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SEVERE MATERNAL MORBIDITY IN ANGOLA

Studies on postpartum haemorrhage, jaundice and clinic-based audit

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“My work consists of two parts; that which I present here and everything that I have not written. It is this latter part that is the important ...”

Ludwig Wittgenstein in a letter to a publisher

ABSTRACT

Background: Angola has recently ended a long period of warfare, which has resulted in an almost complete collapse of public health. In Luanda, the capital, some 70,000 deliveries take place in public facilities. Maternal morbidity and mortality is among the highest in the world. Postpartum haemorrhage is the dominant cause of death. Jaundice of unknown aetiology and obstructed labour with uterine rupture are also common. The obstetric network in Luanda involves a system of referrals of emergencies from 10 peripheral birth units to two central hospitals.

Objectives: The aim of these studies is to analyze part of the mortality, partially to elucidate the prevailing pathology and partially to develop safer routines in obstetric care with the focus on avoiding and treating complications and in referral of obstetric emergencies. We wanted to test a new disposable device, Uniject™ for routine administration of oxytocin as part of active management of the third stage of labour to reduce post partum bleeding. We wanted to understand the aetiology of jaundice among pregnant women and, by clinical audit, to assess the quality of care by studying the “avoidability” of uterine ruptures and time delay and partograph quality in the referral situation.

Methods: In a comparative prospective study we compared post partum blood loss of 782 women with expectative management to 814 women with active management of the third stage of labour (AMTL), while evaluating the effect of Uniject™. A prospective case-control design was used to study jaundice aetiology and its clinical consequences. Twenty pregnant women were compared to 40 controls regarding malaria, HIV, hepatitis A, B, C, E, maternal and neonatal outcome. During two periods, women referred from three peripheral units were studied regarding travelling time and waiting time to see a midwife and to see a doctor, partograph quality, clinical outcome and accordance of diagnosis at the two levels.

Results: AMTL reduced postpartum blood loss by almost 50% and women with a severe blood loss of > 1000 ml were reduced by 80%. Uniject™ was well tolerated. Malaria and hepatitis E were the most common causes found among the pregnant women with jaundice in the study and differed significantly from controls. Around 2/3 of uterine ruptures were judged to be avoidable at the hospital level. All parameters studied in the referral system showed a dramatic improvement in the second period compared to the first.

Conclusions: AMTL should be introduced as clinical routine. Uniject™ can be recommended for logistic and epidemiologic reasons. To minimize the risk for jaundice among pregnant women, malaria prophylaxis has to be implemented as routine among pregnant women. Hepatitis E reflects the basic sanitary conditions, which need to be improved with the emphasis on clean water, separated from sewage. The conclusion regarding avoidability yields information for future education and improvements regarding the deficiencies disclosed. The dramatic improvement in the referral study shows how audit as a means of studying current practices can lead to better quality of care.

Key words: active management of third stage of labour, Angola, audit, jaundice, malaria, hepatitis E, postpartum haemorrhage, uterine rupture, waiting time.

LIST OF PUBLICATIONS

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals I-IV.

- I. Strand RT, da Silva F, Jangsten E, Bergström S. Postpartum hemorrhage: a prospective comparative study in Angola using a new disposable device for oxytocin administration. *Acta Obstetrica et Gynecologica Scandinavica* 2005; 84: 260-265.

- II. Strand RT, Ranque-Franque M, Bergström S, Weiland O. Infectious aetiology of jaundice among pregnant women in Angola. *Scandinavian Journal of Infectious Diseases* 2003; 25:6-7.

- III. Strand RT, Tumba P, Sesa I, Niekowal J, Bergström S. Audit of cases with uterine rupture: a process indicator of quality of obstetric care. *Submitted to Tropical Medicine and International Health*

- IV. Strand RT, Campos , Paulsson G, Campos AP, de Oliveira J, Bergström S. Audit of referrals of obstetric emergencies in Angola – a tool to assess quality of care. *Submitted to International Journal of Gynecology and Obstetrics*

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ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
AIDS	Acquired Immuno-Deficiency Syndrome
ALT	Alanine Amino Transferase
AML	Active Management of Labour
AMTL	Active Management of the Third stage of Labour
ANC	Antenatal Care
AST	Asparate Amino Transferase
AVH	Acute Viral Hepatitis
BW	Birth Weight
CAOL	Coordenação do Atendimento Obstétrico da Provincia de Luanda
CAPEL	Coordenação da Assistência Pediátrica em Luanda
CI	Confidence Interval
CS	Caesarean Section
ELISA	Enzyme Linked ImmunoSorbent Assay
EOC	Essential Obstetric Care
EPI	Extended Program of Immunisation
<i>et al</i>	Et alii (latine) “and others”
FHF	Fulminant Hepatic Failure
GDP	Gross Domestic Product
GPM	Grand multipara
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HBsAg	Hepatitis B surface anti-gene
HCV	Hepatitis C Virus
HEV	Hepatitis E Virus
HIV	Human Immunodeficiency Virus
HNAE	Hepatitis non A-E
IHCAR	Division of International Health
IMCI	Integrated Management of Childhood Illness
IMF	International Monetary Fund

IU	International Units
MAN	Maternidade Augusto N'Gangula
MLP	Maternidade Lucrecia Paím
MM	Maternal mortality
MMR	Maternal mortality Ratio
MPLA	Movimento Popular de Libertação de Angola
MSF	Medecins Sans Frontieres
nd	no data
OMA	Organização de Mulheres de Angola
OR	Odds Ratio
p	probability
P	Plasmodium
PATH	Program for Appropriate Technology
PP	Primi-para
PPH	Post Partum Haemorrhage
PROM	Premature Rupture Of Membranes
RCT	Randomized Controlled Trial
Sida	Swedish International Development Cooperation Agency
SD	Standard Deviation
SPP	Sala de Partos Periférica
STD	Sexually Transmitted Disease
TBA	Traditional Birth Attendant
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
UNITA	União Nacional para a Independência Total de Angola
UR	Uterine Rupture
USA	United States of America
VBAC	Vaginal Birth after Caesarean section
WFP	World Food Program
WHARC	Women's Health and Action Research Centre
WHO	World Health Organization

1. INTRODUCTION

1.1 Background

Life expectancy at birth has increased to a world wide average of 64 years compared to 48 years around 1960 (UNICEF 1997 and 2003). This is mainly a reflection of the dramatic improvement in child survival. Mortality among children under five years of age has been reduced by more than half between 1960 and 1999, from 197 to 82 deaths per 1000 live births (Ibid). At the same time the previous apocalyptic scenarios of population explosion have almost obliterated. There seems to be a global adaptation to the figures above that has affected the total fertility rate. This has dropped from 5.0 births per woman by the end of the 60s to 2.7 in 2001. A further reduction is expected to 2.3 in 2025 (UNICEF 2003). With 2.1 children per woman, a population is estimated to reach a steady state.

Maternal mortality, however, has not shown a similar reduction during the same period. The first estimates of world wide maternal mortality was made in the 1980s and indicated that some 500,000 women die each year from pregnancy- related causes. Contrary to the trends above, the MMR figure shows an increase. The present estimation is close to 600,000 (WHO/UNFPA/UNICEF/World Bank 1999).

Every day, year after year, some 1,600 women suffer this kind of death. The tragedy is aggravated by the fact that these women rarely die from diseases, “but during the normal, life-enhancing process of procreation”. It is difficult to avoid making comparison with other calamities. Every plane crash in the world is reported in most media and the whole world seemed united and chocked by the brutality of the tsunami in South East Asia, Dec in 2004. In spite of the magnitude in number, the suffering of pregnant women seldom gets the attention of newspapers or TV stations, falling into our collective oblivion. Their death is simply no news. Although mourned by their families and children, their fate is not spectacular enough for our common consciousness. The death of one mother is a tragedy; the death of 600,000 becomes statistics.

Pregnancy complications that do not lead to death are more or less forgotten in statistics. These can give severe and lifelong disabilities, e g urine incontinence or fistula. For every obstetric death, there are up to 30 women with complications that will affect them for the rest of their lives (World Bank 1999).

The poor health and nutritional status of the women and the poor quality obstetric care that contribute to their deaths compromise the health and survival of the children they leave behind. Nearly two-third of the world’s yearly 8 million infant deaths result largely from poor maternal health and hygiene, insufficient management of delivery and lack of essential care of the newborn during the neonatal period, before one month of age. The optimistic figure above regarding decline in the infant mortality is largely the effect of immunization campaigns and better control of diarrhea diseases. By contrast, early neonatal mortality rates have changed (WHO/UNFPA/UNICEF/World Bank 1999). Further, among the motherless children who survive the first weeks of life, more than half die within one year and more than 90% before five years of age (Harrison, Bergström 2001).

Maternal disorders represent around 2% of the total “Global Burden of Disease” (Murray, Lopez 1997). Perinatal disorders are now the largest single category of loss of healthy life years in the world.

The technical means of averting almost all maternal deaths have been available for more than half a century. Modern obstetric care has almost extinguished maternal mortality in most high income countries. Were the same level of care implemented world wide, much of the perinatal deaths and complications would certainly also be reduced. See Table 1.

The reason why maternal mortality stands out as a health indicator so far mostly immune to change, is a sad mixture of poverty (lack of resources), mismanagement (wrong allocations regarding cost-effectiveness) and lack of political commitment.

1.2 Definition of maternal mortality

Maternal mortality is defined by the WHO as “the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration or site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental cause”(WHO 1985). This indicates that a fatal complication from an induced abortion is regarded as a maternal death, since it has been caused by the “management” of a pregnancy.

1.3 Maternal mortality, indicators

Maternal death is the ultimate negative outcome of a pregnancy and should be registered in some kind of local health statistics. These often fail in reporting deaths in relation to abortions, ectopic pregnancies and postpartum complications. One way to get around this underreporting is to address the representatives of the population, who most likely never will forget the death of a relative. Researchers may use the so called Sisterhood Method for systematic interviews in order to calculate the “true” figures.

The magnitude of maternal mortality is mostly expressed by four different indicators, which are here presented briefly

1. *Maternal mortality ratio* (MMR) is the most commonly used. This is defined as the number of deaths from pregnancy related causes per 100,000 live births. Similar to the numbers above, these figures vary considerably between different parts of the world. Underreporting and misreporting often make MMR figures inexact. The worldwide MMR average is estimated to around 400.

Sweden now has an MMR of less than 5. The decline has been possible to trace from the middle of the 18th century when MMR was around 1000 (Högberg, Wall *et al* 1986). This is still not an uncommon figure for several of the poor countries today. MMR in Angola was estimated to 1,300 in 1995, but, due to the uncertainty in these figures, it could be as high as 2,100. (WHO/UNICEF/UNFPA 2001). WHO estimates that for every 100,000 live births in Africa there are about 1000 maternal deaths, compared with 276 for Asia, 190 for Latin America and 10 for Europe (Hill, AbouZhar *et al* 2001).

Sri Lanka offers an example of a significant reduction of MMR during a short period of time. At the time of World War II, MMR was more than 1500. Parallel to an implementation of a nation wide system of health facilities where obstetric

complications could be treated, the spread of midwifery skills and family planning, the MMR decreased to 239 within ten years and to 30 today. China, Cuba and Malaysia give similar evidence of the effectiveness of health care interventions, where a system of referral of obstetric complications is crucial. (WHO/UNFPA/UNICEF/World Bank 1999)

2. *Maternal mortality rate* is an indicator, which by its definition is linked to fertility and expressed as the number of maternal deaths per year per 100,000 women aged 15-49 years. A successful program of family planning that leads to a reduction in pregnancy rate will also lead to a decrease in maternal mortality rate, while it does not necessarily have to affect the MMR.

3. *Lifetime risk of maternal death* is perhaps the statistic expression that most dramatically and intuitively depicts the abysmal difference in living (and death) conditions in the world. In some of the least developed countries life time risk may be as high as one in ten, whereas in Scandinavia it is in the order of 1 in 10,000 (Lindstrand, Bergström *et al*). The risk increases with the number of pregnancies and depends of the MMR.

4. *Proportion of all deaths among women of reproductive age*. Although some 25% of all fertile women in the world live in developed countries, only 1% of maternal deaths take place in these countries. So the vast majority – 99% - occur in the less economically developed part of the world. Maternal mortality is also relatively more common in the less developed countries and thereby contributes proportionally more to the “burden of disease” in those parts of the world. In Bangladesh, India and Indonesia for example, more than one out of five deaths among women in childbearing age are related to pregnancy, while in Sweden and the United States less than 0.5% is a maternal death (Maine 1991).

1.4 Causes, direct and indirect

Direct causes of maternal death are usually distinguished from *indirect causes*.

Direct causes are directly conditioned by complications during pregnancy, delivery or the postpartum period (42 days), including abortion complications. Direct causes can thus not occur without pregnancy. The most common direct causes of maternal death are haemorrhage, complications to abortions (often illicit), hypertension/eclampsia, obstructed labour (including rupture of the uterus) and infections. See Figure 1.

Indirect causes of obstetric death are due to conditions aggravated by pregnancy. In developing countries around one fifth to one quarter of maternal deaths are classified as having indirect causes. The most common are malaria, HIV/AIDS, pulmonary tuberculosis, hepatitis, anaemia, sickle cell disease and rheumatic heart disease (Maine 1993).

An individual death is, however, not necessarily due to one single direct cause, but of a combination of causes, some may be direct, others indirect. This often makes allocation of death by causes problematic. (Harrison, Bergström 2001).

Table 1. The diseases estimated to cause most loss of healthy life years in the world, 2001.

Diseases or disease group	% of healthy life years lost	Millions healthy life years lost	Millions of deaths
1. Perinatal disorders	7%	92	2.5
2. Lower respiratory infection	6%	91	3.9
3. HIV/AIDS	6%	88	2.9
4. Unipolar major depression	5%	66	0.0
5. Diarrhoea diseases	4%	62	2.0
6. Ischemic heart disease	4%	59	7.2
7. Cerebro-vascular diseases	3%	46	5.5
8. Malaria	3%	42	1.1
9. Road traffic accidents	3%	38	1.2
10. Tuberculosis	3%	36	1.6
11. Maternal disorders	2%	31	0.5
12. Chronic obstr pulm diseases	2%	30	2.7
13. Congenital malformations	2%	28	0.5
14. Measles	2%	26	0.7
15. Violence	1%	20	0.5
16. Self inflicting injuries	1%	20	0.8
17. Alcohol use disorders	1%	20	0.1
18. Protein energy malnutrition	1%	17	0.3
19. Osteoarthritis	1%	16	0.0
20. Schizophrenia	1%	16	0.0
21. Falls	1%	16	0.4
22. Diabetes mellitus	1%	15	0.9
23. Cirrhosis of the liver	1%	15	0.8
24. Asthma	1%	15	0.2
25. Bipolar disorders	1%	14	0.0
26. Pertussis	1%	12	0.3
27. Alzheimer/ dementia	1%	12	0.4
28. STD (except HIV)	1%	12	0.2
29. Anaemia	1%	12	0.1
30. Drowning	1%	12	0.4
31. Cancer in respiratory tract	1%	11	1.2
Total	100%	1467	56.6

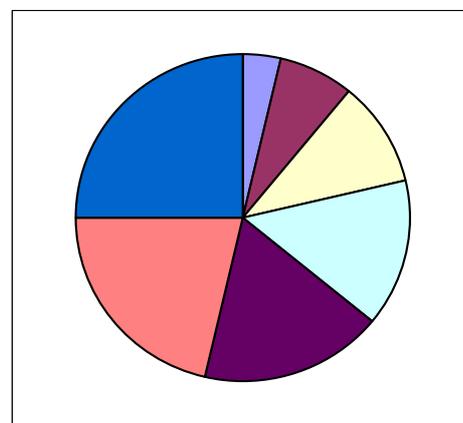
Source: World Health Report, WHO 2002.

1.5 Determinants of severe maternal morbidity and mortality

The background of maternal morbidity and mortality is of course very complex and reflect a combination of socio-economic and health factors. The determinants include malnutrition, anaemia, low age and too early marriages, poverty and illiteracy, harmful practices, denied human rights and denied access to family planning and maternal healthy services. In Figure 1 these underlying threats are illustrated by arrows while the pieces of the circle show the approximate world wide proportions of maternal deaths by causes.

Figure 1. Medical causes and background factors of the global 585,000 pregnancy related deaths yearly (Liljestrand 1999).

- Malnutrition/anaemia →
- Too early marriage →
- Poverty and illiteracy →
- Harmful practices →
- Denied equal rights →
- Denied access to Family Planning & Maternal Health Services →



Haemorrhage 24.8%, Sepsis 14.9%, Hypertensive disorders 12.9% Obstructed labour 6.9% Unsafe abortions 12.9% Other direct causes 7.9% Indirect causes 19.8%

The most important determinant in Figure 1 may suggest that the factors reflecting the overall welfare and equity in a society are more crucial to the health of its people than the quality of medical service, something that has been advocated by some thought-provoking scholars (McKeown 1979; Illich 1975 and Bunker 2001). They focus on the parallel increase of life expectancy and general welfare.

In the history of maternal care there are, however, indicators suggesting that economic development is not the only and definite answer. The historically early decline in Scandinavian and Dutch maternal mortality is often associated with the nation wide implementation of skilled birth attendance (educated midwives) and aseptic techniques for home and institutional births. It is true, that during the same period, there was a gradual overall increase in living conditions and it may thus be difficult to sort out the education of midwives as the single most important determinant in the complex web of an historic process. In England, by contrast, there was no substantial decline in maternal mortality from 1840 to around 1930, while mortality by several other causes declined as general living conditions improved. It was not until the mid-1930s that England, most of Europe and North America experienced a dramatic reduction in maternal mortality, after

which it has no longer been regarded as a major public health problem. This decrease can to a large degree be explained by the introduction of antibiotics, banked blood, transfusions and safer surgical techniques for Caesarean sections, but also by a decline in the virulence of streptococcal infections (Loudon 2000).

An indirect indication of the importance of modern obstetric care is offered by the example of a religious community in the USA, called the Faith Assembly. Members of this community do not make use of modern care, not even in emergency situations. Although relatively prosperous, well educated and well fed, MMR among Faith Assembly women was more than 100 times higher than for the US population in general in 1982, with 872 maternal deaths per 100,000 live births in the community (Kaunitz, Hughes *et al* 1984). This figure is even higher than in contemporary Bangladesh.

In fact, we will never know for certain (beyond hypothesis and indications) whether improvement of medical care, rising living conditions or ecological changes like virulence of infectious diseases, contributed most to the documented decline in maternal mortality. Assuming a synergy of factors seems to offer the most prudent stand point.

1.6 The Safe Motherhood Initiative

In 1985 Rosenfield and Maine asserted that pregnancy related deaths among women in developing countries were a neglected area in medicine, obstetrics and in public health in general. With the emphasis on children, maternal and child health programs had more or less forgotten the mother. Without programs addressing the problems of pregnancy and childbirth, maternal death was not likely to be reduced.

At the international conference in Nairobi 1987, The Safe Motherhood Initiative was launched, and several international conferences and proclamations thereafter have focused on the survival of mothers. In Nairobi, the overall aim of reducing the maternal mortality by 50% by the year 2000 was agreed upon. This was not achieved.

The Safe Motherhood Initiative agreed that interventions to reduce maternal deaths cannot be implemented as so called vertical programs, without relation to other health issues and social and economic development.

“Maternal mortality is not primarily a health disadvantage but a social disadvantage. Safe motherhood interventions should be implemented in the context of broader health programmes, including nutritional advice and micronutrient supplementation, child survival and development, immunization, safe water and sanitation, family planning, the avoidance of unwanted pregnancies, the prevention and the prevention and control of malaria and of HIV/AIDS and other sexually transmitted diseases” (WHO/UNFPA/UNICE/World Bank 1999)

The “holistic” list above may seem paralyzing. Since maternal mortality depends on such an intricate web of background factors, it is indeed difficult not to be overwhelmed and not know where to begin. The Safe Motherhood Initiative has been criticized for this lack of focus (Maine, Rosenfield 1999). In its ambition not to miss out on anything, WHO has included family planning, antenatal care, clean/safe delivery, essential

obstetric care, primary health care and equity for women and safe motherhood as a human right in its program (WHO1993).

1.7 The strategies that failed

In retrospect it may seem surprising but only twenty years ago not only was the magnitude of the maternal mortality uncertain but so were also the strategies for a reduction. Common sense and good reasoning offered more guidance than evidence based medicine which still was a rather esoteric concept. The spirit of the Alma Ata Conference (1977) with its emphasis on public health and community medicine still dominated the agenda and so it was natural to support the work of traditional birth attendants (TBAs). Much energy (and money) was put into educating these women with cultural competence and closeness to the women they were serving. It was simply not known then, but gradually it became clear that maternal survival could hardly be reduced by this approach. Somehow it was not taken into consideration that the TBAs did not have the crucial competence of life saving practice in emergency situations. A subsequent meta-analysis shows that there is no statistically significant or clinical rationale supporting the effect of TBAs on the reduction of maternal mortality (Sibley, Sipe *et al* 2002). And it could also later be estimated that around 15% of women develop potentially life threatening complications during delivery and need some kind of medical assistance. Without access to a major surgical intervention some 1%-3% of parturient women will die (Murray, Lopez 1998).

1.8 Foreseeing the undesirable: the concept of “risk”

Another miscalculation was linked to the concept of risk. It became important to classify women at antenatal care visits into risk categories with the logical assumption that a high risk woman was more likely to suffer some kind of complication. Since big categories like “multiparous women” and “primigravidae” often constituted a large proportion of all pregnant women, the concept did not offer much of a guideline. It later became clear that most women with high risk gave birth without complications and that most complications occurred among low risk women. Most maternal complications cannot be neither predicted nor prevented, save unsafe abortions (Maine, Rosenfield 1999).

The majority of women with severe complications are classified as “low risk” during antenatal care. Complications often evolve rapidly and need prompt professional treatment. The most common of the life threatening complications is postpartum haemorrhage, which mostly develops rapidly without previous warning signs. Time and functioning Emergency Obstetric Care (EOC) are important aspects in saving lives. The times for complications to evolve are approximated in the table below.

Complication	Hours	Days
Haemorrhage, postpartum	2	
Haemorrhage, antepartum	12	
Ruptured uterus		1
Eclampsia		2
Obstructed labour		3
Infection		6

Table 2. Estimated average interval from onset to death for major obstetric complications, in the absence of medical intervention (Maine 1987).

1.9 Essential Obstetric Care

One of the lessons that can be learned from international experience for Safe Motherhood is that the crucial level to save lives is the hospital, where emergency obstetric care can be offered. If this area of “last delay” cannot assist the mother, to whom should she turn?

Emergency obstetric care is divided into Basic and Comprehensive, with the difference being the capacity to administer blood transfusions and perform Caesarean sections in the latter, see Table 3. This is what defines a well equipped hospital from other medical facilities. The logistics and expertise of blood storage is needed and the service of an operation theatre with personnel, including an anaesthesiologist available around the clock.

Table 3. Essential Obstetric Care.

Basic EOC Services	Comprehensive EOC Services
1. Parental antibiotics	
2. Parental oxytocic drugs	
3. Parental anticonvulsants	
4. Manual removal of the placenta	
5. Removal of retained products (vacuum aspiration)	1 – 6. All of those included in Basic EOC
6. Assisted vaginal delivery	6. Assisted vaginal delivery
	7. Surgery (Caesarean section)
	8. Blood transfusion

The interventions included in Essential Obstetric Care address the seven major, direct obstetric complications, constituting some 80% of the most severe morbidity leading to maternal mortality worldwide. Interventions should ideally have a sound support on three levels: (1) the medical safety and efficacy; (2) field intervention safety and efficacy; and (3) effectiveness and cost of large scale implementation. With studies from Vietnam and Bangladesh supporting the implementation of EOC in field settings, the two first levels seem to have satisfied the demands from hard core evidence based advocates (Fauveau, Stewart *et al* 1991; Maine, Akajalin *et al* 1996).

1.10 The severely ill mother: the three phases of delay may imply a maternal death

The concept of “the tree delays” was developed to analyze the different obstacles that threaten to postpone treatment of women with obstetric complications (Thaddeus, Maine 1994).

The first phase of delay involves the decision to seek care. Recognition of illness is defined by the patient’s view, not by criteria defined by health workers. Before deciding to seek treatment, the woman needs to be aware that she has a condition requiring special attention. One purpose with the ANC education is to inform the women about signs of abnormality and danger. Otherwise fever, prepartum haemorrhage or prolonged

labour, for example, may be seen as something natural and inevitable and not recognized as something requiring professional observation. The status of the woman also affects her help seeking behaviour. As an expression of her low esteem, her husband may be reluctant to allocate the necessary family resources associated with a delivery complication. Sex discrimination as a contributory factor to maternal mortality has been largely ignored (Royston, Armstrong 1989).

The second phase of delay concerns transport, the time from the decision to seek medical help to reaching the facility where this assistance is expected. Distribution of facilities, distance and non-existent public transports are the main problem in a situation where there is “too far to walk”. In some countries maternity waiting homes have been provided for women, where they can stay near the hospital the last few weeks of pregnancy.

The third delay is perhaps not as much a matter of time delay as it reflects the receiving of adequate treatment. At the end of the referral line, the woman should expect to receive essential obstetric care (EOC), see below. Instead, insufficient and unqualified staffs, mismanagement of patients, unavailability of blood and shortage of essential drug and equipment constitute the third delay at many places. Often there is a blaming of the patient for seeking care too late, obscuring that the health care system often fails the patient. The levels of delay interconnect in the way that low quality of care at the third level and long distance and troublesome transports at the second level will affect the decision making at first level.

1.11 Indicators of quality of care

Indicators can be divided into three different categories; Structure, Process and Outcome. (Donabedian 1988). Standards within each of these categories have to be agreed upon to allow for comparisons.

Structure indicators address environment, human, financial and physical resources, like the number of facilities offering Essential Obstetric Care to a population of 500,000. *Process* indicators apply to service provision, interaction and collaboration, training and management, while *outcome* indicators refer to results, like maternal mortality (Kwast 1998). Maternal mortality can be regarded as the endpoint indicator, the overall goal is of course to reduce both the number of deaths and the MMR. This final outcome of obstetric care is, however, dependant on a variety of factors, beyond the power of medical care, see Figure 1. These background conditions affect in various ways the women’s likelihood of becoming pregnant, the ability to seek care, the trust in medical institutions and so forth. In Luanda these conditions changed dramatically year by year during the domestic war, with a heavy influx of refugees to the city. With this added pressure on the already overburdened and undersupplied public facilities, slum areas and extreme poverty spread rapidly and it became clear that MMR was too blunt an instrument for assessing quality of obstetric care.

International experience from similar settings has also recognized MMR as an often inappropriate indicator for estimating quality of obstetric care. Instead more attention has been given to process indicators (Pathak, Kwast *et al* 2000; Graham, Wagaarachchi *et al* 2000). It would be simplistic to regard outcome and process indicators as competitive, but there are situations where one is more useful than the other. Outcome

measures are more appropriate for international comparison. As the perspective narrows, to hospitals or departments, process measures become relatively more useful (Mant 2001).

By focusing on the process, it becomes possible to analyze the different types of delays and the links in the chain of health care services. Examples of process indicators are waiting time, “met need”, percentage of Caesarean sections, percentage of birth by skilled attendant, percentage of births at health facility, case fatality etc. Met need is calculated from the expectation that 15% of parturient women need some kind of medical assistance. Case fatality is the percentage of women that die from a specific cause. This indicator makes it possible to evaluate the efficacy of alternative treatments. During the latter part of the 90s, a new protocol for the treatment with magnesium-sulphate was introduced in Luanda to treat women with eclampsia. After this change a dramatic decline in case fatality could be demonstrated (Tomé, da Silva 1998).

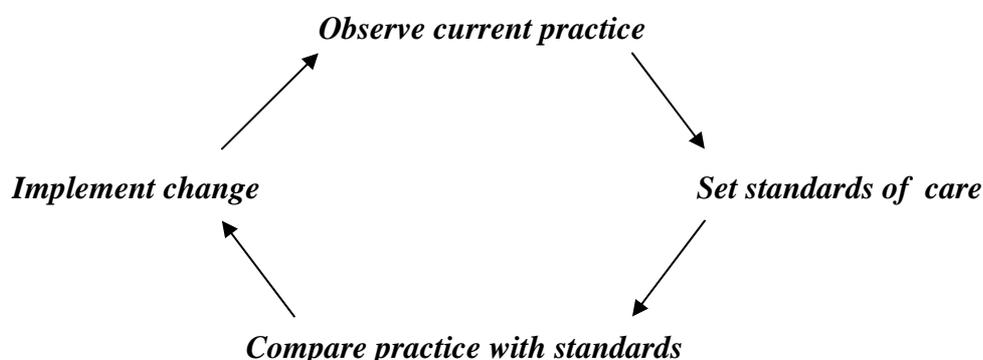
1.12 Audit – a key factor for improvement of obstetric care

Audit is often defined as “The systematic and critical analysis of the quality of medical care, including the process used for diagnosis and treatment, the use of resources and the resulting outcome and quality of life for the patient” (Crombie, Davies *et al* 1977)

The term has long been used in the banking sector, denoting a review by an outsider directed at discovery of mistakes and for the prevention of fraud. (Bergström 2001)

This “re-viewing” is a first cousin to “re-search” and has been adopted as a mean of action-oriented research in medicine. With the critical aim of disclosing and mismanagements and improving quality, focus is often on “avoidability” issues. Clinical practice should be compared to a set of standards. Mistakes or substandard treatment revealed during one audit, should ideally be analyzed and prevented not to re-occur in the future. In other words, the feature of an audit is similar to a “before-and-after” study. Since audits need to be repeated on a regular basis, the process has also been represented by the circle, see below, Figure 2.

Figure 2. The audit circle.



Participation and interaction by all personnel involved in obstetric care were essential. The disclosure of shortcomings may be perceived as threatening, since nobody wants to be associated with substandard care or – even less – a maternal death. A culture of self criticism and confidentiality is important. The conclusions should not be used for individual disciplinary action, but for making recommendations for future improvements (Ronsmans 2001). In order to avoid the blaming inclination of audit, an alternative is audit of “near miss”. This has a more positive connotation. The woman survived. There may be room for appraisal and the woman can contribute with her own version of what happened.

1.13 Post partum haemorrhage

Postpartum haemorrhage (PPH) is the most common single cause of maternal mortality, followed by sepsis, eclampsia, obstructed labour and complications to illicit abortions (Kwast 1991; Liljestrand 1999).

It is estimated that, globally, around 150,000 maternal deaths may be caused by PPH each year (WHO 1994). Field studies in low-income countries and in affluent settings on the prevalence of PPH have demonstrated figures in the range of 10-20% (Prendiville *et al* 1988; McDonald *et al* 1993). Studies in Malawi and in the Philippines, indicate a prevalence of slightly less than 10% (Bullough *et al* 1989; Demographic and Health Surveys 1994), which is also estimated to be the global average figure (WHO 1994).

PPH is defined by WHO as a bleeding \geq 500 ml from the genital tract during the first 24 hours after delivery (WHO 1990). This is an arbitrary limit since a blood loss of 500 ml may be clinically insignificant in countries with low prevalence of pregnancy anaemia, while in many low-income countries, with a high prevalence of severe anaemia, the same blood loss may be life-threatening.

Table 4. Conditions that predispose to postpartum haemorrhage (WHO 1990).

Predating pregnancy	Arising before birth	Arising during labour
Primiparity	Placenta praevia	Induced labour
Grand multiparity (+5)	Placenta praevia with previous Caesarean section	Prolonged / obstructed labour
Idiopathic thrombocytopenic purpura	Abruptio placenta	Forceps delivery
Von Willebrand's disease	Multiple pregnancy	General anaesthesia
Anaemia	Previous 3 rd stage compl.	Epidural anaesthesia
	Intrauterine death	Chorio-amnionitis
	Eclampsia	Disseminated intra-vascular coagulation
	Hepatitis	

Active management of the third stage of labour (AMTL) involves a combination of prophylactic administration of oxytocics, early cord clamping and controlled traction of the cord (WHO 1996). Most of the documentation from the advantages of AMTL has emanated from well-organised units in affluent societies (Prendiville *et al* 1988; Harding *et al* 1989; Begley 1990). Data is limited regarding the applicability of this routine in settings with overburdened delivery units, scarcity of staff and insufficient provision of drugs.

Maternal mortality in Angola is extremely high, as stated in the introduction. In the capital, Luanda, statistics are limited to institutional deliveries, which account for around half of the births in Luanda province. The institutional MMR for 1999 was 888 per 100,000 live births (Estatística anual, CAOL). In 1998 PPH was the cause of death in 21% of the 285 maternal deaths registered in the biggest maternity institution in the city, MLP, a university hospital with about 17,000 births annually.

Due to scarcity of resources no oxytocin was given as a routine in post partum care. Against this background AML represents a potentially valuable approach to improve postpartum care. Such an expected improvement might be further enhanced by the choice of method for oxytocin administration. The Program for Appropriate Technology in Health (PATH) has developed the UniJect™ device, which holds a pre-filled dose of 1.0 ml (= 10 IU) oxytocin in a disposable, cushion-like package with a sterile needle attached. This device has been used in field trials for injectable contraceptives¹⁰ and is a promising technology also for oxytocin administration. It has hitherto not been tested in any low-income country as an ingredient of AML for the prevention of PPH.

1.14 Jaundice during pregnancy

A wide range of possible infectious and non-infectious disorders contribute to jaundice during pregnancy (Rustgi 1989; Lunzer 1989)

In African countries a substantial proportion of jaundice during pregnancy, perinatal problems, and maternal deaths seem to be caused by viral hepatitis (Kwast, Stevens 197; Tsega *et al* 1992; Menendes *et al* 1999).

The spread of hepatitis A and E is known to be facilitated by poor sanitary conditions and to occur more commonly during the rainy season when drinking water can be polluted by latrines (Parker 1978, Mushahwar *et al* 1993).

The blood-borne forms of viral hepatitis, hepatitis B and C, are endemic in sub-Saharan Africa (Ayoola 1988). In the large slum areas of Luanda and a high proportion of deaths has been encountered among pregnant women with jaundice. The two main maternity hospitals in the city, MAN and MLP, had 11,595 and 16,641 births, respectively, during 1998 with 133 maternal deaths at MAN and 285 at MLP. Of these, 19 were related to jaundice of unknown cause at MAN and 58 at MLP, corresponding to 14.3% and 20.4%, respectively, of all maternal deaths that year (Estatística anual, CAOL). The predominant aetiologies of jaundice among these women are unknown.

1.15 Neglected obstructed labour and maternal death

Uterine rupture (UR) is a life-threatening emergency for both mother and foetus. It has been estimated that one in five maternal deaths from haemorrhage is related to UR (Nagaya *et al.* 2000). The prevalence of UR is 0.05-0.8/ 1,000 deliveries in high income countries (Williams Obstetrics 2001), but considerably higher in low-income countries. Earlier African studies show a wide range from 0.8 to 18/1,000 deliveries (Rajab, Mulumba 1998, Diallo *et al.* 1998). A combination of social exploitation of women, lack of medical facilities and delays in seeking, reaching and receiving effective care for various reasons all contribute to these high figures.

Institutional MMR is the only available instrument to assess quality of obstetric care in the capital Luanda and has shown a decrease from 2,070 per 100,000 live births in 1994 to 772 in 1997, see Table 5. Parallel to an escalation of the war and deterioration in the conditions for internal refugees, institutional MMR again increased to 888 in 1999. The total number of institutional deliveries the same year was more than 61,000, accounting for less than 50% of all estimated births in the city. At the two central maternities in Luanda, UR contributed to direct obstetrical deaths in 7% of cases at MLP and 14% at MAN in 1997 (Estatística anual, CAOL). Against this background we decided to review all cases of UR during 1998 and 1999 in MAN, the maternity which had shown the highest mortality due to UR.

There is an increasing awareness that death as an outcome indicator is a blunt instrument for assessing quality of obstetric care. MMR reflects not only the level of medical care, but also various background factors in the society, from the likelihood of becoming pregnant to the propensity and possibility of seeking obstetric care. MMR is based on unreliable figures in a majority of low income countries. The actual number of live births is also uncertain in a setting where a significant proportion of women deliver outside the health system. Maternal deaths have often been shown to be grossly underreported in both developing and industrialized countries (Dye *et al* 1992; Wessel *et al* 1999; Songane, Bergström 2002). With outcome indicators, like the MMR, being recognized as inappropriate, attention has lately focused more on process indicators to evaluate the quality of medical practice (Pathak *et al* 2000, Graham *et al* 2000). By addressing specific questions like the reasons for women's delay in seeking care, the causes of delay in receiving treatment and the risk of being subject to substandard quality of care, the different steps in a process can be studied (Thaddeus & Maine 1994). With process indicators it is possible to analyze the different links in the chain of health care services, their availability, utilization and quality.

Clinic-based audit is among the interventions that have proven to be valuable in maternal health care (Liljestrand 1999). Audit needs to be based on criteria that are realistic to the conditions in the field. Such a list of criteria has been suggested for the management of five life-threatening obstetric complications (Graham *et al* 2000). In cases of UR the criteria are limited to surgery, draining of the bladder and use of an observation chart. In this study the focus is on another aspect of audit by estimating the avoidability of UR (Bergström 2001). By re-viewing the clinical events that preceded

the UR, an overall assessment of each case was made. This analysis started at the time of the patient's admission to the maternity, thus dealing only with factors that were related to the responsibility of the institution, reflecting its quality of care. The purpose of this paper was to reconstruct the chain of clinical events and decisions by health personnel to sort out which URs could have been prevented from those which could not. The purpose was to avoid similar mismanagement in the future.

1.16 The impact of delays for maternal outcome of pregnancy

With the aim of alleviating the heavy overload of patients at the two central maternities, a project was implemented in 1994 as part of the Swedish development co-operation with Angola through the Swedish International Development Cooperation Authority (Sida). This included reconstruction and equipment of nine peripheral birth units (*salas de partos periféricas*, SPP), run by midwives for normal deliveries without the possibility of administering intravenous drugs, blood transfusion or manual exploration of the uterus. Via a system of radio communication and ambulances, rapid referral of patients in obstetric emergencies was made possible. See Study Setting.

In spite of this increased utilisation of the SPPs, the aim to reduce the load of deliveries in the two referral hospitals was not reached. The high number of births at these hospitals remained unchanged or even increased. The central hospital, MLP, continued to register more than 18,000 births in both 1994 and in 1999, while the other maternity MAN increased from more than 9,000 births in 1994 to over 12,000 in 1999. Most likely, these figures reflect the increasing influx of refugees to Luanda.

There is, however, a growing awareness that maternal mortality ratio as an outcome indicator is too blunt an instrument for assessing quality of obstetric care, particularly in low-income countries (Maine 1993; WHO/UNICEF/World Bank 1999)

Maternal mortality in a setting like Luanda depends on much more than the medical service per se and outcome indicators rarely help in identifying which problems that most urgently need to be addressed. It has been shown that less than 50% of women in Luanda give birth in institutions (UNICEF 1997), which implies that the obstetrical outcome of every second pregnancy is likely not to be included in the official statistics. Attention has therefore gradually focused more on process indicators for the assessment of quality of health service and for analysis of the different links in the chain of obstetric care. It would be unwise to view process and outcome measurements as competing with each other; rather it is a matter of circumstances which indicator is regarded most useful (Mant 2001). In a more focused perspective, like evaluating the quality of a referral system, process indicators are more relevant.

Time is often of crucial importance in obstetric emergencies. The different factors that constitute impediments for rapid treatment have been schematically presented as “the three delays” (Thaddeus, Maine 1994). This stepwise model offers a pedagogic analysis of reasons for postponement of treatment in various contexts and is also applicable for referrals of obstetric emergencies from one level of care to another.

2. AIMS

2.1 General aims

The general objective behind these studies was the need to understand more of the causes of suffering and death among pregnant women in Luanda. These women give birth in often chaotic circumstances. The aim of the studies was to illuminate these conditions in order to open up for future improvements. Two examples of direct obstetric mortality are explored; postpartum haemorrhage and obstructed labour (uterine rupture). One example of indirect obstetric death is studied by pursuing the aetiology behind jaundice among pregnant women. Finally, we wanted to study the chain of referral for emergency obstetric care by following the women most in need of professional assistance.

2.2 Study I

The objective of the first study was to introduce the new device for administration of oxytocin, Uniject™, and to evaluate its efficacy and acceptability in clinical practice in an African setting. By including routine administration of oxytocin, we wanted to elucidate whether this approach could help decrease the prevalence of PPH among women in obstetric care with extremely limited resources.

2.3 Study II

The aim of the second study was to elucidate the causes of jaundice among pregnant women in Luanda, hitherto described merely as jaundice of unknown origin. The possible contribution of hepatitis A, B, C and E, malaria and HIV infection was analyzed among jaundiced mothers (cases) and compared with that in pregnant women without jaundice (controls). Clinical outcome for mothers and children was also compared.

2.4 Study III

The purpose of the third paper was to reconstruct the chain of clinical events and decisions to sort out which URs could have been avoided from those which could not in order to reduce similar substandard care in the future.

2.5 Study IV

The purpose of this study was to evaluate the efficacy of the newly established network of peripheral birth units and their relation to the hospitals. By auditing various aspects of emergency obstetric referrals at two different times and by letting the discussions and conclusions from the first study effect the second, we aimed at elucidating the potential impact of audit on quality of care, giving an example of a clinical “audit cycle” .

3. STUDY SETTING

3.1 Angola- a brief presentation

Angola gained its independence in 1975. The country now seems to be ready to leave its tragic and chaotic first decades behind. Along with expectations of economic and social development, there is a growing belief spreading that this time peace is for real. It is hard to imagine that this exhausted country will go back to war.

After the Portuguese withdrawal, the communist-backed party, MPLA, won the upper hand in the power struggle that followed. This escalated to military conflict and the country entered a new phase in its history - a vicious civil war that seemed to drag on forever. With the logic of the cold war USA and South Africa reacted by supporting UNITA, a rival guerilla group, led by Jonas Savimbi and mainly financed by diamond smuggling.

The collapse in 1991 of the Soviet Union, which had invested much interest in Angola, led to a political reorientation as MPLA turned more towards social democracy and eventually gained American support. A peace deal with UNITA was signed "during an outbreak of peace" and free elections followed. The results were rejected by UNITA and after an outbreak of violence in the capital, the guerilla war resumed in 1992. The collapse of a power sharing deal monitored by UN peacekeepers led further mistrust and to full-scale fighting again in 1998.

The war provided an excuse for dos Santos' regime to postpone democratic reforms, as it abandoned the destitute hordes of the country to the care of foreign aid agencies.

Savimbi was shot dead by government troops in February 2002, marking the end of a civil war which has ruined the country and starved a great number of its people. UNITA-soldiers are now collected in camps and reintegrated into society. The guerilla band is turning into a political party that meet face to face with MPLA, not through UN mediators as in previous peace attempts. MPLA generals avoid the word "victory", instead they emphasize that all Angolans are brothers that have suffered from the war and that now all are winners thanks to peace. Reconciliation does seem possible. Absent for two generations, hope has returned to Angola.

Most of the 100,000 ex-rebels have been disarmed and resettled with the help of the logistic knowledge of the army, setting up 34 "quartering areas" The promise of farming tools and vocational training have often failed to materialize, but many have taken initiatives themselves and starting planting crops and building houses.

More than 1.5 million Angolans have returned to their homes (or what is left of them) since spring 2002, far more than expected. However, one year later there were still some

3-4 million internal refugees in the country, according to the government sources. UNITA soldiers and their families constitute some 400,000 of these. In the neighbouring countries around 400,000 refugees remain a majority of whom has expressed their intention to come back. The Angolan government is working together with international aid organizations to prepare for their resettlement.

There are several signs of the new optimism. The economy is booming by an expected GDP growth of 13% this year thanks to peace and to high oil prices (up 40% since last year). Foreign investors meet in Luanda, where new offices and low cost housing are being constructed, while street lighting is making the city safer at night for the people who can afford the hamburgers of South African fast-food chains. Investments are channelled into spreading the mobile-phone coverage out to the provinces and to opening hydro-electric plants, breweries and commercial farms, to mention some. Inflation is down and food is more affordable for the poor. But the slums are still dreadful and the handicapped beggars continue their contribution to street life.

Transports and infrastructure are opening up the country. British Airways has opened a weekly connection to London and domestic airlines are shortening the distances. Travelling by land used to be close to impossible due to the constant threat of ambush. Routs are being re-opened and safer, but roads and bridges are in a terrible state and the de-mining of Angolan soil has only started. The World Food Program (WFP), which still feeds more than a million Angolans, says that the transport of food in peacetime Angola is five times as expensive as in warring Sudan (air transport has to be used).

Quantifying Angola's progress is not easy. Much of demographic statistics are guesswork or estimates. In spite of warfare and approximately 600,000 people killed, the population of Angola has grown to some 13.5 million inhabitants and doubled since 1970. Luanda, which was built for half a million people, now harbours around a quarter of Angola's entire population. The demographic pyramid has an extraordinary broad base as almost 50% of Angolans are under 15 years and only 5% are older than 60 years of age.

BNP per capita is 475 US dollars (2003), but the distribution of wealth in the country is extremely skewed. Ministers claim that corruption is declining, something that off course is hard to prove. Human Right Watch, a New York-based lobbying group, in the beginning of 2004 accused Angola's rulers of having filched or misspent 4.2 billion US dollars during a five year period and to years earlier the International Monetary Fund (IMF) had reported that 0.5 billion dollars disappeared from the national treasure in 2001. The government rejects both these allegations.

While half of Angola's children are malnourished and an estimated 500, 000 people are on the brink of starvation there are 20 super-rich Angolans worth 100 million US dollars or more, according to the Economist Intelligence Unit. Six of the seven richest on the list are state officials. Commercial interests have often been classified as state secrets. Oil revenues are now being published yearly and although the figures are imprecise, this is seen a first step towards more transparency.

Oil accounts for 90% of the government's income. Angola's rich oil fields and diamond mines are not only a blessing for the country but also provide motives for new conflicts. Elections, long overdue, are scheduled for September 2006 and Eduardo dos Santos who has led the country since 1979 has announced that he will step down both as president of MPLA and of the country. Hopefully this election, the first in twelve years, will give Angolans a chance to influence their future and start dealing with corruption, which has drained the country of much of its potential wealth (The Economist 2000-2004; Utrikespolitiska Institutet 2004)

Figure 3. Map of Angola



3.2. Sida and CAOL

By the time the World Health Organisation (WHO) launched the Safe Motherhood Programme, the province of Luanda had only two public maternities, *Maternidade Lucrecia Paím*, (MLP), and *Maternidade Augusto N'Gangula*, (MAN). Maternal mortality ratio (maternal deaths per 100,000 live births, MMR) was estimated to be between 600-1000 and institutional MMR to around 1,700 - some of the highest figures in the world. Between 50 and 80% of the women in Luanda gave birth without contact with health institutions. Traditional birth attendants (TBAs) assisted only in an estimated 1% of deliveries.

The existing maternal health services were not fit to handle the situation. Beside insufficient financing and lack of skilled personnel, there was also a complicating division of leadership between primary, secondary and tertiary levels. By forming CAOL (*Coordenação do Atendimento Obstétrico de Luanda*) important providers of

maternal health were united in one organisation to co-ordinate their tasks and implement national norms and policies in Luanda Province. Non governmental and locally active international organisations such as Angolan Women's Association (OMA), MSF, UNICEF and UNFPA were also invited to take part. Angola expressed interest for co-operation with Sida (*Swedish International Development Cooperation Agency*) (Anderson Brolin, Wessel 1999).

Sida wanted to contribute with "strategic inputs" to the Angolan health system and commissioned Dr. Staffan Bergström to analyse the prerequisite for Swedish co-operation and to suggest strategies for the future (Bergström 1986). His report was handed over to Sida at the beginning of 1988 with the advice to focus on Luanda Province. The situation in the capital was in several aspects worse than in many of the provinces at that time. Luanda was also recognised for its central role in communicating standards to the rest of the country. Sida decided to assist the CAOL programme and focused its support during the initial phase to strengthen CAOL economically and by offering technical advisers – one doctor and one midwife. The arrival of a Swedish obstetrician in 1990 can be regarded as the starting point of the co-operation.

By the end of the same year the first operational plan for 1991-1995 was elaborated with the main objective to fight maternal mortality. The strategy focused on reducing low-risk-deliveries at the hospitals by opening peripheral birth units, increase the referral of risk deliveries to the hospitals by improving the selection procedure, make home deliveries safer by training TBAs and integrate family planning in maternal care.

The following goals were targeted for 1995:

1. MMR should be reduced to 400.
2. Tetanus for newborns should be reduced to 50 cases per year
3. 20% of deliveries should take place at peripheral units
4. 90% of pregnant women should have at least 3 visits at the antenatal care clinics (ANC) and be immunised against tetanus.
5. All centres for Mother and Child Health Care should have family planning integrated in the postpartum controls.
6. Trained TBAs should assist in at least 10% of home deliveries. (This goal was later to be abandoned)

In December 1991, a conference was held on maternity without risks (*Maternidade sem Risco*). The participants suggested forming a special committee in each peripheral unit and hospital to analyse causes of maternal deaths. This has however proven difficult to implement on a regular basis, but during the period 1998 and 1999 monthly clinical audits was achieved at MAN, prepared by the author.

In the discussions during the conference two alternative perspectives on reducing mortality were expressed. The first emphasised the improvement within the health system while the other stressed measures outside this sector such as community work, family life education, involvement of schools and mass media etc. At times this latter

view has been brought up again, but has not really made any impact on the way CAOL has been working.

Sida has since contributed with supplementary salaries, primarily for midwives but later also for other health staff categories. Sida has procured and distributed drugs, supply and equipment for both the nine peripheral birth units being constructed and for the two hospitals where also extensive repair work of the buildings was provided. It has been frustrating to meet the neglect of the Angolan government which has contributed very little to the programme. Swedish support has more and more got the character of compensation for this lack of engagement. Another incidence that influenced the programme in the beginning was that the Swedish gynaecologist resigned in 1991, considering the circumstances impossible for professional work. He was later replaced by other gynaecologists and specialists in public health working as long term consultants.

With CAOL as a model, in 1997 CAPEL (*Coordenação da Assistência Pediátrica em Luanda*) was founded as an integrating organisation stressing the aiming at including both the mother and the child in the overall objective of reducing maternal and child morbidity and mortality. As in CAOL, the emphasis has been on improving the peripheral health units and hospitals outside the University Paediatric Hospital. The global programme for Integrated Management of Childhood Illness (IMCI) can be described as the core strategy in CAPEL. IMCI documents have been translated into Portuguese and used in training modules. Both Brazilian and Swedish paediatricians have been engaged in this training. A Swedish specialist in neo-nathology has spent recurrent periods of clinical, “on-the-floor” education and supervision on the peripheral level. Sweden has also since long supported the Extended Programme on Immunisation (EPI) in Angola through its support to UNICEF.

The number of institutional births has increased dramatically since the completion of the project – from around 36,000 births in 1994 to almost 59,000 in 1999. The major part of this change has taken part at the peripheral level, but the high number of hospital births has remained unchanged or even increased. Most likely these figures reflect the influx of refugees to Luanda during this time. See Table 5.

The programme has also been provided with ambulances and a network of radio communication in order to achieve rapid referrals of obstetric emergencies from the peripheral units to the hospitals, where surgical procedures can be performed and the more advanced cases be treated. During this period two hospitals with 24-hour service of Caesarean section have been added to the network. In the first case there was an upgrading of staff at the operation theatre, in the other an inauguration of a brand new hospital, built with the aid from Spain.

In the beginning of the Sida’s involvement, there were few trained midwives available in Luanda. The maternity service was mainly provided by nurses. Midwife courses were started in various areas such as antenatal care, risk screening and delivery assistance. In 1998 an 18 months midwifery boarding school was opened with the aim of educating 40 midwives per year from different provinces of Angola. Midwives have also participated together with doctors in regular seminars, which were co-ordinated by short term Sida consultants. These meetings provided opportunities not only for ardent discussions but

also for presentations of local studies on pregnancy complications. Several midwives presented their own papers and contributed to the notion of a continuous upgrading of the status of their profession.

The population in Luanda has increased dramatically during the last decade with an annual growth of some 15% and poses an almost insurmountable challenge to maternal care and the health sector as a whole. Some 70% of women still give birth at home and both institutional and total MMR remain extremely high, the latter virtually unknown (UNICEF 1997). Maternal mortality is low at the peripheral units. This could indicate that the referral system is working well, but it is also known that many of the referred women never continue to the hospitals.

The meagre interest previously demonstrated by Angolan politicians regarding the health of the people has motivated Sida to phase out its support. Angola with its vast resources of diamonds and oil is a rich country. In a new period of peace, its wealth should be allocated to the immense task of offering basic education, sanitation and health to a people that has been severely neglected and - demographically speaking - belongs to the future.

Table 5. Institutional births, Luanda 1994-1999 (Estatística anual, CAOL).

	1994	1995	1996	1997	1998	1999
MLP						
Births	18 611	17 099	16 453	17 424	16 641	18 663
Maternal deaths	421	340	261	264	285	358
Live newborns	17 227	15 923	15 229	16 236	15 529	17 586
MMR	2 443	2 135	1 713	1 626	1 853	2 035
MAN						
Births	9 303	8 217	8 940	11 711	11 595	12 138
Maternal deaths	108	108	86	127	133	151
Live newborns	8 720	7 635	8 363	10 882	10 772	11 373
MMR	1 238	1 414	1 028	1 167	1 235	1 328
Peripheral Units						
Births	8 441	11 803	15 276	24 714	26 756	30 516
Maternal deaths	3	8	4	4	7	13
Live newborns	8 589	11 456	14 836	24 007	26 325	29 892
MMR	35	70	27	17	26	43
Total						
Births	36 355	37 119	40 669	53 849	54 992	61 317
Maternal deaths	532	456	351	395	425	522
Live newborns	25 695	35 014	38 428	51 125	52 626	58 851
MMR	2 070	1 302	913	772	807	887

4. SUBJECTS AND METHODS

4.1 Study I

The first study was carried out between March 1998 and May 2000 at the MLP. The heavy flow of parturient women did not permit all women to be included. It proved necessary to define a time and an area not to interfere with the ordinary activity. This was done by limiting the study to the work hours between 8 AM and 3 PM and by studying women in only two rooms of the labour ward. Twelve midwives and four doctors were appointed for the study, taught the practical procedures and instructed in filling in the study protocols.

Due to prevailing constraints in human and material resources and to the load of patients, it was judged impossible to design a randomised controlled trial. Instead we opted to perform a comparative study.

The *first part* comprised parturient women in the labour ward of MLP studied between the 3rd of March and the 28th of May 1998 (n=782). The women enrolled were in daytime spontaneous labour for vaginal delivery, presenting with a dilatation of the cervix of at least 3 cm at the first vaginal examination. Women with obstetric emergencies and multiple pregnancies were excluded. At the time of the study, parturient women in the third stage of labour did not routinely receive any oxytocic medication and the umbilical cord was not actively pulled unless excessive bleeding called for action. Instead the delivery of the placenta was passively observed, in what could be referred to as a physiological or expectant management of the third stage of labour. These women are referred to as “Group 1” below. Vaginal bleeding immediately after birth and during the first two hours postpartum was collected and measured. This was done using a plastic sheet placed underneath the parturient woman directly after birth and allowing blood to be collected for measurement in a bucket while the women remained in a birthing position. The same bucket was then placed under the woman while she moved to a so called cholera bed, below which the bucket was located for a total of two hours after delivery. Such a cholera bed has an opening in the middle, thus making it possible to collect the lost blood during this first period of rest without using swabs or sanitary pads.

The cut off time of two hours was selected for practical reasons taking into consideration the heavy work load of the labour ward, yet including the two most critical hours of PPH. Time interval between birth and expulsion of the placenta was registered, as well as basic obstetrical data (type of presentation, episiotomy, birth weight, complications and drugs given). Any bleeding beyond two hours and other late complications were not possible to cover.

Among the women with PPH, we wanted to identify those with the most severe bleeding, who were in urgent need of treatment to reduce maternal morbidity/mortality. Severe PPH is here defined as a blood loss of ≥ 1000 ml.

Prolonged labour was calculated from partographs and was defined as duration of labour which exceeded by more than four hours the time limit set by an arbitrary standard of one hour per cm cervical dilation and two hours added for the expulsion phase.

The second part of the study consisted of an intensive, introductory course for midwives and doctors concerning AMTL encompassing routine administration of 10 IU oxytocin with the UniJect™ device, early cord clamping and gentle traction of the cord for delivering the placenta.

The third part included 814 women giving birth between the 8th of November 1999 and the 10th of May, 2000, with the same inclusion criteria, methods and protocol as in the first group. This second group was treated according to the principles of AML described above and is referred to as “Group 2” below. The UniJect™ devices were stored in a refrigerator in the labour ward during the study period and were distributed daily to the midwives. These were trained to use UniJect™ for intra-muscular injection into the thigh of the parturient women directly after delivery of the new-born as soon as multiple pregnancy had been clinically excluded. The duration of the third part was longer than the first part due to renovation work of the maternity ward during this period.

4.2 Study II

The second study was conducted between April 30 and June 15 1999 at the two largest maternities in Luanda, MLP and MAN, to which pregnant women with severe jaundice were either referred or admitted directly.

Twenty pregnant women were included as cases. They had been admitted to hospital because of illness and clinical jaundice and were consecutively encountered during the morning rounds performed by the principal investigator (RS). For each case, two apparently healthy referent women were chosen from the labour ward at the same hospital the same morning. The first two women encountered with normal blood pressure, absence of proteinuria and who declared that they had no other known disease, were enrolled as referents. Long-term follow-up was not possible because of the practical difficulties of tracing patients once they had left the hospital. Hence, registration of the clinical outcome was limited to the duration of the hospitalization of each woman.

Serum alanine aminotransferase (ALAT) levels were analyzed locally by using a Reflotrone® (Roche, Mannheim, Germany) at MLP. Serum samples were drawn from all patients and referents and serum aliquots were frozen at -18° C and later transported for serological investigations at Huddinge University Hospital in Stockholm, Sweden. Antibodies against HIV1 and 2 were tested by commercial second generation AxSYM ELISA and HBsAg, anti-HBc, anti-HAV, anti-HCV and anti-HEV by commercial AxSYM ELISA. All tests originated from Abbott Laboratories, North Chicago, Ill.

Malaria slides were initially read locally and later rechecked at Huddinge University Hospital. Thick and thin blood films were stained with 3% Giemsa. Microscopy was performed by a highly experienced laboratory technician at Huddinge University

Hospital. One hundred visual fields were examined before any slide was considered negative.

4.3 Study III

The third study was based on 43 patients records of uterine rupture during 1998, which were studied retrospectively and 67 cases during 1999, were studied along with clinical audits at one maternity hospital in Luanda, MAN.

UR was defined as a tear in the uterine wall, excluding the uterine cervix, associated with maternal or foetal symptoms requiring surgical intervention. During the two year period there was a total of 116 cases of UR (49 in 1998 and 67 in 1999) and we were able to collect and analyze 110 of these patient records.

The 43 cases retrieved in 1998 were analyzed using available patient records. Basic obstetric data were collected from the admission sheet, including previous uterine scar, place of residence and number of antenatal care visits. Estimates of gestational age were based either on the last menstrual period or on clinical examination. By studying partographs and documented clinical observations, a tentative diagnosis on admission was established and an interval between diagnosis of either impending UR or UR and interventions was calculated. Additional circumstances, such as progress and management of labour, use of uterotonic drugs, type of delivery and surgical procedures. Complications and maternal and foetal outcomes were also included. We wanted to differentiate those URs that occurred after admission to hospital from those that had occurred earlier, at home, at the peripheral units or during transport. Referral documents from the peripheral birth units were also analyzed.

In 1999 each new case with UR was audited and analyzed the day after surgery. The final analysis of the cases was then undertaken by the authors according to the same standard protocol as previously used. At that time no new clinical recommendations or routines had been introduced after the initial retrospective analysis.

All cases were analyzed according to avoidability. By stating that a UR could have been avoided, we mean that it could have been prevented by using the treatment available at the hospital, had obstetric vigilance and practice been of good quality. The patients' records and partographs were the main sources of information in this analysis. If, e.g., the so called "action line" of the partograph was not respected by either comment or action, the UR was considered "avoidable".

4.4 Study IV

The fourth study also took place in Luanda and was carried out in two periods; the first part between April 23 and July 24 in 1998 and the second part between Dec 1 in 1998 and Feb 28 in 1999. Three SPPs were selected for the study: Cazenga (C), Palanca (P) and Sambizanga (S). These were included of practical reasons as they are all situated relatively close to the hospitals at a distance of between two and six km. We postulated that this would result in high compliance to referral advice and a similar time for transport.

The first part included 157 women referred for obstetric emergencies. The chief midwife of each SPP had an established routine of monthly visits to the hospitals to

which they had referred patients for collection of records. The frequency of these visits was increased to enable data collection on a weekly basis for the SPPs included in the study. Records were brought to the study group consisting of six midwives and one of the authors (PC) for analysis according to a study protocol. Diagnosis and treatment provided were registered. Besides outcome indicators of maternal and neonatal deaths, process indicators of waiting time, over all case fatality rate, Caesarean section rate and partograph quality were studied. Transport and waiting time is central in referring obstetric emergencies. Partographs had recently been introduced as an obstetric tool and were evaluated according to a list of criteria and subdivided into categories of good, acceptable or poor quality. A good quality partograph should have relevant information on birth protocols and information on foetal heart rate, rupture of membranes, cervical dilatation at least every 4th hour, station of presenting part at least every 4th hour, blood pressure, time of birth, time of placental expulsion and Apgar score. With three or more of these items missing, the partograph was considered of bad quality.

In the following audit sessions, the organizational deficiencies of the referral system disclosed and the incompleteness of records and data were presented, analyzed and discussed at two local seminars. A majority of doctors and midwives employed in institutional obstetric care in Luanda participated. Emphasis was put on further education in the use of partographs. Courses for midwives and doctors were implemented at both the hospitals and the SPPs. The WHO material on the partograph (WHO 1994) was translated into Portuguese, distributed and explained during these lectures.

The second part of the study comprised 92 referrals from the same SPPs. During this part, the chief midwives of the two hospitals were also engaged in the study. The records of referred patients, which they had retrieved, were returned to the responsible midwives of the SPPs twice weekly. These records were then analysed every second week by the study group, using the same study protocol as in the previous collection of data.

For all studies Ethical clearance has been given by the ethical committee at Karolinska Institutet, Stockholm, Sweden and by Agostinho Neto University, Luanda. Angola.

The Fisher's exact two-tail test or Chi square methods were used to test categorical variables. A p-value < 0.05 indicated statistical significance.

5. RESULTS

5.1 Study I

The results of this study are summarised in Tables 6-11.

There was no maternal death in the groups studied. The two groups did not differ concerning age ($p=0.50$), proportion of primiparous women ($p=0.13$) and grand multiparous women ($p=0.13$).

Blood loss and interval between birth of the baby and delivery of the placenta decreased significantly with AMTL (Table 6 and 11). The percentage of parturients with a small bleeding (≤ 200 ml) was significantly less in Group 1 than in Group 2 ($p < 0.005$). Severe PPH also showed a significant difference in the two groups and was detected among 59 women (7.5%) in Group 1. In seven of these, the cause of heavy bleeding was laceration of the cervix. In Group 2 severe PPH was detected in eight women (1%), four of those being caused by cervical lacerations (Table 6).

The prevalence of PPH was significantly lower among both primiparous and grand multiparous women in Group 2. Within these groups there was no difference among these two parity categories. The proportion of PPH was lowest among women with parity 2- 3 within both groups. (Table 7).

Macrosomia of the baby (birth weight ≥ 4000 g) was detected in 11 cases in Group 1, of whom nine had PPH. In Group 2 there were 32 cases of macrosomia and six of those were associated with PPH. The prevalence of PPH was lower in Group 2 than in Group 1 among women giving birth to newborns weighing ≥ 4000 gram ($p < 0.005$) The same holds true when comparing women with low birth weight newborns (Table 8).

Prolonged labour occurred with similar prevalence in the two groups (around 5%). Few of these women were treated with oxytocin stimulation. The reduction of PPH after prolonged labour was significant when AML was used (Table 9).

Episiotomy is still used as a routine in primiparous women in Luanda, resulting in an overall prevalence of almost one third of all deliveries. The bleeding caused by episiotomy might contribute to the post partum blood loss. We found a slight increase in blood loss among women having had episiotomy in Group 2 (borderline significance, $p= 0.05$), but no such difference in Group 1 (Table 10).

Stillbirth occurred in 21 cases (2.7%) in Group 1 and in 14 cases (1.7%) in Group 2. Of these 8 and 11, respectively, had no cardiac activity registered at the first examination after admission to the maternity ward and could therefore be regarded as pre-labour foetal deaths. Of all stillbirths, one case in Group 1 and two cases in Group 2 had PPH.

The intervals between birth of the baby and expulsion of the placenta are shown in Table 11. In Group 2 the placenta was delivered in less than 10 minutes in 89.4% of the parturients as compared to only 5.4% in Group 1 ($p < 0.001$). The difference between the two groups was less marked after 30 minutes.

The prevalence of retention of the placenta depends on the definition of the normal time of the third stage of labour. Using the WHO criteria, we found only one case altogether.

In Group 1, 71 patients (9.9%) had a placenta not delivered before 30 minutes, compared to 2 patients (0.3%) in Group 2 (p<0.001).

Manual removal of the placenta was rare in both groups. Of the six cases in Group 1, five were associated with PPH (out of which two had severe PPH). In the single manual removal of the placenta recorded in Group 2, bleeding was normal.

Table 6. Prevalence of categories of blood loss before and after the introduction of AMTL with UniJect™.

Blood loss	Group 1 n=782	Group 2 n=814	p value
< 200 ml	116 (15.0%)	399 (48.9%)	<0.001
≥500 ml	316 (40.4%)	67 (8.2%)	<0.001
≥ 1000 ml	58 (7.5%)	8 (1.0%)	<0.001
Mean blood loss	447 ml	239 ml	<0.001

Table 7. Prevalence of PPH according to parity before and after the introduction of AMTL with UniJect™.

Parity	Prevalence of PPH	Prevalence of PPH	p value
	Group 1 (n=782)	Group 2 (n=814)	
1	100/262 (38.2%)	39/304 (9.5%)	<0.001
2-3	104/278 (37.4%)	17/288 (5.9%)	<0.001
≥4	112/241 (46.3%)	21/222 (9.5%)	<0.001

Table 8. Proportion of PPH related to birth weight (BW) before and after the introduction of AMTL with UniJect™.

Birth Weight (g)	Prevalence of PPH Group 1 (n = 778*)	Prevalence of PPH Group 2 (n = 807*)	p-value
1000 ≤ BW < 2500	44 / 113 (38.9%)	6 / 67 (9.0%)	< 0.001
2500 ≤ BW < 4000	262 / 654 (40.1%)	55 / 707 (7.8%)	< 0.001
BW ≥ 4000	9 / 11 (81.8%)	6 / 33 (18.2 %)	< 0.001

*Data missing and exclusion of BW < 100

Table 9. Prolonged labour and PPH before and after the introduction of AMTL with UniJect™.

Patient category	Group 1 (n=750)*	Group 2 (n= 810)**	p-value
Women with prolonged labour	35 (4.7%)	42 (5.2%)	0.64
Prolonged labour and PPH	19 (54.3%)	5 (11.9%)	<0.005
Prolonged labour with oxytocin stimulation	3 (8.6%)	6 (14.3%)	0.51

* No data in 32 cases ** No data in 4 cases

Table 10. Episiotomy and blood loss post partum before and after the introduction of AMTL with UniJect™.

	Episiotomy		No episiotomy		Mean difference together with 95% CI
	No of women	Blood loss (ml) Mean (SD)	No of women	Blood loss (ml) Mean (SD)	
Group 1 (n = 750)	219	444 (272)	531	446 (312)	-2 ml (-47 ml, 42 ml)*
Group 2 (n = 810)	274	249 (205)	536	234 (195)	16 ml (-14 ml, 45 ml)*

*No significant difference in blood loss in episiotomy / no episiotomy subgroups before and after the introduction of AML.

Table 11. Duration of the third stage of labour before and after the introduction of AMTL with UniJect™.

Interval between birth and expulsion of the placenta	Group 1 (n = 714)	Group 2 (n = 768)	
0-9 min	38 (5.3%)	687 (89.4%)	
10-19 min	463 (64.8%)	71 (9.2%)	
20-29 min	142 (19.9%)	8 (1.0%)	
30-39 min	63 (8.8%)	2 (0.3%)	
40-49 min	4 (0.6%)	0 (0.0%)	
50-59 min	3 (0.4%)	0 (0.0%)	
≥ 60 min	1 (0.1%)	0 (0.0%)	
Mean time	16.2 min	4.4 min	(p < 0.001)

5.2 Study II

The 20 jaundiced pregnant women (cases) enrolled had a mean age of 21.9 years (range 15 –38 years) of whom 11 were primigravidae (55%). Ten of the women had a gestational age of ≤ 24 weeks. Mean gestational age was 25.3 weeks. Only one woman was estimated to be at term. The 40 parturient women without jaundice (referents) were all at term and had a mean age of 24.7 years (range 17-37 years) of whom 7 (20%) were primigravidae.

The overall clinical outcome differed dramatically between cases and referents. Thus six (30%) of the 20 cases died, five had spontaneous abortions and six had stillbirths (among the cases that recovered, there were three spontaneous abortions and three stillbirths). Among referent women there was no maternal death ($p < 0.001$) and one stillbirth ($p < 0.005$). Since the referent group consisted of women at term and in labour, there was no abortion in this group.

Liver injury as reflected by ALT levels differed between cases and referents. In six cases (30%) with jaundice ALT levels were raised above the upper limit of the normal range ($0.63 \mu\text{cat/l}$) versus only 1/40 (2.5%) mothers in the referent group ($p < 0.007$). Serological markers for hepatitis A, B, C and E among cases and referents are presented in Table 1. No difference in prevalence of hepatitis A and B markers was seen between cases and referents, but 10%, irrespective of group, were found to be HBsAg carriers. Significantly more cases than referents were positive for antibodies against hepatitis E (anti-HEV), 40% versus 12.5%, ($p = 0.02$). We also found two women in the referent group who were anti-HCV positive whereas no case had such antibodies. Antibodies against HIV were detected in three referents (7.5%) but in none of the cases ($p = 0.54$).

Malaria was found significantly more often among cases than among referents 9/19 (47.5%) versus 2/40 (5%), ($p < 0.001$). One slide in the case group was missing. All parasites found were *P. falciparum*. The local malaria diagnoses were less accurate. Hence, among the 11 positive malaria slides diagnosed in Stockholm, four were not detected in Luanda. Furthermore, among the 11 positive malaria slides in Luanda, five turned out to be negative when re-examined in Stockholm. This reflects the difference between a highly qualified research laboratory and a routine laboratory service in an overburdened setting.

The presence of anti-HEV and/or *P. falciparum* parasitaemia in relation to maternal death or recovery among the cases is given in Table 2. No significant difference in prevalence of anti-HEV or presence of *P. falciparum* was seen among the cases who died and those who survived. In fact presumed dual infection with malaria and hepatitis E was not encountered in any woman who died but in two women who recovered.

Table 12. Prevalence of hepatitis A, B, C and E serological markers, HIV antibodies and positive malaria slides among cases and referents.

Parameter	Cases (n=20)	Referents (n=40)
HBsAg-pos	10%	10%
Anti-HBc-pos	70%	75%
Anti-HAV-pos	100%	100%
Anti-HCV-pos	0%	5%
Anti-HEV-pos	40%	12.5%*
HIV	0%	7.5%
Malaria	47.5%	5%*

* Significant difference

Table 13. Prevalence of hepatitis E antibodies and *P. falciparum* parasitemia among pregnant women with jaundice related to mortality.

	Maternal death (n=6)	Maternal recovery (n=14)
Anti-HEV positive	33% (2/6)	43% (6/14)
Malaria positive	50% (3/6)	46% (6/13*)
Malaria or HEV	83% (5/6)	92% (12/13)*
Malaria and HEV	0	15% (2/13*)

* One slide missing

5.3 Study III

The prevalence of UR was 4.9/1,000 deliveries for the two periods studied with 116 cases among 23,733 deliveries (4.2/1000 in 1998 and 5.9/1000 in 1999). There were 15 maternal deaths (13.6%) representing 10.8% of all direct obstetric causes of maternal death in the two-year period.

The mean age of women with UR was 28.3 years. No woman was under 15 years of age and 20 women (18.1%) were ≥ 35 years of age. Parity ranged from 0 to 10 (excluding the index delivery) with a mean of 3.7 previous deliveries. There were seven (6.4%) primigravida and 51 women (43.6%) were classified as grand multiparous (≥ 4 previous deliveries).

A previous Caesarean section (CS) was documented in 31 women (28.2%). The overall CS rate during the two year study period was 7.2%.

More than 50% (56 women) had at least two antenatal care visits, nine women had one visit and data were missing in the remaining records. All women suffering a UR came

from Luanda or its vicinity. All but six women came from areas within 6 km from the hospital (data lacking in 3 cases).

Ninety-nine (90%) of the women were considered at term (≥ 37 completed weeks of gestation). One UR occurred at only 19 estimated weeks after the woman had received repeated doses of misoprostol due to missed abortion. Another case, classified as foetal death occurred at 27 gestational weeks and with a birth-weight of 500 g. The woman was 30 years old, in her fifth delivery and was admitted for pre-eclampsia with a blood pressure of 170/110 and absence of foetal heart activity. She was treated with misoprostol vaginally and oxytocin intravenously for the induction of labour. After one hour UR was suspected and the patient was taken to the operation theatre. A macerated foetus and a left side UR was found and a subtotal hysterectomy was performed.

Oxytocin was used to augment labour in thirty-four women (30.9%) with prolonged labour. One of them had undergone a previous CS. Misoprostol was used for induction of labour in eight women (7.3%), three of whom were due to foetal death (including the woman of 19 weeks of gestation). No women treated with misoprostol had a previous uterine scar. Forty patients (36.4 %) had received some kind of uterotonic treatment, of whom two had received both misoprostol and oxytocin.

Perinatal mortality was at least 70 %. This figure accounts only for the 74 stillbirths documented (in five patient records data was missing). Information on neonatal deaths, not registered in direct association with the UR, was often impossible to retrieve and is therefore omitted here. Malformation was not documented in any of the records studied.

The duration between diagnosis of UR/ impending UR and intervention is presented in Table 14. In 48 women (43.6%) the diagnosis was set prior to birth or surgical intervention, in 38 women (34.5%) during laparotomy and in 24 women (21.8%) after vaginal birth. As expected the foetal presentations differed from women with no UR (Table 15).

Birth weight data was lacking in 15 cases (13.6%). Of the remaining cases there were nine children (9.7%) with a birth weight less than 2,500 g, (not including the two early pregnancies of 19 and 27 weeks of gestation). In only eight cases (8.6%) there was a registered birth weight of >4000 g.

Corporal rupture occurred in five women and in 90 patients the rupture was in the lower segment of the uterus, including two posterior ruptures. Longitudinal rupture including both corpus and the lower segment was registered in seven cases. Information on type of rupture was lacking in eight patient records.

Hysteroraphy was performed in 50 women, subtotal hysterectomy in 36 and total hysterectomy in 16. In the latter two groups, there were also three cases of suture of bladder injury. In eight records data was lacking regarding type of surgery.

Among other complications we found eight cases of sepsis and five cases of shock, which led to the death of four women. There were also two fatal cases of disseminated intravascular coagulation. Two cases of ligation of the ureter and three cases of vesico-vaginal fistulas had uneventful maternal outcome.

The analysis of avoidability required a number of arbitrary distinctions. We opted to consider an interval between diagnosis and intervention of less than 60 minutes, as being operationally acceptable, given the extraordinary logistical constraints in this overburdened setting. In 13 patients the diagnosis was set before or at admission and in 11 patients within one hour after admission with immediate preparation for surgery. We regarded these 24 cases of UR and six of the cases when UR was diagnosed after vaginal delivery without evidence of mismanagement as non-avoidable. In nine cases, the operation theatre was busy, leading to a delay in intervention. According to our definition of avoidability, the URs of these women were considered non-avoidable, giving a total of 39 cases (20 in 1998, 19 in 1999). The remaining 71 cases of UR (64.5%) were regarded avoidable at the hospital level.

Table 14. Interval between diagnosis of UR/impending UR and intervention.

Time (min)	Number of patients
0-9	45 (38 during surgery)
10-30	10
31-60	20
61-120	15
121-180	7
No data	13
Total	110

Table 15. Type of fetal presentation in parturient women with and without diagnosed uterine rupture (UR), respectively.

Presentation	UR	No UR	p-value
Cephalic	79 (82.3%)	22,498 (94.8%)	<0.01
Breech	7 (7.3%)	926 (3.9%)	<0.01
Transverse	10 (10.4%)	309 (1.3%)	<0.01
Total	96 (100%)*	23,733 (100%)	

* Data missing in 14 cases, including one twin delivery.

5.4 Study IV

The total number of births and referrals admitted to hospitals during the two study periods are presented in Table 16.

The proportion of referrals differed widely between the SPPs; from 1.7% in Palanca in May 1996 to 28.7% in Cazenga in January, 1999.

Basic obstetric data. Mean age was 24.1 years in both periods of the study. Young women, primiparous and grand multiparous women are among categories usually regarded at high risk of pregnancy complications. Women < 20 years of age constituted 36%, primiparous women 43% and grand multiparous women (≥ 4 previous births) 32% in the first period. The corresponding figures in second period were 29%, 40% and 22% respectively. These differences are not statistically significant.

Diagnosis. In both periods the most common reason for referral was prolonged labour. The diagnostic alternatives in the first study protocol resulted in a large category called "other diagnosis". In order to get a more differentiated picture, the list of alternatives was extended in the second period and some categories were subdivided into more specific diagnoses. Some women were also referred with more than one diagnosis. See Table 17.

The agreement on diagnosis at the SPPs and the hospitals was almost total in the second period of the study. In only two cases did they differ; one was diagnosed as foetal distress but turned out to be a normal birth, the other was a missed diagnosis of a twin pregnancy. In the first period records were too incomplete to make a meaningful comparison of diagnosis.

Waiting time. The first period of the study demonstrated a mean waiting time of 13.7 hours from admission to hospital to first evaluation by a doctor.

During the audit this question was much discussed and it was decided that referred patients should be seen with highest priority at the hospitals and not have to join the waiting line together with other patients. In the second period waiting time was studied more in detail.

Mean transport time from the peripheral unit to the central hospital was 36 min (range 15-225 min). After arrival to the hospital, mean waiting time to see a midwife was 9 minutes and to the first evaluation by a doctor 71 minutes (range 0-510 min). This mean waiting time was 54 minutes at MAN (where 5 of the patients were met immediately at arrival by a doctor and 59% had to wait for less than 30 minutes) and 71 minutes at MLP (57% waited < 30 min). The mean total time from leaving the SPP to first assessment by a doctor was 104 minutes (range 15-570 min). With virtually the same transport time, mean total time was 92 minutes at MAN, compared to 108 minutes at MLP, but this difference is not statistically significant.

Treatment. The receiving hospitals had developed a more active stand regarding admission and treatment of referred patients after the audit. In the first period Caesarean section (CS) was performed in 13% of referred cases, uterotonic treatment was used in

15% and vacuum extraction in 2%. The corresponding figures for the second period were 30%, 24% and 4%, respectively. Only the difference in CS is statistically significant ($p < 0.005$).

The proportion of referred women who were left with neither medical evaluation nor treatment mentioned in the patients' records decreased from 45% in the first period to 27% in the second ($p = 0.007$).

Partographs. The quality of partographs differed to the advantage of the SPPs when compared to the overburdened delivery wards of the hospitals at both periods of the study. The poor partograph quality of hospitals disclosed at the audit initiated further education in its proper use. This was reflected in the second period with a significant increase in partograph quality over time at both levels. See Table 18.

Outcome. In the first period there were 27 deaths among the traced 157 referrals, giving an over-all case fatality rate of 17.8%. In the second period no maternal death was registered. Foetal outcome was not addressed properly in the first period. In the second period, there were eleven stillbirths (12.0%).

After the completion of the study, it was found in the books of the SPPs that during the first period 398 women were registered as "referrals". The corresponding figure for the second period was 429. Thus, the 157 and 92 women who could be traced at the hospitals constituted only a minority of all women registered as referrals (39.4% and 21.4%, respectively). Only these could be included in the analysis above.

Table 16.

Number of births and referrals from three peripheral birth units in Luanda

Referrals are given as percentage of total number of women entering the units.

Birth unit	Sambizanga		Palanca		Cazenga	
	Births	Referrals	Births	Referrals	Births	Referrals
May 1996	203	19	113	2	516	149
June 1996	213	13	114	6	469	109
July 1996	213	18	104	5	498	77
Total	629	50 (7.4%)	331	13 (3.8%)	1,483	335 (18.4%)
Dec 1998	152	14	45	5	380	106
Jan 1999	141	5	54	8	344	139
Feb 1999	172	22	57	4	407	126
Total	465	41 (8.1%)	156	17 (9.8%)	1,131	371 (24.7%)

Table 17. Reasons for referral of obstetric emergencies in Luanda during two periods of referral audit*.

Diagnosis	1996	1998/9
Prolonged labour	45 (28.7%)	28 (29.2%)
Haemorrhage, pre partum	23 (14.6%)	8 (08.3%)
Haemorrhage, post partum	**	1 (01.0%)
Anaemia	**	2 (02.1%)
Previous CS	16 (10.2%)	7 (07.3%)
Hypertension /pre-eclampsia	28 (17.8%)	10 (10.4%)
Coma/convulsions	***	3 (03.1%)
Abnormal presentation	-	12 (12.5%)
Fever	-	2 (02.1%)
Foetal distress	3 (01.9%)	-
PROM	-	7 (07.3%)
Others	37 (23.6%)	16 (16.7%)
No data	5 (03.2%)	-

* *Some referrals had more than one diagnosis.*

** *Haemorrhage pre- and post partum and anaemia referred to as one group in 1996.*

*** *Hypertension/pre-eclampsia and convulsions referred to as one group in 1996.*

Table 18. Quality of partographs during two periods of referral audit in Luanda.

Quality	Referring units 1996	Referring units 1999*	Receiving hospitals 1996	Receiving hospitals 1999**
Good	18 (11%)	73 (95%) p<0.001	0 (0%)	41 (46%) p<0.001
Acceptable	108 (69%)	3 (4%)	14 (9%)	30 (34%)
Bad	31 (20%)	1 (1%)	143 (91%)	18 (20%)
Total	157	77	157	89

*15 partographs missing,

** 3 partographs missing

6. DISCUSSION

It might be argued that lack of focus is not only a trait of Safe Motherhood, but also of these studies. This was motivated by the heterogenic nature of obstetric emergencies and the often chaotic situation at the hospitals. This was hardly the setting for more refined, in-depth research as long as basic obstetric care was in an urgent need of improvement. Very little research had previously been published within the field of obstetrics in Angola. There was no tradition to follow. We wanted to illuminate important aspects of the care offered to parturient women in Luanda. The objective was to elucidate serious morbidity with the aim of reducing maternal mortality. Counting the sick and the dead was a starting point, but without studies on care itself, there was hardly any chance to reduce the numbers.

With the turbulent situation in the country and the overflow of refugees in Luanda, we realized that other factors than merely medical would contribute to maternal mortality. Should we study the effect of different treatment on maternal mortality, the results would be affected by the changing scenes “out there”. Besides, to obtain clear, non-disputed evidence for best treatment is never an easy endeavour. Even in settings with a high MMR, a maternal death is a relatively rare event. This means that in order to conduct a randomized controlled trial (RCT- the golden standard of study design) to study the impact of an intervention on maternal mortality, large populations have to be included. It can be calculated that in order to observe a reduction in mortality of 10% in a setting with MMR of 500/ 100,000 live births (confidence interval 95%, statistical power 80%) not less than 233,000 women are needed in each of the intervention and the comparison group. Large studies are expensive and complicated. To address the problem of sample size, the researchers have to prolong the study period or to widen the geographical study area. However, both these measure will add new difficulties in interpreting the results. This is the reason why many seemingly simple questions regarding obstetric care and maternal mortality still remain unanswered (Paxton, Maine *et al* 2005).

After the initiation of Safe Motherhood, there was a rapid proliferation of indicators proposed by a range of agencies to monitor the goals set up at international conferences. WHO has later edited a reduction of these indicators. See Table 19 (WHO 2000). Out of the 17 indicators of reproductive health, only the two of Essential Obstetric Care focus on the reducing maternal mortality. They did not convey much help in selecting critical areas for clinical studies.

Table 19. Reproductive Health Indicators for Global Monitoring

1. Total Fertility Rate
2. Contraceptive Prevalence
- 3. Maternal Mortality Ratio**
4. Antenatal Care Coverage
5. Births attended by skilled health personnel
- 6. Availability of basic essential obstetric care**
- 7. Availability of comprehensive essential obstetric care**
8. Perinatal mortality rate
9. Low birth weight prevalence
10. Positive syphilis serology prevalence in pregnant women
11. Prevalence of anaemia in women
12. Percentage of obstetric and gynaecological admission owing to abortion
13. Reported prevalence of women with FGM
14. Prevalence of infertility in women
15. Reported incidence of urethritis in men
16. HIV prevalence in pregnant women
17. Knowledge of HIV-related prevention practices

The studies presented here are examples of central problems and concepts in obstetric care in a low income country. We have studied aspects of the two *direct* pregnancy complications that contribute to death; postpartum haemorrhage and obstructed labour carried to its extreme of uterine rupture. Viral hepatitis, an *indirect* complication, is also often among the leading causes of maternal mortality. Audit and the use of partographs are among the interventions that have proven valuable in maternal health (Liljestrand 1999). In the last two studies we have used audit to highlight the concept of avoidability and waiting time and partograph quality respectively. All four studies were carried out at hospitals with EOC facilities. The level of EOC fluctuated, since blood was often lacking (in spite of reiterated attempts to create functional blood banks).

6.1 The third stage of labour

Previous studies on AMTL have mainly been performed in high-income countries. This study is the largest investigation made in a low income country where blood loss is not only clinically assessed, but measured. Uniject™ for routine administration of oxytocin in a postpartum situation is here systematically evaluated for the first time.

We have demonstrated that this management of the third stage of labour significantly reduces blood loss during the first two hours postpartum compared to expectant management and that the duration of the third stage of labour is significantly reduced.

The normal duration of the third stage of labour has been subject to different views with a range of 10–60 minutes (Tandberg *et al* 1999). In a survey of 1,300 normal deliveries,

without the routine of AMTL, Cooms and Laros (1991) found an average duration of 6 minutes for the third stage of labour and in only 3.3% the duration exceeded 30 minutes. In the present study, the mean time for placenta delivery was 16.4 minutes in Group 1 and 4.4 minutes in Group 2, a reduction in agreement with other studies.

The prevalence of retention of the placenta varies in different reports from 0.6% to 5.5% depending on the definition used for the normal duration of the third stage of labour (Tandberg *et al* 1999). It has been suggested that retained placenta could be more common in practice with routine administration of oxytocin (Begley 1990; WHO 1996). Neither the present study, nor a retrospective report from Ghana (Geelwood *et al* 2002) could confirm this risk. There have also been concerns that cord traction could cause inversion of the uterus (WHO 1996). We did not encounter any such case.

More importantly, we did not find any maternal death during this study. This could partially be explained by the fact that the most dramatic cases of antepartum bleedings have been excluded as they were treated in the operation theatre on an emergency basis. We also believe that the study situation itself with more attention to the problem of bleeding and improved vigilance by the personnel, helped in avoiding fatal complications.

6.2 AMTL - a package solution?

Just as “active management of labour”, AML, is a combination of different actions, “active management of the third stage of labour, AMTL, is also a “package management” and the relative importance of each action is not entirely clear.

WHO has given attention to PPH in a number of documents. A Technical Working Group, convened by WHO in 1989, analysed nine published reports of controlled trials in which oxytocic drugs were compared with either placebo or no routine prophylactic regimen in the third stage of labour, directly after the birth of the child. It was found that routine use of oxytocic drugs reduces the risk of PPH by about 40% (WHO 1989). The same magnitude of haemorrhage reduction has later been confirmed in a Swedish study (Nordström *et al* 1997).

A meta-analysis of AMTL has been published in the Cochrane Database (including the additional components of early cord clamping and controlled cord traction) (Prendiville *et al* 2002). The conclusion is that AMTL yields significantly less bleeding (by an average of 78 ml) and a shortening of the third stage of labour (by an average of 3.4 minutes). The most important finding, however, is the reduction of pathologic bleeding postpartum (≥ 500 ml) by 66% (OR = 0.34; 95% CI 0.28, 0.41). “Controlled cord traction” and “early clamping” together contribute to an important proportion of the PPH reduction in AMTL.

The relative weight of each component is difficult to establish. Trials to study each action separately appear to yield elusive results. Controlled traction of the cord is claimed to shorten the duration of the third stage of labour. While the clinical significance of diminishing this time in a non-bleeding woman by some minutes can be questioned, it does seem reasonable to assume that the risk of PPH increases in proportion to the delay of the placenta delivery.

Cord clamping

Variations in timing of cord clamping failed to demonstrate any difference in cord adherence, neonatal or maternal outcomes in a randomised controlled study (Oxford Midwives research Group 1991). An Australian study reached the same conclusion, while also including the risk of foeto-maternal transfusion at late clamping by using the Kleihauer test. No case of transfusion was found (Thomas *et al* 1990).

Neonatal considerations

The timing of clamping of the umbilical cord has been a controversial question for a long time. The estimated volume of placental transfusion varies from 20% to 60% of the existing blood volume, depending on the time of clamping and the position of the baby (Usher *et al* 1963). When the neonate is placed on the mother's abdomen and clamping is performed only once the cord stops pulsating, a more recent study has demonstrated that the blood volume of the newborns is 32% higher than in babies whose cords were clamped immediately after birth (Nelle *et al* 1995). These findings have severe implications on AMTL, as it is presently defined. A comparison of 9-month-old infants has shown higher serum ferritin values among those whose cords were being clamped late (Haschke F *et al* 1993). Iron deficiency is associated with impairment of mental and psychomotor development. This may be of critical clinical and economic importance among children in low-income settings. For these children, threatened by malnutrition, there is a risk that the decreased placental transfusion caused by early clamping could be detrimental to their well being.

The widespread acceptance of early clamping was never founded on studies evaluating the risk of depriving newborns this physiological volume of extra blood. A large clinical trial regarding the paediatric effect of early versus late clamping is needed and the result has to be taken into consideration when defining – or re-defining - the management constituting AMTL.

Delivery is a dynamic event which makes it a complex situation to study. Trials regarding individual factors of AMTL and their effect on various outcomes, must take this complexity into consideration. Not only do future trials need to be large enough to have a statistical chance of answering the question posed. They also have to account for the confounding factors and variations of a real life phenomenon. Among those are the progress and duration of delivery and actions taken during first and second stage of labour; parity, size and possible age of the parturient and size and presentation of the child.

6.3 Which uterotonic drug?

The uterotonic drug is the most important component in the AMTL package. Ergometrine was extracted by Moir in 1932 and is the oldest of the uterotonic drugs in use. Methyl ergometrine was later developed and used mainly in the USA with the same indication. Synthetic oxytocin (“syntocinon”) was introduced in 1956 by Sandoz

Products Ltd. This is now used as intravenous infusions all over the world to induce labour. A combination of 0.5 mg ergometrine and 5 IU oxytocin was later introduced as “syntometrine” in the 3rd stage of labour. As 10 IU of oxytocin showed the same effect as syntometrine, without the side-effects of nausea and hypertension associated with ergometrine, this was later to become “the drug of choice”.

Storing of drugs in ambient temperatures in tropical countries often poses problems to their continuous potency. This is the case with many vaccines and also with ergometrine, making refrigerators necessary links in the health chain. In settings where ergometrine cannot be stored at a temperature of < 8° Celsius, it is recommended that it should not be used more than one year after its manufacture (Walker *et al* 1988). A systematic research programme by WHO focused on comparing injectable ergometrine, methylegometrine and oxytocin and could demonstrate the superiority of oxytocin (WHO 1993). The better stability, equal cost and less side-effects are reasons why oxytocin is the drug of choice in AMTL, regardless of climate.

Misoprostol

Misoprostol (Cytotec®) is a synthetic prostaglandin E₁ analogue, which originally was designed to reduce gastric acid production in the ventricle and to be used against peptic ulcer. It has also proven effective for medical abortions in the first and second trimester and for the induction of labour. In contrast to oxytocin, prostaglandins have an effect not only by initiating uterine contractions, but also by ripening the cervix.

Oxytocin

WHO has conducted a double blind and randomized multicentre trial, comparing misoprostol and oxytocin in the management of the third stage of labour. (Gülmezoglu *et al* 2001). The study included 9,264 women who received 600µg misoprostol orally and 9,266 women who received IU oxytocin by an intravenous or intramuscular injection immediately after birth. The number of women in each group who had a postpartum haemorrhage exceeding 1000 ml and the number of women who needed further uterotonic treatment were studied.

In the misoprostol group 4% had a bleeding of >1000 ml compared to 3% in the oxytocin group (p<0.0001, RR 1.39). Additional uterotonics were given to 15% of the women with misoprostol and to 11% to women with oxytocin (p<0.0001, RR 1.40). Side effects like shivering (RR 3.48) and raised body temperature (RR 7.17) were more common in the misoprostol group. It was concluded that 10 IU oxytocin is preferable to 600 µg oral misoprostol. The conclusion has later been criticized as an example where statistical significance does not convey clinical relevance. The difference between 3% and 4% is indeed 25%, but this is hardly of practical, clinical importance. The fact that misoprostol can be stored at room temperature and does not need refrigeration should also be taken into consideration as should the risk of an uncontrolled spread of Cytotec® for illicit abortions.

An oxytocin preparation, which is resistant to variations in temperature, is on the list of the drugs most wanted in the future (Kaplan, Laing 2004). Research in this area has

been meagre since the beginning of the 90s. Such a heat stable preparation would make oxytocin effectiveness less depending on refrigeration and less vulnerable to electrical black outs.

Uniject™

In most low-income countries budgetary constraints in the health sector require simplified technology in public health. Parenteral oxytocin is needed for AMTL. By using Uniject™ the logistical problems of syringes and needles are avoided. The device showed to be well appreciated by both midwives and parturient women. Since Uniject™ cannot be reused, it does not add to the risk of transmission of blood borne pathogens²⁷. Recently attention has been drawn to the association of unsafe injections and the rapid spread of HIV/AIDS in Africa (Gisselquist *et al* 2002). The importance of this argument and the results of this study imply that production of large quantities of Uniject™ will be justified. This would offer a presumably less costly and less risky alternative than the prevailing routine.

6.4 Measuring blood loss

Blood loss after delivery is usually not measured but more or less roughly estimated in clinical practice. This often leads to an underestimation of 20-40% (Newton 1966) or even more when bleeding exceeds 300 ml (Razvi *et al* 1996).

The lack of accuracy can be expected to be more serious in low-income countries, where time and staff constraints frequently impede accurate assessment of postpartum blood loss. Also bleeding within normal limits may still be fatal in parturient women with severe anaemia.

Direct measurement

Blood loss can be assessed either by visual estimation, indirect measurement or direct measurement. *Visual estimation*, even by an experienced obstetrician, is known often to result in serious under-estimation (Brant 1967). Although estimated mean blood loss may agree with laboratory results, further analysis might show that the diagnosis of PPH is frequently missed (Razvi *et al* 1996).

Indirect measurement of vaginal blood loss can be carried out by a variety of methods, e.g. comparison of pre- and post-delivery serum plasma and haemoglobin concentrations (Coller *et al* 1944) or tagging red cells with various isotopes (Garhes *et al* 1962). To date, none of these methods have been found appropriate in low income countries.

Direct measurement has been used by some authors, though they do not describe in detail how the known difficulties are taken into consideration (Prendiville *et al* 1988; Nordström *et al* 1997).

Hill *et al* (1989) described the use of a plastic drape beneath the buttocks of the patient during delivery but postpartum measure was limited to ten minutes. All women, who had not delivered the placenta by that time, were subject to manual removal. This intervention cannot be justified in cases without bleeding, since most placentas will be delivered spontaneously

anyway and the exploration of the uterine cavity always poses a risk of infection. It is therefore dubious, for ethical reasons, whether such a study could be repeated today.

Recognizing that estimates of postpartum blood loss is inaccurate and that the measure in millilitres does not necessarily imply clinical relevance has motivated a search for other indicators. It has been suggested that physiological changes (e.g. low blood pressure) that threatens the life of the woman, would be a more accurate definition of PPH (McCormick *et al* 2002). This is not convincing. Individuals have different physiological blood pressure, a decline in blood pressure can be caused by other conditions than bleeding and the evaluation of a clinical condition is as arbitrary as the routine estimation of blood loss. Therefore, in research situations it should be mandatory to accept the trouble of actually measuring what is studied, not just making clinical estimates. Several previous studies fail in this respect. If we want to study the effect of a certain treatment on PPH, shortcuts like blood pressure should not be acceptable.

Cholera beds

Collecting postpartum blood loss is often untidy work Blood may be mixed with amniotic fluid and urine, soaked into sponges and linen, dispersed into buckets and spread on the floor. This is why we want to recommend our simple method of collecting blood by using a cholera bed, described in the Subjects and Methods chapter. We have compared our results with those presented by other authors, using other methods (Strand *et al* 2002). A direct comparison is however difficult because of differences in management of the third stage of labour and time of observation. We have found only one other study of similar design in which AMTL was practised and blood was collected during two hours after delivery (Razvi *et al* 1996). Their method consisted of a quantification of the blood loss by calorimetric measurement of haemoglobin content in several layers of absorbent paper. See Table 20.

The outcome of direct measurement described here appears to be well in agreement with the above-quoted study, having a similar design, but using a more elaborate method. No towels or pads are needed during the period in the cholera bed and the woman is allowed to bleed through its opening. The method deserves to be considered also in studies in affluent countries, since the problem of a satisfactory estimation of blood loss is the same regardless of economical conditions. The difficulty of measuring postpartum bleeding can be overcome, particularly in resource-scarce settings without the use of advanced laboratory equipment.

Table 20. Postpartum bleeding in two studies with similar design and an observation period of two hours postpartum.

Study	Sample size	<150 ml	> 500 ml	≥ 1000 ml	Mean blood loss
Razvi et al	112	45 40.5%	9 8.1%	0	227 ml
Strand et al	814	368 45.2%	67 8.2%	8 1%	239 ml

In Group 1, the prevalence of PPH was more than 40% (a figure reduced to 29.5% when excluding women with a bleeding of exactly 500 ml). This prevalence is unexpectedly high, but not unique. In the Swedish study referred to above (Nordström *et al* 1997) 35.9% of women not treated with oxytocin had PPH (> 500 ml). The authors find no explanation for this, except the inaccuracy in blood loss estimations. Even if we have to concede that even measurements have a component of subjectivity, we want to stress that apart from most other studies, we have measured, not merely estimated, the blood loss and therefore dare trust these figures.

Contributing factors might comprise liver damage, secondary to the high prevalence of hepatitis in Luanda. (Strand *et al.* unpublished results). Such an association is beyond the scope of this paper, but may suggest a field for future studies.

6.5 Pain

Postpartum pain has rarely been the focus of investigations, probably because it is less severe than pain during labour and there is a feeling that the "critical phase" of parturition is over. With the introduction of the new practice of Uniject™ we wanted to assess its effect on postpartum pain (Jangsten *et al* 2005). Expression of pain was assessed by two methods. A Verbal Rating Scale was used for quantitative measures and semi-structured interviews based on a questionnaire estimated pain and satisfaction with care in a qualitative approach.

Birthing women's perception of pain and pain tolerance is influenced by various factors: the individual's previous experience, anxiety, cultural standards and education, etc. The accuracy of memory and recalling labour pain is widely discussed with many methodological problems (Niven, Murphy-Black 2000). A study from Israel has shown that women with low educational levels had higher ratings of pain during labour than highly educated women. Holdcroft *et al* 2003). It has not been possible to demonstrate any difference between labour pains recorded immediately after delivery and recalled two days later (Turner *et al* 1987).

It was feared that the introduction of yet another intervention (Uniject™ injection) might aggravate the perception of pain. This did not appear to have been the case.

The principal finding of the study is that women receiving oxytocin did not report significantly more pain than women without administration of oxytocin. Hence, the introduction of AMTL, with the approach utilised, would presumably be acceptable in this population.

6.6 Jaundice

There are numerous aetiologies behind the symptom of jaundice. We have focused on some of the most likely infectious agents without a systematic ruling out of other causes. We did not have the possibility to perform liver biopsies in this study. Results from other authors (Khuroo, Kamili 2003; Dilawari, Singh *et al* 1994) suggest that

fulminant hepatic failure (FHF) may be the definite cause of mortality in hepatitis E virus (HEV) infection.

This study shows that HEV and malaria are associated with jaundice among pregnant women in Luanda and may indirectly or directly contribute to morbidity and mortality among these women. The prevalence of anti-HEV antibodies and presence of *P. falciparum* parasitaemia was significantly higher among the jaundiced cases than among the pregnant women serving as controls. It might have been expected that the combination of these two infections would have been more lethal than either one separately, but this could not be demonstrated. In this small study, this could merely be a reflection of chance.

Chronic hepatitis B virus infection did not seem to contribute to the maternal morbidity and mortality since the prevalence (10%) was the same among cases and referents. This carrier rate mirrors rates often found in countries in sub-Saharan Africa (Ayoola 1988).

Hepatitis E is an enterically transmitted acute viral hepatitis (AVH), causing large-scale epidemics in endemic areas in various low-income parts of the world, like Somalia, Ethiopia and India (Tsega, Krawczynski *et al* 1993; Bile, Isse *et al* 1994 ; Dilawiri, Singh *et al* 1994) Contaminated drinking water is the source of outbreaks of epidemics, with rivers more vulnerable than wells (Bile, Isse 1994). Mortality in pregnant women with acute hepatitis E virus infection may reach 20-30%, which is considerably higher than in non-pregnant women (Tsega, Krawczynski *et al* 1993; Kumar, Beniwal *et al* 2004).

HEV has been detected in many animal species and a zoonotic origin has been suggested (Meng *et al* 1999). HEV was identified rather recently (Reyes *et al* 1990), which indicates that most studies on AVH were done before tests of HEV were available. Patients negative for hepatitis A virus (HAV) and hepatitis B virus (HBV) were previously classified as hepatitis non-A, non-B. Around half of those has been associated with HEV, while the rest remains unknown, probably caused by other viral agents, classified as hepatitis nonA-E (HNAE) (Mallia, Nancekivell 1982).

Studies on AVH in affluent settings have not demonstrated a special predilection to pregnancy and the clinical course has been similar among pregnant and non-pregnant women. The aetiology of AVH in the high income countries is dominated by HAV (40%), HBV (30%), HCV (25%) and HNAE (2%) (Centres for Disease Control 1992). In low income countries, the aetiology is different and the most common cause of sporadic AVH is HEV (40%), HNAE (25%), HBV 22%, HCV (9%) and HAV (4%) (Khuroo, Rustgi *et al* 1994).

Pregnancy seems to increase the human susceptibility to HEV. In epidemics, the incidences of jaundice among pregnant women is almost ten fold compared to men and non-pregnant women (Khuroo, Kamili *et al* 1995). The infection is also more severe in pregnant women, especially in the third semester. The main reason of mortality in epidemics is the high rate of FHF in this group (Khuroo, Kamili 2003).

Khuroo and Kamili (2003) reported a study from Srinagar, India, that well illustrates the association of HEV infection and serious pregnancy complications. They compared

pregnant and non-pregnant women of childbearing age with sporadic AVH regarding clinical outcome, serology for hepatitis, biochemical parameters and biopsies of the liver in selected group of patients and all fatal cases (post-mortem). The incidence of HEV was twice as high among pregnant women (86% compared to 42%). The risk to develop FHF increased six fold in pregnancy (62% compared to 10%) HEV could be detected in almost all cases (96%) of FHF. The major complications of FHF were cerebral oedema and disseminated intravascular coagulation, both occurring more often among pregnant women. Cerebral oedema contributed to a worse prognosis for FHF patients. Less than half of patients with FHF survived.

Their finding that patients with FHF and HEV infection had the best chances of survival seems contradictory. This has also been reported from Pakistan (Hamid, Jafri *et al* 1996) where no clinical nor laboratory feature was found which could accurately distinguish acute HEV infection from acute fatty liver of pregnancy. Patients with FHF and HEV had a better prognosis than other groups with FHF, mortality 16% vs. 68%. A study from Indore, India, reported seemingly the opposite: mortality was highest among HEV infected women with FHF in the third trimester (Jaiswal, Jain *et al* 1999). The conclusive interpretation yields that HEV infection poses the greatest risk of developing FHF in comparison with other causes. However once FHF is established, the association with HEV has a better prognosis than FHF by other causes.

The incidence of HEV among pregnant women with jaundice in Luanda was 40%, less than half of what was detected in Srinigar. This is most likely an effect of the exclusion criteria used in Srinigar to rule out non hepatitis causes and include only *sporadic* AVH. In Luanda all pregnant women with jaundice entered the study.

Maternal mortality in the Srinigar study was almost of the same magnitude as in the Luanda study; 24% and 30 % respectively. The proportion of stillbirths and abortions, however, was much higher in Luanda: 55% compared to 5%. The results from another study by Khuroo *et al* (1995) suggest a vertical transmission of HEV, which could explain morbidity and mortality among offspring. In five out of eight children born to mothers with HEV in the third trimester, they could detect the virus in cord or birth blood samples.

To conclude the comparison we found HEV less associated with AVH and jaundice among pregnant women, but more lethal in Luanda than in Srinigar. In 60% of the women with jaundice in Luanda anti-HEV antibodies could not be demonstrated. This indicates that we are still far from an explanation to the high morbi-mortality. It is likely that future aetiological discoveries or further understanding of mixed infections will contribute to the answer.

HEV infection is an example of “pathology of poverty”. The virus is rare in high income countries with safe distribution of clean water. Cases have mostly been reported to be imported. Anti-HEV antibodies have been detected in sporadic cases of AVH in the United Kingdom suggesting the risk of previous underestimation (McCrudden, O’Connell *et al* 2000). The preventive effect of an acceptable level of hygiene should have highest priority in building post war Angola. The HEV prevalence of 12.5% among the controls indicates the spread of the virus in the city. Luanda was built for a

population of some 500,000, but now harbours some 3-4 millions inhabitants, the majority living under deplorable conditions. With drinking water and sewage facilities in disarray, there is a constant risk of new outbreaks not only of HEV, but also of other epidemics. Improvement of the infrastructure, in particular sanitation with construction of safe water supplies well separated from latrine areas, is the most basic means to reduce the incidence of hepatitis E in the city. Vaccination would be another route of preventive action. A recombinant vaccine against HEV is about to be tested in phase II and phase III trials (Emerson, Purcell 2001). These two measures of preventive medicine together offer a realistic possibility to decrease the outbreak of HEV.

Malaria (*P. falciparum*) was found to be the second infectious agent with a statistically significant association to jaundice in the study. *P. falciparum* during pregnancy increases the risk of maternal anaemia, abortion, stillbirth, prematurity, intrauterine growth retardation and low birth weight (Brabin 1991). The susceptibility to malaria is highest in the second and third trimester and also the first 60 days into the post partum period (Diagne, Rogier *et al* 2000). The risk seems to be particularly elevated during the first pregnancy with higher parasite density (Bell 1995).

Fifty patients with jaundice and confirmed *P. falciparum* were studied by Kochar, Sing *et al* (2003). They found a combination of mostly conjugated hyperbilirubinaemia and increased levels of AST and ALT. Liver biopsies showed hepatocellular necrosis. Together these signs are evidence of a hepatocytic dysfunction to which the authors suggest the term “malarial hepatitis”

The high mortality among pregnant women with jaundice indicates that one of the important tasks at ante-natal care (ANC) clinics is to check for malaria and administer prophylactic treatment on a routine basis. Infected women should receive effective treatment and be referred for hospital treatment when necessary.

The possibility of reducing malaria morbidity in Africa is pursued in new strategies for “rolling back” malaria. Studies from Kenya (Parise, Aiyisi *et al* 1998) and Malawi (Steketee, Wirima *et al* 1996) have tried to target “high risk pregnancies” for prophylactic treatment in order to decrease the risk for *P. falciparum* resistance to development for Chloroquine. In a study on icteric pregnant women in Nigeria, it was concluded that haemolysis was the most common mechanism giving rise to jaundice. This was interpreted as a sign of pyrimethamine-resistant *P. falciparum* (Anyia, Oshi 1999).

SP (sulphadoxine-pyrimethamine, Fansidar®) given at the first ANC visit and at the beginning of the third semester has proven highly effective in reducing periphery and placental malaria parasitaemia. The same regimen has also been tested in Mozambique among nulliparas and 1-paras below 21 years of age and resulted in increased mean birth weight, placenta weight and a prolongation of gestational age (Challis)

Such a simple preventive treatment might also be suitable in the Luanda setting. Along with the sanitary improvements suggested above this would reduce the risk of malaria infection among pregnant women.

6.7 Audit of avoidability

Outcome indicators of quality of obstetric care have proved to be inappropriate for comparison over time. Process indicators are more appropriate when evaluating efforts in safe motherhood (Campbell *et al* 1997).

We have used audit of clinical practice in two of the studies. The avoidability of UR in study III and waiting time and partograph quality in obstetric emergencies in study IV are examples of morbidity-specific process indicators.

The study on UR disclosed that almost two out of three cases could in some respect be traced to inadequate obstetric care at the level of the hospital receiving the parturient women. UR is one of the most serious complications that can be prevented in a setting with good obstetric vigilance and partograph culture.

The concept of avoidability of maternal death has previously been used in studies from low-income countries and revealed severe deficiencies in care (Wessel *et al.* 1999, Granja *et al.* 2001). A high proportion of avoidability of maternal deaths is, however, not confined to low-income countries (Purificação-Araujo 1985). The specific question of avoidability and UR has rarely been addressed.

There are reasons to assume that regular audits have to be repeated in order to ensure the improvement that has been achieved. In practical life this is often difficult. In a paper on audit of “near misses” from 12 hospitals in four African countries, Filippi *et al* reported failure of sustaining the audit practice in a majority of hospitals after the end of their project (Filippi *et al* 2004).

Approaches on how to carry out the revolving cycle of re-evaluation vary from informal discussions of selected cases to structured reviews of large number of cases using statistical analysis. The criterion-based clinical audit is an example of the latter, quantitative, method monitoring the extent to which different complications are treated according to a set of explicit criteria (Graham *et al* 2000). This would give information of the treatment of UR, but would fail in identifying the avoidability in each case of obstructed labour leading to UR.

In order to consider our results in an African context, we wanted to compare them with those of other studies from sub-Saharan Africa (Rajab, Mulumba 1998; Diallo *et al* 1998; Balde *et al* 1990; Elkady *et al* 1993; Fekadu *et al* 1997; Adanu, Obed 2001; Zanconato *et al* 1994; Ola, Olamijulo 1998; Ekele *et al* 2000, Nkata 1996).

We estimate that 24 women (21.8%) had a UR before or just after admission to the hospital, which is the same proportion as in Maputo. In the present study the diagnosis of UR was made either after vaginal delivery or during surgery in 56.3% compared to 80% in Maputo (Zanconato *et al* 1994). In Lagos, on the other hand, 75% of the URs were diagnosed before surgery (Ola, Olamijulo 1998). The variation in these figures reveals differences not only between countries, but also between regions, as shown in the reports from different parts of Nigeria (Diallo *et al* 1998; Ola, Olamijulo 1998; Ekele *et al* 2000). The study from Botswana (Rajab, Mulumba 1998) was based on few

cases, but might suggest a more effective obstetric care than in the other settings. These and similar studies have been displayed in Table 21.

Table 21. Comparison of studies on uterine rupture in African settings

<u>Country</u>	<u>Ref</u>	<u>No</u>	<u>Year</u>	<u>Prev.</u> ‰	<u>MM</u> %	<u>PM</u> %	<u>Scar</u> %	<u>GMP</u> %	<u>PP</u> %
Angola	Current	110	98-99	4.9	12.8	75.4	28.2	46.3	6.3
Botswana	Rajab	18	93-96	0.8	0	22.2	61.0	nd	nd
Conakry/G.	Balde	81	85-86	8.4	20.9	75.3	21.0	nd	nd
Egypt	Elkady	126	79-88	2.7	21.4	73.2	23.0	68.3	3.2
Ethiopia	Fekadu	245	91-95	nd	5.3	98.0	9.8	50.6	0.8
Ghana	Adano	106	95-98	2.2	1.8	77.1	24.7	nd	nd
Mozambique	Zanconato	96	90-91	2.4	7.3	62.9	45.8	29.6*	3.1
Nigeria	Ola	80	85-92	5.0	17.5	86.3	27.5	25.0	7.5
Nigeria	Ekele	43	95	13.5	38.0	98.0	10.0	nd	nd
Nigeria	Diallo	50	nd	18.0	16.0	96.0	nd	nd	nd
Zambia	Nkata	32	93-94	17.2	43.8	nd	9.4	18.8	43.
									8

*Abbreviations used: Ref: reference, first author; MM: maternal mortality; PM: perinatal Mortality; Scar: Previous CS; GMP: grand multiparous women (≥ 4 births; *in Mozambique ≥ 5 births); PP: primiparous women.*

A previous CS is the most common among risk factors for UR (Williams Obstetrics 2004). However, with close monitoring of the wellbeing of both mother and foetus and with availability of obstetric, anaesthetic and surgical staff around the clock, attempted vaginal birth after caesarean section (VBAC) has been recommended by several authors (ACOG 1996; Enkin 1989). Yap *et al* (2001) reported 17 cases of UR out of 2,033 VBAC (0.8%), with no maternal death and two neonatal deaths of low gestational age. In low-income countries, VBAC has been questioned. A meta-analysis of 17 sub-Saharan studies found, however, a prevalence of UR of 2.1% and concluded that VBAC is relatively safe and can be practiced, provided that there is access to emergency CS (Boulvain *et al* 1997).

Misoprostol was associated with UR in eight cases in this study, among which there was one missed abortion at 19 weeks. UR has previously been reported after treatment with misoprostol as early as in the 9th gestational week of a woman with previous CS (Eman, Greenhalf 2000). The risk of UR after induction of labour should not be neglected (Majoko *et al* 2002).

Grand multiparity is often considered a risk factor for UR (Williams Obstetrics 2001), especially in combination with oxytocin stimulation. The risk of UR has been reported to be elevated 20 times in women who are para 7 or more (Fuchs *et al* 1985), although Bique *et al* (1999) found no case of UR among 165 grand multiparous women induced with vaginal misoprostol in their study from Mozambique. Primiparity, on the other hand, is no guarantee against UR. Most other settings have not reported a proportion of primiparous women as high as in Luanda (6.3%). This is surpassed only in a study from rural Zambia, where primiparous teenagers living far from the hospital were at greatest risk (Nkata 1996).

Macrosomia of the baby increases the risk of foeto-pelvic disproportion and thereby, theoretically, the risk of UR. Only two children with a birth weight of > 4,500 g were found in this study. Over the last decades there has been an increase in birth weight in some high-income countries with no reported parallel increase in UR (Meeuwisse, Otterblad-Olausson 1995). This suggests, again, that UR is mostly a diagnosis related to inadequate quality of care.

In conclusion, we have found that a majority of URs could have been avoided and represent an area for possible improvements regarding this obstructed labour. During the second year the personnel was aware of the ongoing study and the risk of being scrutinized at regular audits. We therefore expected to find a higher proportion of non-avoidable UR, a lower case fatality rate and a lower prevalence of UR. The reasons why this did not occur are not clear. The elevated number of births in 1999 (12,138, compared to 11,595 in 1998) might have implied the passing of yet another limit at which quality of care is hampered in an already heavily overburdened situation. As long as structural changes are not made to meet unmet need, improved audit and monitoring of women at risk and appropriate medical interventions may not be sufficient.

6.8 Audit of waiting time and partographs

In this study we have demonstrated a substantial improvement of quality of care over time regarding referrals of obstetric emergencies along with efforts to sensitise staff both in the referring and the admitting health units. By using the results from the first study for a clinical audit, sub-standard care with long waiting times, poor quality partographs and high mortality figures were revealed and provoked a challenge for improvement. Special areas of concern were identified and after a partograph education programme, a second data collection took place. A dramatically reduced waiting time, an improved vigilance with use of partographs and a more proactive stand by the hospitals, all helped in reducing the maternal mortality to zero in the second study period.

During the last years much emphasis has been given to the correct use and interpretation of the partograph in the in-service training of hospital staff in Luanda. A local translation of the WHO material on partograph use (WHO 1994) has been completed, printed and distributed to midwives and doctors at lectures and seminars. There is no doubt that the partograph has meant dramatic improvement in the perception of the birthing process in countries where no such notion was present before (Bergström

2000). We believe that the partographs studied give a fairly accurate picture of the clinical situation. Therefore it has been part of both audit studies.

With the deplorable results in the first data collection, an improvement was to be expected by the mere focusing on the problems. Even if an improvement could be expected, this simple example of feed-back nevertheless illustrates the importance of audit of process indicators in clinical practice.

The problem of follow-up

A large proportion of women, who were registered as “referred” in the books at the SPPs were not possible to trace at the hospitals. One explanation could be the unacceptably high referral rate at Cazenga. Many of the referred women from there were probably not really in an emergency situation and were not motivated to continue to the hospital. It could be argued that this loss to follow-up disqualifies the above findings since they are based on traced referrals only. This is however an inherent problem when studying referrals of obstetric complications in African settings. Similar figures have been reported from e g Tanzania (Kowalewski *et al* 2000), Morocco (Belghiti *et al* 1998) and Ghana (Martey *et al* 1998).

The technical aspects of referrals may be too narrow a focus since the number of non-traced persons gives rise to further questions. In resource-scarce settings like the current one, patients may feel forced to base their decisions not on what is medically sound, but on what is economically possible and culturally appropriate (Kwast 1996).

Although many women in Luanda deliver without assistance, it should be recognised that the public medical services work in competition with alternative health systems. Our observations indicate that many of the referred women had preferred home birth with the help of a friend or a traditional birth attendant to a delivery in an overcrowded maternity ward. It has been shown that expert-defined risk has little influence on women’s decision to seek care. Apart from financial pressures, many women have been found to fear discrimination and disrespect (Kowalewski *et al* 2000). Unfortunately these factors have a bearing also in Luanda where negative perceptions of the hospitals may make women hesitate to seek care and the demand for informal user-fees seems to breed a fatalistic attitude among birthing women: “From where will we take that kind of money? You stay home and hope for the best”.

Prolonged labour was the single most common reason for referral in both periods. The two collections of data did not occur at the same time of the year. We therefore expected to find differences in reasons for referring. In the second study protocol we listed fifteen diagnostic alternatives but still did not register common severe diagnoses like malaria and jaundice. Referrals of obstetric emergencies have been the focus of several African studies during the past decade and obstructed/ prolonged labour is repeatedly one of the main indications (Martey *et al* 1998; Lompo *et al* 1993; Van Coeverden *et al* 1994) In the study from Burkina Faso (Lompo *et al* 1993) maternal mortality increased proportionally with the distance to the hospital, which illustrates one of the “delays” in obstetric care (Thaddeus, Maine 1994).

The emphasis put on partograph education and the decision to give highest priority at the hospitals to referred women were crucial for the final results. In studying waiting time we were mainly concerned with the duration of transport and the “admission to treatment interval”. Only few such studies have been published previously. A reduction of the same magnitude as in this paper has been demonstrated for women with obstetric complications from some other African settings. In a general hospital in Nigeria, a mean interval of 11 hours decreased to 1.5 hours after intervention (Sabitu *et al* 1997). At a teaching hospital, the same team could demonstrate a reduction in both waiting time (from 3.7 hours to 1.6) and overall case fatality rate (by 21%) (Ifenne *et al* 1997).

“Decision to delivery interval” has recently been reported in a paper from Abidjan among cases of life-threatening obstetric emergencies (with a median time of 4.8 h and 2.8 h respectively from the two hospitals studied) (Gohou *et al* 2004). Routine records in low-income countries are often too poor in information to allow for analysis of time of decision-making and have not been included in the audit of referrals. In the UR study, however, we have also addressed the “decision to delivery interval” indicator.

Audit of clinical practice thus yields process indicators that can contribute to enhance quality of obstetric care, yield suggestions for further education and improvement of clinical routines and facilitate their monitoring over time. This would not be possible with only the information from an outcome indicator.

7. CONCLUSIONS

7.1 Study I

This study has demonstrated a more dramatically beneficial effect of AMTL than in the quoted meta-analysis from more affluent countries. To our knowledge this is the most extensive prospective study in Africa elucidating the role of AMTL and the first time Uniject™ is used in a prospective study on PPH. In most low-income countries budgetary constraints in the health sector require simplified technology in public health. Parenteral oxytocin is needed for AMTL. By using Uniject™ the logistical problems of syringes and needles are avoided. The device showed to be well appreciated by both midwives and parturient women. Since Uniject™ cannot be reused, it does not add to the risk of transmission of blood borne pathogens. Recently attention has been drawn to the association of unsafe injections and the rapid spread of HIV/AIDS in Africa. The importance of this argument and the results of this study imply that production of large quantities of Uniject™ will be justified. This would offer a presumably less costly and less risky alternative than the prevailing routine. AMTL should be used a routine also in low income countries and Uniject™ has proven to be part of appropriate technology.

7.2 Study II

The case fatality rate among women with jaundice during pregnancy and their offspring is extremely high. In many cases the cause of this mortality remains unclear. We have

shown that *P. falciparum* parasitaemia and hepatitis E are associated with jaundice in the setting studied. Hence, preventive measures for malaria and hepatitis E should be implemented. The most basic need in Luanda is functioning infrastructure of clean water and sewage. Together with directed preventive measures against malaria among pregnant women and a future vaccine against hepatitis E, there is a possibility to reduce the numbers of women with jaundice.

7.3 Study III

The majority of URs in this study could have been avoided. This represents the proportion of substandard care and the level of possible improvement regarding this complication. During the second year the personnel was aware of the ongoing study and the risk of being scrutinized at regular audits. We therefore expected to find a higher proportion of non-avoidable UR, a lower case fatality rate and a lower prevalence of UR. No such improvement could be detected and the reasons why this did not occur are not clear. The elevated number of births in 1999 (12,138, compared to 11,595 in 1998) might have implied the passing of yet another limit at which quality of care is hampered in an already heavily overburdened situation. As long as structural changes are not implemented, improved audit and monitoring of women at risk and appropriate medical interventions may not be sufficient. Performing morbidity-specific audit by highlighting major weaknesses in obstetric care is an important tool to sensitize staff on the issue of avoidability.

7.4 Study IV

Audit of referrals of obstetric emergencies addresses a process indicator of related to EOC. We have studied the time duration for patients from peripheral birth unit to admission at the receiving hospitals. This gives an example of how process indicators, contrary to outcome indicators, help to identify shortcomings, elucidate reasons therefore and act upon the results. This study has shown a dramatic shortening of waiting time, an increase in CS rate, high agreement in diagnosis between peripheral and central units as well as an increased quality of partographs.

In spite of the statistical limitations of the study, we cautiously interpret the findings as signs of an improved quality of care regarding the referral of obstetric emergencies in Luanda during the periods studied. Future studies also need to include factors affecting patients' reluctance of being referred.

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