# A Perinatal Health Framework that Incorporates a Lifespan Approach and a Multiple Determinants Model

A Working Paper

*by*

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## Introduction

Current policy and practice approaches to improving the outcome of pregnancy and perinatal care are based, generally, on an individual-level epidemiological model of addressing known risk factors. As new risks for poor perinatal outcome are identified, these are incorporated into the model. Some efforts have been made to incorporate multiple risk factors into programs of care, but these are still grounded in an intervention mode that begins with pregnancy. This, in part, led to the enormous emphasis on early entry into prenatal care. The initial enthusiasm for prenatal care as an all-encompassing strategy, however, has faded as it became increasingly clear that the relationship is more complex.[1] Despite great strides in improving prenatal care utilization among American women, there has not been a concurrent decline in indicators of adverse pregnancy outcome. Key perinatal indicators have remained stagnant or worsened in the past decade, and the U.S. continues to rank near the bottom for these indicators compared to rates in other developed counties.[2] A new approach offers the opportunity to achieve improvements in perinatal health.

## Rationale for a New Framework: Integrating a Lifespan Approach with a Multiple Determinants Models

The new framework we will propose is one that integrates a lifespan approach with a multiple determinants model. The framework is grounded in the current context of perinatal health in the United States, including both health systems issues and demographic and population aspects. In this section, we seek to provide a rationale for why such a framework is now needed in order to advance both study and practice related to perinatal health in the U.S.

First, some of the most powerful influences on pregnancy outcome are related to health influences on women that occur long before pregnancy begins. For example, a woman's nutritional status may be strongly influenced by practices beginning in childhood.[3, 4] Thus in order to achieve sufficient levels of folate in early pregnancy, adequate nutrition may need to be ensured not just in the few weeks or months prior to pregnancy but possibly years before childbearing begins. Similarly, although infection during pregnancy is a strong risk factor for preterm delivery,[5-8] the problem of sexually transmitted infections may need to be addressed before and between pregnancies to be effective in preventing adverse outcomes. While earlier frameworks have shown some recognition of the importance of the preconceptional period,[9-11]

most have limited the scope of their attention and have failed to place preconceptional forces in the context of women's health across the lifespan. The focus has been on addressing factors in the few weeks to months prior to conception by targeting women who are planning their pregnancies. Even if this approach were effective, nearly one-third of pregnancies in the U.S. are believed to be unintended (unwanted and/or mistimed).[12] This high rate of unintended pregnancy underscores the importance of promoting a woman's health regardless of her pregnancy plans. A "lifespan" approach to pregnancy outcome identifies the antecedents of poor perinatal outcome and links behaviors and risks across time, not solely during those periods in which a woman is pregnant.

Second, as in the case of chronic disease prevention programs, efforts to improve the outcome of pregnancy may need to adopt a "multiple determinants" model that integrates the social, behavioral, environmental, and biological forces that shape pregnancy. Such a model would go beyond specific individual risk factors to provide a framework for showing the interrelationships between factors, and pathways by which factors might influence perinatal and women's health. For example, while it has long been understood that poverty influences risk, the pathways and possible intervention points have not been elucidated. Again, the implications for practice and policy are that the integration of these various domains may be an essential step to improvements in perinatal health.

Third, the demography of pregnancy has changed dramatically in the last few decades[13-15] so that approaches that simultaneously consider the entire lifespan as well as multiple determinants may need to be adopted to achieve improvements in perinatal outcomes. While teen pregnancy and early childbearing have declined, the adolescent period remains important and retains the particular challenge of addressing issues of early sexual activity. But attention must now be given to the delayed childbearing occurring among older women who have spent years in the work force and enter pregnancy with a completely different set of biological and social issues than younger women. A framework for improving perinatal outcomes provides a structure that takes account of these differences.

In this paper we attempt to link the current thinking about lifespan perspective and multiple determinants with an approach to pregnancy in the different age periods. We use the newly available research literature to identify particular moments and strategies for effective interventions. Unfortunately, there may not be any proven interventions available during some

of these periods. Our goal, however, is to create a framework for the logic of such new intervention strategies.

The audiences for this paper include policy makers, public health practitioners, clinicians in leadership positions, and researchers. Policy makers need to understand why some of the formerly promoted strategies may not have had their intended outcomes; our framework provides a more complex, but perhaps realistic way of thinking about pregnancy outcome. Practitioners face the daunting challenge of how to use such information. Above all, this framework will give them a reason to link service domains across time and create a context for the health of women across the lifespan. Finally, this framework may be useful to the research community in developing intervention trials that will test the relationships and bring forth new knowledge on which to judge its value.

**Women's Reproductive Periods and Definitions**

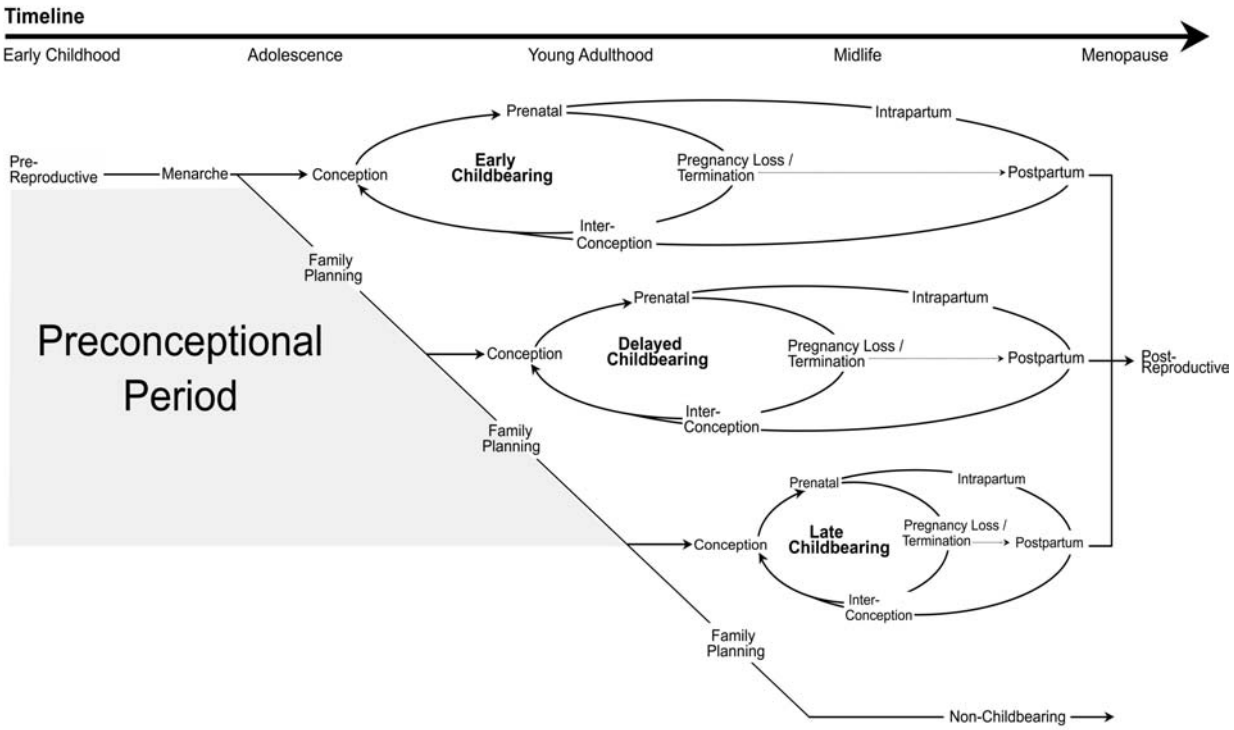
Because the framework proposed here is based on a life-course perspective and focuses on the preconceptional and interconceptional periods, we first define these concepts and specific terms. The period prior to pregnancy, particularly the first pregnancy, is often referred to as the "preconceptional" period. However, some consider preconceptional to represent only a brief period prior to pregnancy (a planning period). Furthermore, many refer to the period between pregnancies as the "interconceptional" period; this encompasses the entire time between pregnancies, including the "preconceptional" period. More broadly, this would be what is known as "women's health."

We also note that while pregnancy is considered to be the demarcation separating pre- and interconceptional intervals, utilization and access to prenatal care rarely begin with conception or even the first trimester. Recognizing that it is unlikely that women will have contact with a provider (beyond a laboratory test confirmation of pregnancy) during the early stages of the most sensitive period of fetal development, current guidelines from a number of groups recommend not only early prenatal care but also the receipt of preconception care.[9, 16, 17]

Figure 1 provides a schematic representation of the potential reproductive periods and paths within a woman's life course. Each cycle of pregnancy encompasses a prenatal (beginning at conception), intrapartum (labor and delivery), postpartum, and interconception period. Figure 1 depicts these cycles graphically as one recursive cycle (a "template") that can repeat until a

woman reaches the end of her reproductive years (menopause). The length of the interconceptional periods may vary for any given woman. Finally, the number of cycles can vary between women. For example, one woman may experience several short cycles (i.e., several pregnancies, closely spaced) while another experiences one or two long cycles (i.e., a few pregnancies with long interludes).

Figure 1.




Each cycle also explicitly models the potential for pregnancy loss or termination rather than a live birth. Women with the same number of live births (i.e. same parity) may experience differing numbers and lengths of cycles as a result of cycles that end in loss or termination. The period between a loss or termination and the next conception is often unmarked but is important to delineate as sizable numbers of U.S. women will experience a loss or termination of pregnancy. The rate of clinically recognized loss is approximately 12-14% of recognized pregnancies.[18-21] It has been estimated that 43% of women will have had an abortion by age 45.[22]

Figure 1 provides an illustration of hypothetical reproductive cycles of just 4 women. The figure does not display the length of time spent in each period or delineate the precise time of initiation. The timeline, or axis, for the figure is a woman's age, from her early childhood to the end of her reproductive years.

There are obviously a multitude of reproductive paths that could be hypothesized and simulated. We have highlighted these four possible paths in our schematic because each emphasizes a key issue with regard to reproductive trajectories. The first reproductive path describes the trajectory for a woman who becomes pregnant in her early twenties. (We have chosen not to model or examine in detail adolescent childbearing as it relates to this model.) The preconceptional period is abbreviated but the interconception periods that follow may be lengthy or short. In the second path pictured in Figure 1, childbearing is "delayed" and so too is the first reproductive cycle. In this case, the preconceptional period is lengthy and future interconception periods will vary but will be short if a woman continues childbearing. This is but one trajectory for women; a woman may delay her first birth but not her first pregnancy. The third path illustrated in Figure 1 portrays the experience of a woman who engages in late childbearing (i.e., late 30s through 40s). The length of the preconceptional period is extended relative both to women in the first path ("early"/adolescent childbearing) and the second path ("delayed" childbearing). As there is little time remaining in her reproductive years after even one reproductive cycle, the interconceptional period or periods will likely be brief. Finally, the fourth path is that of a woman who never becomes pregnant or gives birth.

As noted above, strategies for improving perinatal health have primarily focused on the prenatal, intrapartum, and immediate postpartum periods of a woman's reproductive cycles. This primary attention to the period during and directly following pregnancy fails to adequately address the impact of women's health on maternal and infant outcomes. Figure 1 focuses attention toward the preconceptional and interconceptional periods in a woman's life course as target points for intervention in addressing perinatal health. Regardless of the path taken and the number of pregnancies, a woman will spend the bulk of her reproductive life span in either preconceptional or interconceptional periods. Figure 1 provides the underpinnings on which to build a perinatal health framework that considers all aspects of a woman's life course in addressing perinatal health.

**A Multiple Determinants Framework for Perinatal Health**

Our framework marries a life-course perspective, incorporating forces that influence the health of women through successive stages of their lives and their reproductive cycles, with a multiple determinants model. Beginning in childhood/adolescence, attention focuses on the influences on health as women mature and on the forces that have implications for women's health beyond their reproductive period. Integral to the framework are the phases of the reproductive cycle described above. Specific outcomes to be addressed include traditional measures of infant and maternal mortality, as well as newer indices of maternal and women's health and morbidity.

The perinatal health framework presented is an adaptation of the Evans and Stoddart[23] model of the determinants of health. While acknowledging the direct influence that biological, behavioral, environmental, and social factors have on health status, the Evans and Stoddart model more importantly provides a framework for understanding the interrelations between such factors. It distinguishes between concepts of disease, health and functioning, and well-being, providing a more comprehensive means of assessing health status than that encompassed by traditional health models. Organized in four hierarchical levels, Figure 2 provides a framework for assessing the multifactorial determinants of adverse perinatal and women's health outcomes.

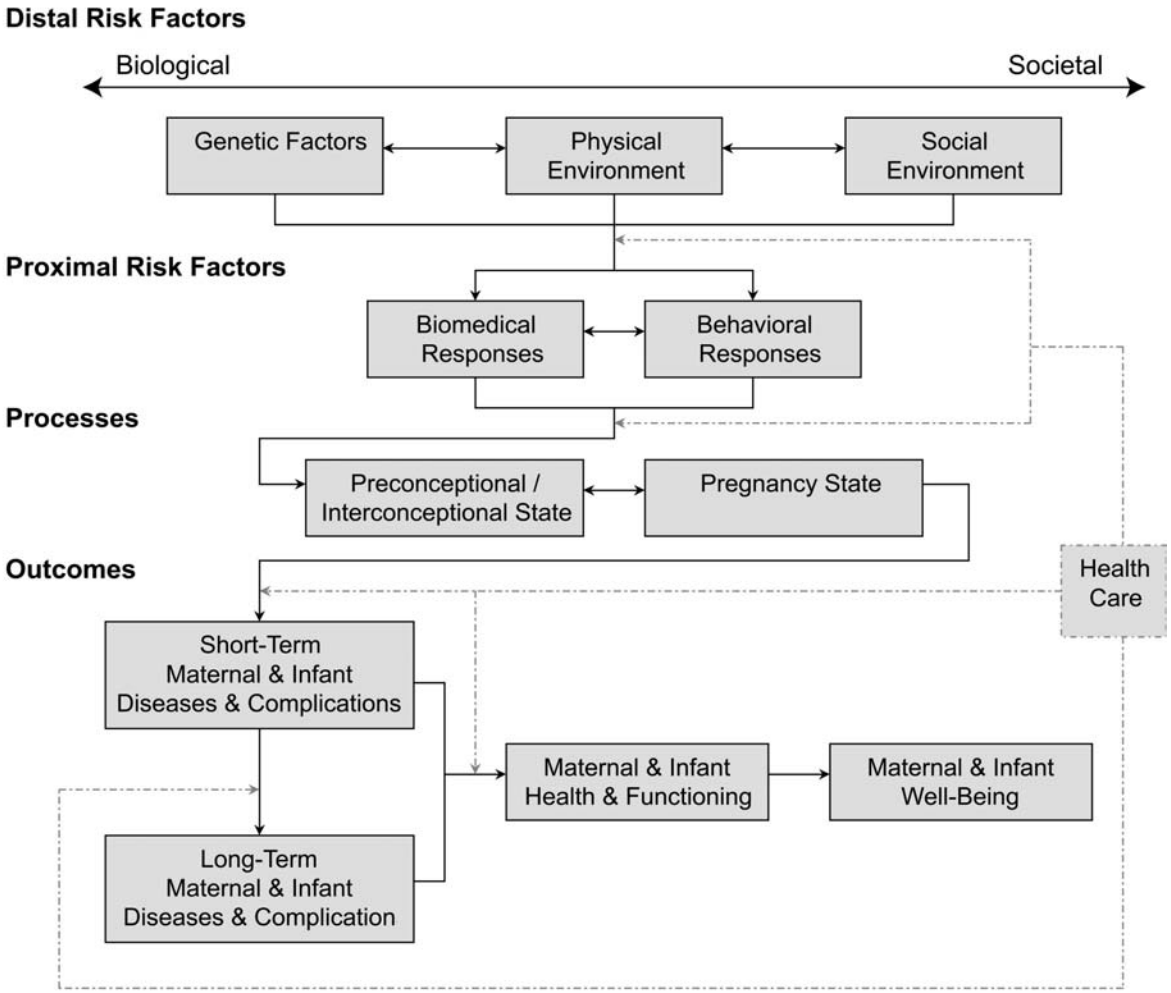
We have constrained the model by limiting the determinants and outcomes to the perinatal health arena, encompassing both the woman and her offspring. Following our presentation of the model, we examine how various factors would be conceptualized. Our emphasis is on how factors relate to the preconceptional and interconceptional periods, and how multiple factors interact to influence the outcomes.

The schematic of the framework implies directionality with the distal factors leading to the proximal factors which are then mediated by the processes of conception and pregnancy to lead to the array of outcomes. The aim of the figure is not to display all possible connections. Rather, we are seeking to describe what we judge to be the critical components and connections that can aid in development and implementation of effective strategies for improving perinatal health.

At the distal level, the framework brings focus to risk factors that place an individual or population at greater susceptibility to proximal risk factors. While having the potential to directly influence individual health status, distal factors are more relevant in terms of increasing

or decreasing an individual's predisposition towards developing compromising health conditions, engaging in high-risk behaviors, or being exposed to potential toxins. The primary categories of distal risk factors are genetic factors, the physical environment, and the social environment.

Figure 2.




At the proximal level of the framework, risk factors that have a direct impact on individual health status are represented by two categories, behavioral and biomedical responses. This distinction between the behavioral and biomedical characteristics of proximal risk factors

highlights the relationships between high-risk or protective behaviors and a women's health status, as well the influences of the physiological and biological characteristics of specific health conditions. Both behavioral and biomedical responses provide important targets for intervention.

The interaction between distal and proximal risk factors determines an individual's overall health status. It is the interrelationship between a woman's health status directly prior to conception and the changes and demands of pregnancy that is one of the primary influences on perinatal health outcomes.

Evans and Stoddart include four groups of outcomes: diseases and complications, health and functioning, well-being, and prosperity. Our framework applies three of the four groups of outcomes to perinatal health (prosperity is not included). For each set of outcomes, we differentiate between maternal (e.g., preeclampsia) and infant (e.g., preterm birth) outcomes. We have also separated the "diseases and complications" into short-term and long-term outcomes. The levels of the framework and elements within each level are listed in Tables I through III and are described in greater detail below.

**Distal Risk Factors**

Distal risk factors (Table I) range from biological to social. At the extreme end of the continuum are the genetic factors. While there have been almost no studies of how a particular genetic mutation relates to key perinatal health outcomes, studies of familial associations have hinted at a role for genetic factors. Studies of birthweight in twins and/or siblings have reported correlations of the magnitude and pattern expected if genetic factors play a role.[24-29] Gestational age and preterm birth do not appear to have strong familial correlations as examined in intergenerational studies of perinatal outcomes.[30-32] Consistent with studies of siblings, intergenerational studies have also found evidence of familial associations with regards to birthweight.[31-37] However, associations between generations may be due to characteristics strongly influenced by immutable genetic factors, such as mother's height, as well as persistence of adverse social circumstances, such as poor nutrition associated with poverty. Studies are rarely able to definitively separate the underlying factors. The potential interaction between genetic and environmental factors has rarely been examined but may not be negligible. In a recent study by Wang and colleagues, strong evidence of an interaction between smoking and a genetic polymorphism was reported with regard to the outcome of birth weight.[38] Furthermore,

while there are few reports of gene-environment interaction, there are a number of studies supporting a role for familial and possibly genetic influences on perinatal health.

| **Table I: Distal Risk Factors** |
|---|
| **Genetic Factors** |
| • Twinning |
| • Intergenerational Factors |
| **Physical Environment** |
| • Air Pollution |
| • Crowding |
| **Social Environment** |
| • Individual: SES, race, stress |
| • Neighborhood: physical, economic, social, political |
| • Intergenerational Factors |

The physical environment, captured by conditions such as air pollution and crowding, falls somewhere between the biologic and the social ends of the continuum of distal risk factors. Evidence of adverse effects of air pollution (e.g., carbon monoxide, particulate matter, sulfur dioxide) on perinatal health is just beginning to emerge.[39-42] Most of these studies are from countries with much higher levels of pollutants than would be found in the U.S. with the exception of one study based in Southern California.[41] While air pollution would appear on its face to be a biologic variable, it may be strongly associated with social factors and difficult to disentangle from them. Crowded living conditions may have biologic roots as well as having effects that are mediated by social factors. The effects of crowding have infrequently been the focus of perinatal health studies. However, a recent study examined the effects of housing on the health of preterm infants in the first year of life. Overcrowding had an adverse effect on the health of preterm infants, but not on the health of the term infants.[43]

At the far end of the continuum is the social environment. At the individual level, the social environment is frequently defined as a woman's or her family's socioeconomic status (SES). A number of perinatal outcomes are associated with SES, even when it is operationalized in simplistic fashion. For example, maternal and family income and educational levels correlate

with preterm delivery and low birth weight in the U.S. as well as other developed countries.[44-47] However, the multiple dimensions of SES are not encompassed by education and income alone; racial differences may result in social inequities despite "equal" education and income. Measures of material hardship and deprivation may need to be refined and used in order to fully estimate the effects of SES. Another individual level social factor that is strongly correlated with perinatal health across all outcomes is maternal race. Black women in the U.S., for example, are at much higher risk of preterm delivery.[48]

In the past decade, stressors (the sources of stress) and related factors have also emerged as potential risk factors for adverse perinatal outcomes.[49-55] Most researchers are just beginning to appreciate the potential effects of stressors as well as the complexity of studying this construct. This is another perinatal risk factor for which a multiple determinants model is especially needed. Part of the influence of the social environment has also been conceptualized as the residential neighborhood context. Neighborhoods have physical, economic, and social features that may influence health behaviors and outcomes. There is a growing literature on the effects of neighborhood context on health[56-68] with a few studies specifically examining perinatal health.[69, 70] The social environment can also be examined through intergenerational research in perinatal health. As stated earlier, investigators have reported perinatal outcomes to be correlated across generations.[31-37] These associations can be interpreted as evidence of genetic factors or alternatively may indicate the persistence of social factors (e.g. poverty) across generations. Studies which measure both the underlying genetic and social factors directly may shed light on how these distal factors operate and their meaning.

The distal factors are the foundation for Figure 2. They exert their influence throughout a woman's reproductive life, and may be addressed irrespective of the cycles and paths delineated in Figure 1. The emphasis of prior frameworks on the perinatal period may have led to us overlooking those factors which are all encompassing and unlikely to be resolved by perinatal interventions alone.

**Proximal Risk Factors**

The criteria for selection of the proximal factors (Table II) in our framework include consideration of the existing body of scientific knowledge on the factors that influence perinatal health as well as the feasibility of achieving changes in those factors in the U.S. population.

First, we selected only those factors for which there was scientific evidence of an effect on perinatal outcomes (whether morbidity or mortality). Second, consistent with our embrace of a lifecourse perspective, factors were chosen if effective intervention was unlikely to achieve change unless the woman's health during the preconceptional/interconceptional periods was addressed. Third, we selected only those factors that could potentially be addressed without requiring major changes in the preceding level of the framework (distal risk factors), particularly the social environment and genetic factors. Finally, we included only factors for which we have infrastructure and experience in addressing in the pregnant population. We view expanding efforts to address factors in the non-pregnant population as potentially more feasible if there is already research in the pregnant population.

| **Table II: Proximal Risk Factors** |
|---|
| **Biomedical Responses**<br>• Infection<br>• Nutrition<br>• Chronic Disease<br>• Infertility |
| **Behavioral Responses**<br>• Alcohol Use<br>• Drug Use<br>• Smoking<br>• Nutrition<br>• Sexual Behavior<br>• Assisted Reproductive Technology Utilization |

It should be readily apparent that these proximal factors co-exist (i.e., a woman may have a chronic disease and be receiving ART services). While this may be stating the obvious, it is important to consider the implications of the multivariate nature of the model. Efforts to assess the potential impact of addressing proximal factors (such as attributable risk estimation) must find a way to account for the overlap. Furthermore, interventions to address these factors must address multiple factors simultaneously. It might be necessary to develop a range of strategies to

address a particular factor and the choice of interventions will differ depending on the co-occurrence of other factors.

*Nutrition*. Nutritional factors including prepregnancy weight and weight gain, as well as intake of specific nutrients play a role in perinatal health. For example, low levels of folic acid intake in early pregnancy are associated with an increased risk of neural tube defects.[71] The risk relates to exposure during such an early period of pregnancy that many women do not know they are pregnant. Even those women who are aware that they have conceived are unlikely to have access to medical care early enough for effective clinical intervention in this area. Strategies to address intake of folic acid must therefore focus on the period prior to pregnancy. Prepregnancy weight and weight gain are other nutritional factors that may need to be considered relative to the preconceptional and interconceptional periods. Obesity may contribute to maternal morbidity during the pregnancy,[72] and high weight gain, while often beneficial for the fetus,[73] may contribute to obesity and its associated health problems for the mother postpartum.

*Infection.* There is renewed attention recently to the impact of reproductive tract infections (RTIs) on adverse perinatal outcomes (e.g., spontaneous abortion, preterm delivery).[5-8] RTIs include sexually transmitted infections (STIs) as well as bacterial vaginosis, a relatively common infection that does not appear to be predominantly sexually transmitted. Prenatal screening and treatment may lead to improved outcomes, but studies have not uniformly found this approach to be effective.[5-8, 74-77] This may be an area in which attention to the periods of time outside of pregnancy may yield benefits.

*Smoking.* There is an abundance of literature on the risks of adverse perinatal outcomes associated with smoking, ranging from delayed time to conception[78] and birth defects[79-84] to placental abruption[85-88] and LBW.[89] Infant mortality rates are also higher for women who smoke during pregnancy.[73] Smoking reduction and cessation during pregnancy clearly benefit the mother, fetus, and infant[90-92] but it is not clear that all risks return to baseline if a woman begins her pregnancy as a smoker.

*Alcohol Use.* As with smoking, alcohol use may adversely affect outcomes across the continuum. However, the evidence is not as strong for alcohol use as it is for smoking, and there are certainly safe levels of consumption with regard to the woman's own health. The effects of alcohol abuse or heavy alcohol use during pregnancy on fetal alcohol syndrome (FAS) and fetal alcohol effects (FAE) have been consistently noted in a number of studies.[93-96] Adverse effects have not been consistently seen with lower levels of exposure, whether chronic or acute. There may be safe levels of alcohol consumption although we do not know yet what levels those are. As the adverse effects of alcohol on the fetus/infant appear to be related to neurologic development that begins very close to conception, this is another area of behavior in which exposure preconceptionally is important to consider.

*Drug Use.* As with smoking, these are potentially addictive behaviors that can adversely affect outcomes across the continuum. While abuse of most of these substances certainly leads to acute and chronic adverse health effects for the woman, the evidence of detrimental effects on her pregnancy is less consistent. The specific effects of substance use during pregnancy depend on the type and amount of drug used, the mother's overall health, the gestational age of the fetus at the time of use, and the functional state of the placenta.[97, 98] Reduced birth weight of infants exposed to cocaine prenatally has generally been upheld in studies, even recent ones in which adjustments were made for confounding factors.[97] Cocaine has also been reported to increase the risk of placental abruption and spontaneous abortion.[98]

*Chronic disease*. Chronic diseases as well as the treatment of such diseases often have wide ranging effects on a woman's health. There is some direct empirical evidence that chronic disease is associated with poorer maternal, fetal and infant outcomes. In studies of pregnant women with specific chronic diseases, a wide range of diseases have been reported to increase the risk of adverse fetal and infant outcomes, such as low birth weight and preterm birth. These illnesses include asthma[99-101], diabetes[102], hypertension[103] and renal disease.[104] There is also indirect evidence of an association of adverse maternal and infant outcomes with chronic disease. In a study of women who delivered a preterm low birth weight infant, Haas and McCormick[105] reported that 29.7 percent of the mothers had been hospitalized for a non-pregnancy related condition, usually a chronic disease, during the five year follow up period.

*Assisted Reproductive Technology (ART).* The increasing use of ART[106, 107] has enormous implications for perinatal health in the U.S. population. This is clearly a high-risk group of women for a number of reasons. First, multiple gestation pregnancies and births are much more frequent with ART[106]; the rate of multiple gestation pregnancies has increased dramatically in the U.S. in the past two decades as a result.[108, 109] Multiple gestation pregnancies have a much higher risk of adverse outcomes for the fetus and infant[107, 110-112] as well as the mother.[113] Second, even ART treatment that results in a singleton birth may carry more risk. Studies have reported increased risks of adverse perinatal outcomes among women who have had ART treatments and deliver singletons.[114-116] This may be because factors leading to infertility also increase the risk of adverse perinatal outcomes. Alternatively, it may be that the ART treatment interferes with normal development.

**Processes**

In Figure 2 we include a "processes" level in the framework that connects the framework to the life course of the woman described in Figure 1. We have explicitly identified the transition from the preconceptional/interconceptional state to the event of conception and the pregnancy state.

**Outcomes**

Our framework includes three groups of outcomes (Table III), each differentiating between mother and infant (including fetus): 1) diseases and complications; 2) health and functioning; 3) well-being. We have explicitly separated short-term from long-term diseases and complications as these groupings are consistent with the way in which perinatal outcomes are grouped for monitoring and research purposes. We made no attempt in our examples however, to limit the identified outcomes to those associated with the proximal risk factors. Our intent is to call attention to a broader array of outcomes than is typically considered.

| Table III: Maternal and Infant Outcomes | |
|---|---|
| **Short-Term Maternal Diseases and Complications**<br>• Hemorrhage<br>• Preeclampsia<br>• Gestational Diabetes<br>• Cesarean Section<br>• Antenatal Hospitalizations<br>• Emergency Department Visits<br>• Maternal Mortality | **Short-Term Infant Diseases and Complications**<br>• IUGR<br>• Preterm Birth<br>• Low Birthweight<br>• Congenital Malformations<br>• Respiratory Distress Syndrome<br>• Sepsis |
| **Long-Term Maternal Diseases and Complications**<br>• Postpartum Depression<br>• Pregnancy Weight Gain Retention<br>• Urinary Incontinence<br>• Risks During Subsequent Pregnancies<br>• Cancer<br>• Osteoporosis | **Long-Term Infant Diseases and Complications**<br>• Cerebral Palsy<br>• Chronic Pulmonary Disease |
| **Maternal Health and Functioning**<br>• Life Expectancy<br>• Limitations of Daily Living Activities | **Infant Health and Functioning**<br>• Learning Disabilities |
| **Maternal Well-Being**<br>• Economic Stability | **Infant Well-Being**<br>• School Achievement<br>• Employment |

Many of these outcomes, such as low birth weight, are already monitored on an ongoing basis and most at least periodically. There are some notable exceptions, particularly those that are maternal (e.g., morbidity measured by emergency department visits). Furthermore, some of these outcomes are not only missed by current systems of monitoring, they are not even widely accepted as part of perinatal health despite evidence that they are related to a woman's reproductive life cycle. Health and function could be measured by limitation-of-activity type measures but a fuller examination of this issue is required. Functional outcomes, such as academic achievement and professional attainment, are potential measures to assess well-being.

There is growing evidence that some "short-term" perinatal outcomes have adverse effects on well-being. In a twenty-six year follow up of the 1970 British Birth Cohort, Strauss reported that adults born small-for-gestational age had small but significant deficits in academic achievement and larger and significant deficits in income and professional attainment.[117] Comparing siblings from the U.S. Panel Study of Income Dynamics, Conley and Bennett found that low birth weight was associated with lower educational attainment net of socioeconomic status.[118] These studies not withstanding, these two groups of outcomes, health and functioning and well-being, are more difficult to understand, measure, and monitor. Yet these are indeed the outcomes by which success of our efforts must ultimately be judged.

**Health Care**

Figure 2 shows that health care can modify the relationships between the various components of the perinatal health framework. Health care, in this context, is defined as the broad range of activities from primary prevention, societal level programs that could be targeted to preventing young adolescents from having unplanned pregnancy to medical interventions that screen for or treat specific disease processes. The mix of preventive and therapeutic will vary at different levels of the model.

At the very first level of the model, the health care activities that potentially modify the impact of distal risk factors on perinatal health are more global and primary in nature. For example, governmental policies could provide better health insurance for all low-income women, and thereby improve their health status preconceptionally. Similarly, national efforts to promote better nutrition, reduce environmental and occupational exposures, and reduce violence against women will benefit all women.

At the next level, health care services may also modify individual biomedical and behavioral responses that constitute the proximal risk factors for perinatal health. Many of the health care activities related to these constitute a mix of secondary prevention and treatment services including smoking cessation programs, screening and treatment for perinatal infection, effective management of underlying chronic disease and others. The provision of this health care occurs prior to the beginning of the reproductive cycle and may also extend into prenatal care. Primary prevention activities include such initiatives as folic acid supplementation and interventions to prevent smoking initiation.

The interaction between preconception and pregnancy may be influenced by a variety of family planning and contraceptive approaches to preventing, delaying and timing pregnancy as well as a wide array of more technical services - assisted reproductive technologies - to promote fertility. These health and medical care interventions are provided at the individual level.

Finally, at the outcome level of our model, health care services, including tertiary level services, are provided to individual level women and infants to improve the outcome of pregnancy and likelihood of survival without complications. These interventions are the best known. They include more comprehensive prenatal care, prevention of preterm delivery, managing multiple pregnancy, high quality labor and delivery obstetric care, maternal-fetal medicine, and neonatal intensive care.[119-122] It should be emphasized, however, that these services may be delivered to individuals, but to be effective, must also be organized at the societal level into regionalized perinatal systems.[123-125]

**Interrelationships Between Levels/Sections and /or Between Proximal Factors**

In Figure 2, the relationships among levels of the model are shown. We have also illustrated relationships between groups of factors within a level. For example, the bi-directional arrow connecting "physical environment" and "social environment" is intended to represent the potential association between these two groups of factors within the distal factors level. Figure 2 is not, however, a pictorial representation of potential relationships between factors within a group. For example, pollution and crowding are both factors grouped within "physical environment" and they may well relate to one another. Therefore many potential links between factors underlie the basic framework depicted in Figure 2. The goal of our framework and our depiction of the framework is not, however, to exhaustively identify every possible association. Rather, we wish to highlight the critical pathways that strategies must consider in order to achieve success.

**Applications of the Framework**

We have presented a framework that integrates a life course perspective with a multiple determinants model. Our intent is to influence the way in which perinatal health concerns are approached in both the research and practice domains. In this section of the paper, we seek to provide illustrations of how the framework might be applied. We show how strategies to address

selected proximal factors for adverse perinatal outcomes might be informed by our framework. In particular, by examining proximal factors of relatively greater importance for those who engage in either early or late childbearing, we illustrate the intersection of the lifespan perspective (Figure 1) with multiple determinants (Figure 2).

*Nutrition.* Our proposed perinatal framework leads to interventions that address nutritional factors in the periods outside of pregnancy. Folate has received considerable attention with regard to the need to address the pre- and interconceptional periods. Based on a 1998 national telephone survey, the March of Dimes Birth Defects Foundation reported that 68 percent of women reported ever having heard of or read about folic acid, a 31 percent increase from 52 percent in 1995.[126] However, according to the Centers for Disease Control and Prevention, folic acid supplementation prior to pregnancy has only risen to 29 percent, an increase of 4 percent over 3 years.[126] Based on data from the USDA 1995 Continuing Survey of Food Intake by Individuals, less than half of adult women consume diets containing 100 percent of the RDA for folate with little variation by age.[127] In the U.S., fortification of cereals and grains with folic acid began shortly after 1996 in an effort to decrease the risk of neural tube defects in pregnancy.[128] This is a clear example of a factor for which there is evidence that deficiencies cannot be effectively addressed during pregnancy and why we need a framework that explicitly considers the periods outside of pregnancy. Except for the recent mandate to fortify food, folate supplementation has been an issue largely consigned to "pregnancy planning". Nonpregnant women who are not planning a pregnancy are not targeted with interventions. Yet the high rate of unintended pregnancy in the U.S.[12] necessitates that this group be the focus of efforts in this area.

*Infection.* The rates of all sexually transmitted infections (the majority of RTIs) are much higher in the United States than in any other developed country, and the rates of many sexually transmitted infections have been increasing.[129] Rates of sexually transmitted infections as well as RTIs overall are highest among poor women and minority women,[129] the same groups at high risk for adverse perinatal outcomes. While sexually active women of all ages are susceptible to such infections, younger women are at the highest risk, with two-thirds of all cases occurring in

persons under 25 years of age. The increased burden of infection for young women is related to both higher-risk behaviors and biological differences.[129]

RTIs, even if treated, may lead to pelvic inflammatory disease and cause tubal damage resulting in infertility. This means that infection years before a woman intends childbearing may affect the health of the woman and infant. Research on RTIs in pregnancy also suggest that strategies may need to be developed to target the problem of infection outside of pregnancy. Treatment of infections during pregnancy may reduce the risk of adverse outcomes but results have not been consistent.[5-8] In the case of bacterial vaginosis, a recent large randomized clinical trial of treatment did not achieve reductions in the preterm delivery rate[74] in contrast to three other randomized clinical trials in this area.[75-77] Reasons for this failure to achieve improved outcomes may include recurrence or persistence of the infection. Goldenberg has hypothesized that some women may suffer from chronic persistent infections, seemingly asymptomatic, that are harbored in the uterus between pregnancies.[8] These possibilities suggest, again, that the perinatal period may be too limited to address these issues. A model that explicitly includes the periods outside of pregnancy is needed to develop approaches to prevention and treatment of infections.

*Chronic Disease*. While no one chronic disease is common among women of childbearing age, taken as a group, chronic diseases affect substantial numbers of women.[130, 131] While some chronic conditions are very common in younger women, such as asthma, most chronic conditions increase in frequency with age. Furthermore, the longer a woman has had a chronic condition, the more likely it is that her health has been adversely affected. Therefore, as more women postpone or continue childbearing into their 30s and 40s,[13, 14] the increased prevalence of chronic disease as women age underscores the potential importance of addressing chronic diseases in the context of pregnancy-related care and services.[132] Finally, the burden of chronic disease falls disproportionately on two overlapping subpopulations of women at increased risk for adverse perinatal outcomes: poor women and minority women.[132] While chronic diseases can be managed during pregnancy with an effort to minimize any adverse sequelae, even chronic diseases that are well controlled may adversely affect a single important physiologic function (e.g., respiratory function) and thereby represent a potential risk to the fetus and mother. Treatment itself may have adverse effects. In addition, particular treatments may be

teratogenic and/or hazardous to the mother in pregnancy; therapies may need to be modified for women who are pregnant or at risk for conception. Pregnancy may also exacerbate chronic diseases; women with cardiovascular or renal disease may experience difficulty with the increased demands pregnancy places upon their body's already compromised systems.[133, 134] Haas and colleagues[135] recently reported that women were four times more likely to be hospitalized antenatally if they had a history of chronic hypertension and two times more likely if they had a history of diabetes mellitus.

Interventions that increase the practice of protective behaviors, such as proper nutrition and exercise, as well as those that seek to reduce negative factors, such as smoking and stress, are important steps towards reducing the incidence and sequelae of chronic conditions and concurrently improving perinatal outcomes and women's overall health. Adolescents may be a critical group to target for prevention. There is growing evidence that healthy behaviors adopted in adolescence (e.g., physical activity, diet) continue at least into young adulthood.[3, 4]

Misra and colleagues have examined the issues of chronic disease and perinatal health to identify opportunities where women's health and perinatal health interventions can intersect more beneficially, including broadening strategies aimed at improving perinatal health to emphasize a woman's overall health regardless of childbearing status or plans and using perinatal health care as a bridge to ongoing care for women.[132] Therefore, chronic disease is another factor for which strategies may be more effective if conceptualized based on a framework that integrates the life course and a multiple determinants model.

*Assisted Reproductive Technology (ART)*. While there is some evidence that ART may increase risk in singleton gestations,[114-116] the high rate of adverse outcomes for the mother and infant is largely a consequence of the increased rate of multiple gestation pregnancies that occur as a result of ART. ART is particularly important to consider for women engaging in late childbearing. While ART is utilized by women across the lifespan, women who initiate childbearing in their late 30s and 40s are more likely to experience infertility and to utilize ART services.[136] Women who engage in late childbearing, as discussed above, are also more likely to have chronic conditions and there may be interactions with ART.

One strategy might be to develop clinical practice guidelines to limit the number of conceptuses implanted or to monitor ova released. However, such approaches may not be

entirely successful, particularly in the U.S. Using a broad framework such as we have proposed here, the focus shifts to the antecedents of infertility which may be far removed. This would require attention to women's health prior to conception, perhaps even reaching into adolescence and childhood. Among the known causes of infertility, the single greatest contributor is a sexually transmitted infection.[136-138] The prevention and treatment of infections prior to and between pregnancies, particularly in young women who may be years away from initiation of childbearing, would be one strategy to improve perinatal health that would follow from examination of ART within our proposed framework. Our framework provides the structure to conceptualize and develop strategies that take into account these multiple determinants of pregnancy outcome.

**Conclusion**

In this paper we propose an integration of a multiple determinants model with a life course framework to focus attention on risk factors that influence perinatal outcomes, but that occur prior to and between pregnancies. This work takes advantage of new research on these risk factors and organizes them into a framework that broadens the traditional approach to addressing pregnancy outcomes by prenatal care related activities.

We believe that such rethinking of the factors that influence the outcome of the perinatal period will be useful to practitioners, policy-makers, and researchers, especially by linking interventions and risk factors that are often viewed as existing in distinctly separate arenas. A major impediment relates to the fragmentation of the perinatal health system and the larger health system in this country. Care that is not exclusively for pregnancy or newborns is often outside the system with few if any real linkages. In general, family planning strategies to prevent unwanted and unplanned pregnancy are not systematically linked to prenatal care. Preparation for pregnancy needs to begin in childhood with knowledge of nutrition, safe sex, family planning, and physical fitness. Yet, again, there is little linkage between care for pre-adolescent girls and adult women of reproductive age. Care for infections, an important and preventable risk factor for poor perinatal outcomes, is too often separated from the perinatal health system. Furthermore, maternal chronic conditions may constitute a major risk for adverse perinatal outcomes but are not often viewed as being in the domain of pregnancy care. We have built on past work in this area and view this framework as representing an important shift in this field.

However, we do not expect that this will be the final framework developed in this area. We see this as a contribution to an ever evolving set of ideas.

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