
Preface

Nutrition and Health in Developing Countries, Second Edition, was written with the underlying conviction that global health and nutrition problems can be solved only through a firm understanding of the different levels of causality and the interactions between the various determinants. Although the book focuses on the problems in developing countries, we recognize that as a result of globalization, there is no longer a clear distinction between health and nutrition problems between the developed and the less-developed world. Emerging diseases such as HIV/AIDS, tuberculosis, and obesity show how the world is connected, and that knowledge about health and nutrition problems is also essential for professionals in developed countries. The objective of *Nutrition and Health in Developing Countries, Second Edition*, is to provide policymakers, nutritionists, students, scientists, and professionals with the most recent and up-to-date knowledge regarding major health and nutritional problems in developing countries. This specific knowledge is presented to facilitate an integrated approach to health research, programs, and policy. As such, the approach represents the tension inherent in combining diverse disciplines. This book is meant as a synthesis, and it is not meant as an exhaustive treatise of all infectious diseases or every nutrient deficiency in developing countries as such information is generally accessible in other textbooks.

We have greatly expanded the second edition to 34 chapters and have included new chapters relevant to humanitarian emergencies, including a case study of the Indian Ocean tsunami in 2004, food in humanitarian relief, food policy, the emerging role of supermarkets in developing countries, homestead food production, aging, ethics, and the adverse impact of parental tobacco use on child health in poor families. These new chapters reflect the increasing complexity and changes that are occurring in developing countries. The Millennium Development Goals of the United Nations call for major progress in eradicating extreme poverty and hunger, in reducing child mortality, and in improving maternal health; we hope that these chapters provide insight and solutions that will help to attain these goals.

Nutrition and Health in Developing Countries, Second Edition, begins with a historical overview of the idea of nutrition and development, and shows how the concepts of progress and development evolved from the Enlightenment and shaped the basic precepts underlying work in nutrition and public health for the last two centuries. Many people working in public health may be impressed by the conditions often found in developing

countries today: high infant mortality, widespread malnutrition, goiter, tuberculosis, and other health problems. However, similar conditions were faced by public health and policy makers in the early 20th century in Europe and the United States. A better understanding of nutrition and implementation of this new knowledge into policy helped to eradicate many nutritional and infectious diseases. An appreciation of these historical examples may help avoid “reinventing the wheel,” a phenomenon apparent in some nutrition and health research conducted in developing countries today.

The first section of *Nutrition and Health in Developing Countries, Second Edition*, focuses on the major health indicators in developing countries: maternal mortality, low birth weight, neonatal mortality, infant mortality, and child growth and development. The differences in mortality rates between developing countries and industrialized countries are presented in these chapters and are striking, with the disparity greatest for maternal mortality. In many circumstances, the application of known, effective interventions could reduce the large disparities in mortality between developed and developing countries.

The second section of the book deals with major infectious diseases in which nutrition plays a role: diarrheal diseases, acute lower-respiratory infections, measles, malaria, tuberculosis, and HIV infection. There is a purposeful overlap between these chapters on specific health problems and subsequent chapters on nutritional deficiencies (e.g., the role of zinc in prevention and treatment of diarrheal diseases). This approach was used to emphasize the different perspectives that may be taken either from the standpoint of infectious disease or from a specific nutrient.

In the third section of the book, the general problem of malnutrition and specific deficiencies in vitamin A, vitamin D, zinc, iron, and iodine and multiple-micronutrient deficiencies are presented. Large advances have been made in our understanding of micronutrient malnutrition in the last three decades. Vitamin A deficiency is a major cause of childhood morbidity, mortality, and blindness in developing countries, and it is apparent that many diverse approaches are needed to eliminate this problem. New research shows that zinc deficiency is widespread, and that zinc supplementation can reduce morbidity from diarrheal and respiratory diseases. Iron deficiency remains the most common micronutrient deficiency among women and children worldwide, and its reduction will be a major challenge. The elimination of iodine deficiency disorders through widespread use of iodized salt appears to be an attainable goal in the near future. As micronutrient deficiencies often occur together due to limited consumption of good dietary sources, there is a shift in focus to combating these deficiencies in combination.

The fourth section of the book deals with new emerging issues of countries in an intermediate stage of development, such as the nutrition transition in which many nutritional deficiencies decline and other health problems, such as obesity, diabetes, and cardiovascular disease, become more prominent. Life expectancy is increasing in most developing countries, which raises new concerns about nutrition in older adults. Another pressing problem in developing countries is rapid urbanization, as observed in large cities such as Mexico City, Lagos, Dhaka, and Jakarta, and there are new challenges in achieving food and nutrition security in these settings. Although tobacco control has not usually been considered a problem related to child health and survival, new findings from Bangladesh, India, and Indonesia show that, among poor families, smoking diverts precious resources from food to tobacco, with an adverse impact on quality of diet and an associated higher level of child malnutrition and mortality of infants and children

under 5 years old. In many countries, especially in Asia, the prevalence of smoking is 50% to 75%, which has serious implications for child health. Tobacco control is placed front and center as a child survival strategy.

The fifth and final section of *Nutrition and Health in Developing Countries, Second Edition*, deals with special topics such as humanitarian emergencies, the role of food in humanitarian relief, homestead food production, how supermarkets are changing agricultural economics and food security, food policy, benefits of multimicronutrient supplements in children, use of nutritional surveillance data, ethics in public health research, and the Indian Ocean tsunami of 2004 as a case example of emergency relief. The book closes with a broad view on nutrition and health policy, analytical frameworks for public policy analysis, and thoughtful insight into the development and implementation of sound public policy in public health and public nutrition.

During the preparation of this Second Edition, we were deeply saddened by the passing of our friend and colleague, François Delange, the Executive Director of the International Council for Control of Iodine Deficiency Disorders. He was strongly dedicated to the elimination of iodine deficiency disorders, and he will be greatly missed by the international nutrition community.

We wish to thank our lovely series editor, Adrienne Bendich, for the kind support and encouragement that she has been giving us over the last decade. Her enthusiasm and breadth and depth of knowledge regarding the complex field of nutrition has been an inspiration for all of us.

As editors, we are pleased to bring together this group of authors from diverse backgrounds of clinical nutrition, medicine, immunology, infectious disease, epidemiology, public health nutrition, anthropology, health policy, economics, and disaster planning. We hope that this book will stimulate further thought, comprehensive and effective policies and programs, and research across disciplines in the goal of improving health and nutrition in developing countries to reach the Millennium Development Goals by the year 2015.

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Maternal Mortality in Developing Countries

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2.1 INTRODUCTION

According to the latest estimates of the World Health Organisation (WHO) and the United Nations International Children's Emergency Fund (UNICEF), 529,000 women still die every year from complications of their pregnancy, and nearly 90% of these deaths are in sub-Saharan Africa and Asia [1]. Obstetric complications continue to represent the major cause among women of childbearing age, far ahead of tuberculosis, suicide, sexually transmitted diseases, or AIDS [2]. While developed countries have made enormous progress in bringing down the huge death rates associated with pregnancy, women in developing countries continue to face very high risks of death and disability as a result of pregnancy. The risk of a woman dying as a result of pregnancy or childbirth during her lifetime is about 1 in 6 in the poorest parts of the world compared with about 1 in 30,000 in Sweden [3].

The growing awareness of the continuing high rates of maternal mortality during the early 1980s led to the launch of the Safe Motherhood Initiative in Nairobi in 1987. After this "call for action," governmental and nongovernmental organisations joined forces to reduce the huge burden of maternal mortality in the world. Substantial progress has been made in documenting the extent of maternal ill health, and many of the actors involved have now embraced safer motherhood as among the highest priorities in public health practice. As a result, the reduction of maternal mortality is now one of the major targets promoted within the Millennium Development Goals set up by the United Nations in 2000 [4]. The recent *World Health Report* [2] also marked two decades of attention for Safe Motherhood and highlighted key strategies that may make pregnancy safer.

The aim of this chapter is to review the evidence underlying the strategies proposed to reduce the huge burden of maternal mortality. It starts off by documenting the magnitude of maternal mortality while briefly highlighting the problems associated with its measurement. After a review of the main factors known to contribute to maternal mortality, the strategies that have been proposed to reduce the high levels of maternal mortality in the world are discussed.

This review explicitly focuses on the evidence linking maternal mortality with effective strategies, ignoring the fact that some of these strategies, while perhaps not proven effective to reduce maternal mortality, may have beneficial effects on the health of the unborn child or the woman in general. In doing so, an incomplete picture of intervention strategies to improve perinatal and women's health in developing countries is presented. It is important, however, to separate the different entities to gain a better understanding of what we can hope to achieve in reaching the goal of a reduction in maternal mortality in poor countries.

2.2 MAGNITUDE AND CAUSES OF MATERNAL MORTALITY

2.2.1 *Measuring Maternal Mortality*

The measurement of maternal mortality is surprisingly complex. The factors that make maternal mortality difficult to measure include (1) the uncertainty about the precise time period during which pregnant women are at higher risk of adverse health effects; (2) the lack of insight into the causes of death that are indirectly attributable to the pregnancy; and (3) the underreporting of pregnancy as a cause of death. In addition, the relative rarity of maternal deaths (in statistical terms) makes interpretation of trends in maternal mortality over time or between geographical areas very difficult.

Traditionally, a death is defined as maternal if it occurs during pregnancy or within 42 days of its termination [5]. The length of the postpartum period at risk has varied substantially, however, and the tenth revision of the *International Classification of Diseases (ICD-10)* now acknowledges the need for an extended time period referring to "late maternal deaths," which occur after 42 days and up to 1 year after delivery [6] (Table 2.1).

Table 2.1

Definition of maternal mortality (*International Classification of Diseases, Tenth Edition*)

Maternal death: The death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes

Late maternal death: The death of a woman from direct or indirect obstetric causes more than 42 days but less than 1 year after termination of pregnancy

Pregnancy-related death: The death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause of death

Direct obstetric death: The death of a woman resulting from obstetric complications of the pregnant state (pregnancy, labour, and puerperium); from interventions, omissions, incorrect treatment; or from a chain of events resulting from any of the above; includes conditions such as hypertensive diseases of pregnancy, haemorrhage, dystocia, genital tract sepsis, spontaneous or induced abortion.

Indirect obstetric death: The death of a woman resulting from previous existing disease or disease that developed during pregnancy and was not due to direct obstetric causes but was aggravated by physiologic effects of pregnancy

Source: Adapted from [6].

Not all deaths during or shortly after pregnancy are due to the pregnancy. Traditionally, deaths from direct and indirect obstetric causes have been included in the maternal mortality statistic, while deaths from accidental and incidental causes have not (Table 2.1). Deaths from direct obstetric causes such as eclampsia, haemorrhage, obstructed labour, or puerperal sepsis are undoubtedly attributable to the pregnancy as such conditions can only occur in pregnant women. Far less certainty exists, however, regarding indirect obstetric causes, particularly those due to infectious diseases. The notion of “diseases aggravated by the pregnancy” is not straightforward, and some diseases may merely coincide with the pregnancy without being aggravated by it. In addition, the verbal autopsy methods on which most cause-of-death ascertainment are based may be unreliable, particularly for indirect causes of maternal death [7]. In settings that rely on verbal autopsy methods, all deaths in pregnant or recently delivered women are commonly included in the maternal mortality statistic (whether or not they are attributable to the pregnancy), except for deaths due to unintentional and intentional injuries [7–9]. However, it is becoming increasingly clear that the burden of indirect causes may have been underestimated, particularly in Africa, where the prevalence of HIV is high [10].

The exclusion of deaths from accidents, homicides, or suicides from the maternal mortality statistic is a matter of controversy, and there is a growing awareness that such deaths may, at least in part, be caused by the pregnancy [11, 12]. In India, deaths due to domestic violence were the second largest cause of death in pregnancy (16%) [13]. In Matlab, Bangladesh, 20% of deaths of pregnant unmarried women were due to suicide compared to 5% for married women, and pregnant girls were nearly three times more likely to die from violent causes than nonpregnant girls [11, 14]. Studies in developed countries suggested that suicide may be precipitated by pregnancy, and that some accidents may be pregnancy related, although a recent study in the United Kingdom did not support these findings [12, 15]. Authors of a recent systematic review of violence and pregnancy-related mortality have called for further research in this area, arguing that very few rigorous epidemiological studies exist [16].

Many pregnancy-related deaths still go unnoticed or unreported, and substantial errors in the estimates of maternal mortality persist [17, 18]. Correctly measuring maternal mortality requires not only a complete registration of deaths in women of reproductive age, which in many countries may be lacking, but also the recognition that the woman was pregnant or recently delivered at the time of her death. Deaths during early pregnancy, such as those due to abortion or ectopic pregnancy, are often not recognised or reported as pregnancy related, and death certificates often omit the notion of pregnancy. The verbal autopsy techniques on which many cause-of-death assignments are based may have poor reliability [7].

Maternal mortality is usually expressed in two different ways: the maternal mortality *rate* and the maternal mortality *ratio*. The rate is expressed as maternal deaths per 100,000 women of reproductive age. The maternal mortality ratio—sometimes erroneously called the maternal mortality rate—refers maternal deaths to the numbers of live births. The maternal mortality rate and ratio measure very different kinds of risks. The ratio measures the risk of death a woman faces with each pregnancy, whereas the rate measures the risks to women, whether or not they are pregnant. The rate is a compound measure of the level of fertility and the risks associated with each pregnancy. Any intervention lowering fertility will automatically lower the maternal mortality rate but

not necessarily the ratio. As many assessments of progress in Safe Motherhood aim at separating the effects of lowering fertility from those directly aimed at improving the health of women once they are pregnant, the maternal mortality ratio has now become the preferred statistic [19]. Denominator information for the maternal mortality ratio is also easier to capture routinely, from hospital records or vital registration.

The problems in the measurement of maternal mortality are such that maternal mortality has not always been recommended as an outcome measure against which to assess programme successes. Although hopes were raised that morbidity would be a good alternative measure, it has proven very difficult to measure the prevalence of maternal morbidity at the community level [20, 21]. In fact, very little is known about the incidence of obstetric complications in developing countries. The use of facility-based data has been suggested as an alternative means to study programme effectiveness, and experience so far has been encouraging [9, 22, 23]. Investigation of women who had a near-miss obstetric morbidity, for example, may provide useful insights into the pathways leading to maternal death [24, 25]. Whether the measurement of near-miss or other life-threatening complications can inform programme success at the population level, however, is not known.

2.2.2 *Medical Causes of Maternal Mortality*

In developing countries as a whole, maternal mortality ratios range from 55 per 100,000 live births in eastern Asia to 920 per 100,000 in sub-Saharan Africa (Table 2.2). In many countries of East, Central, and West Africa, maternal mortality exceeds 1,000 deaths per 100,000 live births.

The majority of maternal deaths in developing countries are due to five major direct obstetric complications: haemorrhage, infection, unsafe abortion, hypertensive disorders of pregnancy, and obstructed labour [19] (Fig. 2.1). While huge variations are seen in the relative contribution of each of the direct obstetric causes to mortality, deaths from intra- or postpartum haemorrhage tend to be the leading cause of death, with about one quarter of all deaths attributed to severe bleeding. Estimates for deaths from unsafe abortion have varied substantially, but the consequences of illegal abortions may still be

Table 2.2
Estimates of maternal mortality by United Nations regions (2000)

<i>Region</i>	<i>Maternal mortality ratio (maternal deaths per 100,000 live births)</i>
Sub-Saharan Africa	920
Southern Asia	540
Oceania	240
Southeastern Asia	210
Western Asia	190
Latin America and the Caribbean	190
Northern Africa	130
Commonwealth of Independent States	68
Eastern Asia	55

Source: From [4].

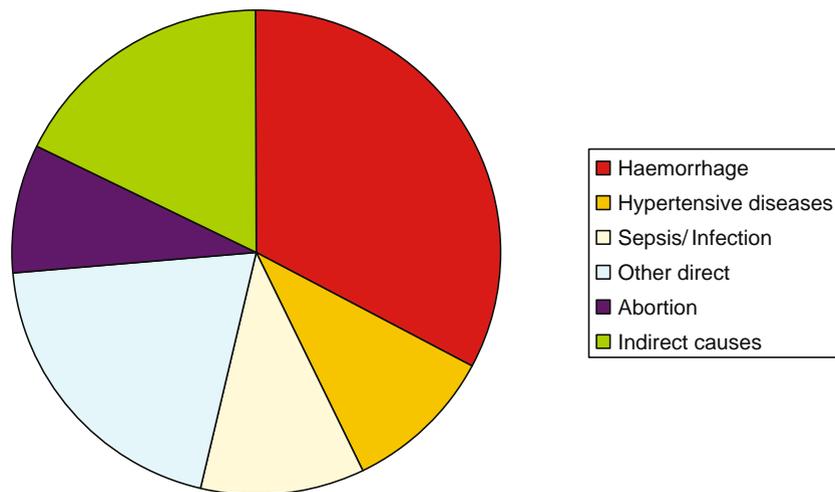


Fig. 2.1. Main causes of maternal death. (Adapted from [19].)

underestimated. Some authors have suggested that postpartum sepsis, a condition that carries a huge risk for the mother, may be declining in certain areas [26].

WHO has estimated that approximately 17% of maternal deaths worldwide are due to the so-called indirect obstetric causes, including anemia, cardiovascular diseases, and infections [19]. These figures are based on a small number of studies, however, and in settings with a high prevalence of HIV/AIDS, the contribution of infections may have increased [10, 27]. While there is no doubt that certain chronic diseases such as diabetes or cardiovascular disease or infections such as hepatitis are aggravated by the pregnancy, the common belief that the stresses of pregnancy lead to a breakdown of immune resistance allowing infectious diseases to set in is not always supported by strong epidemiological evidence [28]. The widely acknowledged association between tuberculosis and pregnancy, for example, has been challenged, and the authors concluded that tuberculosis is not associated with pregnancy [29]. Similarly, whether pregnancy accelerates the progression of HIV in HIV-infected women is still uncertain [27, 30], although a study in Uganda suggested that the risk of HIV acquisition may rise during pregnancy [31]. The overall impact of HIV on pregnancy-related mortality remains unclear [27]. Adverse effects of malaria during pregnancy on maternal health have been documented, but the increased prevalence and density of malaria parasitaemia in pregnant women are not necessarily associated with symptoms in the mother [32, 33]. The frequency and severity of malaria are of greater magnitude during pregnancy and the early postpartum period than outside pregnancy [34, 35]. In settings with low malaria transmission, the effects of malaria are particularly severe [36]. Malaria may also increase the risk of maternal death through its effect on maternal anemia [37].

Severe anemia is believed to be an important cause of maternal death in developing countries, although much of the evidence is circumstantial [38]. Mild anemia in pregnancy may go unnoticed, but the potential adverse effects of pregnancy increase as hemoglobin levels fall. Very severe anemia with hemoglobin levels of less than 4 g/dL can lead to heart failure and death from shock [39]. It has also been suggested that anaemic mothers are less able to tolerate blood loss during childbirth, although this has never been empirically verified [40]. Severe anemia in pregnancy has been reported as the main cause of 8–23% of maternal deaths in some hospitals and 11–16% in community-based studies [41–43]. It was also the main cause of near-miss obstetric events in several African hospitals [25]. In Tanzania, symptoms such as severe weakness, pallor, shortness of breath, and peripheral oedema, which may be suggestive of anemia, were present in nearly half of maternal deaths [42]. In a hospital study in western Kenya, reproductive age women with hemoglobin levels below 6 g/dL were eight times more likely to die than women with a hemoglobin level of more than 6 g/dL [44]. In a multivariate analysis, severe anemia and HIV status were significant predictors of mortality, while pregnancy status was not. In other words, severe anemia carries a huge risk of death for women of reproductive age, but pregnancy may not aggravate that risk.

2.3 STRATEGIES TO REDUCE MATERNAL MORTALITY

The strategies that have been promoted as potentially effective ways to overcome the high rates of maternal mortality have been multiple [45], and substantial changes have occurred in recent decades. Initial efforts since the 1950s have focused on antenatal clinics and maternal education, followed by an emphasis on family planning [22]. In the 1970s, training and promotion of traditional birth attendants (TBAs) were introduced, while the 1990s were dominated by an emphasis on increased access to and quality of obstetric care. More recently, a new magic bullet has been introduced, namely, the nutritional supplementation of pregnant or reproductive age women.

Relatively few of the strategies proposed in this recent time period have involved the medical profession directly as interventions such as family planning or antenatal care were thought to be deliverable by community health workers. Many of the suggested strategies were modelled after the experience with child survival programmes, and the desire for finding so-called cheap and community-based interventions has left many of the interventions unchallenged for long. Only in 1991, when Maine et al. published their influential work using evidence from the Kasongo study did the emphasis shift to the importance of professional delivery care [46]. Ensuring skilled medical attendance at delivery has now become the leading goal for maternal health programmes [45].

In reviewing the evidence in support of certain strategies, it has to be borne in mind that there is very little *direct* evidence linking maternal health interventions to maternal mortality [45]. The absolute numbers of maternal deaths are generally small, and large populations are needed to investigate the determinants of maternal mortality. For this reason, evidence from randomised controlled trials, the gold standard in health care evaluations, is seldom available to those trying to understand the strategies underlying maternal mortality reductions. Our knowledge so far is largely based on historical precedent in Western countries and on so-called thought experiments [47]. A main priority is the implementation of an effective intrapartum care strategy [45].

2.4 SOCIOECONOMIC DEVELOPMENT, WOMEN'S EDUCATION, AND MATERNAL MORTALITY

There is no doubt that the poorest countries suffer the highest burden of maternal mortality. The maternal mortality ratio is often quoted as the statistic that most clearly highlights the huge gap between developed and developing countries. The women's lifetime risk of maternal death is almost 40 times higher in the developing than in the developed world; and the highest maternal mortality ratios of 1,000 per 100,000 live births found in some regions of eastern and western Africa are as much as 100 times higher than those observed in some Western countries [3].

Yet, the relationship between high levels of maternal mortality and poverty is not straightforward. When De Brouwere and colleagues [48] mapped the maternal mortality ratios by gross national product (GNP) per capita for countries with a GNP per capita below US \$1,000 in 1993, the estimates ranged from 22 to 1,600 per 100,000 without any clear association with the level of economic development (Fig. 2.2). Countries with a similar GNP per capita such as Vietnam, Uganda, and Burundi (US \$170–180), for example, had maternal mortality ratios of 160, 1,200, and 1,300 respectively. Similarly, Loudon [49], in his excellent review of historical trends in maternal mortality in Western countries, could not explain the huge differences in the levels of maternal mortality between the United States, England and Wales, and the Netherlands in the earlier part of 1900s by differences in the social or economic context prevailing at that time in each of these countries (Fig. 2.3). In the 1920s, the United States experienced maternal mortality ratios as high as 689 per 100,000 live births, a figure not unlike many developing countries today. The Netherlands, in contrast, had already reached levels as low as 242 deaths per 100,000 live births, while England and Wales were at an intermediary level of 433. Loudon [49] remarked that, "Maternal mortality, unlike infant mortality, was remarkably insensitive to social and economic factors per se but remarkably sensitive to standards of obstetric care."

In most countries, the better-off are more fully covered by maternal health services than the poorest, and poor–rich differences are greater for higher-level than for primary

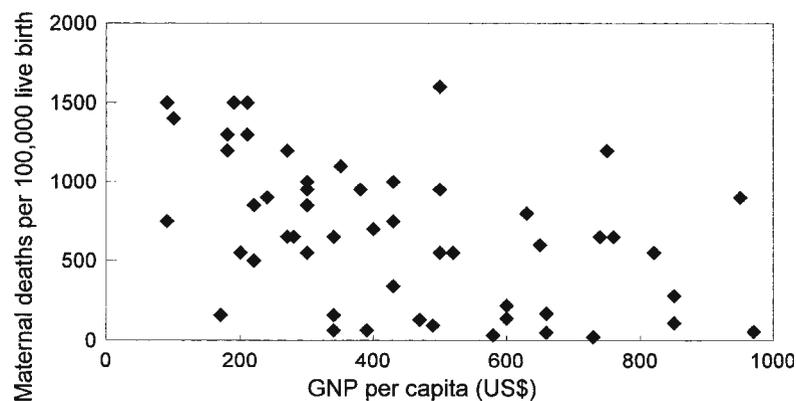


Fig. 2.2. Maternal mortality ratios by gross national product (GNP) per capita for countries with GNP <\$1000. Adopted with permission from [48].

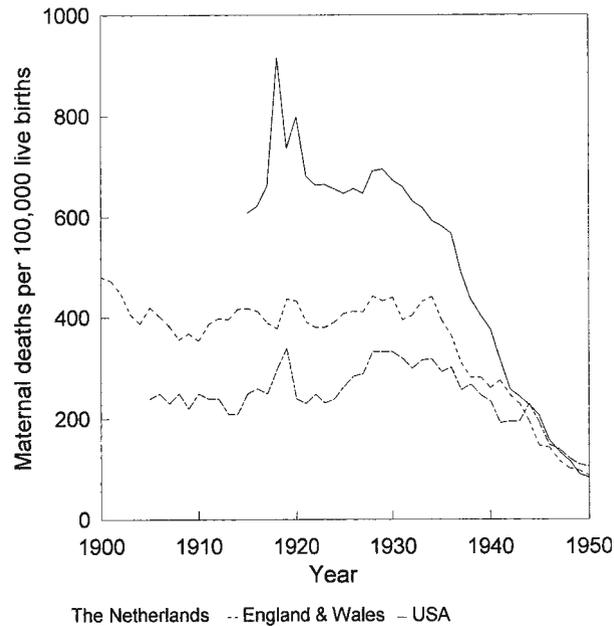


Fig. 2.3. Maternal mortality in the Netherlands, England, Wales, and USA, 1900–1950. Adapted with permission from [49].

care [50]. Data on within-country variation in maternal mortality are scarce, although a study suggested strong associations in six countries with demographic and health survey data [51]. In Indonesia, a third of all maternal deaths were in women from the poorest quintile of the population, whereas fewer than 13% of maternal deaths were in women in the richest quintile [51].

The relationship between women’s education and maternal mortality is relatively well established. Using data from 11 demographic and health surveys, Graham and colleagues showed a strong association between maternal education and maternal mortality [51]. A cross-country analysis conducted by Shen and Williamson [52] also showed that women’s level of education *relative to* men’s education was a strong predictor of maternal mortality level, together with two other women’s status variables (age at first marriage and reproductive autonomy). Interestingly, others have also shown that while maternal education was not associated with an increased risk of maternal death, a higher level of education in men was protective against maternal mortality [13]. These studies highlight the importance of women’s status in safe motherhood.

2.5 FAMILY PLANNING AND MATERNAL MORTALITY

During the 1980s, family planning was presented as one of the key strategies for maternal mortality reduction in developing countries [39, 53]. If accepted by a large proportion of the population, and if used continuously for prolonged periods, contraceptive methods should, at least in theory, contribute to lowering the high levels of maternal

mortality. Family planning may prevent unwanted pregnancy (and illegal abortion), redistribute births from high- to low-risk categories, reduce the total numbers of births, and have direct benefits from the contraceptive methods themselves [54]. Yet, various reports examining the potential impact of family planning on the reduction of maternal mortality have suggested disappointing effects [54–57].

There is no doubt that widespread use of contraceptives will reduce the total numbers of maternal deaths and hence lower the maternal mortality *rate* as fewer women will be exposed to the risks of pregnancy. However, the effects on the maternal mortality *ratio*, that is, the risk of death once a woman is pregnant, are thought to be minimal [54–56]. The vastly lower mortality ratios in the developed world when compared to developing countries cannot be attributed to changes in the demographic distribution of births [49, 54].

There is considerable evidence that the extremes of maternal age affect the risk of dying in pregnancy, and studies generally also confirmed the excess risk of first births and births of higher order [54, 58]. What is less clear is whether age and parity act independently of one another or whether the effects persist after taking into account the possible confounding effect of socioeconomic status. At very young ages, the growth of the bony pelvis is immature, and childbearing in girls less than 16 years old has been shown to carry huge risks [59]. Experiences from industrialised countries, however, suggest that pregnancies in very young girls may be only marginally more risky than in older women [60–62]. In a review article, Zimicky [58] concluded that, “While the evidence is suggestive rather than conclusive, it seems that ages below 20 and above 30 enhance the simple parity-specific patterns.”

The widely held view that short birth intervals affect the risk of maternal death has not been supported by strong empirical evidence [56, 58, 63]. The results of a large study from Matlab, Bangladesh, did not find an association between the preceding birth-to-conception interval and the risk of maternal mortality [63]. In a more recent study in Latin America, very short (<6 months) interpregnancy intervals were associated with higher risks for maternal death, third trimester bleeding, puerperal endometritis, and anemia [64]. Long interpregnancy intervals (longer than 59 months) had significantly increased risks of preeclampsia and eclampsia, however, and these effects may outweigh those of short intervals.

Eliminating births to very young, old, or high-parity women will not have a major impact on the survival chances associated with pregnancy [54, 55]. Although the risks of maternal death tend to be highest in the extremes of reproductive performance, most births, and by consequence maternal deaths, occur in the low-risk groups. Moreover, first births are generally at highest risk, and family planning programmes, by inducing a relative shift from high-parity–high-risk groups to first-birth–high-risk groups, will have little effect on the overall level of maternal mortality.

2.6 NUTRITION AND MATERNAL HEALTH

During pregnancy, growth of the foetus and the uterus induces an increase in the demand for energy and many nutrients, including iron, folic acid, calcium, vitamin A, and zinc. In chronically malnourished populations, micronutrient supplementation appears attractive as a potential intervention to reduce maternal and foetal mortality because

it is believed to be cheap, safe, and easier than the more fundamental changes in society that may be required [65]. Widespread appeals for the promotion of micronutrient supplementation of pregnant or reproductive age women have been made, and some agencies have incorporated supplementation strategies in their policy agenda [66, 67]. This section analyses the evidence linking energy and micronutrient deficiencies with an increased risk of maternal mortality. As very few studies have been able to explore such direct links, efforts are made to explore the potential for energy and micronutrient deficiencies to reduce life-threatening maternal complications.

2.6.1 Direct Effects of Energy or Micronutrient Deficiency on Maternal Mortality

Recent reviews of evidence from randomised controlled trials provided very little support for a direct link between micronutrient deficiencies in the mother and her risks of dying in pregnancy. There is at present no evidence of benefit from routine micronutrient supplementation during pregnancy in reducing the mortality risks associated with pregnancy [68–81]. Few studies were done in communities with micronutrient deficiencies, however, and most trials were not sufficiently large to draw meaningful conclusions regarding effects, beneficial or harmful, on maternal mortality.

Results from a large, randomised, double-blind, placebo-controlled trial of vitamin A and β -carotene in Nepal suggested that vitamin A or β -carotene may be associated with a 40% reduction in maternal mortality [8]. The trial was well conducted and involved the supplementation of more than 40,000 women of reproductive age with weekly doses of placebo, vitamin A (7,000 μ g retinol equivalents), or β -carotene (42 mg or 7,000 μ g retinol equivalents). Causes of death were ascertained using verbal autopsy methods. The investigators observed a reduction in mortality during pregnancy and within 12 weeks after delivery, from 704 deaths per 100,000 live births in women receiving the placebo to 426 and 361 deaths per 100,000 live births in the vitamin A and β -carotene groups, respectively (Fig. 2.4). The authors suggested that, “Raising the intake of preformed vitamin A or provitamin A carotenoids towards the values recommended for pregnancy or lactation, presumably by supplementation or by dietary means, can complement antenatal and essential obstetric services in lowering maternal mortality in rural South Asia.”

An accompanying editorial suggested that further work is needed before putting the findings of this trial into practice [82]. Methodological difficulties (particularly loss to follow-up), the fact that the effect was most pronounced in the group of causes least likely to respond to supplements (deaths from injuries), and the possible teratogenic effects of vitamin A supplementation led the author to conclude that further evaluation of benefits and possible hazards is needed before the findings can be translated into policy. In addition, the study leaves us uncertain whether the appropriate intervention is vitamin A or β -carotene, whether the supplementation should be delivered before conception or antenatally, and whether it is feasible for programmes to administer supplementation weekly [83]. Given these uncertainties, it is rather astonishing that certain agencies have already opted for the supplementation of pregnant women with vitamin A during antenatal care [84]. Two large trials in Ghana and Bangladesh are currently ongoing and may shed some light on the role of vitamin A in the reduction of maternal mortality.

Historical data from Western countries do not provide compelling evidence that the general health status of women affects their risk of dying in childbirth. Loudon [49]

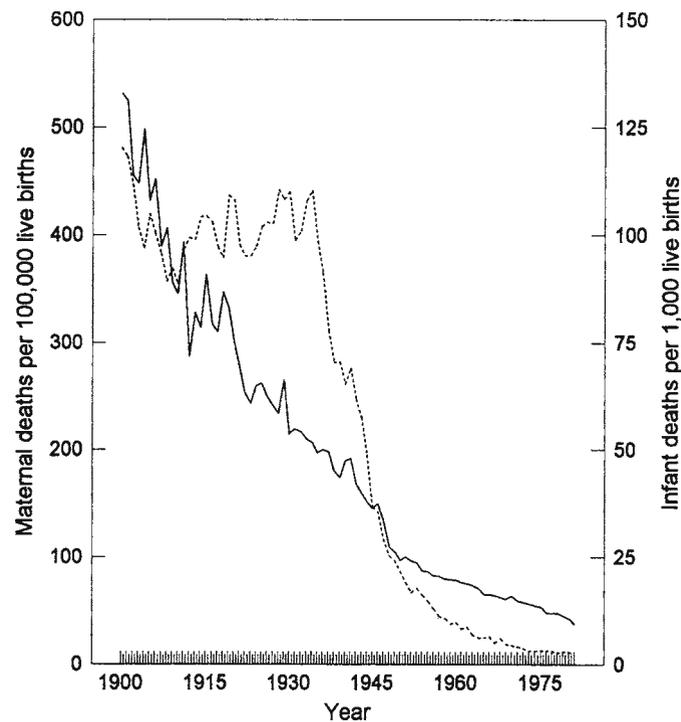


Fig. 2.4. Infant and maternal mortality in England and Wales, 1900–1980. Based in part upon [49].

was puzzled by the paucity of evidence showing that an improvement in the health of the mothers reduced maternal mortality in Western countries. Although the standard of living rose throughout Britain after 1880, and although Loudon regarded the health of mothers as a key determinant of the level of maternal mortality, he could find no evidence supporting such an association. The sharp contrast between the trends in infant and maternal mortality between 1900 and 1980 in England and Wales provide very useful insights (Fig. 2.5). Infant mortality rates, which were widely believed to be associated with increased living standards and improved nutrition, declined steadily throughout that period. The maternal mortality ratio, on the other hand, remained high until 1940 and declined sharply thereafter.

Pantin, on the other hand, suggested that the declines in maternal mortality on the Isle of Man before 1911 may have been attributable, at least in part, to improved maternal health [85]. Recent studies that examined the plausibility of adverse effects attributable to micronutrient deficiencies during pregnancy tended to focus on perinatal and neonatal outcomes [86–90].

In the absence of strong evidence of a direct link between nutritional deficiencies and maternal mortality, the next step is to search for evidence of a link between nutritional deficiencies and obstetric complications. The associations that merit attention include (1) malnutrition and obstructed labour; (2) calcium deficiency and preeclampsia;

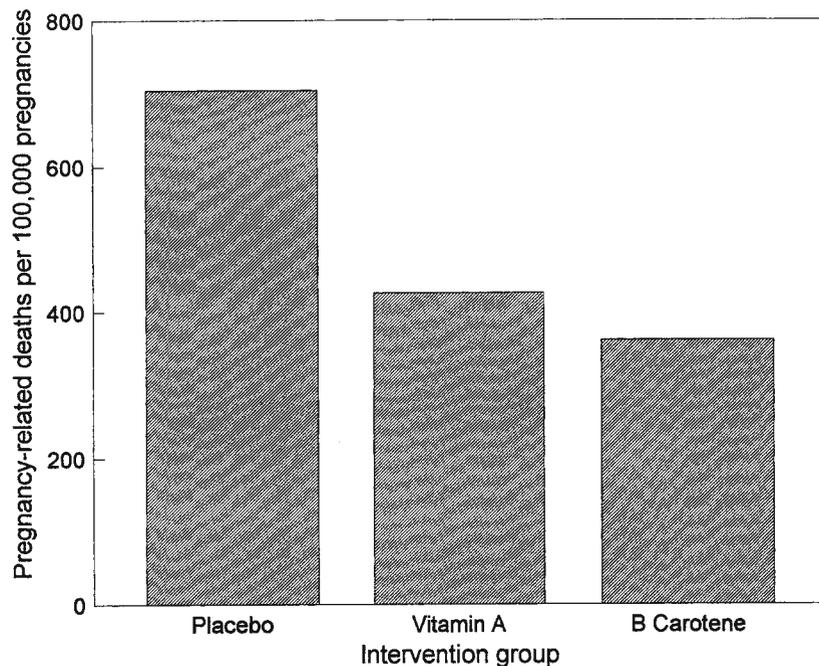


Fig. 2.5. Effect of vitamin A or beta-carotene on maternal mortality. Adapted from [8].

(3) iron deficiency and anemia; (4) vitamin A deficiency and anemia or infection; and (5) zinc deficiency and haemorrhage or infection. We also look at evidence for the efficacy of multiple micronutrient supplements in preventing obstetric complications.

2.6.2 Malnutrition and the Risk of Obstructed Labour

The association between short stature and an increased risk of cephalo-pelvic disproportion is well established [91, 92]. In a review of 14 studies, the WHO found that women in the lowest quartile of height had a 60% higher risk of assisted delivery than women in the top quartile, and the findings were consistent across study sites [92]. Although assisted delivery does not always equate cephalo-pelvic disproportion, it is probably a good marker for dystocia in settings where caesarean sections are only done in extreme circumstances. The nature of the effect appears to be relative rather than absolute in that, whatever the average height of the population of women, the lowest tenth percentile is always at higher risk [91]. The conventional cutoff for low height of 150 cm, for example, does not hold true in the Bangladeshi population, with half of these women below that cutoff, yet only women shorter than 140 cm are at increased risk of prolonged labour [93].

The WHO meta-analysis did not find evidence for an association between poor anthropometric measurements such as mid-upper-arm circumference, prepregnancy weight or body mass index (BMI), attained weight or BMI during pregnancy and weight

gain during pregnancy, and increased risks of assisted delivery [92]. In fact, most of the anthropometric indicators had an inverse relationship with assisted delivery in that thinner women had a lower risk of assisted delivery than their better-nourished peers. This, according to the authors, is plausible “insofar as a low body mass index indicates a thin mother, probably with limited calorie intake, for whom foetal growth is likely to be constrained, thus reducing the likelihood of assisted delivery” [92]. This adaptive mechanism, although adversely affecting foetal survival, may protect the mother.

It has been suggested that the low levels of maternal mortality among Scandinavian women before 1930 could be partly due to the fact that they had a stronger build, had a broader pelvis, and suffered less rickets. This hypothesis was invalidated by the observation that recent Scandinavian immigrants in the United States suffered as many high risks of maternal death as their “native” peers [49]. The high levels of maternal mortality in the United States at that time were in large part attributable to mismanagement of the delivery by doctors [48, 49].

Nutritional advice in pregnancy appears to increase the pregnant woman’s energy and protein intake, but the implications for maternal health cannot be judged from the available trials [94]. Kramer and colleagues also stated that, “Given the rather modest health benefits demonstrated with actual protein/energy supplementation, the provision of such advice is unlikely to be of major importance.” The assertion that the increased foetal size that may accompany nutritional supplementation may lead to an increased risk of prolonged labour [95] has not been empirically tested. High-energy supplementation of pregnant women in the Gambia led to a significant increase in the head circumference of babies [96]. However, the small size of this increase and the impressive reduction in perinatal mortality suggest that the supplementation was unlikely to have increased the incidence of cephalo-pelvic disproportion.

While certain risk factors, such as a small pelvis in a short woman or in growing teenage girls, generally fall under the broad heading of “nutritional” factors, the strategies to either prevent or treat them are not necessarily nutritional. Stunting caused by early malnutrition cannot be reversed in adulthood. Although nutritional supplementation in childhood may enhance future height [97], it is uncertain what the small gains in average attained height mean in terms of preventing difficult labour. Improved labour management is probably the most appropriate strategy for preventing adverse health effects in stunted women. The low risks associated with pregnancies in very young girls in Western countries do suggest that adequate labour management can ensure a safe delivery in these girls [60–62].

2.6.3 Calcium Deficiency and the Risk of Preeclampsia

The association between high calcium intake and a low incidence of hypertensive diseases in pregnancy was first shown in a study among the Mayan Indians in Guatemala in 1980 [98]. The traditional practice of soaking corn in lime before cooking was associated with an unusually high calcium intake and a low incidence of preeclampsia and eclampsia. A similar association between high calcium intake and a low prevalence of preeclampsia has also been reported from Ethiopia and was later confirmed by further epidemiological and clinical studies [68].

Low calcium intake may cause high blood pressure by stimulating parathyroid hormone or renin release and inducing vasoconstriction by increasing intracellular

calcium in vascular smooth muscle and intensifying smooth muscle reactivity [99]. Calcium supplementation has been postulated to act on smooth muscle reactivity by reducing parathyroid hormone release and intracellular calcium. By the same mechanism, calcium supplementation has been suggested to reduce uterine smooth muscle reactivity and prevent preterm labour and delivery [100].

Reviews of calcium supplementation trials during pregnancy provide strong support for the supplementation of pregnant women with calcium as a means of preventing pregnancy-induced hypertension and preeclampsia in communities with low calcium intake [68]. Supplementation with 1–2 g calcium daily was associated with a 42% reduction in risk of hypertension with or without proteinuria (10 trials) and a 65% reduction in risk of preeclampsia (11 trials). Among women with low dietary calcium intake, risk of hypertension and preeclampsia was reduced by 62% (five trials) and 71% (six trials), respectively. The absence of an effect of calcium on either the incidence or the severity of preeclampsia in nulliparous low-risk women in the largest study to date [101] does cast doubt on the potential benefits of calcium supplementation in low-risk women with adequate dietary calcium intake. The findings of this study, however, do not call into question the potential role of calcium supplementation in populations whose dietary calcium intake during pregnancy is inadequate [102]. A multicountry trial is being conducted by WHO among 8,500 nulliparous women living in areas of low calcium intake in six middle-income countries. The results of this trial will determine whether calcium supplementation should become recommended policy in such areas.

There is very little evidence linking poor nutritional status (expressed by anthropometric indicators) during pregnancy and preeclampsia [92]. A systematic review of risk factors for preeclampsia found that higher body mass indices were associated with increased risk of preeclampsia [103].

Preeclampsia has also been linked to oxidative stress, and supplementation with antioxidants has been suggested as an effective way to improve vascular endothelial function and prevent preeclampsia. In a pilot study, vitamin C and E supplementation of pregnant women at increased risk of preeclampsia substantially reduced the risk of preeclampsia [104]. The sample size was small, however, and larger trials in different populations, with attention for safety, particularly for the infant, are needed before adopting such a strategy [105].

2.6.4 Iron Deficiency and Anemia

During pregnancy, the demands for iron may increase because of the expansion of the red cell mass and the deposition of substantial amounts of iron in the foetus and the placenta [38]. These increased demands are partially offset by the cessation of menses and the increased absorption of iron during pregnancy. During pregnancy, the hemoglobin and serum iron concentrations fall, and the needs for additional iron increase as the pregnancy progresses [38]. Iron supplementation in pregnancy has become routine practice throughout the world.

In developing countries, anemia during pregnancy is very common. WHO [106] estimates that more than half of pregnant women in developing countries may be anaemic (defined as hemoglobin below 11 g/dL). The prevalence of severe anemia (defined as hemoglobin below 8 g/dL) is not well documented, and it is not certain that the prevalence of mild anemia mirrors the prevalence of severe anemia. Stoltzfus [107] summarised

data from six different populations on the prevalence of anemia (Table 2.3). While the prevalence of overall anemia was similar in the six sites, the prevalence of moderate-to-severe anemia was markedly different. Rush and Brabin et al. concluded that severe but not moderate anemia was associated with a higher risk of maternal mortality; hence, the prevalence of mild anemia may not be in itself a good marker of risk [108, 109].

There is little doubt that iron supplementation of around 60 mg elemental iron daily in pregnancy improves maternal iron status during pregnancy and immediately after delivery in both industrialised and developing countries [75, 110]. Increases in hemoglobin, haematocrit, serum ferritin, and serum iron are usually apparent within 3 months. Routine iron supplementation results in a substantial reduction in the proportion of women with a hemoglobin level below 10 or 10.5 g/dL in late pregnancy. Some questions remain, though, not least whether iron supplementation reduces the incidence of severe anemia [108, 111]. Most trials exclude severely anaemic women, and the assumption that the supplementation of the entire population of pregnant women would cause a shift in the distribution of anemia such that the prevalence of very severe anemia would decrease has not been empirically tested.

Despite the long-standing universal practice of iron supplementation in pregnancy, it is surprising how little is known about its effects on pregnancy outcome. A review of randomised controlled trials of routine iron supplementation during pregnancy concluded that while the trials demonstrated a positive effect on hemoglobin levels at delivery and at 6 weeks postpartum, there was very little information on a possible effect on maternal or foetal outcomes [75]. A trial of routine versus selective iron supplementation during pregnancy in Finland suggested that caesarean sections and postpartum blood transfusions were more common among the selectively supplemented group, but the authors

Table 2.3
Prevalence of mild, moderate, and severe anaemia in various populations

<i>Population</i>	<i>Sample size</i>	<i>Anaemic^a(%)</i>	<i>Hb < 10 g/ dL (%)</i>	<i>Hb < 9 g/ dL (%)</i>	<i>Hb < 8 g/ dL (%)</i>	<i>Hb < 7 g/ dL (%)</i>
Nepal, 3 months postpartum	613	81.4	28.4	13.6	6.3	2.4
Central Java, 3 months postpartum	146	71.9	15.1	2.7	2.1	2.1
Zanzibar, not pregnant	583	71.7	26.2	13.0	8.9	5.3
Nepal, pregnant	1,052	69.8	40.5	20.8	9.5	4.9
Shanghai, pregnant	826	66.2	25.3	5.5	0.8	0.2
Peru, pregnant	670	44.3	14.5	4.3	<0.1	<0.1

Source: From [107].

^aAnaemic = Hb < 11 g/dL in pregnant women and < 12 g/dL in nonpregnant women.

warned that such effects may have been due to reactions of midwives and doctors to low haematocrit values [112]. From the available evidence, no conclusions can be drawn on the effects of iron supplementation during pregnancy on its outcome for the mother.

Limited compliance with iron supplementation is thought to be a major reason for the low effectiveness of anemia prevention programmes in developing countries [113, 114]. Reasons for noncompliance include inadequate program support, insufficient service delivery (particularly unavailability of iron supplements), and patient factors such as fear of side effects [115]. Weekly rather than daily supplementation with iron appears to be promising [116–118].

In developing countries, anemia in pregnancy may only in part be due to iron deficiency. Malaria, HIV, vitamin A deficiency, and intestinal parasites may be equally important causes [119–123]. It has been demonstrated conclusively that drugs given routinely for malaria to low-parity women prevent severe anemia [124]. Intermittent presumptive treatment with antimalarials (and insecticide-treated nets) is recommended for all pregnant women in areas of holoendemic malaria [125, 126].

2.6.5 Vitamin A Deficiency and the Risk of Anemia or Infection

In children, vitamin A has been associated with sharp reductions in mortality and the severity of infections. The hypotheses underlying such an association have mainly centred on the immunity-impairing effects of vitamin A deficiency. During pregnancy, four pathways have been suggested through which vitamin A supplementation (or its precursors) may improve the maternal health status [127, 128]. First, vitamin A may decrease the risk of bacterial and viral infections during pregnancy through its beneficial effects on maternal immunity. Second, vitamin A may improve the mother's haematological status. Third, vitamin A may enhance the implantation and development of the placenta. Fourth, vitamin A deficiency has been associated with pregnancy-induced hypertension.

Vitamin A deficiency has not often been shown to be associated with infections during or after pregnancy. Circumstantial evidence suggests that vitamin A or β -carotene deficiency may be associated with puerperal infection, bacteriuria, and vaginal candidosis [129–131]. Christian and colleagues found that Nepali women with night blindness were twice as likely as normal pregnant controls to report symptoms such as lower abdominal pain, painful urination, vaginal discharge, or convulsions or swelling of the face and hands [132]. Women's reports of reproductive ill-health are unreliable, however, and should not be taken to represent medically defined illness [20, 21].

Retinol is known to be decreased by the acute-phase response of infections, even in the presence of adequate liver stores of vitamin A [133]. Therefore, vitamin A serum concentrations may be markers of infection rather than causally related to it. The randomised controlled trial of vitamin A and β -carotene supplementation in women of reproductive age in Nepal failed to find an effect of supplementation on mortality from sepsis or infection [8]. There is so far no direct evidence supporting an association between vitamin A supplementation and the risks of severe infection during or after pregnancy in malnourished populations.

Vitamin A deficiency is thought to contribute to low hemoglobin levels [128]. Vitamin A supplements given to pregnant women in Indonesia reduced the prevalence of nutritional anemia, suggesting a possible causal role of vitamin A, but this finding

was not reproduced in two trials in Malawi [134]. Among HIV-positive women in South Africa, supplementation with megadose β -carotene combined with preformed vitamin A had no detectable effect on self-reported pre- or postpartum HIV or pregnancy-related symptoms but did appear to protect against postpartum weight loss, especially among women with low serum retinol or high CD4 counts [135, 136]. In a trial of multivitamin supplementation (with or without megadose β -carotene, 30 mg/day, plus vitamin A) among HIV-positive women in Tanzania, megadose β -carotene plus vitamin A did not contribute to the improved hemoglobin levels attributed to the multivitamins [137].

There is no direct evidence linking vitamin A deficiency to the risk of obstetric haemorrhage or plausible biological pathways underlying a potential association between vitamin A or β -carotene deficiency and uterine atony, the leading cause of postpartum haemorrhage. Vitamin A and its precursors may be essential for the placenta as the placenta has been shown to have higher concentrations of retinol-binding protein and β -carotene than other body tissues [138]. In HIV-1-infected women, supplementation with multivitamins, but not vitamin A, has been shown to increase the weight of the placenta [137]. Sharma et al. reported a significant reduction in serum antioxidants, including β -carotene, in pregnancies complicated by abruptio placentae compared to normal pregnancies [139]. As with infections, however, the low concentrations of vitamin A and β -carotene may be the result of the stress of placental abruption rather than its cause.

A number of observational studies have found a higher prevalence of vitamin A or β -carotene deficiency among women with preeclampsia [140–143]. As mentioned, such observational evidence should not be interpreted as causal as decreased retinol might be a consequence of acute-phase reaction or a decrease in circulating serum protein associated with the preeclampsia. Two randomised controlled trials of fish oil supplementation (which is rich in vitamin A) in pregnant women found no significant effects on preeclampsia [144, 145].

Unlike β -carotene, vitamin A may be highly toxic when taken in high doses, and its teratogenicity is still a subject of debate [82, 146, 147]. In a large cohort study, US women consuming more than 10,000 IU of vitamin A per day were found to have a fivefold increased risk of defects associated with cranial-neural crest tissue than women consuming 5,000 IU or less [147]. However, a large case-control study found no association between periconceptual vitamin A exposure of more than 10,000 IU and malformations [148]. It is now generally accepted that the supplements suggested for malnourished women in developing countries are safe.

The most compelling potential mechanism of action of vitamin A and its precursors is through improvements of the immune and haematological status of the pregnant woman. The Cochrane Review of vitamin A supplementation during pregnancy concluded that, despite positive findings from Nepal and Indonesia, further trials are needed to provide evidence of a beneficial effect on maternal mortality and morbidity and to elucidate the mechanism behind any such effect [135].

2.6.6 Zinc Deficiency and the Risk of Haemorrhage or Infection

Zinc supplementation in infants may reduce the incidence of diarrhoea and acute respiratory infections [149, 150], and it has been suggested that zinc may therefore also influence maternal health [19]. Zinc plays an important role in many biological

functions, including protein synthesis and nucleic acid metabolism. Certain reports have suggested an association between serum zinc deficiency and dysfunctional labour, placental ablation, and haemorrhage [151–154]. Others have not found such associations [155]. Observational studies have to be interpreted with caution, however, as zinc values vary significantly by gestational age, and zinc deficiency may be a consequence rather than a cause of pregnancy complications [152].

There is no evidence to date supporting a beneficial effect on maternal health of routine zinc supplementation during pregnancy [76]. A well-conducted randomised controlled trial in pregnant women in the United Kingdom found no effect of zinc supplementation on pregnancy complications such as pregnancy-induced hypertension, abnormal labour, postpartum haemorrhage, or postpartum infection [76]. Hunt et al. found a significantly lower risk of pregnancy-induced hypertension among Hispanic women living in the United States who had received zinc supplements during pregnancy but found no effect on infections or bleeding during pregnancy [156].

There are very few trials of zinc supplementation in pregnant women with a poor dietary intake. A study in Peru showed that adding zinc to antenatal iron and folic acid supplements may increase maternal zinc status [157]. Among African American women with relatively low plasma zinc concentrations, daily zinc supplementation increased plasma zinc concentrations and birth weight [158]. The implications of improved maternal zinc status for maternal health, however, are unknown.

2.6.7 Multiple Micronutrients

As might be expected given the inconsistent and conflicting evidence described for single micronutrients, trials of multiple micronutrient supplementation during pregnancy have yet to demonstrate a clear benefit for the mother. In Mexico, multiple micronutrients did not improve hemoglobin levels any more than iron only [159]. In Nepal, multiple micronutrients plus vitamin A did not improve hemoglobin levels any more than iron and folic acid plus vitamin A [160].

Different results were obtained in two trials in sub-Saharan Africa. In Tanzania, a daily micronutrient-fortified beverage was associated with a 51% reduction in risk of predelivery anemia compared with iron and folic acid [161]. Among HIV-positive women, also in Tanzania, daily multivitamins (20 mg vitamin B₁, 20 mg vitamin B₂, 100 mg vitamin B₃, 25 mg vitamin B₆, 50 µg vitamin B₁₂, 500 mg vitamin C, 30 mg vitamin E) with or without megadose (30 mg/day) β-carotene plus vitamin A were associated with increased CD4, CD8, and CD3 counts; increased postpartum hemoglobin levels; and reduced risk of weight loss and low rate of weight gain in the third trimester [137, 162, 163].

Several trials (in Pakistan, Nepal, Bangladesh, Indonesia, and Guinea-Bissau) of routine multiple micronutrient supplementation are being conducted as a collaborative effort overseen by the UNICEF/UNU (United Nations University)/WHO Multiple Micronutrient Supplementation During Pregnancy (MMSDP) Study Team [164]. Members of this team have agreed on a formulation based on the US recommended daily allowance (RDA): 2,664 IU vitamin A, 1.4 mg thiamin, 1.4 mg riboflavin, 18 mg niacin, 1.9 mg vitamin B₆, 2.6 µg vitamin B₁₂, 70 mg vitamin C, 200 IU vitamin D, 10 mg vitamin E, 0.4 mg folic acid, 30 mg iron, 15 mg zinc, 2 mg copper, 65 µg selenium, and 150 µg iodine [165].

A lower dose of iron than recommended by WHO (60 mg) is justified on the grounds of improved absorption and utilisation when iron is combined with vitamins A, C, and riboflavin and because a 60-mg dose would require a 30-mg dose of zinc to offset a negative effect of iron on absorption of zinc. A lower dose of iron would also improve adherence by reducing side effects; severely anaemic women can be given additional iron supplementation. Calcium was omitted due to concerns over tablet size and reduction in bioavailability of iron and zinc. Magnesium was omitted because there were no strong arguments in favour of its inclusion, and vitamin K was omitted because deficiency is only likely in cases of severe malnutrition. Only one trial (Indonesia) was originally powered to measure an effect on maternal mortality, but this trial has failed to reach the planned sample size.

The Nepal team has reported no difference in hemoglobin levels between the group supplemented with multiple micronutrients and the group supplemented only with iron and folic acid [166]. Unpublished data from the Guinea-Bissau team confirmed this finding even among a group given double the RDA formulation. The MMSDP trials have been designed to permit a meta-analysis of the combined data, an approach that has not been possible with many other micronutrient trials due to heterogeneity in study design, including the type of supplementation given to the control group, selection by hemoglobin status, dosage, compliance, duration of supplementation, gestational age at enrolment, and the prevalence and severity of nutritional deficiencies, anemia, and infections.

2.8 ANTENATAL CARE

Antenatal care has long been seen as the backbone of maternal health services. The primary rationale for the widespread introduction of antenatal care has been the belief that if a predominantly healthy population is screened, early signs of, or risk factors for, morbidity and mortality can be detected and intervention implemented [167]. Antenatal care has been widely seen as an intervention that could be introduced at the community level and has been presented as among the most cost-effective strategies to improve women's and children's health [39, 53].

Reviews examining the effectiveness of formal risk assessment in pregnancy have concluded that the risk approach may not be effective in preventing maternal death or in ensuring rational use of resources [19, 46, 167, 168]. The low predictability of some of the major causes of maternal death—postpartum haemorrhage, shock, and sepsis—had been recognised as early as 1932 [169]. Evaluations of the performance of risk-scoring systems in developing countries have also shown that complications such as dystocia and postpartum haemorrhage cannot be adequately predicted [91, 93, 170]. The low predictability of such adverse maternal outcomes has led to a shift in the emphasis of safe motherhood strategies from universal antenatal care to universal access to professional delivery care [19].

The narrow focus on the failure of sociodemographic factors, physical characteristics of women, or clinical signs during pregnancy to adequately predict obstructed labour or postpartum bleeding has led us to overlook the potential wider role of antenatal care. Antenatal care clearly has value for the detection and treatment of pregnancy-related complications (i.e., malaria, severe anemia, urinary infections, hypertensive diseases)

and the prevention of potential problems (i.e., HIV, malaria) [168]. A model of antenatal care that emphasises fewer (i.e., five or less) visits and actions that are known to be effective may be as effective as the more standard multivisit model routinely practiced in middle-income countries [171]. In addition, antenatal care offers an opportunity for informing the woman about the risks associated with the pregnancy and about her options for professional care during delivery. Women seeking antenatal care may also be more likely to seek professional care during delivery [93]. Antenatal care may not be an efficient strategy to identify those most in need for obstetric service delivery, but if promoted in concurrence with effective environment of care (EOC), and delivered in skilled hands, it may become an effective instrument for better use of EOC services.

2.9 TRAINING OF TRADITIONAL BIRTH ATTENDANTS

It has long been recognised that women should not give birth alone. As it was not deemed feasible to provide access to professional medical care for all women, and as women throughout the developing world were already giving birth in the presence of TBAs, the training of such attendants appeared to be an attractive option. The training of TBAs was also in accordance with empowerment of the community, a growing paradigm during the 1970s and 1980s, and that period saw the emergence of the training of hundreds of thousands of TBAs. TBAs were expected to screen women during antenatal clinics and to provide a clean environment for giving birth. It was also hoped that they could be integrated into the health system and be recognised as official health personnel [48].

Training of TBAs has not proven to be an effective strategy for reducing maternal mortality [45, 48]. In a quasi-experimental study from the Gambia, Greenwood et al. showed that the use of TBAs may have a positive effect, but 3 years after the programme began maternal mortality remained as high as 700 per 100,000 [172]. In Bangladesh, training of TBAs had no effect on maternal mortality [173]. A comprehensive review of the role of TBAs in the reduction of maternal mortality concluded that the impact of their training on maternal mortality is low [174]. Although there has been recent renewed interest in the role of TBAs or other community-based providers in the reduction of maternal mortality, results remain inconclusive [175, 176]. It is now clear that TBAs will have little impact on maternal mortality, and that facilitating access to professional medical care would be a more effective strategy [46, 177, 178].

The reasons for the failure of TBA training are multiple [46]. There is a large variation in the skills and experience of TBAs, and some may have little more skill than holding the woman in their arms, while others master a good number of basic obstetric skills through years of experience. Resources to provide the necessary supervision and support have often been lacking [179]. Traditional knowledge is rooted in the local culture and may be difficult to change. Most important, the content of the training programme has never been clear [46].

2.10 ACCESS TO PROFESSIONAL DELIVERY CARE

The past two decades have seen a shift from community-based strategies to reduce maternal mortality to an increasing emphasis on the role of professional care at the time of delivery [45]. Historical data provide the most compelling evidence for the crucial role of obstetric care in the decline of maternal mortality. There can be no doubt that the

remarkably steep and sustained decline in maternal mortality in all Western countries from 1935 onwards is due to increased access to high-quality obstetric care compounded by major advances in obstetric techniques [49]. Factors such as the discovery of antibiotics in the 1940s, the use of blood transfusion and ergometrine during the Second World War, and safer methods for caesarean section and induction of labour since the 1950s all contributed to the extraordinary decline in maternal mortality in Western countries [49]. While in the 1920s some Western countries were still at levels of maternal mortality currently seen in developing countries, improved delivery care caused their levels to decline to as low as 20 deaths per 100,000 in a period as short as 30 years. The main obstacles to increasing the expansion of care is the shortage of skilled providers and health care infrastructure, substandard quality of care, and reluctance of women to use maternity care because of high cost and other factors [180, 181].

Support for the crucial role of obstetric care is also provided from a current example in the United States. Members of a religious group who received no antenatal care and who delivered at home without trained attendance had a maternal mortality ratio about 100 times higher than the statewide rates [182]. Although the numbers of maternal deaths were small, the maternal mortality ratio of 872 deaths per 100,000 live births among Faith Assembly members was significantly higher than the ratio of 9 deaths per 100,000 among the remainder of the population. These findings suggest that, even in the United States, absence of skilled obstetric care greatly increased the risk of maternal death.

How to best organise maternity services to ensure that all women have access to highly skilled care for childbirth remains a matter of debate. As shown in the Netherlands, hospital delivery for all women is not necessary to achieve very low levels of maternal mortality. Similarly, the Swedish success in the late 19th century was a result of the training of professional midwives in the systematic use of aseptic techniques, while hospital births were uncommon [183]. Doctors, in fact, have often been shown to be the cause of high levels of maternal mortality [49, 85]. In Egypt, where a large proportion of the women deliver in a hospital, more than half of the maternal deaths have been attributed to inappropriate management by obstetricians (Table 2.4) [184]. Health care systems have been said to contribute to rather than to prevent maternal mortality

Table 2.4
Avoidable factors for 718 maternal deaths in Egypt (1992–1993)

<i>Avoidable factors</i>	<i>Number of deaths (%)</i>
No or poor antenatal care	239 (33)
Delay in seeking medical care	304 (42)
Unwanted pregnancy	36 (5)
Substandard care from general practitioner	87 (12)
Substandard care from obstetricians	334 (47)
Substandard care from traditional birth attendant	84 (12)
Lack of drugs, supplies, and equipment	15 (2)
Lack of blood bank	15 (2)
Lack of transportation	28 (4)
No avoidable factors	54 (8)

Source: Adapted from [180].

[185]. Encouraging women to give birth in health centres where a team of midwives and midwife assistants provides delivery care is probably the most effective and efficient way of ensuring access to a skilled attendant in poor countries [180].

Direct evidence from developing countries that increased access to obstetric care can reduce maternal mortality is scarce. The few quasi-experimental studies addressing the potential role of professional care in the reduction of maternal mortality in developing countries have not been able to provide conclusive evidence. The findings from a large community-based study in Matlab, Bangladesh, for example, which provided support for professional midwifery care in the community, have been questioned repeatedly [186, 187]. Other studies either had very low sample sizes or were poorly designed [172, 188–192].

The available evidence suggests that low mortality can be achieved with a variety of different models of health care. Rural China, for example, reached low levels of maternal mortality despite nonprofessional attendance at home births, while Malaysia reached low mortality by training a large body of professional midwives to attend home deliveries [178]. Other countries such as Sri Lanka have reached low levels of mortality in the presence of nearly universal institutional delivery rates [19]. What is certain is that all countries that have successfully managed to make motherhood safer have done so within a context of universal financial and geographical access to skilled care and with a backup system of hospital care for those requiring higher-level referral [2, p. 68; 45].

One of the key messages emerging from the Safe Motherhood technical consultation held in Sri Lanka in 1997 was that maternal mortality reduction could not occur in the absence of a change in the political environment around women's health. Reductions in maternal mortality in Western countries would also not have been possible without a political commitment to do so. This commitment involves the necessity to document the magnitude of the problem, the recognition that most maternal deaths are avoidable with the currently available technology, and most importantly, the active mobilisation of qualified health professionals and the community [48]. Without a willingness of decision makers to take up their responsibility and health providers to be held accountable for their actions, the decline could not have taken place. WHO also emphasises that national commitment at a high level and by health care providers will be necessary to ensure that implementation of the actions required by the mother–baby package will be feasible and sustainable.

2.11 SUMMARY AND CONCLUSIONS

Maternal mortality is one of the statistics showing the largest degree of disparity between developed and developing countries. Poverty contributes to this disparity but does not explain it completely as countries with similar levels of socioeconomic development have widely ranging levels of maternal mortality.

Historical data from Western countries provide the most compelling evidence regarding which strategies will most likely contribute to the decline of maternal mortality in less-developed countries. Sustained reductions in maternal mortality will be possible if modern high-quality obstetric care will be made available to all women through a system of professional midwifery and referral hospital care in a context of political commitment and accountability of health providers. There is very little evidence from the

industrialised world supporting the direct role of strategies involving family planning or nutrition in the improvement of the health of pregnant women.

Nutritional supplementation of pregnant or reproductive age women has been proposed as a new strategy for the reduction of maternal mortality in developing countries. The suggestion for a possible role for nutritional supplementation has largely emanated from the beneficial effects micronutrient supplementation may have on child survival. The evidence so far in support of such a strategy in pregnant women is scant, except for calcium supplementation, which has been convincingly shown to be associated with a reduction in the incidence of preeclampsia. Further research is needed before micronutrient supplementation can be introduced as a complementary strategy to increasing the access to and quality of professional obstetric care for all women.

The adoption of a strategy of intrapartum care in health centres is a top priority needed to reduce maternal mortality by two thirds by 2015, the Millennium Development Goal for maternal health [45, 191]. The goal of reducing maternal mortality is linked with other Millennium Development Goals discussed in other chapters of this book, including poverty reduction, women's empowerment, child survival, and infectious diseases [191].

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