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Review

Integrating Evidence and Causal Mapping of Factors Which Influence Medication-Taking Behavior of Pregnant Women at Risk of Hypertensive Disorder: A Scoping Review

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Abstract: Preeclampsia is a form of gestational hypertension that usually appears after the 20th week of pregnancy. Evidence suggests that low-dose aspirin (LDA) effectively reduces the risk of developing preeclampsia, but the uptake rate remains low. This scoping review aims to synthesize and integrate existing knowledge domains relevant to the factors that influence women's medication decisions during pregnancy, and to develop a causal explanation for at-risk women's LDA uptake decisions. We introduced systems thinking to map the variables and develop causal loops to show variable interactions and causal explanations guided by the Theory of Planned Behavior. We extracted 65 variables, and grouped them into provider- (n = 19), patient- (n = 39), and system-level (n = 7) factors. By identifying variable interactions, we built a theory to explain various causal pathways leading to LDA treatment uptake. Mapping the variables and supporting the relationships of these variables with theories and concepts increases our study's generalizability to medication decisions for other pregnancy complications.

Keywords: preeclampsia; aspirin; pregnancy; decision; adherence; causal; systems thinking

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1. Introduction

Making medication decisions during pregnancy is a complex process. Preeclampsia (PE) is a common hypertensive disorder that generally appears after the 20th week of pregnancy and affects 4% of pregnancies in the United States [1]. Although maternal mortality associated with PE and eclampsia decreased from 17 per 100,000 live births in 1999 to 8 per 100,000 live births in 2018 in the United States, 7% of maternal deaths were still attributed to PE and eclampsia in 2016–2018 [2,3]. The relative risks of an adverse outcome—such as acute renal failure, cerebrovascular accident/transient ischemic attack, disseminated intravascular coagulation, deep vein thrombosis, myocardial infarctions, pulmonary embolism, hemorrhage, pulmonary edema, seizure, thrombocytopenia, and death—associated with mild and severe PE were two and three times higher than for women without PE [4]. Pregnancy outcomes associated with PE include early induction of labor or Cesarean delivery, preterm birth, neonatal seizure, and neonatal mortality [5]. PE accounts for 6% of all preterm births and 19% of medically indicated preterm births in the United States [6].

Women with a personal or family history of PE, multifetal gestation, chronic hypertension, diabetes, kidney disease, and age over 35 years are at increased risk of PE [7]. In

the United States, PE is more prevalent among African Americans primarily due to social factors, such as environmental and historical inequities that influence health exposure, access to care, and inequitable distribution of resources [7].

Despite the benefits of low-dose aspirin (LDA) for pregnancy outcomes for women at high risk of PE, reported LDA uptake rates have varied from 47% to 79% [8–13]. We define uptake rate as the percentage of at-risk women meeting the American College of Obstetrician and Gynecologist criteria (i.e., are eligible) for LDA who initiate or adhere to a daily intake of LDA. The counseling rates on LDA for at-risk women range from 36% to 75% [8,10,14], and between 31% and 95% of providers would recommend LDA to at-risk women [8,9,11,15,16]. The prescription rates for eligible women for LDA span from 3% to 83% [14,17–19]. The reasons for nonadherence to LDA treatment include pill burden [20], intentional and nonintentional omission [20,21], miscommunication with healthcare providers [20,21], fear of drug use during pregnancy [22], socioeconomic issues [23], healthcare system factors [23], personal factors such as limitations in knowledge of the complications of PE and preterm birth [21,23], and prior experience [21]. Given the multiple factors that span individual, social, healthcare organization, and system spheres, it is imperative to examine the interactions of these factors and their influence on pregnant women's medication decisions.

This scoping review aims to synthesize the best available evidence to integrate existing knowledge domains relevant to factors influencing women's medication decisions during pregnancy to develop a causal explanation for at-risk women's decisions to take LDA. Our knowledge integration efforts differ from conventional scoping reviews in three ways: (1) we include a wide range of studies that adopt diverse research methods; (2) we map the causal relationship of the synthesized knowledge; and (3) we propose an alternative framework for synthesizing knowledge obtained from the literature review and for guiding further analysis and aggregation by other researchers.

2. Theoretical Framework

We adapted the Theory of Planned Behavior (TPB) to integrate and synthesize the findings. The TPB postulates that a human's intention to change a behavior is influenced by three broad and context-specific factors, i.e., attitude toward that behavior, subjective norms, and perceived behavior control (Figure 1) [24]. Attitude toward a specific behavior refers to the degree to which the individuals' favorable or unfavorable evaluation and assessment of the behavior can be changed. A subjective norm is a social factor that characterizes the social pressure one perceives to perform or not perform the behavior in question. Lastly, perceived control belief represents the perceived difficulty of performing the behavior, and this factor accounts for the individual's experience and expected obstacles. These three factors are conditioned upon three other factors: behavioral belief, normative belief, and control belief.

An individual's behavioral belief influences his or her attitude toward the behavior intended to be changed or vice versa. Individuals may associate certain attributes, values, or goals with their behavior. Their attitudes evaluate each of their beliefs toward that behavior. These attitudes will be called upon whenever the individuals need to evaluate that behavior [25].

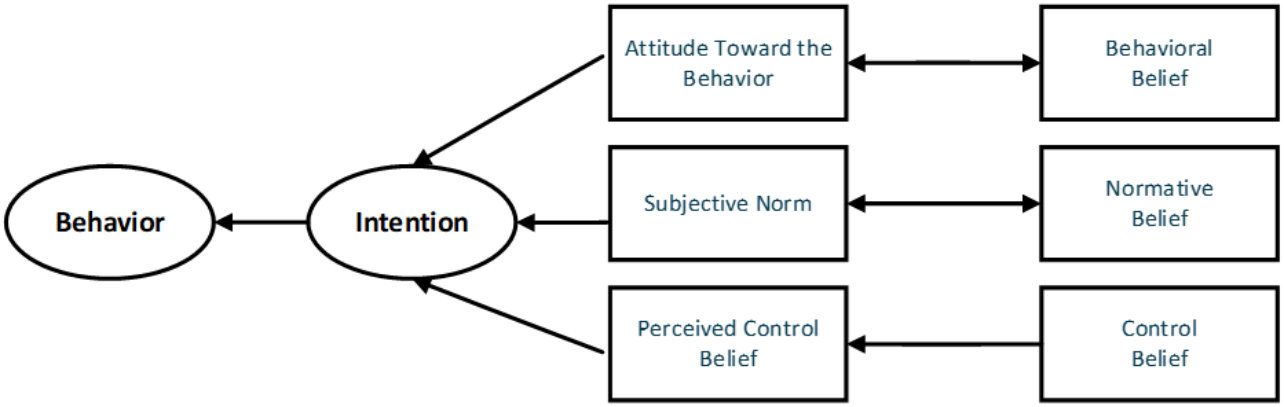

Figure 1. Conceptual framework of the theory of planned behavior proposed by Icek Azjen (Ajzen, 1991 [24]).

Normative belief is related to the probability that the important referent individuals or groups approve or disapprove of a certain behavior. An individual's normative belief influences his or her perceived subjective norm or vice versa.

Ultimately, the presence of required resources and opportunities determines individuals' intentions and actions to modify behavior. The more resources and opportunities individuals believe they possess, the greater their perceived control over their behavior. This perception may be influenced by the experience of people in their surroundings or information circulated in the community. Control belief affects an individual's perceived control belief or vice versa. Altogether, one's attitude toward the behavior, the subjective norm, and the perceived control belief alter one's intention and subsequently change one's behavior.

Next, we introduced systems thinking and applied the TPB to connect the variables and explore the causal mechanism of the medication decisions of pregnant women at risk for PE (Figure 2). We divided "behavior" into "Initiation Rate" and "Adherence Rate" to separate the LDA treatment acceptance process into two stages. Women take the first LDA pill first, followed by adherence. Collapsing the initiation and adherence rates would form an incorrect assumption that other factors will affect the initiation and adherence rates equally. The variable "Intention" was removed from the TPB model because most of the literature assumes women's intentions to take medication are reflected in their decisions to initiate and adhere to the medication. Thus, studies using questionnaires and statistical analysis to attempt to quantify patients' intentions to take medicine [26] did not add further insight to our study, which aims to understand the causal relationships between variables. The numbers along the arrows in Figure 2 represent the information extracted from the studies listed in the Reference section. These variables identified in the boxes in the causal map (Figure 2 and Supplementary S1) have direct relationships with behavioral, normative, and control beliefs in three broad categories: patient (pink), provider (blue), and system level (green). We used thicker arrows to represent relationships cited by five or more studies.

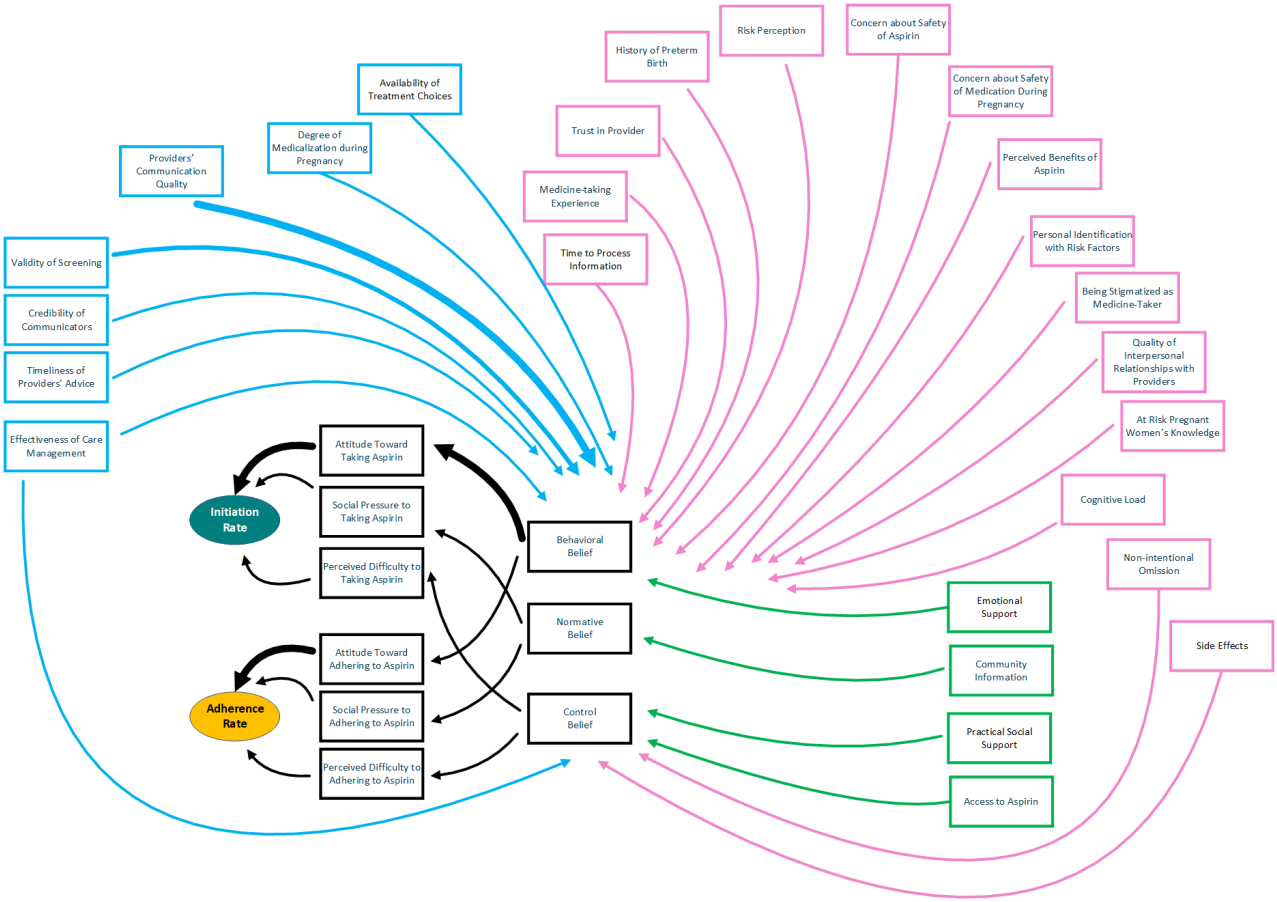

Figure 2. Causal map with variables that influence low-dose aspirin (LDA) initiation and adherence directly (see Supplementary S2 for details on the references cited by number in the small boxes). Pink boxes—patient factors; blue boxes—provider factors; green boxes—system-level factors.

3. Materials and Methods

3.1. Protocol and Registration

This scoping review was conducted according to the Joanna Briggs Institute Manual for Evidence Synthesis (JBIMES) [27]. The framework was developed by Arksey and O'Malley [28], and subsequently revised by Levac et al. [29] and Peters et al. [30]. A detailed protocol for this scoping review was published on 17 January 2024, and is available at https://bmjopen.bmj.com/content/bmjopen/14/2/e074775.full.pdf (accessed on 1 September 2024).

3.2. Eligibility Criteria

The inclusion and exclusion criteria were developed according to the population–concept–context (PCC) framework. The populations covered by captured studies include pregnant or postpartum women, caregivers, families and peers of pregnant and postpartum women, medical professionals, and community members. The concepts captured by this literature review included perceptions, views, patterns, acceptance and refusal, tendencies, probability, service accessibility and utilization, and facts from peer-reviewed studies or the grey literature. The context of these studies was pregnancy-related hypertensive disorders with a focus on pre-eclampsia. Captured studies may be quantitative, qualitative, or mixed-method studies, reviews, proceedings, and book chapters in English and were published between 1980 and 2023 because 96% of all studies captured by our search criteria were published during this time. We excluded non-English literature to accommodate the

reviewers' language proficiency. We used a snowballing strategy to retrieve theoretical and macro-level studies to extract system-level factors.

3.3. Information Sources and Search Strategy

The database searches were conducted in January 2023 and updated in January 2024 and April 2024. We adopted a two-step search strategy. First, we used some keywords to identify relevant studies in PubMed. Then, we formulated a comprehensive search strategy with the keywords identified. We searched PubMed, Embase, CINAHL, and Web of Science databases with a comprehensive query designed by a Stanford University Lane Medical Library research librarian [31]. This query was (aspirin OR ((medication OR treatment OR therap*) AND (prophyl* OR prevent*))) AND (adher* OR compliance OR attitude OR refus* OR "noncompliance" OR "nonadher*" OR belief OR Ethnograph* OR qualitative OR interview OR Phenomenological OR "focus group*") AND (preeclampsia OR "pre eclampsia" OR eclampsia).

3.4. Study/Sources of Evidence Selection

The search strategy (Supplementary S2) yielded 1818 studies from four electronic databases. Another 74 studies were identified from the reference lists of these publications. After removing duplicates and screening the titles and abstracts, 1277 studies were selected for full-text screening. A total of 39 studies met the inclusion criteria. The search process is outlined in the PRISMA flow chart in Figure 3. In the selection round, two research team members independently assessed the titles and abstracts in Covidence. Studies were selected according to the inclusion and exclusion criteria. Studies without an abstract were selected for full-text screening. In the second selection round, three team members independently screened the full texts of the selected studies.

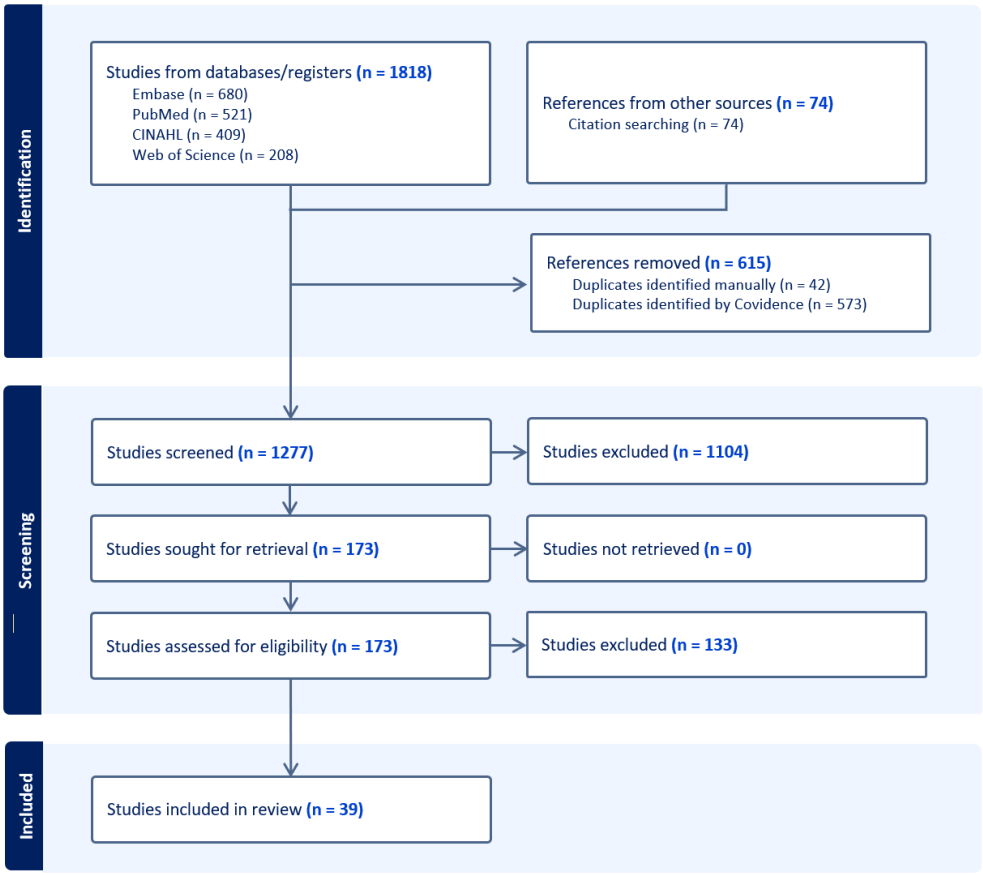

Figure 3. PRISMA flow chart.

3.5. Data Charting Process

Three members extracted variables and recorded the variables and reasons for exclusion in the pre-designed variable extraction sheet for each full-text screened study. We screened a designated number of studies and extracted variables in batches, followed by meetings to compare, discuss, and decide which variables to keep. Information on the included papers was recorded, including the author's name, year of publication, journal's name, keywords, study aim, abstract, country where the research was conducted, and type of publication. For studies that did not include data collection location, the country of origin was extrapolated by using the first author's affiliation. Other study characteristics captured included roles of the persons for whom information was provided in the study (e.g., patient, provider, community), the system component in which the extracted variable fit (e.g., patient, provider, system level), dependent variable (i.e., the variable to which the extracted variable corresponds), nature of the relationship between the extracted and dependent variable (positive or negative), and explanations. When conflicting views arose among members, they consulted a senior reviewer about the eligibility of an article.

3.6. Synthesis of Results

The text excerpts from the studies that indicated the relationships between the extracted and dependent variables were thematically coded in discussions among the three members. The basic information and extracted data were entered into a Microsoft Access database built for this study. This database is accessible by readers at https://purl.stanford.edu/bm278dg3221 (access on 7 October 2024). The extracted variables and the corresponding independent variables were presented in the form of a causal map and causal loops. The relationships between variables were inferred from the text.

The causal map was developed and refined as new themes emerged. The TPB was central to the causal map (Figure 2). The extracted variables that were directly related to the factors influencing the beliefs of women at risk of PE and their LDA treatment uptake were grouped and placed around the TPB according to the relationships captured in the selected papers or inferred from the selected theoretical and conceptual papers. The variables were grouped by provider (blue), patient (pink), and system-level (green) factors. Medication initiation and adherence rates are the two outcome variables for this study.

Causal loops are a diagramming tool used in system dynamics simulation and modeling methodology [32]. Causal loop diagrams (CLD) enable the conceptualization of the real-world system with feedback loops and explain how these loops or structural assumptions cause the behavior of a system or simulation model [32]. An arrow indicates the direction of influence of one variable on another. The relationships between variables are supported by the information in the captured papers we reviewed. The sign, plus or minus, indicates the type of influence. A plus sign indicates that, when the originating variable increases, the receiving variable also increases. A negative relationship means that an increase in the originating variable will decrease the receiving variable. If the originating variable causally influences the receiving variable and the receiving variable also causally influences the originating variable, a feedback loop is formed. The letters in the loop characterize the behaviors of the loops when they are perturbed in response to a variable change. A reinforcing loop (R loop) reinforces the perturbation; a balancing loop (B loop) counters the perturbation and steers the loop's behavior toward an implicit or explicit goal set for the system.

4. Results

4.1. General Characteristics of Sources of Evidence

Most of the included studies were published after 2010 (n = 41, 89.1%). Information about the selected studies, including title, author's name(s), published year, geographic location, paper type, and population characteristics, is presented in Supplementary S3. Studies reported most commonly on populations in the United States (n = 23), followed by the United Kingdom (n = 6), the Netherlands (n = 5), Denmark (n = 2), Australia (n = 1), Sweden (n = 1), and Canada (n = 1). Most of the studies were research papers (n = 32); others included extended abstracts (n = 2), commentaries (n = 1), posters (n = 3), and reports (n = 1). Among the included studies, 37 covered patient perspectives, seven investigated factors associated with the providers, and three explored the community's influence on pregnant women's medication decisions. Some studies included more than one perspective.

4.2. Causal Map

The causal map (Figure 2) demonstrates the relationship between the extracted variables and LDA initiation and adherence connected by the Theory of Planned Behavior.

4.2.1. Provider Factors

Seven provider factors were identified (Figure 2). The factors covered most commonly in our review were providers' communication quality [9,10,20,33–37] and validity of screening [10,11,13,16,37]. Other factors included the availability of treatment choices [38], degree of medicalization during pregnancy [10], the credibility of communicators [39], timeliness of providers' advice [39], and effectiveness of care management [20,40]. The effectiveness of care management was also shown to influence control belief [40]. Most of the provider factors could influence women's behavioral beliefs, except for the effectiveness of care management, which also influences control belief.

Education about aspirin treatment and consistent communication between providers and patients increased at-risk women's uptake rates [20,41]. Provider recommendations were essential [35], but at-risk women reported a lack of memory about aspirin treatment counseling [9,34]. About 40% (n = 315, N = 754) of at-risk women received provider consultation on PE while 35% (n = 267) did not [34]. The remaining 16% did not remember whether they received any information. Among those who received counseling, only 37% (n = 115) indicated that they understood most of the information provided.

The screening and LDA recommendation practices varied among providers. Among 301 eligible women, only 31% (n = 92) received recommendations for LDA [16]. At-risk women with multiple "moderate" risk factors were often not given an LDA prescription. However, women with one "high" risk factor of either diabetes (73%), a history of hypertensive disorder (72%), chronic hypertension (71%), or autoimmune disease (33%) were more likely to be prescribed LDA.

4.2.2. Patient Factors

We identified fifteen patient factors. These factors were related to women's experiences, values, beliefs, and perceptions, such as risk perception [40,42,43], perceived benefits of aspirin [10,15], non-intentional omission [12,44], personal identification with risk factors [10], side effects [42,44], concern about medication during pregnancy [10], trust in providers [45], time to process information [40], medicine-taking experience [40], history of preterm birth [46], concern about the safety of aspirin [10,12,46], being stigmatized as a medicine taker [40], quality of interpersonal relationships with providers [47], at-risk pregnant women's knowledge [42], and cognitive load [15].

Some at-risk women were unable to relate the PE-related risk factors to PE [40], while some avoided taking preventive medication during pregnancy for fear of the potential side effects [10]. Limited knowledge about the consequences of PE on their fetuses' and their own health and limited understanding of the increased risk of cardiovascular disease later in life also lowered the women's risk perception of PE [42]. Providers' mixed messages about the safety of LDA increased at-risk women's concerns and thus contributed to non-intentional omission [40]. In the UK, inconsistent recommendations or prescriptions of LDA by providers were mainly caused by the "off-label" use—the practice of prescribing a medication for a different use than for which it is approved—of LDA during pregnancy [40]. Some general physicians and midwives in the UK were reluctant to prescribe LDA and left the decision to the obstetricians. At-risk women would stop the treatment when they encountered side effects, such as gastrointestinal issues or vaginal spotting [44]. More than 30% of at-risk women reported unintentional omission, and about 10% forgot two or more tablets in a week [12]. Taking multiple vitamins and other medications or taking LDA at night could lead to unintentional omission [44].

4.2.3. System-Level Factors

We identified a limited number (n = 4) of system-level factors. The studies suggested that emotional and practical social support [48], access to aspirin [40], and community information [20] influenced at-risk women's LDA treatment uptake. Patients not receiving emotional support were 35% more likely to not adhere to treatment [48]. Practical social support, such as tangible support, practical assistance, reminders, or not living alone, strengthened treatment adherence [48]. System barriers to LDA dispensaries influenced adherence. Some pharmacies failed to stock up on LDA, leading women to either postpone the initiation of the LDA treatment or skip the pills occasionally [40]. Women who communicated with other at-risk women through social media were found to be more likely to initiate or adhere to LDA treatment throughout their pregnancies [38].

4.3. Loops and Major Factors Influencing Loops

Figures 4–7 show the expanded causal map, including an additional layer of variables identified by the information extracted from a second round of review of the selected papers, which affect and interconnect the patient-, provider- and system-level variables. The interactions between these variables led to the formation of feedback loops. We identified seven reinforcing loops (R1–R7) and one balancing loop (B1). Depending on the relationship between the patients' average mental health score and risk perception, one loop could be reinforcing (R6) or balancing (B1). We highlight the importance of further investigation of the relationships between these two variables because the nature of this relationship can change the polarity of the loop, which subsequently changes the underlying causal explanations of the factors and expected LDA uptake significantly. The identified polarities of the relationships between variables and the causal map combined with loops are shown in Supplementary S4 and S5, respectively.

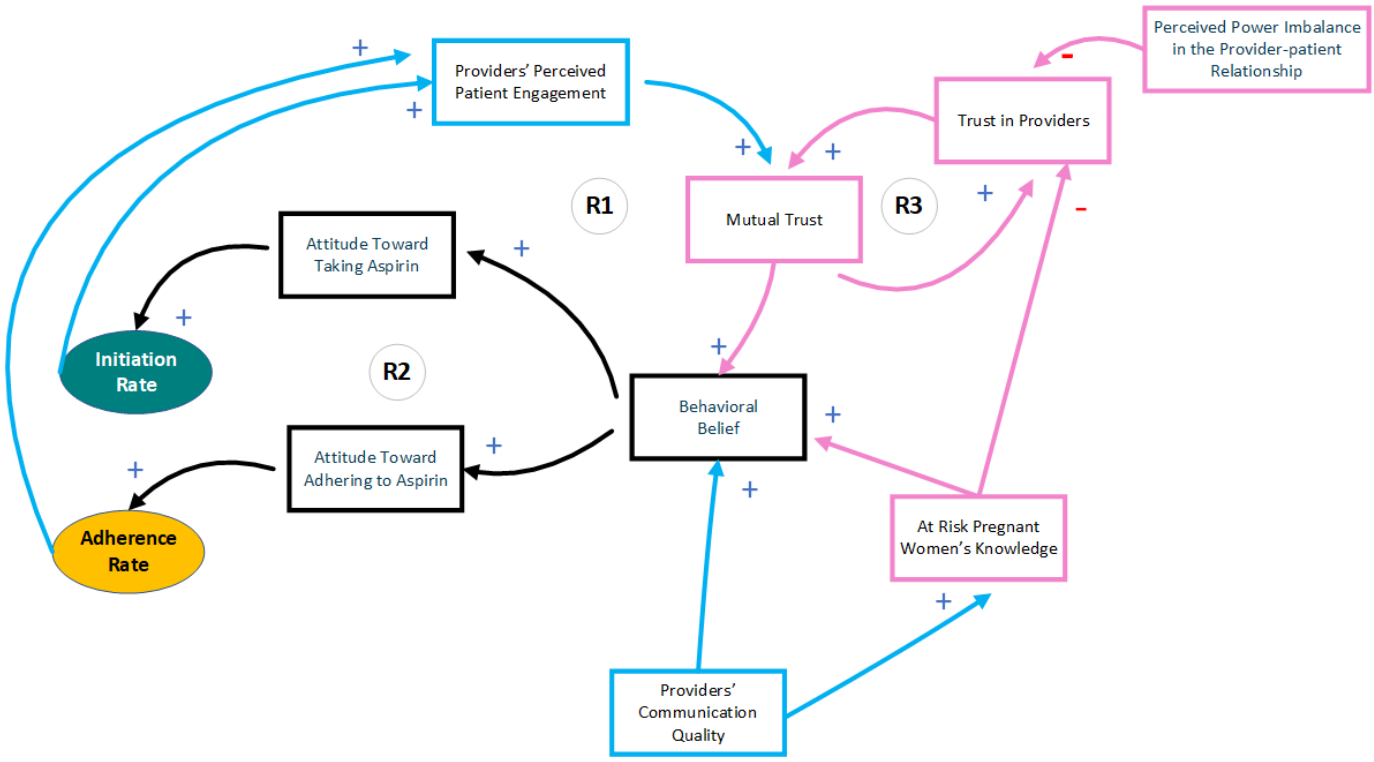

Figure 4. Causal loop explaining the relationship between mutual trust and low-dose aspirin initiation and adherence and other influencing factors.

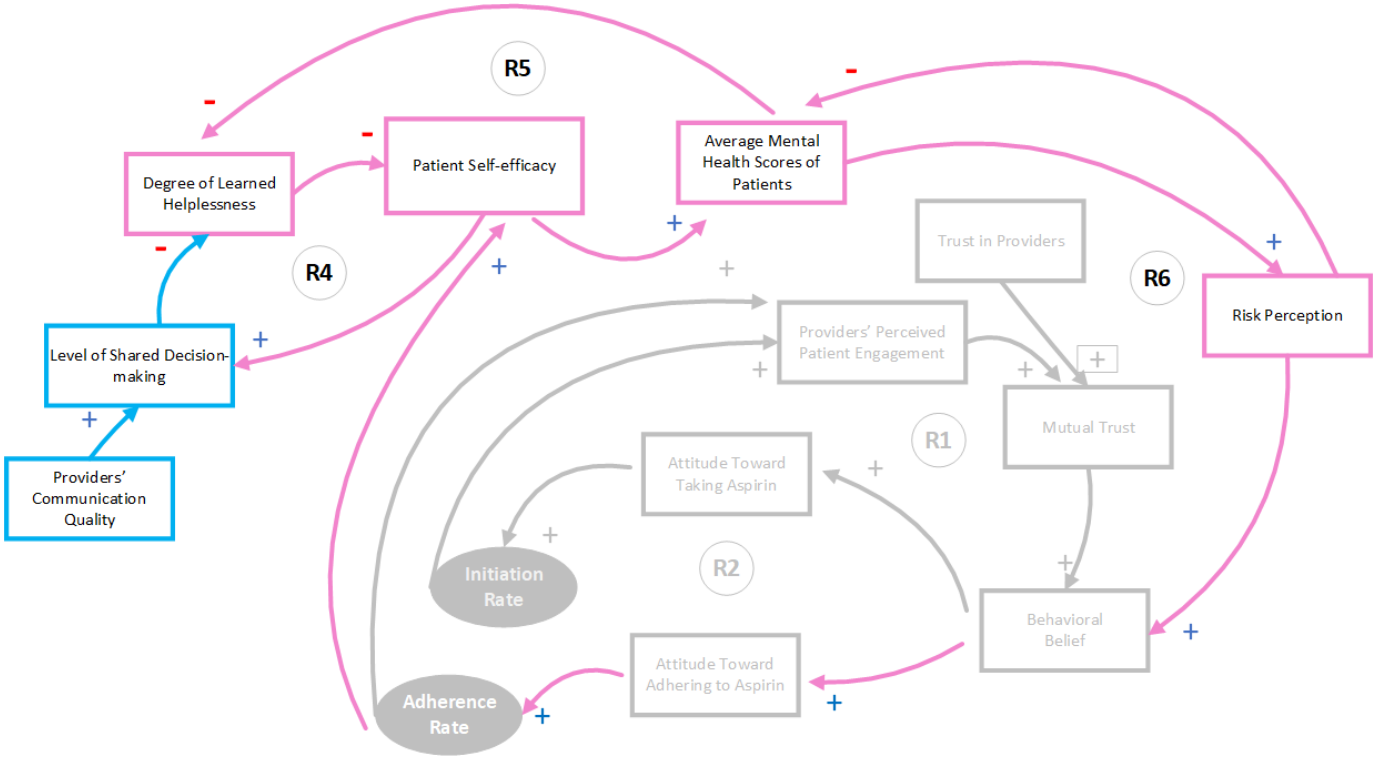

Figure 5. Causal loop explaining the relationship between shared decision-making, patient self-efficacy, mental health, risk perception, trust, and low-dose aspirin initiation and adherence.

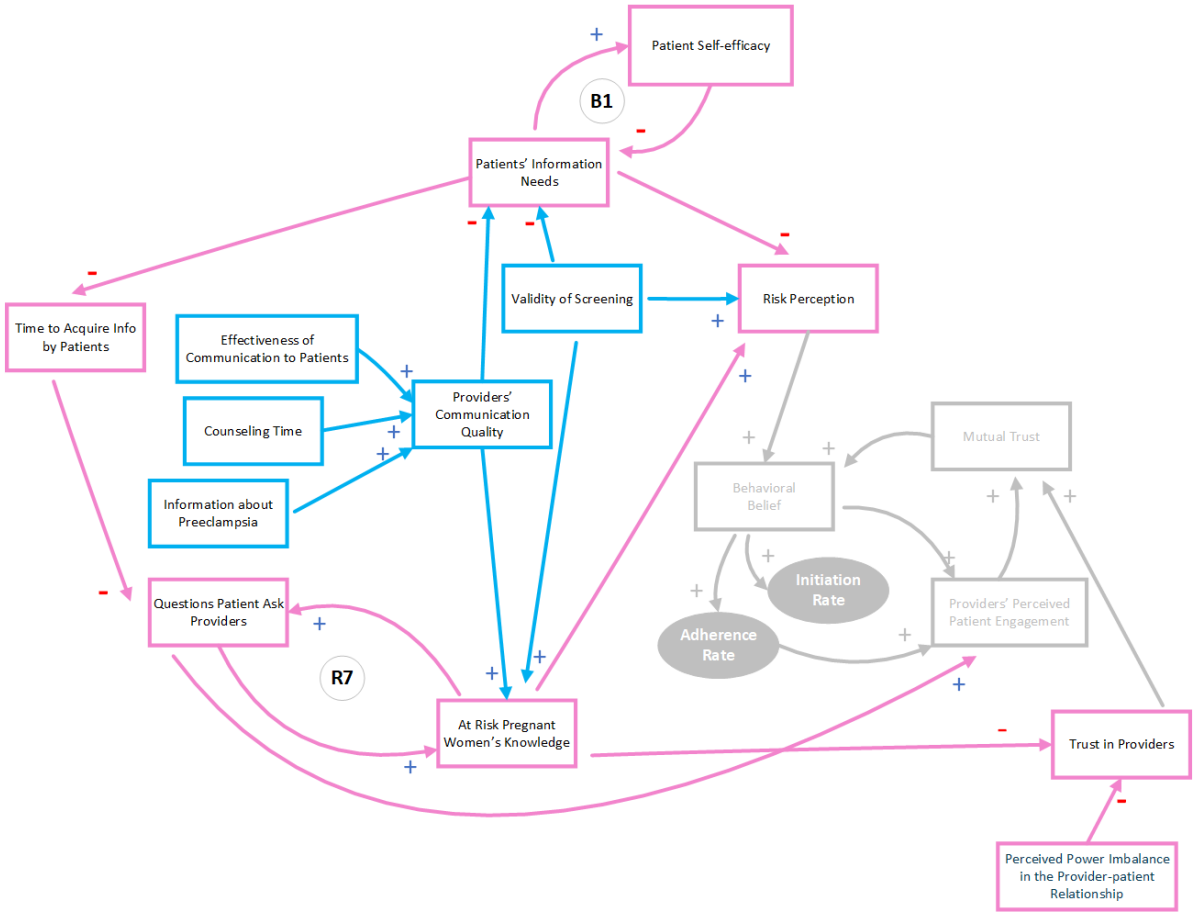

Figure 6. Causal loop explaining the relationship between at-risk women's knowledge, information needs, low-dose aspirin initiation and adherence, and other influencing factors.

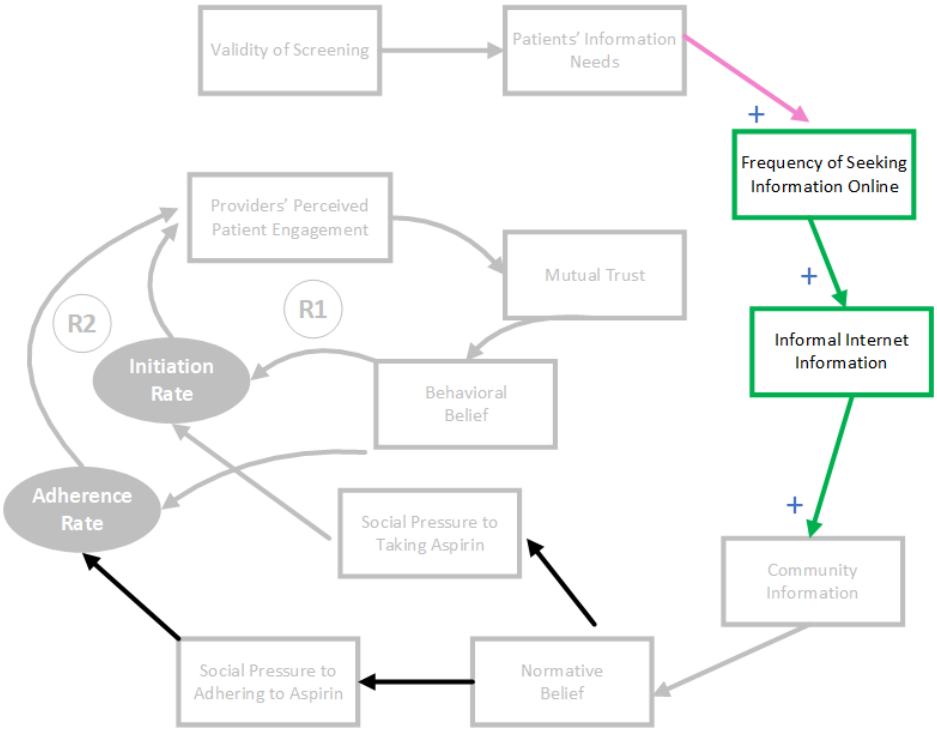

Figure 7. Causal loop explaining the relationship between internet information seeking and low-dose aspirin initiation and adherence.

4.3.1. Loops R1, R2, and R3—Mutual Trust and LDA Uptake

Providers' Perceived Patient Engagement and LDA Initiation Loop (R1) and LDA Adherence Loop (R2)

The main loops, R1 and R2, which are both reinforcing, depict the effect of mutual trust on LDA initiation and adherence rates (Figure 4). A stronger perception of patients' engagement in treatment was found to strengthen mutual trust between providers and women at risk of PE [47,49]. With a higher providers' communication quality [20,33–35] and at-risk women's knowledge [42], women felt encouraged and, thus, accepted or adhered to LDA treatment. Increased LDA initiation (R1) and adherence (R2) contributed to stronger patient engagement [49].

Trust in Providers and Mutual Trust Loop (R3)

Together, women's trust in providers [49] and providers' perceived patient engagement [47,49] formed mutual trust. Patients who trusted their providers were more willing to reveal their information to the providers [49] and adhere to the providers' recommendations and medication [45]. When providers begin trusting patients, patients are more likely to reciprocate and strengthen their relationships with the providers and their ability to trust (R3).

Providers' communication quality and at-risk pregnant women's knowledge positively influenced women's behavioral beliefs. In a survey of 754 women who visited the Preeclampsia Foundation website, 42% (n = 315) received counseling on PE from their prenatal care providers, and 35% (n = 267) and 16% (n = 121) of the women indicated that they had no counseling or no recollection, respectively [34]. Of the women who received counseling and fully understood the provider's explanation (n = 169), 74% (n = 125) reported symptoms to their providers, visited the hospitals, monitored blood pressure, stayed in bed, or complied with the recommended treatment. In the UK, among 160 midwives who responded to an online survey, 35% (n = 60) skipped LDA counseling with their patients due to "conflicting views", a "deficit of resources", and unclear responsibility division [43]. The inconsistent messaging, stemming from the "off-label" use of LDA, from providers and the dispensary system confused women and discouraged them from accepting the treatment [43]. Some midwives were willing to provide information but were reluctant to prescribe LDA [43]. Midwives had limited time to provide counseling on PE in addition to other pregnancy-related topics during patient visits [43]. Women with higher health literacy tended to perceive PE as a severe condition [50], were more likely to ask their providers more questions, express their needs accurately, and receive more health education [49]. These interactions encouraged shared decision-making, which could counteract patients' perceived powerlessness [49]. Women's knowledge was also influenced by the providers' communication quality [8,10,34,43,49,50].

Trust in providers was found to be influenced by mutual trust, at-risk pregnant women's knowledge, and perceived power imbalance in the provider–patient relationships. The patients' self-efficacy increased when they felt empowered by providers who promoted shared decision-making [49]. Authoritative providers tended to deepen the patient's belief that their conditions were unalterable, which led to low treatment acceptance, loneliness, and depression [49]. Sometimes, women with less education tended to trust their providers more [51]. At-risk pregnant women claimed that the information they received during their antenatal visits reinforced their adherence to LDA treatment [42].

4.3.2. Loops R4, R5, R6 or B1—Shared Decision and Self-Efficacy

Shared Decision and Patient Self-Efficacy Loop (R4) and Patients' Mental Health and Self-Efficacy Loop (R5)

Figure 5 illustrates the reinforcing relationship between shared decision-making and patient self-efficacy (R4). Better provider communication and fostering shared decision-making could have reduced patients' "learned helplessness", a circumstance when the providers' actions became disempowering. Thus, patients or their families stopped advocating for themselves because they perceived a lack of control over treatment and health outcomes and the confidence and emotional capacity to speak up [49]. Empowerment increases women's self-efficacy, which is an individual's belief in achieving specific goals that might influence his or her life [52]. Treatment adherence was positively related to self-efficacy, which related to depression negatively [53]. The variable "Average Mental Health Score of Patients" captures the stress, anxiety, and depression in women related to pregnancy complications. The higher the self-efficacy, the higher the mental health score. Better mental health mitigated women's fear of asserting their needs and, thus, reduced the degree of learned helplessness among the women and their families [49]. The reinforcing loop, R5, describes the importance of empowering women with resources to reduce their stress and anxiety levels.

Risk Perception and Adherence Rate Loop (R6)

Women with complicated pregnancies tended to show higher levels of self-assessed pregnancy-related risk and anxiety compared to women with uncomplicated pregnancies [54]. Risk perception and anxiety showed a significant positive correlation (0.36, $N = 208$, $p < 0.001$) [54]. Correlation implies association, which is a variable providing information about another variable, but not causation [55,56]. Hence, we hypothesize a positive bi-directional relationship between at-risk women's mental health and risk perception. However, some women failed to perceive the risk of PE on their health and their unborn children, and their lower perceived risk affected LDA uptake [42], despite the provider's explanation of PE risk factors [40] (R6). In a survey, about 10% ($n = 4$) of women stated the concern of side effects as the reason for non-adherence [12]. Providers also exhibited their risk perception toward prescribing LDA. About 40% of the providers avoided conversation about LDA with their patients due to the "off-label" use of LDA [43]. The reinforcing R5 loop depicts the positive relationships between LDA adherence, self-efficacy, mental health, and risk perception.

4.3.3. Loop B2 and R7—Patient Information Needs and Women's Knowledge

Women's information needs affect their risk perception (Figure 6). Women screened and determined to be at high risk of PE exhibited two types of behavior [57]. "Danger managers" focused on the maternal consequences of PE, had a strong sense of internal control, and developed coping strategies, such as information seeking, positive behavioral change, and cognitive appraisal. However, this type of woman had a low sense of risk despite being determined by providers as high-risk. On the contrary, the "fear managers" focused on the fetal consequences of PE, had a strong sense of internal control, and developed threat minimization and avoidance coping strategies. These women also showed a low risk perception.

The validity of screening technologies, especially ultrasound, but not blood tests, increased the confidence of at-risk women in providers' recommendations [58]. The validity of screening and patients' information needs to form a negative relationship. Women who relied on ultrasound monitoring to receive information about their fetuses' health were less likely to monitor their well-being and fetal movements and receive additional

information [57]. Trust in providers is also negatively related to patient's perceived power imbalance between providers and patients [49].

B1—Patients' Information Needs and Self-Efficacy Loop

In addition to screening, patient self-efficacy also changed patients' information needs [57]. Both danger and fear managers sought information online and developed their coping mechanisms [57]. Highly activated patients were more likely to prepare questions for a doctor visit, ask about treatment guidelines for their condition, and seek out health information, including comparisons of the quality of healthcare providers [59]. Thus, resourceful women had lower information needs from their providers. The negative B1 loop describes a negative relationship between patient self-efficacy and patient information needs. Women with higher information needs seek information and form coping strategies, which eventually contribute to lower information needs once women are confident that they can manage their conditions.

Patient engagement is pivotal in health reform. Of 216 women who were screened and determined to be at risk of PE, 43% (n = 92) did not think the assessment applied to them [10]. Of 92 women, 42% (n = 39) did not receive information about PE. This study implies that most at-risk women understood their risk of PE and accepted providers' recommendations for LDA treatment, while others may lack the information to understand their risks [57]. In an online survey of 1226 women, 81% (n = 990) of participants indicated that they received information from their providers about medication during pregnancy [60]. Among the women who stopped or modified their medication (n = 468), 64.4% (n = 321) did so according to providers' advice. Passive patients who refrained from asking questions could be perceived as disengaged by the providers [49]. The loop R6 hypothesis is that the more questions the women ask their providers, the more knowledge they will gain. Anderson and Dedrick revealed that women with a less formal education trusted their providers more [51]. Hence, the relationship between at-risk pregnant women's knowledge and trust in providers is negative. However, this relationship is unclear because women also expressed that the information they received impacted their treatment adherence [42].

R7—Patients Asking Questions and Knowledge Accumulation Loop

At-risk women's knowledge is also conditioned upon providers' communication quality. Women who received information from their providers and understood the signs and symptoms of PE were more likely to report the symptoms to their providers and adhere to treatment [34]. Knowledge enabled women to recognize the risk of PE and led to earlier diagnosis and treatment [34,50]. Providers who followed the risk-based care recommendation and discussed LDA as an option for at-risk women also influence LDA adherence positively [10]. Educated patients received more information from their providers, could ask more specific questions, and expressed their needs precisely [49] (R7). Nevertheless, inconsistent messaging, the confusing roles of prescribing providers, concern for the off-label use of LDA, and prescription patterns interfered with information dissemination between providers and patients and lowered the quality of communication [43].

Three variables affect providers' communication quality: effectiveness of communication with patients, counseling time, and information about PE. Some providers felt inadequate in providing counseling on LDA treatment to their patients [43]. A long list of discussion topics, requirements for providers to abide by regulations and manage reimbursement and institutional procedures, and limited counseling time left little room for midwives and physicians to educate women about PE and LDA treatment [40,49].

Although patients desired more support and communication from the providers [33], they might not fully understand the information shared by providers [34], which could

potentially lead to the misperceive of the risk of PE [50]. When the providers failed to share sufficient useful information, they shifted the burden to the patients to search for information elsewhere [61].

4.3.4. Influence of Community Information on LDA Uptake

Figure 7 exhibits the relationships between online information-seeking behavior and normative belief, social pressure, LDA initiation, and adherence rates. After receiving information about PE from their providers, some women sought information online to explore other women's experiences [57,62,63], while some reread the information leaflets thoroughly [63]. Searching for information online sped up information retrieval. Over 50% of the women would look for information online more often at the beginning of their pregnancy [62]. Even the fear managers, women who developed threat minimization and avoidance coping strategies, chose information online selectively to avoid anxiety-provoking information [57]. Participating in social media to communicate with other women or speaking with friends with similar experiences would eventually increase the stock of community information, leading to a higher LDA uptake [20].

5. Discussion

Our scoping review extracted 65 variables influencing at-risk women's perceptions of PE and LDA, which eventually affect their actions and medication decisions. Our search strategy was designed to capture as many relevant studies of healthcare systems in high-income settings as possible and to identify the variables in these systems that could potentially affect the decisions of women who are at risk of preeclampsia to take low-dose aspirin. These variables were grouped into provider- (n = 19), patient- (n = 39), and system-level (n = 7) factors.

We argue the importance of identifying and understanding the key variables and their interactions in various pathways that affect the initiation of and adherence to LDA. These key variables were (1) the providers' communication quality, (2) level of shared decision-making, (3) validity of screening, (4) at-risk pregnant women's knowledge, (5) degree of learned helplessness, (6) patient self-efficacy, (7) average mental health score of patients, (8) risk perception, (9) patients' information needs, (10) time to acquire information by patients, (11) questions patients ask providers, (12) frequency of seeking information online, (13) informal internet information, and (14) mutual trust.

The providers' communication quality directly affects women's belief systems and their knowledge, along with the validity of screening and the questions asked of providers (Figure 3). Women learned about symptoms to monitor from screening, thus increasing their knowledge, their reporting of symptoms to their providers, and adherence to LDA treatment [34]. Women were likely taught that taking medication during pregnancy could lead to side effects, which might harm their fetuses [10,40]. Education efforts will be undermined if women are unconvinced that LDA is safe to take and will reduce the risk of developing PE (Table 1).

Table 1. Major findings and insights.

	Findings	Insights and Actions
1.	Women learned about symptoms to monitor from screening, thus increasing their knowledge, their reporting of symptoms to their providers, and adherence to LDA treatment. However, they were likely taught that taking medication during pregnancy could lead to side effects, which might harm their fetuses.	Education efforts will be undermined if women are unconvinced that LDA is safe to take and will reduce the risk of developing PE.
2.	Providers' communication quality directly affects women's belief systems and their knowledge, along with the validity of screening and the questions asked of providers.	Women learned about symptoms to monitor from screening, thus increasing their knowledge, their reporting of symptoms to their providers, and adherence to LDA treatment.
3.	Providers developed trust in their patients when patients were engaged and followed their advice. Patients corresponded with their providers and built stronger relationships with their providers when they trusted that their providers genuinely cared about their well-being, leading to patients being more likely to adhere to their treatment plans.	Monitoring the perceived power imbalance and at-risk women's knowledge and periodically updating providers on their patients' treatment uptake are crucial to keeping their trust in their patients.
4.	The perceived imbalance between providers' and patients' status may negatively affect patients' trust in providers.	A platform for providers to keep track of patients' uptake and adherence to treatment and emphasizing shared decision-making in the physician–patient relationship will be useful in promoting mutual trust.
5.	The relationship between at-risk pregnant women's mental health state and risk perception reported in the literature is unclear. The increase in at-risk women's mental health state could increase or reduce risk perception.	If interventions increase patient self-efficacy and lead to higher risk perception, women will form a positive outlook on LDA treatment and adhere to it. As their adherence to the treatment increases, they may be more confident in managing the treatment. Women's confidence in managing their treatment will help reduce their anxiety and stress levels. Better mental health leads to higher risk perception, and LDA uptake will increase. If the relationship between mental health and risk perception is negative, the increase in mental health due to increased self-efficacy may lower the perceived risk of PE. Women who are less anxious and stressed might perceive PE as less risky. Then, consistently sharing more accurate and precise information and screening results with the women and their families will help remind women about the risk of PE.
6.	At-risk pregnant women's knowledge might influence their trust in providers positively or negatively.	If more knowledge leads to lower trust in providers, other strategies to maintain or increase the trust in providers are essential.
7.	At-risk women sought information online and advice from their families. The more information is shared online, the more community information accumulates.	Measuring and monitoring misinformation in the community is also critical. Misinformation that discounts the risk of PE and the benefits of LDA might undermine the effort to increase the LDA treatment uptake.

The mutual trust loop (R3) is pivotal to keeping the reinforcing loops R1 and R2 dominant or growing. Monitoring the perceived power imbalance and at-risk women's knowledge and periodically updating providers on their patients' treatment uptake is crucial to keeping their trust in their patients (Figure 3). The literature reported the lack of

trust in providers or health systems as a critical variable that hinders patients' adoption of providers' recommendations [45]. Providers developed trust in their patients when patients were engaged and followed their advice [47]. Patients corresponded with their providers and built stronger relationships with their providers [49] when they trusted that their providers genuinely cared about their well-being [47], leading to a higher adherence rate [45]. However, the perceived imbalance between providers' and patients' status may negatively affect patients' trust in providers. This finding suggests that a platform for providers to keep track of patients' uptake and adherence to treatment and emphasizing shared decision-making in the physician–patient relationship will be useful in promoting mutual trust (Table 1). Studies showed that higher knowledge among at-risk women could lead to higher treatment adherence [42]. Contrarily, women with lower education tended to trust their providers more [51]. This contradicting information warrants further investigation because the positive or negative relationship between at-risk pregnant women's knowledge and trust in providers might require different strategies to increase LDA uptake.

Learned helplessness, self-efficacy, and mental health state are central variables in adjusting the risk perception of at-risk women toward PE (Figures 4 and 5). Establishing the space to engage women and their families to discuss their needs with their providers may increase women's confidence in co-managing their treatment. A high mental health score and positive attitude help to mitigate women's learned helplessness. The reinforcing loop R5 demonstrates that a lower degree of learned helplessness increases women's self-efficacy toward LDA treatment and elevates their mental health state. It is important to study the relationship between these two variables further because a positive relationship between mental health and risk perception will form a reinforcing loop (R6). Interventions that increase patient self-efficacy may lead to a higher risk perception in this loop, which may help women shape positive attitudes and beliefs in LDA treatment. As their treatment adherence increases, they may be more confident in managing their treatment. If better mental health leads to higher risk perception, at-risk women's confidence in managing their treatment will help alleviate their anxiety and stress levels. This positive loop (R6) will fuel self-efficacy and the mental health state to keep risk perception high. Subsequently, LDA uptake will increase. If the relationship between mental health and risk perception is negative, the increase in mental health due to increased self-efficacy may lower the perceived risk of PE. Women who are less anxious and stressed might perceive PE as less risky. This negative loop (B1) slows the growth in LDA uptake through self-efficacy.

Due to the uncertain relationship between women's mental health state and risk perception, we should evaluate and monitor the other three paths that influence risk perception closely: validity of screening, patients' information needs, and at-risk pregnant women's knowledge (Figure 5). Women noted that PE screening was informative, and their knowledge of PE improved after learning from their screening results [58]. Unfortunately, some women failed to relate the screening results to their risk of PE [10]. Educating at-risk women and their families about the validity of the screening and result interpretation is crucial (Table 1). As women obtain more information and their need for information is reduced, they adjust their perceived risk of PE. Simultaneously, women gather more information, and their self-efficacy grows. Then, the need for information reduces. The negative loop B1 will eventually curb the growth of patients' information needs and indirectly limit the increase in risk perception. Fueling up the reinforcing loop R7 by making the information-acquiring process shorter involves encouraging women to ask their providers for information. Preparing tools for women to guide them to ask questions specific to their needs will build up women's knowledge base and perceived risks of PE.

Finally, the importance of information circulated in the community, especially over the internet, should not be overlooked. In addition to obtaining comments from their

families, at-risk women also sought information from women with similar experiences [20]. The more frequently the women and their family members seek and share information online, the more the community's information grows. However, measuring and monitoring misinformation in the community is also critical (Table 1). Misinformation that discounts the risk of PE and the benefits of LDA might undermine the effort to increase the uptake of LDA treatment. Correct community information shapes the normative behavior of at-risk women and encourages LDA treatment uptake.

Our theory-building approach, through mapping out the variables and supporting the relationships of these variables with theories and concepts, increases our study's generalizability to medication decisions for other pregnancy complications. The new system theory provides a comprehensive view of the important variables and causal pathways that may alter at-risk pregnant women's medication decisions and behaviors. The newly identified loops are important findings because they help us understand the ripple effects of the interactions of variables in the loop. A complex system usually contains several negative feedback loops to self-correct the system and positive feedback loops to grow the system exponentially [64]. Meadows alleges that reducing the gain from a growing and dominating positive loop is more effective than driving growth in the negative loop to curb the growth in the positive loop. However, our review implies that R1–R3 (Figure 3) and R4 and R5 (Figure 4) are weak reinforcing loops. Promoting growth in these five reinforcing loops is essential to increasing the LDA uptake rate. If women's mental health and their risk perception have a positive relationship, a dominant loop R6 will threaten LDA treatment uptake because low mental health might lower risk perception, causing R6 to dwindle.

Literature reviews about factors influencing medication decisions for gestational hypertension are limited. Vinogradov et al. coded their data using the COM-B framework to integrate key facilitators and barriers at different phases of adherence to LDA treatment [65]. The COMB-B framework is a diagnostic tool that identifies areas that need to change to promote actual behavioral changes. The framework comprises three interrelated domains: capability, opportunity, and motivation. The authors reveal five themes associated with LDA adherence during pregnancy: insufficient knowledge, necessity concerning balance, access to medicine, social influence, and lack of habit. Náfrádi et al. synthesized evidence from the literature to explore the relationship between patient empowerment and medication adherence [66]. In a more general view, Oladejo and Bewley's systematic review highlights patients' characteristics, including socioeconomic status and lifestyle, such as education, age, forgetfulness, and missing doses, as common factors [67]. These authors also acknowledged the paucity of evidence regarding pregnant women's adherence to medication, potential bias due to self-reported adherence, and the lack of consistent definitions for medication adherence. The authors suggested that the scant study of physician–patient interactions could lead to the misinterpretation that non-adherence was due to patients' problems.

Our scoping review differs from Vinogradov et al. and Oladejo and Bewley's literature review in two important ways: the objectives and methodology. Our scoping review aimed to extract and map factors related to medication for hypertensive disorders during pregnancy to produce a causal explanation from the system perspective. Hence, our selected literature includes studies covering factors associated with medication decisions for gestational hypertensive disorders, reasons for treatment adherence, non-adherence, and acceptance, as well as theoretical and conceptual papers. The theoretical and conceptual papers support the linkages of the extracted variables.

Methodologically, our data synthesis approach is similar to that of Vinogradov et al., which maps variables with the support of a framework. However, the COMB-B framework

is relatively limited in scope. Our 65 synthesized variables were grouped into provider-, patient-, and system-level variables and integrated into a causal map with TPB as the core component to explain the relationships between beliefs, attitudes, intention, and behavior, i.e., initiation and adherence to LDA. Subsequently, eight causal loops were discovered from the interactions between the variables to form causal explanations for medication decisions for women at risk of PE. Ultimately, the new variables linked to the TPB created a new theory about how women decide to take LDA to prevent PE. Thus, the causal loops reflect system complexity and provide novel insights into key opportunities to shape system behavior to promote LDA uptake. Future work includes building a system dynamics simulation model using the information from this study, followed by group model-building workshops to elicit information in areas with limited coverage in the literature.

Some study limitations should be acknowledged. The quality of studies in this review could be inconsistent. The search query was designed to include as many relevant English studies as possible. Nevertheless, this search strategy only led to 39 captured studies. Hence, we did not appraise the quality of the captured studies. Also, the generalizability of the system mapped out could be limited, given that the information was extracted from a small number of papers. Readers who plan to build on the findings from this study are encouraged to investigate further to define a system for the context of their research.

Supplementary Materials: Supplementary S1—Causal Map is available at https://purl.stanford.edu/qw261hj6965. Supplementary S2—Literature Review Search Strategy is accessible through https://purl.stanford.edu/zj395jx5411. Supplementary S3 for the basic information of selected paper is available at https://purl.stanford.edu/zb628cc1002. Supplementary S4 for the detailed extracted variable information and relationships is available at https://purl.stanford.edu/ck435tc6944. Supplementary S5—Causal Map with Causal Loops can be accessed at https://purl.stanford.edu/yh177jf1991 (all accessed on 1 September 2024).

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