatrix} \\ \rightarrow & y[k] = g(y[k]; y[k-1]), \ \exists g \in \mathcal{G}_{sMFI} \end{aligned}$$

Other conditions can be proved to be maximal in a similar manner and omitted due to space requirements.

□