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A systematic review of the treatment and management of pre-eclampsia and eclampsia in Nigeria

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systematic review

ENDING Eclampsia

A SYSTEMATIC REVIEW OF THE TREATMENT AND MANAGEMENT OF PRE-ECLAMPSIA AND ECLAMPSIA IN NIGERIA

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List of Abbreviations

ANC	Antenatal care
BP	Blood pressure
CFR	Case fatality rate
CS	Cesarean section
dBP	Diastolic blood pressure
DFID	Department for International Development
EML	Essential Medicines List
EmOC	Emergency obstetric care
EmONC	Emergency obstetric and newborn care
HDP	Hypertensive disorders of pregnancy
HELLP	Hemolysis, elevated liver enzymes, low platelet count
LBW	Low birth weight
MCSP	Maternal and Child Survival Program
MD	Maternal death
MDG	Millennium development goals
$MgSO_4$	Magnesium sulphate
mmHg	Millimeters of mercury
MMR	Maternal Mortality Ratio
MOH	Ministry of Health
Ob/Gyn	Obstetrician and gynecologist
PE/E	Pre-eclampsia and eclampsia
PHC	Primary healthcare center
PIH	Pregnancy-induced hypertension
PNC	Postnatal care
PTB	Preterm birth
RH	Reproductive Health
sBP	Systolic blood pressure
USAID	United States Agency for International Development
WHO	World Health Organization

Background and Introduction

Despite significant declines in maternal mortality rates, sub-Saharan Africa continues to face the burden of maternal deaths due to pregnancy related complications. Nigeria is one of the ten most dangerous countries for a woman giving birth and is reportedly responsible for 14% of the world's maternal deaths (National Population Commission [Nigeria] & ICF International, 2014). Nigeria's MMR is estimated to be 576 deaths per 100,000 live births; one in 30 women in Nigeria will die from a cause related to pregnancy or childbirth (NPC & ICF International, 2014). Poor health systems, lack of trained staff and quality of care, low levels of education, poverty, patriarchal societies and women's lack of agency to make decisions about their own healthcare needs are some of the factors contributing to the high maternal mortality and morbidity (NPC & ICF International, 2014)

Pre-eclampsia and eclampsia (PE/E), pregnancy-related hypertensive disorders, are consistently cited as a leading cause of maternal morbidity and mortality Nigeria. In addition to maternal morbidity and mortality, PE/E can increase the likelihood of preterm or stillbirth (Onyearugha, & Ugboma, 2012; Olusanya & Solanke, 2012b; Owolabi et al., 2008). Both PE/E are preventable and the deaths due to PE/E can be avoided through timely detection and management of complications during and after pregnancy (The World Health Organization, 2011).

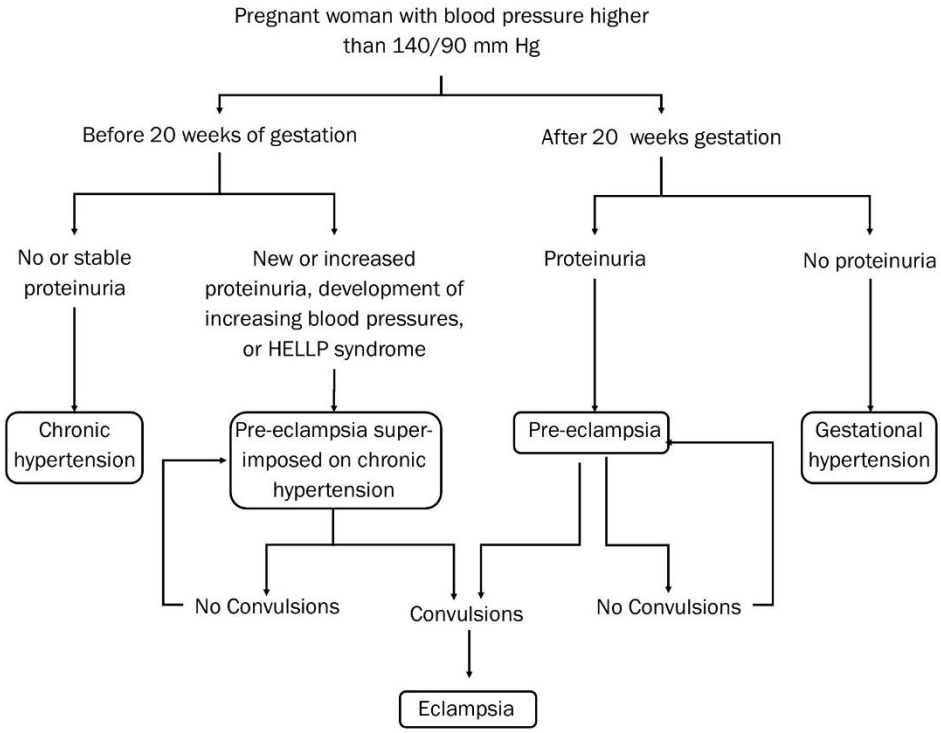
To fully appreciate the enormity of the problem at country level, we conducted a systematic review of published papers on PE/E in Nigeria from 2000-2015 in order to understand the key challenges, gaps and interventions related to the prevention and treatment of pre-eclampsia and eclampsia.

WHAT IS PRE-ECLAMPSIA AND ECLAMPSIA?

While the medical cause of eclampsia is unknown and definitions of the condition vary, there are some generally-accepted signs and symptoms that are used to diagnose pre-eclampsia and eclampsia in pregnant women. Pre-eclampsia is a condition where a woman experiences a rapid elevation of blood pressure to $\geq$ 140/90 mmHg (hypertension) and high levels of protein in the urine (significant proteinuria $\geq$0.3g/day or $\geq$30mg/mmol of urinary creatinine in random sample) after 20 weeks gestation (Magee et al., 2015). If untreated, it can progress to eclampsia, characterized by seizures, and other complications such as kidney or liver damage and ultimately death of the mother and/or fetus.

Diagnosing pre-eclampsia and managing it before it progresses to severe pre-eclampsia or eclampsia is a critical strategy to promote maternal and newborn health. Pre-eclampsia can be managed and eclampsia can be prevented by routine screening of blood pressure and protein levels in urine for pregnant women during antenatal care (ANC) visits. Health care providers can manage high BP in pregnant women using antihypertensive drugs that are safe during pregnancy, prevent and control eclamptic convulsions with injectable magnesium sulphate ($MgSO_4$) and, if at PHC facility, should refer the woman for follow-up monitoring and management of PE/E.

FIGURE 1 Diagnosing pre-eclampsia and eclampsia



Adapted from: Wagner, L.K. (2004)

The World Health Organization (WHO) recommends three main evidence-based approaches to prevent maternal mortality due to PE/E (The World Health Organization, 2011):

1) **Preventing** the incidence of PE/E by screening all pregnant women for signs and symptoms during antenatal care (ANC) check-ups. Preventative interventions include: calcium supplementation during pregnancy, low-dose aspirin prophylaxis and family planning methods to delay pregnancies.
2) **Detecting** early signs of PE by measuring blood pressure and protein levels in the urine during ANC visits to monitor and manage pre-eclampsia.
3) **Managing** severe cases of PE/E by administering anti-convulsant therapy—magnesium sulphate ($MgSO_4$) —to stop seizures followed by careful monitoring of the pregnant mother and her fetus and plan timed delivery of the baby.

The World Health Organization recommends use of $MgSO_4$ as the standard method of preventing eclampsia in women with severe pre-eclampsia and of treating eclampsia (The World Health Organization, 2011). Women treated with $MgSO_4$ have a 67% lowered risk of recurrent seizures compared to women who were treated with diazepam and phenytoin (Euser & Cipolla, 2009). Despite its proven efficacy, this inexpensive drug is often underutilized for various reasons including lack of awareness and continued use of outdated methods (like diazepam and phenytoin), poor access to supplies, and insufficient number of trained personnel to administer $MgSO_4$ (Yeager & Patel, 2012).

PRE-ECLAMPSIA AND ECLAMPSIA IN NIGERIA

In Nigeria, approximately 34% of pregnant women receive no antenatal care, putting them at higher risk of maternal mortality (NPC & ICF International, 2014). A recent, nationwide cross-sectional survey found that pre-eclampsia and eclampsia is the leading cause of maternal mortality in Nigeria and is responsible for 28.2% of maternal deaths; the other main contributors to maternal mortality are hemorrhage (24.4%) and pregnancy-related infection/sepsis (14.2%) (Oladapo et al., 2015).

This systematic review of peer-reviewed literature published after 2000 aims to identify the interventions adopted to treat and manage pre-eclampsia and eclampsia. It specifically looks at issues around the quality of care, gaps in the evidence, and barriers to accessing services for PE/E in Nigeria.

NIGERIAN HEALTH SYSTEM AND MATERNAL HEALTH POLICIES

Nigeria is Africa's most populous nation of 162.5 million people. The Nigerian health system divides hospitals into primary, secondary, and tertiary hospitals with referral linkages between them (Tukur et al, 2009). In addition, Nigeria divides levels of governance into three distinct and independent entities, which are: federal, state, and local governments. The tertiary healthcare systems are managed by the federal government, the secondary institutions by the state government and the primary health care by the local government authorities, with no formal connection between these levels of care (Tukur et al, 2009). Patients with Pre-eclampsia and eclampsia are often referred from primary to secondary and tertiary health facilities for management. Delays in care are common due to lack of knowledge from the patient and poor understanding of the seriousness of the condition, as well as differing governance structures in the healthcare system.

Some of the key national policies and strategies adopted in Nigeria to address the high MMR include: Safe Motherhood Initiative launched in Nairobi in 1987, the road map for accelerating the attainment of MDG 4 and MDG 5 in 2005, FIGO's Safe Motherhood and Newborn Health Committee Initiative (2006-2011), the Integrated Maternal Newborn and Child Health (MNCH) Strategy in 2007, the Midwives Services Scheme (2009) which was launched by the National Primary Healthcare Development agency, USAID's Saving Mothers, Giving Life initiative (2012) and their Maternal and Child Survival Program (MCSP) and DFID's Maternal and Newborn Child Health Programme. The Federal Ministry of Health has included all of the necessary drugs for the management of hypertensive disorders of pregnancy (Labetalol, Hydralazine, Methyldopa, Nifedipine, magnesium sulphate, and calcium gluconate), on the national Essential Medicines List (EML) which was last updated in 2010 (Federal Ministry of Health Nigeria, 2010). The inclusion of these drugs on the EML means that every facility should maintain a regular supply of these medications; though this is not always the case. While some of these efforts have put a focus on the high maternal mortality rate in Nigeria, much remains to be done to address some of the challenges in the delivery of services for the prevention and treatment of pre-eclampsia/eclampsia. It will be necessary to re-visit some of the policies and on-going programs and explore how we may improve some of the gaps in health management to achieve better maternal health.

Methods

This systematic literature review was conducted in three phases to collect, organize and analyze the published literature on pre-eclampsia and eclampsia in Nigeria.

IDENTIFYING ARTICLES FOR REVIEW

Search of Databases

The research team developed two sets of key terms related to pre-eclampsia and eclampsia that captured citations for peer-reviewed papers related to detection, management, and prevention of PE/E (Appendix I). The first search was designed to capture results that do not mention PE/E explicitly and the second search included the MeSH terms for PE/E and the rare complication known as, HELLP syndrome. The two searches were run in bibliographic databases including: PubMed, ScienceDirect, World of Science, Cochrane, POPLINE, and Wiley Online Library. These searches used a combination of terms linking various aspects of the diagnosis, treatment, and prevention of pre-eclampsia, eclampsia and hypertensive disorders of pregnancy. Searches were limited to articles published from 2000 to 2015 (April).

To accommodate the large number of key terms included in the second search, the terms were divided into three sub-searches to avoid any inadvertent omissions. The exact combinations of search terms used can also be found in Appendix I. The three sub-searches resulted in a high volume of duplicate citations.

Google Search

In an effort to identify any articles that may have been missed during the database searches, a simple google search was done using the following search terms:

> "eclampsia" or "pre eclampsia" or "preeclampsia" or "pre-eclampsia" AND Nigeria

From the articles identified, the same search was run on the website or database hosting those articles. These sites included: Hindawi.com, African Journals Online (AJOL), Journal of Obstetrics and Gynaecology Canada (JOGC), Journal of Family and Reproductive Health (JFRH), Guttmacher Institute, International Federation of Gynecology and Obstetrics (FIGO). A final effort was made to ensure capture of any relevant articles by running two simplified searches in PubMed, results were duplicates with articles that had already been identified, and the searches were:

> [“task shifting” AND Nigeria AND (“Magnesium sulfate” OR “magnesium sulphate”)]
>
> and
>
> [(“magnesium sulfate” OR “magnesium sulphate”) AND Nigeria].

Articles were excluded prior to phase I review if they were duplicate citations, if they pertained to non-human subjects, or if it was evident from the title that the article was not related to Nigeria (e.g. specifically identified the location of the study as somewhere other than Nigeria).

Titles and abstracts for the articles were imported into an excel spreadsheet adapted from “Excel Workbook for 2 Screeners” by Helena VonVille, licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License, available online at http://libguides.sph. uth.tmc.edu /excel_SR_workbook.

PHASE I: EXCLUSION CRITERIA

During Phase I of the systematic review two independent reviewers KK and IC conducted title and abstract screening to determine if the abstracts should be included or excluded in the next phase of the review. Abstracts were excluded if they were:

1) Not about Nigeria,
2) Not related to pregnancy; (for example: abstracts about male subjects and abstracts that discussed hypertension but not in pregnancy were excluded),
3) Not related to PE/E or associated risk factors, symptoms, or complications.

The two screeners then reconciled their reviews and in cases where it was unclear from the abstract if an article would provide relevant information, the screeners consulted the full text of the article.

PHASE II: INCLUSION AND EXCLUSION

In the second phase, the two reviewers read the full texts of the remaining articles to determine their relevance and eliminated any papers that were not related to PE/E, did not focused enough on Nigeria or did not provide any substantive data or observations specific to Nigeria, and any papers for which a full text could not be acquired.

PHASE III: CATEGORIZATION

Finally, the remaining articles were sorted into five types of papers—based on the main topic of each—that were found during the systematic review.

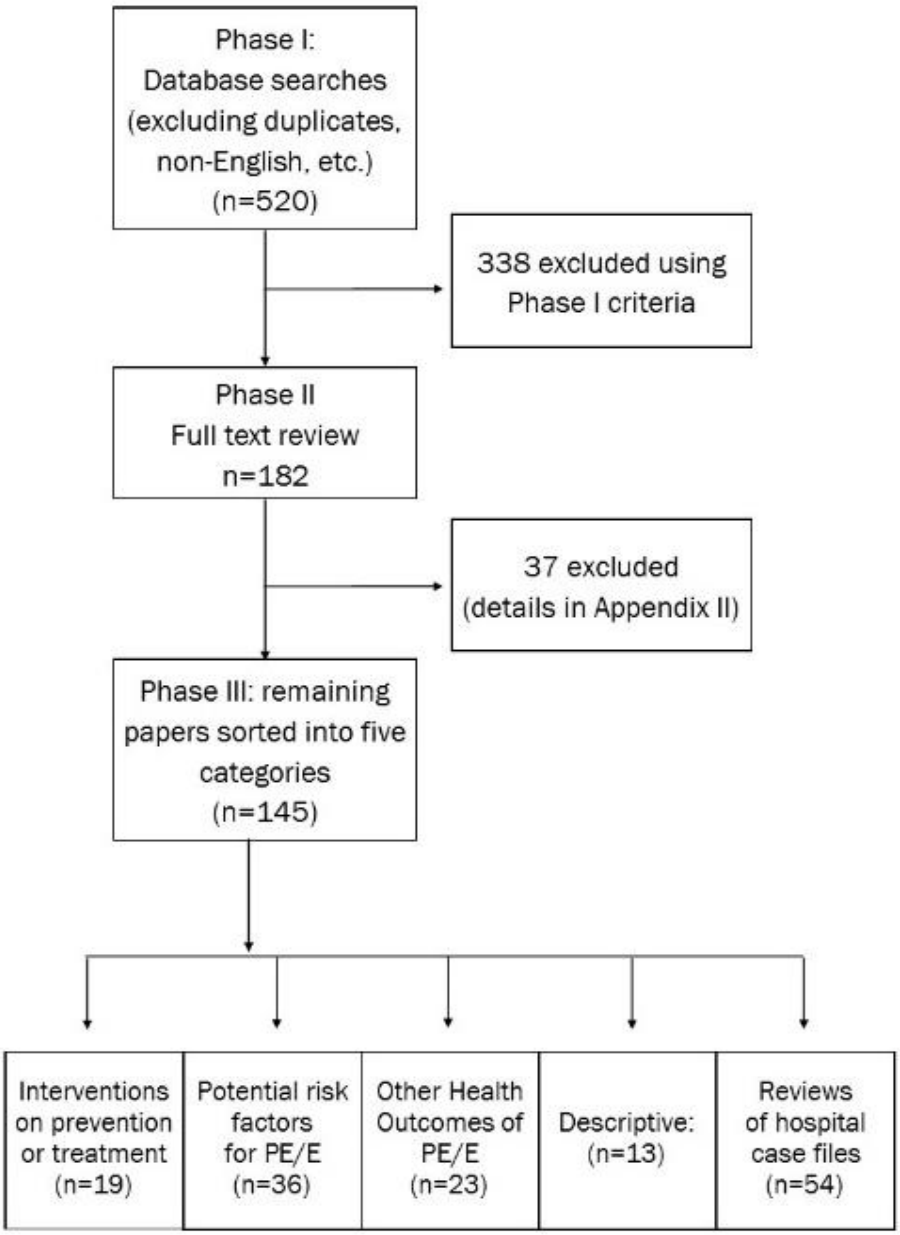
1) Intervention: papers that explore questions related to prevention and treatment of PE/E
2) Potential risk factors for pre-eclampsia and eclampsia
3) Other health outcomes associated with pre-eclampsia and eclampsia
4) Descriptive papers: including program descriptions/summaries and literature reviews
5) Reviews of hospital case files summarizing maternal mortality rates, causes of maternal mortality and the proportion of maternal mortality attributable to PE/E (and other hypertensive disorders in pregnancy).

The goal was to identify articles that presented evidence on interventions that addressed the diagnosis, treatment, or prevention of pre-eclampsia or eclampsia.

Results

After removing duplicate citations and those that were obviously unrelated to this review, the initial database searches identified 520 abstracts which were included in Phase I review. The two reviewers removed 338 articles that were deemed to not fulfill the inclusion requirements for Phase I. During Phase II, 37 articles were removed because they did not provide enough, relevant information specific to Nigeria or a full text document could not be located (details in Appendix II). A total of 145 articles were included in the systematic review.

FIGURE 2 **Flow diagram of systematic review methods and results**



SUMMARY OF TOPICS FROM THE LITERATURE

Strategies for prevention and treatment of PE/E

Nineteen studies relating to strategies for the prevention and/or treatment of PE/E were identified in this systematic review. Key data was extracted from these papers and compiled in a summary table (see Appendix III). These articles look at possible strategies for reducing mortality due to pre-eclampsia and eclampsia in Nigeria.

There were six major topics that emerged from these nineteen papers looking at best practices for preventing and treating PE/E including: confirming $MgSO_4$ is safe and effective, testing different dosing mechanisms, determining different methods for delivering patients with PE/E, improving case monitoring, creating and incorporating policy and management guidelines, and re-training of providers/task-shifting to lower cadres.

$MgSO_4$ is safe and effective

Two papers confirm that magnesium sulphate is a safe and effective treatment for eclampsia and is a better option than other anticonvulsants like diazepam. Altman et al. performed a randomized placebo-controlled trial (known as the Magpie Trial) that showed that in 33 countries (including Nigeria) which demonstrated that $MgSO_4$ is safer and more effective for controlling fits in eclamptic women than diazepam (Altman et al., 2002). The Magpie Trial was the first large, multi-country, randomized trial to generate evidence on the safety and efficacy of $MgSO_4$ in women with eclampsia; this study lead to the determination that $MgSO_4$ is the drug of choice and should be used over other anticonvulsants to control eclamptic fits.

The second paper, Ugwu et al. involved a before-and-after comparison of health outcomes based on retrospective case review from hospital records (Ugwu et al., 2011). During the three year study period, the University of Nigeria Teaching Hospital, Enugu, saw 77 cases of severe PE; 47 of whom were treated with diazepam and 30 of whom received $MgSO_4$. Only one woman experienced recurrent seizures, and she had been treated with diazepam. During the study, no maternal deaths occurred due to severe PE, however, women in the diazepam group were more likely to experience prolonged hospital stay.

$MgSO_4$ dosage

There are currently two predominant regimens for administering $MgSO_4$ to women with severe PE, impending eclampsia, or eclampsia: the Pritchard regimen and Zuspan regimen. The Pritchard regimen has been considered the 'gold standard' treatment method in low resource settings since 1925, but there is no evidence to show that this is best and most efficient mode of treating convulsions associated with PE/E. The Zuspan regimen requires more medical skills and equipment (involves setting up an infusion pump).

Four papers identified in this review looked at the question of dosage and tested alternate regimens. One was a descriptive comparative study conducted at the Federal Medical Centre in Katsina where women presenting with severe PE during the two study periods received a different dosage of $MgSO_4$ (Okusanya et al., 2012). The 54 women who were enrolled during the first study phase received a 10g dose of $MgSO_4$ and 49 women in the second study phase received the 14g associated with the standard Pritchard regimen. Overall, the health outcomes from both groups were comparable: similar rates of vaginal delivery, onset of convulsion/recurrent convulsion, maternal death, and neonatal Apgar score were not significantly different between the two groups.

Ekele and Ahmed conducted an experimental pilot in 2002-2003 that used the same loading dose of $MgSO_4$ but limited the maintenance doses for 12 hours following the loading dose (compared to the 24 hours stipulated in the Pritchard regimen)(Ekele & Ahmed, 2004). Thirty-three women participated in this study and the results seem to indicate that the primary outcome of interest—rate of recurrent convulsion—in these women (6.0%) is comparable to the rate documented in the large $MgSO_4$ Collaborative Eclampsia Trial (Magpie Trial) that followed the standard, Pritchard regimen (4.7%).

The other two papers looking at the dosage question were randomized control trials. Chama and Geidam randomized 112 patients into standard treatment group (Pritchard) and a shortened postpartum course which involved administering only two IM injections four hours apart (Chama & Geidam, 2013). The findings indicated that the shortened postpartum course was as effective as the Pritchard regimen to manage eclampsia. While Chama and Geidam shortened the postpartum maintenance in their study, Abdul et al. instead modified the antepartum loading and maintenance doses (Abdul, et al., 2013). During their study, Abdul et al. randomized 72 patients into standard dose (n=33) and low dose (n=39) groups. The low dose regimen reduced the amount of $MgSO_4$ required in the standard, Pritchard. The women in the low dose group received a 9g loading dose (4g IV, 2.5g in each buttock) followed by 2.5g in alternate buttocks every four hours. Though the sample size was small, this study found no significantly different rates in maternal or perinatal mortality or in Cesarean section (CS) rate.

Delivery methods for PE/E cases

The only definitive treatment for eclampsia is to end the pregnancy by delivering the baby and placenta. It is, therefore, understandable that PE/E leads to increased rates of cesarean section (CS) deliveries in populations with high rates of PE/E. Afolayan and Tukur explore two different aspects of labor and delivery in order to determine which methods have the best outcomes for mother and baby.

Afolayan et al. conducted a retrospective case review that compared complication rates between using general anesthesia or spinal anesthesia during caesarean section deliveries among eclamptic women (Afolayan et al., 2014). The study showed that maternal and perinatal survival among eclamptics are better among those who received spinal anesthesia during their caesarean section procedure.

Tukur examines the outcomes for eclamptic mothers and their babies who underwent caesarean section versus those who had labor induced using misoprostol (Tukur et al., 2007). Their study found that although both methods were effective, misoprostol requires more time to fully induce labor and should therefore only be used when prompt and safe caesarean section is not available.

Improved case management and monitoring

Case management and monitoring can be modified and improved and at different stages throughout the development of the condition; three papers looked at strategies to improve case management for women with PE/E. One looks at a strategy to manage early PE, one incorporates a tool for streamlining monitoring and treatment, and the third tests the role of serum magnesium levels in eclamptic patients as a way to prevent and detect $MgSO_4$ toxicity.

In a prospective, case-control study conducted in Enugu, 749 consecutive cases of pre-eclampsia admitted to the University Teaching Hospital were recruited; 175 cases were deemed to be 'early onset' (before 30 weeks gestation) and made up the study group and 574 served as controls (Onah & Iloabachie, 2002). All participants were tested for blood count, serum electrolytes, urea and creatinine, liver function, clotting profile, urinalysis and ultrasonography. When necessary, they were treated with antihypertensives (alpha-methyldopa used antepartum and hydralazine used in the event of a hypertensive crisis) and diazepam (to control convulsions). The women in the early onset group were conservatively managed using antihypertensives and diazepam until maternal and/or fetal risks meant that continued conservative management was considered dangerous; 80% gained more than two weeks gestation using this method of management. Women in the late onset group were delivered promptly, especially if the woman was beyond 34 weeks gestation. While conservative management may improve fetal outcomes, this study saw an increase in maternal morbidity and mortality among the study group participants which was likely due in part to facility delays and the unavailability of $MgSO_4$. The authors suggest that conservative management has potential to improve fetal outcomes but in order to improve maternal outcomes, institutional delays need to be reduced and $MgSO_4$ needs to be available.

Ameh et al. developed a monitoring chart that simplified the paperwork and compiled all relevant details onto one sheet (Ameh et al., 2012). The improved chart, the LIVKAN chart allows for the patient's blood pressure to be tracked over time as well as the number and timing of convulsions, patient's level of consciousness,

proteinuria, respiratory rate, deep tendon reflex. Furthermore, any drugs needed to manage high BP (hydralazine, nifedipine, labetolol), eclamptic fits ($MgSO_4$), or $MgSO_4$ toxicity (calcium gluconate) are also recorded in the chart. Missing from the chart, however, is methyldopa, another antihypertensive that is usually affordable and available. In order to assess the effectiveness and acceptability of the LIVKAN chart, Ameh et al. trained 118 skilled birth attendants on its use and followed up with questionnaires. The study found that 98% of the participants thought that the LIVKAN chart was an improvement over the existing monitoring system and would be useful at their level and at lower levels to improve care and documentation of referral. The challenges cited include: low availability of blank charts and high workload due to paperwork. Overall, the chart appears to improve monitoring of PE/E by combining monitoring and treatment guidelines and allowing for 24 hour surveillance of a patient experiencing PE/E in one single page.

Finally, whenever a patient is treated with $MgSO_4$, she must be monitored for indications of toxicity from $MgSO_4$. Ekele and Badung quesiton the role of serum magnesium levels in patients receiving $MgSO_4$ as an indicator of possible toxicity. During their prospective study, they recruited 19 patients who presented with eclampstic convulsions and were treated using $MgSO_4$; blood samples were taken from patients prior to administration of $MgSO_4$ to assess whether there was a significant change in serum magnesium levels (Ekele & Badung, 2005). This small study found that serum magnesium levels in eclamptic patients do not change drastically and they remain within therapeutic levels and conclude, therefore, that serum magnesium level estimation is not necessary in patients with eclampsia being treated with $MgSO_4$.

Policy and management guidelines

Establishing policies and institutionalizing guidelines support clinical efforts to manage cases of PE/E. Three papers included in this review examined the impact of guidelines and policies on maternal mortality related to PE/E. Nkwocha et al. looked at the impact of a global call to action—the Safe Motherhood Initiative—that was adopted in Nigeria in 1990 and called for a reduction in maternal mortality by 50% by 2000. Igwegbe et al. assessed the impact of a facility-specific policy and Ezugwu et al. looked at guidelines within a specific facility to assess the effect on maternal mortality due to PE/E.

Nigeria launched the Safe Motherhood Programme in 1990 with the express purpose of reducing maternal mortality by half in ten years (Nkwocha et al., 2006). Nkwocha et al. reviewed hospital cases from eight years before (1981-1989) and eight years after (1990-1998) the introduction of this initiative in Nigeria. The study found that while the overall MMR decreased by 8% between the two study periods, maternal deaths due to PE/E increased after 1990. Prior to 1990, PE caused 4.4% and eclampsia caused 10.5% of maternal deaths, after 1990 these rates increased to 13.9% and 17.9%, respectively. These findings indicate that PE/E represents a priority area that requires more focus in order to reduce the associated maternal death.

In 2005, the Nnamdi Azikiwe University Teaching Hospital (NAUTH) introduced a “Service Compact” (SERVICOM) contract in response to a federal proclamation to provide all Nigerians with “basic services to which each citizen is entitled in a timely, fair, honest, effective and transparent manner” (Igwegbe, Eleje, Ugboaja, & Ofiaeli, 2012). The SERVICOM charter at NAUTH included mandates including: elimination of fee-for-service for all emergency services (which included emergency obstetric services), prompt and appropriate treatment, and monitoring of services and record keeping. Igwegbe et al. reviewed hospital records from before and after the introduction of the SERVICOM charter at NAUTH to determine if the policy had any effect on maternal mortality. Overall, the maternal mortality rate at the facility from 2004-2010 was 1,098 per 100,000 live births and eclampsia contrubuted 25% of the maternal deaths. Before SERVICOM, the 2004 maternal moratily rate was 1,567 per 100,000 live births compared to 691 per 100,000 in 2010. Igwegbe et al. showed that introducing a policy like the SERVICOM charter can improve quality of care, timeliness of treatment and maternal health outcomes which may have implications for maternal outcomes related to PE/E.

In 2008, the Enugu State University Teaching Hospital adopted evidence-based guidelines aimed at reducing maternal mortality (Ezugwu et al. 2014). This study reviewed hospital records from three years before the

institutionalization of the guidelines and three years after in order to compare the maternal outcomes at the facility and to determine if the guidelines had an impact. The guidelines were identified through PubMed and Google scholar; they were adapted to the local context and included guidelines on the management of severe PE using the Pritchard regimen. The three years after the introduction of the guidelines at the facility showed a 43.5% reduction in MMR when compared with the three years prior to the guidelines. The case fatality rate fell by 80% (from 15.8% to 2.7%) after introducing the guidelines and training providers on them. This study by Ezugwu et al indicates that institutionalization and training on guidelines related to management of PE/E can reduce maternal mortality.

Re-training and task-shifting

The final major theme that emerged from the literature on strategies for improving prevention and management of PE/E is focused on increasing access through provider knowledge and skills. Five studies were on training, re-training and task-shifting as a way of improving access and quality of care for patients with severe PE/E.

In a multi-state study, Okonofua et al. conducted a before-and-after trial in six health facilities that sought to test the impact of training various professionals (Ob/Gyns, doctors in training, nurses, midwives and others) on the proper treatment of PE/E cases using the Pritchard regimen, antihypertensives, and monitoring the patient (Okonofua et al., 2013). To establish a baseline and identify gaps in knowledge, the researchers reviewed hospital records from January to May 2008 and conducted in-depth interviews (IDIs) with providers to inform development of the training materials. The endline data was prospectively collected for one year after the intervention. Incidence of eclampsia was comparable at baseline and endline but the case fatality rate decreased from 15.1% at baseline to 3.2% at endline. This study found that the trainings successfully built the capacity of the healthcare providers to safely use $MgSO_4$ and effectively reduced deaths due to eclampsia.

Ishaku et al. conducted a case-control study where they assessed whether lower-cadre health workers could detect severe PE/E and safely administer the loading dose of $MgSO_4$. In their study, ten primary health care facilities in Kano state were included, 5 made up the experimental arm and 5 were controls (Ishaku et al., 2013). At the experimental facilities, health workers received training on how to recognize cases of severe PE/E and learned how to administer the loading dose of $MgSO_4$ (10g IM) and refer women for follow up care. In addition to recognizing and initiating treatment for severe PE/E, the PHC providers also received instruction for detecting $MgSO_4$ toxicity and treating it with calcium gluconate. The PHC providers at the control facilities did not give $MgSO_4$ or diazepam. During this study, a higher proportion of women defaulted from experimental facilities than in the control facilities; this was potentially due to the immediate, yet temporary, effect of $MgSO_4$. This study demonstrated that PHC providers can safely and effectively administer the loading dose of $MgSO_4$ in patients with severe PE/E, however referral mechanisms need to be strengthened to reduce the 75% default rate seen in this study.

The remaining three papers are reporting on data collected during the same or complementary studies that were implemented in ten facilities in Kano state from February 2008 to December/January 2009 (Okereke, Ahonsi, Tukur, Ishaku, & Oginni, 2012; Tukur et al., 2011; Tukur et al., 2013).

The intervention trained twenty-five individuals on evidence-based management of hypertensive disorders of pregnancy and use of $MgSO_4$ (five hospital board officials and one midwife and one doctor from each of the ten facilities). These 25 people were considered “Master Trainers” and together trained another 160 health workers. These papers report a baseline case fatality rate of 20.9% compared to 2.3% after the intervention.

This evidence-based intervention was successful because it engaged with stakeholders and it is replicable (Tukur et al., 2011). Training providers on protocols for the treatment of severe PE/E using $MgSO_4$ was determined to be an effective strategy to reduce case fatality due to eclampsia without incurring any significant increase in cost (Okereke et al., 2012). This effective, low-cost, replicable intervention has a positive effect on maternal and fetal mortality and morbidity and should be implemented on a wider scale (Tukur et al., 2013).

Demonstrated and Potential Risk Factors

While the biological mechanism for developing eclampsia remains unknown, many studies look at various attributes or conditions in an effort to identify risk factors for developing PE/E. Among the potential risk factors explored in the literature are: maternal ethnicity, adolescent mothers, sickle cell anemia, parity, and history of hypertension or prior pre-eclampsia. Thirty-six papers looked at demonstrated or potential risk factors for PE/E that had the potential to improve early detection (Appendix IV).

Previously demonstrated risk factors for PE/E that appear in the literature from Nigeria and include: low parity, young age, multiple gestation, history of chronic high blood pressure, previous pre-eclampsia, and not registering or booking at a health facility for ANC (Adokiye & Isreal, 2015; Anorlu et al., 2005; Olusanya, 2011; Osungbade et al., 2008; Owolabi et al., 2008). Three papers looked specifically at young age and determined that adolescence is a risk factor for PE/E, though the papers did not look at explanations for this fact (Adeyinka et al., 2010; Airede & Ekele, 2003; E. I. Nwobodo & Panti, 2012).

While rise in blood pressure is known to be associated with PE/E, one paper investigated whether or not a relative rise versus absolute rise in BP would be better to predict maternal and fetal outcome. After following a cohort of 478 women and tracking blood pressure levels throughout the study period, Onah concluded that fetomaternal outcomes were not significantly affected by relative rise in diastolic BP and concluded that absolute BP is a better predictor of fetomaternal outcome (Onah, 2002).

Twenty-one other papers looked at potential risk factors relating to biomarkers in pregnancy. Each looked at a specific set of biological measures to determine if there were any observable trends or associations between the biomarker and the development of PE/E. These included: various antioxidant vitamins, magnesium or magnesium serum levels, trace element levels, lysosomal enzymes or enzymic antioxidants, among others (Appendix IV). Based on these studies, elevated levels of haptoglobin, malondialdehyde, phenylalanine concentration, blood lead and homocysteine levels were observed in pre-eclamptic women and may contribute to the development of PE/E. Low serum concentrations in zinc, copper, manganese and magnesium, and low plasma calcium, vitamin C and E levels could indicate PE/E or risk of PE/E in pregnant women.

The remaining papers tested the effect of maternal ethnicity, seasonality, past abortion and change in paternity, socioeconomic status and polygamy on a woman's risk of developing PE/E (Abubakar et al., 2009; Attahir, et al., 2010; Chigbu et al., 2009; Familoni et al., 2008; Okafor & Ezegwui, 2010; Olayemi et al., 2010; Olayemi, et al., 2010). All of these studies were specific and small but their findings indicate the potential need for further research into risk factors for PE/E. Abubakar et al. found that the Fulani ethnic group was more likely to progress from PE to eclampsia when compared to Hausa and Kanuri women. Attahir et al. learned that seclusion and polygamy did not have an effect on rates of PE. Okafor reported from a retrospective review of hospital records that women with PE were more likely to undergo CS during the rainy season.

While these findings are certainly interesting, they are looking only at a relatively small number of women and are not sufficient to consider these aspects as risk factors for PE/E.

Other Health Outcomes associated with PE/E

In addition to the common, known health outcomes of PE/E (edema, headache, seizure, and death), other health outcomes are associated with PE/E. Twenty-three papers identified during this review reveal other health outcomes that can affect mother and/or fetus including: fetal malnutrition, poor Apgar scores increased chance of cesarean section (CS), cardiac complications and persistent hypertension (Appendix V).

Among the less-common outcomes associated with PE/E were: orofacial injuries, loss of vision, and paralysis. The orofacial injuries are not caused by PE/E, however, but are the result of objects being forced into the mouths of eclamptic women in a misguided effort to mitigate consequences of the seizures (Adeyemo & Rabiu, 2012; Ndukwe et al., 2004). While change in vision is a more common consequence of PE/E, total loss of vision occurs less often but one such case is reported in the literature (Waziri-Erameh et al., 2003). The literature also revealed

a rare case of a 26-year old woman who was brought into a facility with postpartum eclampsia and was left quadriplegic, a rare yet real consequence of her eclampsia (Okafor & Efetie, 2006).

Since $MgSO_4$ only allows for the temporary management of eclampsia, many women suffering from the condition must be delivered pre-term; this leads to an increase in the number of caesarean section (CS) deliveries that are performed which, in turn, increases the woman's chance of suffering a morbidity or mortality from the procedure (Adeoye et al., 2013; Oladapo et al., 2004; Okafor & Ezegwui, 2010; Okafor, 2009; Ozumba & Anya, 2002). Further to the increase in caesarean sections and associated morbidities and mortality for the mother are the increased negative health outcomes for the fetus/baby. With an increase in pre-term deliveries, there is a heightened burden of low birthweight babies (Olusanya & Solanke, 2012a, 2012b; Onyearugha & Ugboma, 2012a).

Another health outcome of PE/E is HELLP syndrome, a dangerous condition that complicates eclampsia with hemolysis, elevated liver enzymes, and low platelets. HELLP syndrome causes the internal organs to shut down, and left untreated, the mother's health, as well as the fetus' health, will quickly deteriorate (Makinde, 2009).

It is important to remember that PE/E has negative health effects on the fetus/newborn as well as the mother. Eight papers reviewed discuss the fetal/neonatal outcomes associated with PE/E including fetal malnutrition, low birth weight (LBW), preterm birth (PTB), low Apgar score and fetal death. For example, Onyearugha et al. conducted a study based on the hospital records for 48 babies delivered to eclamptic mothers in Abia state. The records showed that 13 babies were LBW <1500g, and 29 (60%) were stillborn and four were severely asphyxiated; the authors suggest that these poor Apgar scores could be impacted by 'asphyxiogenic effect' in utero during eclamptic convulsions (Onyearugha & Ugboma, 2012b).

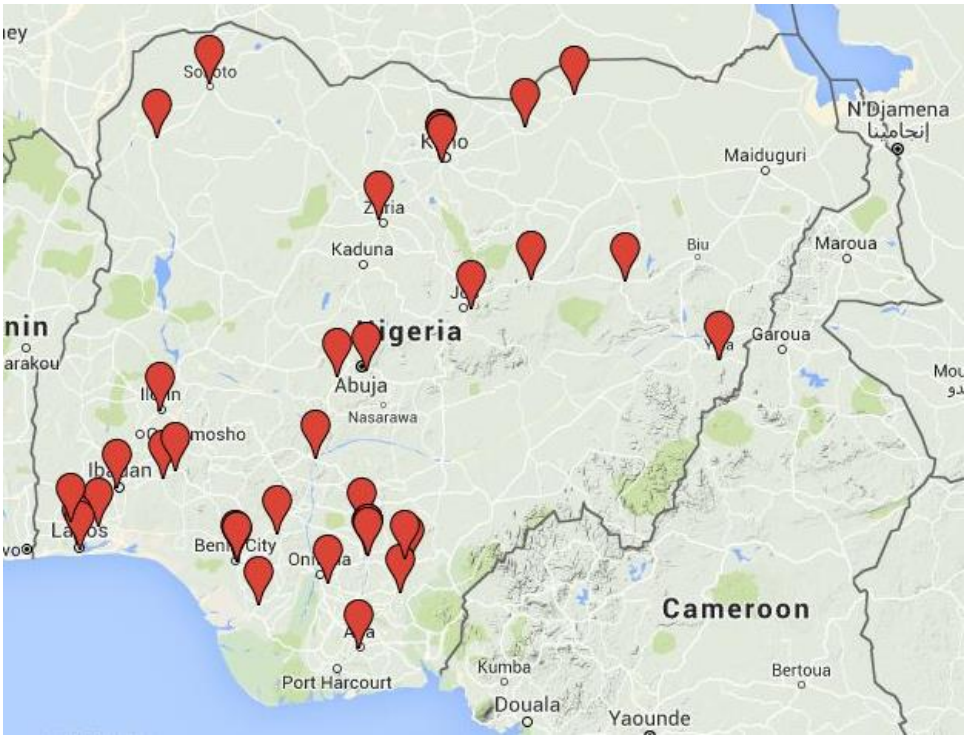
Program descriptions and literature reviews

Thirteen of the papers reviewed were categorized as being descriptive articles and included: project summaries (three), literature reviews (five), purely cross-sectional studies (three), and editorial or correspondence articles (two). Some of the topics covered in these descriptive papers were: verbal autopsy to determine cause of pregnancy-related death in a population, assessment of nurse-midwife educators on causes of maternal mortality, determine whether brief summaries of these descriptive papers relating to PE/E in Nigeria can be found in Appendix VI.

Summaries of hospital case notes and records for PE/E

A majority of the papers collected for this review are a specific kind of a descriptive paper; they are summaries of hospital reports of eclampsia or, more broadly, maternal mortality. The 54 papers that fall into this category report maternal mortality ratios, the attributable proportion of MMR to PE/E, incidence of PE/E, and case fatality rate at a specific facility during a specific time period and do not provide any analysis or interpretation. The facilities are from across the country, with a greater concentration in the South West and South East (Figure 3).

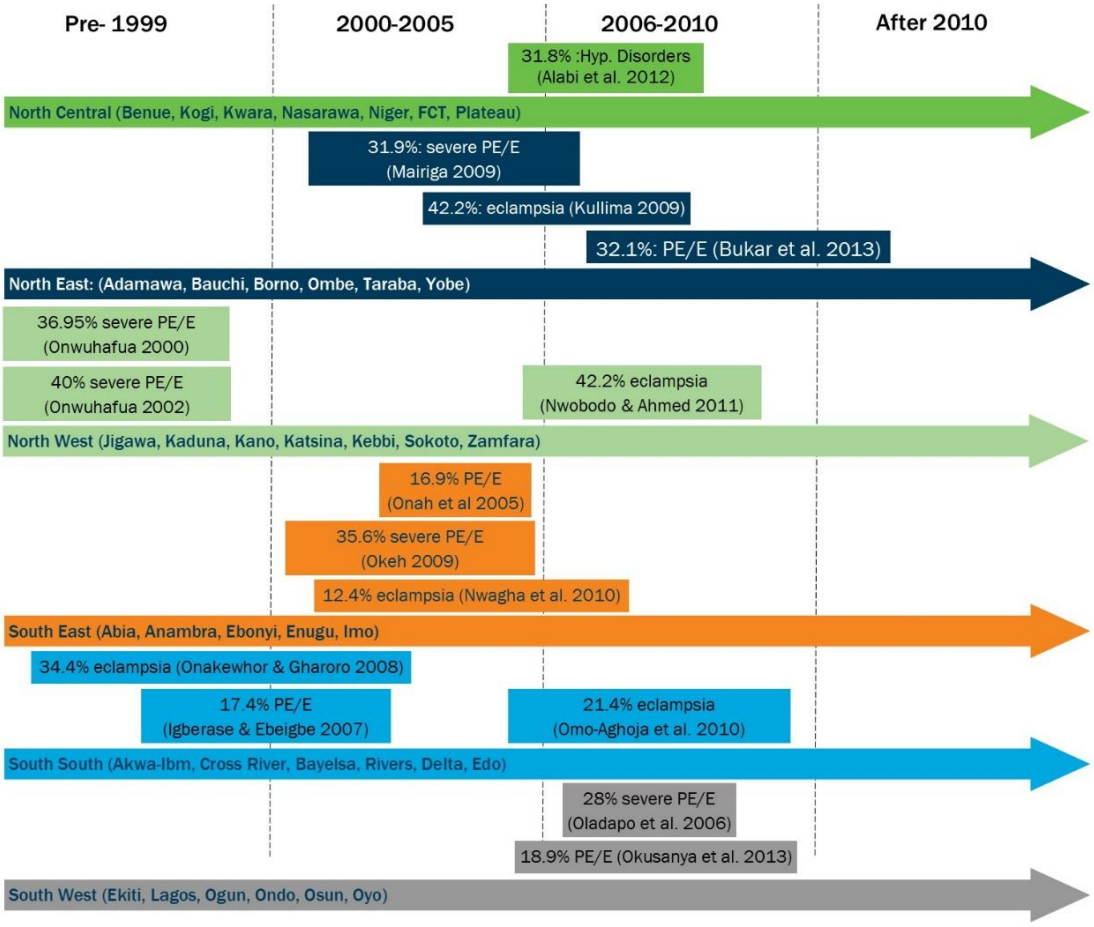
FIGURE 3 **Map of facilities where records were reviewed**



The MMRs reported in these papers cover specific periods of time over the last three decades; Olatunji et al. reviewed data from a facility in Sagamu in Ogun state that included cases from 1988-1997; their review found 92 maternal deaths out of 5,423 deliveries making the MMR at that facility at that time, 1,696 per 100,000 deliveries. The lowest MMRs reported include 463 per 100,000 live births (44 maternal deaths) at the Federal Medical Centre in Kogi state from 2005-2009 (Alabi et al., 2012) and 454 per 100,000 from Edo state in 1996-2000 (Onakewhor & Gharoro, 2008). The highest MMRs reported among these summary papers include one from a rural referral hospital, Baptist Medical Centre, in Delta state. The cases reviewed were from 1994—2003 and revealed 115 maternal deaths out of 5,153 deliveries making the MMR= 2,232 per 100,000 live births (Igberase & Ebeigbe, 2007). Another extraordinarily high MMR of 2,849 per 100,000 deliveries comes from a tertiary facility that experienced 112 maternal deaths out of 3,931 deliveries from 2003-2007 (Kullima et al., 2009). The highest observed MMR comes from Olabisi Onabanjo University Teaching Hospital in Sagamu in Ogun state from 2000-2005 where 75 maternal deaths and 2,509 live births were recorded making the MMR= 2.989.2 per 100,000 live births (Oladapo et al., 2006).

In addition to reporting on MMRs at facilities, the authors also reported on the proportion of MMR that is attributable to PE/E. These proportions also varied, every paper that reported the proportion of maternal deaths caused by hypertensive disorders in pregnancy, PE/E, severe PE/E, eclampsia, was over ten percent (Figure 4). The proportions ranged from 12.4% of 97 maternal deaths (Nwagha et al., 2010) to 42.2% of 277 maternal deaths (Nwobodo & Ahmed, 2011).

FIGURE 4 **Attributable proportion of maternal death due to PE/E as reported in the literature**



Two papers, examined 'maternal near miss' cases to get a larger sample size and a better idea of the causes of severe maternal outcomes even in cases where the woman survived. These also found that a large proportion of cases were due to PE/E. Adeoye et al. saw that hypertensive disorders in pregnancy (which they defined as severe PE/E) caused 37.3% of near miss cases at the maternity units of Obafemi Awolowo University Teaching Hospitals Complex in Ile-Ife from July 2006-June 2007. In a recent cross-sectional study of 91,724 live births, Oladapo et al. found 2,440 severe maternal outcomes (1,451 maternal near-miss and 998 maternal deaths). Of these 2,440 cases, hypertensive disorders (chronic hypertension and PE/E) were the most common cause and contributed 24% of the SMOs and eclampsia was found to be the most frequent complication and resulted in 20% of the maternal deaths (Oladapo et al., 2015).

The papers already discussed in this section were looking at all causes of maternal mortality/maternal near misses and reported on overall MMR and attributable proportion of maternal death to PE/E among other health conditions; the remaining summaries of hospital records look at reports from cases of PE/E specifically and report on prevalence/incidence and case fatality rates. Incidence/prevalence of PE/E ranged from very low: 0.42% (Onwuhafua et al., 2001) and 0.75% (Ikechebelu & Okoli, 2002) to very high: 9.42% (Tukur, Umar, & Rabi'u, 2007). For obstetric complications, the United Nations has set the maximum case fatality rate at 1% of cases; every paper reporting CFR in this literature review found CFR over 1%, most were over 10% and one study found CFR as high as 42.22% (out of 45 cases) (Onwuhafua et al., 2001).

Discussion

GAPS IN PREVENTION OF PE/E

Globally, aspirin and calcium are thought to have a protective effect for women at risk of developing PE/E. This potential prophylactic effect is only very briefly mentioned in a few papers and none of the studies test the effect of these two supplements on the incidence of PE/E. The effectiveness and impact of prophylactic aspirin and calcium are unknown in the Nigerian context.

GAPS IN DETECTION OF PE/E

Terminology and clinical definitions

Throughout the 145 full text articles reviewed in this paper, there is no consistency in terminology used or in clinical definitions for those terms; each paper provides their own definitions with some overlapping criteria.

Among the various terms used throughout the literature were: hypertensive disorders of pregnancy, mild pregnancy-induced hypertension (PIH), PIH, severe PIH, chronic hypertension with superimposed pre-eclampsia, pre-eclamptic toxaemia (PET), severe PET, toxemia of pregnancy, the toxaemia syndrome, mild pre-eclampsia, pre-eclampsia, severe pre-eclampsia, imminent eclampsia, impending eclampsia and eclampsia.

Currently, with the plethora of accepted terms used to refer to varying degrees of PE/E severity, studies are forced to define the clinical parameters for each condition. While some of the definitions contain similarities or overlapping criteria, there are often specific differences between them. Below are a few examples of definitions from the literature

Mild pre-eclampsia

- “a blood pressure of 140/90 mmHg on two occasions 6 h or more apart, or a rise of 30 mmHg systolic or 15 mmHg diastolic from mid-trimester values; proteinuria above (+) on two consecutive urine specimens and significant non- dependent oedema” (Okafor & Okezie, 2005).
- “Pregnancy-induced systole hypertension of 140 to <160 mmHg (or diastole hypertension of 90 to <110 mmHg) with proteinuria of 2+ (100 mg/dL)” (Osinubi, Ajayi, & Adegbola, 2009)

Pre-eclampsia

- “Preeclampsia, a multisystem disorder unique to human pregnancy is defined as the association of pregnancy induced hypertension with proteinuria of greater than or equal to 300mg/24h after 20 weeks of gestation” (Okafor & Ezegwui, 2010)
- “Hypertension after the 20th week of gestation, the diastolic blood pressure >110 mmHg on admission, proteinuria >30mg/dl in random urine specimen or > 300mg in a 24hr urine specimen” (Makinde, 2011)
- “Hypertension (?140/ 90mmHg on two occasions 4h apart) and proteinuria (≥0.3g/dl) in the second half of pregnancy” (Adeyinka et al., 2010)
- “Hypertension (systolic pressure = 169 ± 26.0 mmHg, diastolic pressure = 102 ± 11.0 mmHg), significant proteinuria (368 ± 39 mg/24 h), severe headache, abdominal pain and vomiting.” (Akiibinu, Kolawole, Ekun, & Akiibinu, 2013)
- “Significant proteinuria (>100 mg/day) and high blood pressure (>130/90 mm Hg) irrespective of weight of the patients or the presence of edema. The blood pressure must have manifested on at least two occasions 6 hours or more apart.” (Arinola, Arowojolu, Bamgboye, Akinwale, & Adeniyi, 2006)

- ”Blood pressure of ≥140/90 mmHg on at least two occasions measured at least 6 h apart or a diastolic blood pressure of 110 mmHg at any time or an increase of 30 mmHg and 15 mmHg in the systolic and diastolic blood pressures, respectively from the booking values or a mean arterial pressure of greater than 105 mmHg” with “two midstream urine specimens more than 4 h apart with 2+ protein on dipstix testing or 1+ protein with measured specific gravity of 41.03 and < 8” (Chigbu et al., 2009)
- “Cerebral or visual disturbances, epigastric pain, pulmonary edema or cyanosis, a systolic blood pressure ≥140 mm Hg or a diastolic blood pressure ≥90 mm Hg and proteinuria.”(Glew et al., 2004)

Severe pre-eclampsia

- “The blood pressure is persistently above 160/110 mmHg and proteinuria above 5 g/24 h (+++) and symptoms of headache, blurring of vision, epigastric pain and oliguria.” (UV Okafor & Okezie, 2005).
- “New hypertension with blood pressure of 160 mmHg systolic or diastolic blood pressure of 110 mmHg, or greater, arising after 20 weeks of gestation in a woman who was normotensive before 20 weeks gestation, associated with proteinuria [...] 2+ or more protein on urine dipstick.” (Guerrier, Oluyide, Keramarou, & Grais, 2013)
- “If any two of the following signs were present: (1) systolic blood pressure >160 mmHg or diastolic blood pressure >110 mmHg; (2) proteinuria (>3+ on dipstick [500 mg/dL]); (3) facial oedema.” (Osinubi et al., 2009)

Eclampsia

- “...maternities that presented with fitting or fitted while on admission, had blood pressure equal to or greater than 140/90 mm Hg, at least 2 +proteinuria with or without edema, and had no past history of epilepsy.” (B. Ekele, Bello, & Adamu, 2007)
- “hypertension after the 20th week of gestation, the diastolic blood pressure >110 mmHg on admission, proteinuria >30mg/dl in random urine specimen or > 300mg in a 24hr urine specimen [...] plus headache, blurring of vision and upper abdominal pain [...] and seizures” (O. N. Makinde, 2011)
- “associated with convulsions, oliguria (4400ml/24h), increased tendon reflex, pain in the right hypochondriac region.” (Adeyinka et al., 2010)
- “Occurrence of seizure and/or altered level of consciousness not caused by epilepsy or other convulsive disorders, with signs of severe preeclampsia.” (Guerrier et al., 2013)

Creating specific and clear clinical definitions for these conditions is essential to ensuring that providers around the globe are able to appropriately diagnose and manage the symptoms related to PE/E. Generally speaking, “toxemia” is an outdated term that is not frequently used today to classify types of hypertensive disorders of pregnancy. Given the wide range of definitions related to hypertensive disorders in pregnancy, it is necessary to reduce the number of terms and simplify the definitions to move beyond the implication that interventions vary significantly between each classification, when in fact, the monitoring and management methods are not so different between mild PE and PE or severe PE and eclampsia.

ANC attendance, content, and quality

One message that comes through clearly in the literature is that “booked” patients are less likely to develop PE/E when compared to “unbooked” women. This trend is not surprising as women who attend ANC will be more likely to be screened for PE/E and receive preventative care and careful monitoring before the condition worsens. Women who do not attend ANC are unlikely to be aware of any problem until eclamptic seizures begin. What is not always clear from the literature are the details about which services the women attending ANC are receiving and whether or not they know what danger signs to look for in pregnancy. Attending ANC and receiving all essential ANC services is required for early detection of PE/E and to prevent the women with early signs of preeclampsia from worsening.

GAPS IN TREATMENT OF PE/E

The literature very clearly supports the use of $MgSO_4$ to manage eclamptic convulsions; $MgSO_4$ is not the only weapon that we have against PE/E. If indicators of PE/E are detected early in pregnancy, these symptoms can be managed using antihypertensive drugs before the condition escalates.

Antihypertensives

There is nothing in the literature that specifically reports on the effectiveness and safety of antihypertensives for pregnant women with high blood pressure; a few mention that as part of their treatment procedure, women were receiving antihypertensives to manage their high BP. Using antihypertensive drugs (labetalol, nifedipine, methyldopa, hydralazine) to manage high blood pressure in pregnant women is an important strategy to reduce the number of PE cases that escalate to eclampsia.

Use of $MgSO_4$

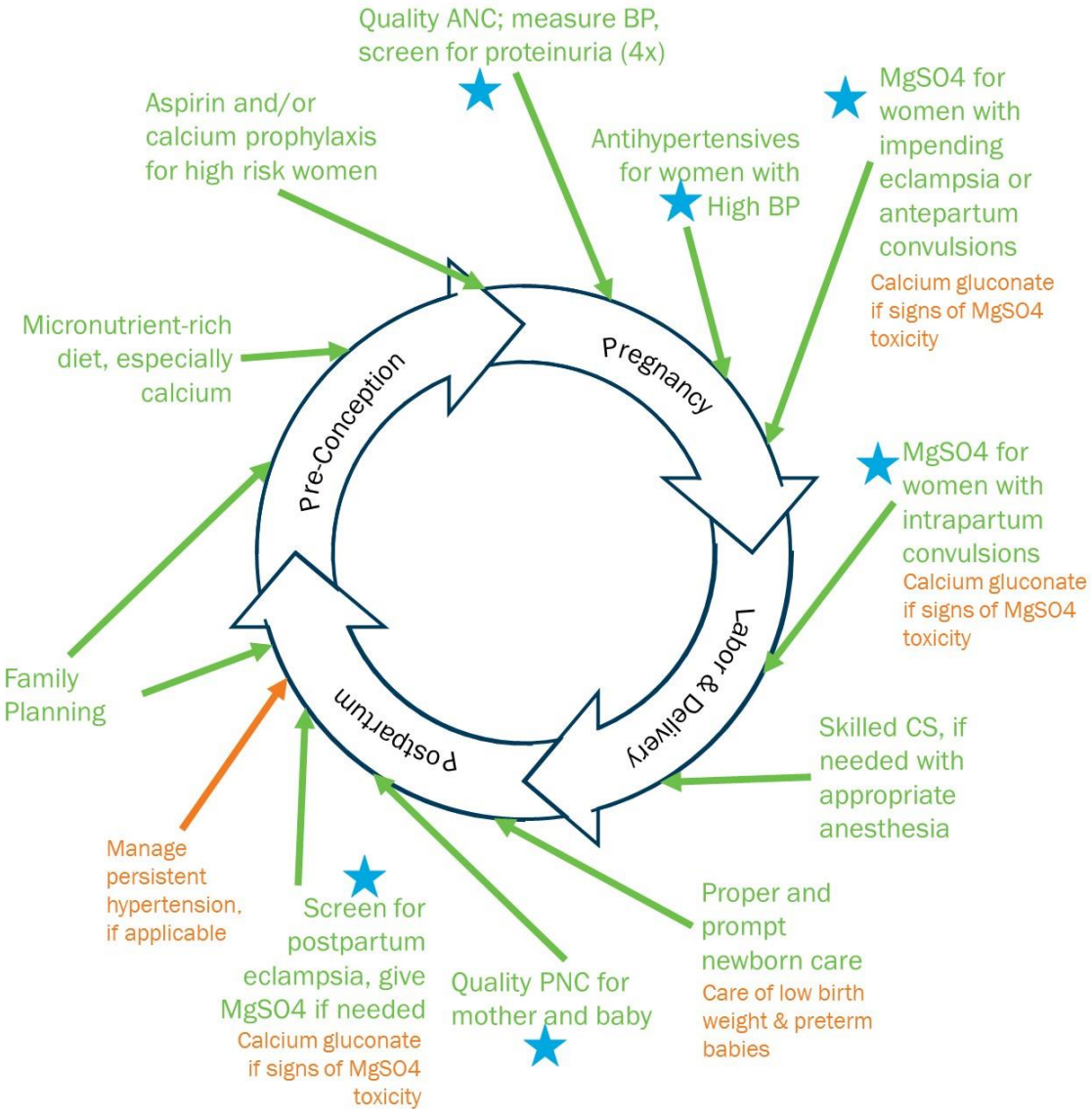
Despite the abundance of evidence demonstrating the safety and effectiveness of $MgSO_4$, its use has remained low, especially in developing countries where it, incidentally, is most needed. Low availability of $MgSO_4$, lack of guidelines on its use (or unawareness of these guidelines), misinformation regarding who can administer the drug, poor knowledge of health workers on its use, fear of toxicity, little incentive for pharmaceutical companies to commercialize the drug (no profit to be made), ready availability of pre-packaged forms of less effective drugs (like diazepam), and lack of support for policy change all contribute to the underutilization of this safe and effective life-saving drug. Even if providers are trained to use $MgSO_4$ and know how and when to use it, sometimes providers choose to use diazepam instead because they are more familiar with it since it was the recommended drug for PE/E in Nigeria for decades before $MgSO_4$ was introduced (Ekele, 2009).

In addition to the relatively low use of $MgSO_4$, there are no studies that demonstrate the lowest effective dose to manage PE/E. As described earlier in this paper, some researchers have started questioning and testing the dosage with preliminary results indicating that a reduced dose—either in amount delivered or timing of doses—can be as effective as the generally-accepted Pritchard regimen.

Conclusion

Throughout the development of a pregnancy, there are many opportunities when PE/E can be prevented, detected and managed; based on the literature, certain gaps exist along this continuum of care. In order to have the most impact, we recommend a multi-level set of interventions that increase community awareness of symptoms of PE/E and ANC health seeking behavior, improve and expand provider skills and knowledge at multiple levels (including PHC) for detecting and treating high BP in pregnancy and PE/E throughout the developmental stages of pregnancy. Figure 5 visualizes the cycle of pregnancy and specific strategies that are currently thought to be the best practices to reduce maternal mortality related to PE/E; the blue stars correspond to opportunities that hold the most potential for significant reduction of incidence of eclampsia and subsequent death.

FIGURE 5 **Opportunities and strategies for preventing, detecting and treating PE/E**



*orange text indicates adverse outcomes for which providers should monitor and be prepared to manage

RECOMMENDATIONS

Develop common language and clear streamlined policies

- Develop simple terminology and associated definitions for global use.
- Continued advocacy to hospital administrators and relevant policymakers to ensure that protocols are followed over time and that the necessary drugs and equipment are procured.

Clarify and define management strategies and dosage

- Determine the minimum effective dose for $MgSO_4$.
- Create and distribute clear and concise guidelines and protocols for treating PE/E with antihypertensives and $MgSO_4$.
- Assess the effectiveness and need of aspirin and/or calcium prophylaxis in Nigeria.

Increase access to quality services

- There should be training and re-training of healthcare providers on recognizing PE/E, managing high BP with antihypertensives, when and how to administer $MgSO_4$, and how to monitor for and treat toxicity.
- Task-shifting can increase the workforce capable of providing life-saving services; PHC providers can and should be able to detect and provide initial treatment (antihypertensives and $MgSO_4$ loading dose) for PE/E and monitor for toxicity.

Engage Community

- Increase community awareness of and access to antenatal care.
- Educate community members on the signs and symptoms of PE/E and when and where to seek treatment.

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Yeager, B., & Patel, S. (2012). *Medicines for Maternal Health; Key Data and Findings*.

Appendix I:

SEARCH QUERIES FOR BIBLIOGRAPHIC DATABASE SEARCHES

Humans*	AND	Pregnancy*	AND	Nigeria*	AND	Seizures* OR Hypertension* OR "Hypertensive Disorders" OR Pregnancy-induced hypertension*† OR Proteinuria* OR "blood pressure"* OR Anticonvulsants* OR "magnesium sulfate" OR "Magnesium Sulphate" OR Aspirin* OR "calcium supplementation" OR Complications
Humans*	AND	Pre eclampsia*† OR eclampsia OR HELLP Syndrome	AND	Nigeria*	AND	"calcium gluconate"* OR "Magnesium sulfate" OR "magnesium sulphate" OR Phenytoin* OR Chlorpromazine* OR Meripidine* OR Diazepam
Humans*	AND	Pre eclampsia*† OR eclampsia OR HELLP Syndrome	AND	Nigeria*	AND	"early diagnosis"* OR Treatment OR "prenatal diagnosis"* OR "health personnel"* OR "prenatal care"* OR "postnatal care" OR "blood pressure"* OR "Aspirin"* OR "aspirin prophylaxis"
Humans*	AND	Pre eclampsia*† OR eclampsia OR HELLP Syndrome	AND	Nigeria*	AND	"maternal death"* OR "maternal mortality"* OR "disease management"* OR Treatment OR "near miss" OR "induced labor"

*denotes use of MeSH terms, when available

†MeSH terms for "pre eclampsia" include alternate spellings, when MeSH terms were unavailable in search, alternative were included and linked using 'OR' "Preeclampsia OR pre-eclampsia OR pre eclampsia"

Appendix II:

PAPERS REMOVED DURING PHASE TWO AND EXCLUSION REASON

Citation	Reason	Notes
Abdul, M. A., Odogwu, K., & Madugu, N. (2011). Gross vulva eodema complicating severe pre-eclampsia/eclampsia: a case series. Nigerian Journal of Medicine: Journal of the National Association of Resident Doctors of Nigeria, 20(3), 380–382.	No Full Text	Obscure Journal, couldn't acquire full text
Adamu, A., Ekele, B., & Ahmed, Y. (2012). W219 PREGNANCY OUTCOME IN 1027 CONSECUTIVE WOMEN WITH ECLAMPSIA. African Journal of Gynecology & Obstetrics, 119(S3), S531–S867.	No Full Text	Abstract published in "poster presentations" supplement of African Journal of Gynecology & Obstetrics. *Full paper version of this abstract was separately identified and included in the review.
Adewole, I., Oladokun, A., Okewole, A., Omigbodun, A., Afolabi, A., Ekele, B., Obed, Y. (2000). Magnesium sulphate for treatment of eclampsia: the Nigerian experience. African Journal of Medicine and Medical Sciences, 29(3-4), 239–241.	No Full Text	Could not locate full text
Atiba, A. S., Abbiyesuku, F. M., Adekanle, D. A., Oparinde, D. P., Ajose, O. A., & Niran-Atiba, T. A. (2014). Malondialdehyde and antioxidant enzymes in second and third trimesters of pre-eclamptic Nigerian women. The Nigerian Postgraduate Medical Journal, 21(2), 150–154.	No Full Text	Local journal, unable to locate full text
Awoleke, J. O., Ajayi, G. O., & Adegbola, O. (2012). Prevalence of Chlamydophila pneumoniae antibodies in women with pre-eclampsia in Lagos, Nigeria. West African Journal of Medicine, 31(4), 253–258.	No Full Text	Could not locate full text
Brabin, B. J., & Johnson, P. M. (2005). Placental malaria and pre-eclampsia through the looking glass backwards? Journal of Reproductive Immunology, 65(1), 1–15.	Not Nigeria	Not enough focus on Nigeria or Nigeria-specific data
Durojaye, E. (2009). {I94} Human rights implications of maternal mortality. International Journal of Gynecology & Obstetrics, 107, Suppl(0), S24 –	No Full Text	Abstract published in "invited presentations" supplement of International Journal of Gynecology & Obstetrics.
Egbodo, C. O., & Oyebode, T. (2012). W248 ECLAMPSIA, PATIENT CHARACTERISTICS AND CONTRIBUTION TO MATERNAL AND PERINATAL MORBIDITY AND MORTALITY: A THREE YEAR REVIEW AT THE JOS UNIVERSITY TEACHING HOSPITAL, NIGERIA. International Journal of Gynecology & Obstetrics, 119, Suppl(0), S785 – S786.	No Full Text	Abstract published in "poster presentations" supplement of International Journal of Gynecology & Obstetrics.
Ezugwu, E., Onah, H., Ezugwu, F., & Okafor, I. (2009). {0282} Low birth weight babies at a tertiary hospital in Enugu, South East Nigeria. International Journal of Gynecology & Obstetrics, 107, Suppl(0), S173 –.	No Full Text	Abstract published in 'Abstracts of XIX FIGO World Congress of Gynecology and Obstetrics'
Fawole, A. O., Sotiloye, O. S., Oladimeji, A. O., Alao, M. O., Hunyinbo, K. I., Sadoh, E. A., & Otolorin, E. O. (2008). Antenatal cardiotocography: experience in a Nigerian tertiary hospital. The Nigerian Postgraduate Medical Journal, 15(1), 19–23.	Not related to PE/E	
FIGO. (2010). Successful advocacy for Government provision of MgSO4 in Nigeria.	Grey Literature	
Fujioka, A., & Smith, J. (2011). Prevention and Management of Postpartum Hemorrhage and Pre-Eclampsia/Eclampsia: National Programs in Selected USAID Program-Supported Countries.	Grey Literature	

Citation	Reason	Notes
George, I., Jeremiah, I., & John, C. (2009). {0340} Perinatal morbidity and mortality associated with eclampsia in a Nigerian tertiary hospital. International Journal of Gynecology & Obstetrics, 107, Suppl(0), S189 –.	No Full Text	Abstract for oral presentation published in supplement
Gordon, R., Magee, L., & Payne, B. (2014). Magnesium sulphate for the management of preeclampsia and eclampsia in low and middle income countries: a systematic review of tested dosing regimens. Journal of Obstetrics and Gynaecology Canada, 36(2), 154–163.	Not Nigeria	Not enough focus on Nigeria or Nigeria-specific data
Ishaku, S. M., Ahonsi, B., Tukur, J., & Oginni, A. B. (2012). 0328 TASK-SHIFTING USING MAGNESIUM SULPHATE (MGSO4) TO TREAT SEVERE PRE-ECLAMPSIA AND ECLAMPSIA IN PRIMARY CARE SETTINGS, IN KANO STATE, NIGERIA. International Journal of Gynecology & Obstetrics, 119, S376.	No Full Text	Abstract for oral presentation published in supplement
Itam, I. H., & Ekabua, J. E. (2001). A Review of Pregnancy Outcome in Women with Eclampsia at the University of Calabar Teaching Hospital, Calabar. Tropical Journal of Obstetrics and Gynaecology, 18(2), 66–68.	No Full Text	Local journal, unable to locate full text or contact authors
Jeremiah, I., & Fiebai, P. (2009). {0419} The unbooked status: a major contributor to maternal morbidity and mortality. International Journal of Gynecology & Obstetrics, 107, Suppl(0), S211 –.	No Full Text	Abstract for oral presentation published in supplement
Familoni, O., Adefuye, P., Olunuga, T., Ayoola-Sotubo, O., & Oritogun, S. (2008). QT Intervals and Outcome of Pregnancy in Patients with Eclampsia. Tropical Journal of Obstetrics and Gynaecology, 25(1).	No Full Text	Unavailable online, attempted to contact author, could not acquire full text.
Nwagha, U. I., Ejezie, F. E., & Iyare, E. E. (2009). Evaluation of serum uric acid levels in normal pregnant Nigerian women. Nigerian Journal of Clinical Practice, 12(1), 83–86.	No Full Text	Unable to access article online, attempted to contact author.
Obiechina, N. J., & Udigwe, G. (2004). Pattern of Eclampsia in Onitsha, Nigeria. Orient Journal of Medicine, 16(1), 16–20.	No Full Text	No response from author
Okafor, C., Follen, M., & Adewole, I. (2007). Opportunities to improve health systems in Africa. A comparative overview of healthcare challenges for stakeholders and strategic planners. Gynecologic Oncology, 107(1, Supplement), S86 – S93.	Not related to PE/E	
Okafor, U. V, Efetie, E. R., Nwoke, O., Okezie, O., & Umeh, U. (2012). Anaesthetic and obstetric challenges of morbid obesity in caesarean deliveries--a study in South-eastern Nigeria. African Health Sciences, 12(1), 54–57.	Not related to PE/E	
Ola, Rotimi E, OT Odeneye, and Olalekan O Abudu. "Eclampsia: A Randomized Double Blind Trial of Magnesium Sulphate and Diazepam in Lagos, Nigeria." Tropical Journal of Obstetrics and Gynaecology, 21.2 (2004).	No Full Text	Obscure Journal, couldn't acquire full text
Oladokun, A., Okewole, A. I., Adewole, I. F., & Babarinsa, I. A. (2000). Evaluation of cases of eclampsia in the University College Hospital, Ibadan over a 10 year period. West African Journal of Medicine, 19(3), 192–194.	No Full Text	Unable to acquire full text
Onah, H. E., & Okaro, J. M. (2001). Caesarean Section in the Delivery of Nigerian Eclamptics. Tropical Journal of Obstetrics and Gynaecology, 18(1).	No Full Text	Obscure Journal, couldn't acquire full text

Citation	Reason	Notes
Onwuhafua, P. I., & Oguntayo, A. (2006). Perinatal mortality associated with eclampsia in Kaduna, Northern Nigeria. Nigerian Journal of Medicine : Journal of the National Association of Resident Doctors of Nigeria, 15(4), 397–400.	No Full Text	Unable to acquire full text
Orazulike, N., Fiebai, P., & Uzoigwe, S. (2009). {0725} The effect of antenatal care on maternal mortality in Port Harcourt, Nigeria. International Journal of Gynecology & Obstetrics, 107, Suppl(0), S301 –.	No Full Text	Abstract for oral presentation published in supplement
Souza, J. P., Gülmezoglu, A. M., Vogel, J., Carroli, G., Lumbiganon, P., Qureshi, Z., … Say, L. (2013). Moving beyond essential interventions for reduction of maternal mortality (the {WHO} Multicountry Survey on Maternal and Newborn Health): a cross-sectional study. The Lancet, 381(9879), 1747–1755.	Not Nigeria	Not enough focus on Nigeria or Nigeria-specific data
Tukur, J., & Muhammad, Z. (2010). Management of eclampsia at AKTH: before and after magnesium sulphate. Nigerian Journal of Medicine, 19(1), 104–7.	No Full Text	Journal not available online prior to 2011
Tukur, J., Babatunde, A., Salisu, I., & Ayodeji, O. (2012). I369 EXPANDING THE USE OF MAGNESIUM SULPHATE IN NIGERIA. International Journal of Gynecology & Obstetrics, 119S3, S161–S260.	No Full Text	Abstract for oral presentation published in supplement
Uzoigwe, S. A., & John, C. T. (2004). Maternal mortality in the University of Port Harcourt Teaching Hospital, Port Harcourt in the last year before the new millennium. Nigerian Journal of Medicine : Journal of the National Association of Resident Doctors of Nigeria, 13(1), 32–35.	No Full Text	Unable to acquire full text
van Lonkhuijzen, L., Stekelenburg, J., & van Roosmalen, J. (2012). Maternity waiting facilities for improving maternal and neonatal outcome in low-resource countries. The Cochrane Database of Systematic Reviews, 10, CD006759.	Not related to PE/E	
von Dadelszen, P., Sawchuck, D., Justus Hofmeyr, G., Magee, L. A., Bracken, H., Mathai, M., … Roberts, J. M. (2013). PRE-EMPT (PRE-eclampsia-Eclampsia Monitoring, Prevention and Treatment): A low and middle income country initiative to reduce the global burden of maternal, fetal and infant death and disease related to pre-eclampsia. Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health, 3(4), 199–202.	Not Nigeria	Not enough focus on Nigeria or Nigeria-specific data; Nigeria is part of the PRE-EMPT project, but this paper merely included Nigeria in a list of countries.
Wahab, K. W., Sanya, E. O., Ademiluyi, B. A., & Bello, A. H. (2014). Posterior reversible encephalopathy syndrome complicating postpartum eclampsia in a Nigerian: case report. The Nigerian Postgraduate Medical Journal, 21(3), 266–268.	No Full Text	Unable to acquire full text
Watila, M., Omeiza, B., & Kwari, S. (2015). Seizure occurrence, pregnancy outcome among women with active convulsive epilepsy; one year prospective study. Seizure.	Not related to PE/E	Related to seizure associated with epilepsy; eclamptic patients were excluded from the study
Yakasai, I., Dikko, B., Sunday, A., & Tukur, J. (2009). O1018 Free maternity services in Kano State Nigeria–Use of magnesium sulphate as key to reduction of maternal mortality. International Journal of Gynecology	No Full Text	Abstract for oral presentation, published in supplement
Yeager, B., & Patel, S. (2012). Medicines for Maternal Health; Key Data and Findings.	Grey Literature	

Appendix III:

SUMMARY TABLES OF 19 INTERVENTIONS TO IMPROVE PREVENTION/TREATMENT OF PE/E

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of methods/intervention	Main findings/ limitations Conclusions/ Recommendations
Abdul, M., Nasir, U., Khan, N., & Yusuf, M. (2013). Low-dose magnesium sulphate in the control of eclamptic fits: a randomized controlled trial. Archives of Gynecology and Obstetrics, 287(1), 43–6.	Randomized Controlled Trial	Labour Unit, Obstetrics and Gynecology Federal Medical Centre, Azare, north-eastern Nigeria January to August 2008 72 patients recruited, 39 randomized into low-dose group, 33 were in standard regimen group	Prevalence rate of eclampsia = 4.2% CFR= 5.5%	Standard dose: 14g loading dose of MgSO4 (4g IV, 10g IM) followed by IM maintenance dose of 5g every four hours Low dose: 9g loading dose of Mg SO4 (4g IV, 5g IM) followed by IM 2.5g every four hours	• Primigravidas: 57% of cases. • 44% intrapartum, 26% antepartum, and 15% postpartum eclampsia. • Recurrent convulsion rate did not differ between the study groups. • There were more cesarean deliveries and perinatal deaths in the low-dose group, but the difference was not statistically significant. • Other maternal complications, including mortality, were not significantly different between the groups. • Limitations: small sample size and the study was not blinded. • Conclusions: more studies needed to determine whether a low-dose regimen of MgSO4 should be standardized.
Afolayan, J. M., Nwachukwu, C. E., Esangbedo, E. S., Omu, P. O., Amadasun, F. E., & Fadare, J. O. (2014). Evolving pattern of spinal anaesthesia in stable eclamptic patients undergoing caesarean section at University of Benin Teaching Hospital, Benin, Nigeria. Nigerian	Retrospective case review	University of Benin Teaching Hospital, Benin City, Nigeria January 1, 2011—December 31, 2012 99 cases of eclampsia	Incidence of eclampsia: 170 in 10,000 = 1.7%	Patients' case notes were reviewed; clinical and demographic data was extracted and analyzed.	• 58.59% antepartum, 29.29% intrapartum, 12.12% postpartum eclampsia • 68.73% of cases were nulliparous and 84.1% did not receive ANC at the hospital • 82 underwent caesarean section; 13.4% of whom were <20 years old, 39% were between 25-29 years old, and 52.4% were 30+ years old • Of patients who underwent c/s, 65 (79.3%) had spinal anaesthesia and 17 (20.7%) had general anaesthesia. • This study concludes that maternal and perinatal survival is better when the patient undergoes spinal anaesthesia than those who had general anaesthesia.

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of methods/intervention	Main findings/ limitations Conclusions/ Recommendations
Journal of Medicine, 23(4), 288–295.					
Altman, D., Carroli, G., Duley, L., Farrell, B., Moodley, J., Neilson, J., … Magpie Trial Collaboration Group. (2002). Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. The Lancet, 359(9321), 1877–90.	Randomized placebo-controlled trial Magpie Trial	Was conducted in 33 countries, including Nigeria. 10, 141 women		10, 141 women who had not given birth or were <24 h postpartum, blood pressure 140/90 mmHg or more and proteinuria of 1+ (30mg/dL) or more. Randomized to: Magnesium sulphate (n=5071) or placebo (n=5070)	• While this study does not report findings specific to Nigeria, it is listed here as it was the Magpie Trial that definitively demonstrated the safety and effectiveness of MgSO4 for the management of severe PE/E. • This trial found that MgSO4 reduces the risk of eclampsia (and probably risk of maternal death) by half with no substantive harmful effects for mother or baby.
Ameh, C. A., Ekechi, C. I., Tukur, J., & J, A. C. E. C. T. (2012). Monitoring severe pre-eclampsia and eclampsia treatment in resource poor countries: skilled birth attendant perception of a new treatment and monitoring chart (LIVKAN chart). Maternal and Child Health Journal, 16(5), 941–946.	Cross-sectional	Katsina, Nigeria 118 participants (skilled birth attendants) over five workshops in 2010	N/A	LIVKAN chart was developed and providers were trained on its use. Participating providers were interviewed using a semi-structured questionnaire to assess the usefulness in the chart and assess the quality of care for severe PE/E.	• The goal was to assess the usefulness of the treatment monitoring tool (LIVKAN chart) in improving quality of care for severe PE/E using questionnaires • 98% reported that the LIVKAN chart was better than existing monitoring system and would be useful for improving care. 73% said the chart would be useful at lower levels and improve documentation of referral. • Some challenges to using the LIVKAN chart were high workload (45%) and irregular supply of blank charts (53%). • The chart combines monitoring and treatment guidelines (anticonvulsant, anti-hypertensive, IV fluids, calcium gluconate and delivery) and allows for 24h of monitoring using fewer pages.
Chama, C., & Geidam, A. (2013). A shortened versus standard matched postpartum magnesium sulphate regimen in the treatment of eclampsia: a randomised controlled trial: original article. African Journal of Reproductive Health, 17(3), 131–136.	Randomised Controlled Trial	Labour ward of University of Maiduguri Teaching Hospital January and June 2011 98 eclamptic mothers	Incidence 6.41% (141 out of 2,201 deliveries)	Eclamptic mothers were randomized and received either the standard or shortened postpartum regimen. Fetomaternal outcomes were measured and compared.	• 21 of the 141 had previously received anticonvulsants (mainly diazepam) from referring health facilities and 8 had other complications and were excluded • The remaining 112 participants were randomized to receive either the standard Pritchard regimen of $MgSO_4$ or a shortened postpartum course: two doses of IM $MgSO_4$ are given four hours apart. (14 had incomplete information and 98 were included in the analysis) • Primary outcome measure was recurrence of fits • The shortened course was found to be as effective as Pritchard for the management of eclampsia

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of methods/intervention	Main findings/ limitations Conclusions/ Recommendations
Ekele, B., & Ahmed, Y. (2004). Magnesium sulfate regimens for eclampsia. International Journal of Gynecology and Obstetrics, 87(2), 149–150.	Experimental pilot	Usmanu Danfodiyo University Teaching Hospital January 2002—December 2003 33 women		Patients were treated with a modified regimen that limited $MgSO_4$ administration to 12 hours (vs. 24) and the authors' primary outcome of interest was recurrent convulsions.	• Pritchard regimen involves use of MgSO4 with a habitual 24h administration of maintenance doses after initial loading dose • This small study tested an alternate regimen that is the same loading dose as in Pritchard (4g IV and 5g each buttock) and maintenance doses every four hours for 12 hours. • Recurrent convulsion rate was 6.0% (comparable to 4.7% found in the Collaborative Eclampsia Trial • Since cost of magnesium sulfate has been underestimated, according to the authors, reducing the amount needed to manage PE/E is better. • Recommend a larger, multicenter randomized (12h vs 24h) trial is needed to validate these findings.
Ekele, B. A., & Badung, S. L. H. (2005). Is serum magnesium estimate necessary in patients with eclampsia on magnesium sulphate? *African Journal of Reproductive Health*, 9(1), 128–132.	Prospective	Usmanu Danfodiyo University Teaching Hospital, Sokoto January—December 2002 19 patients		Blood samples were taken from consecutive patients treated for eclampsia with $MgSO_4$ prior to administration of the loading dose and subsequent maintenance doses serum magnesium levels were estimated Modified Pritchard regimen was used (loading dose of 4gIV over 10 mins followed by 10g of deep IM $MgSO_4$; followed by maintenance doses of 5g every four hours. Patients were monitored for $MgSO_4$ toxicity and calcium gluconate was available, Blood samples were taken before each maintenance dose	• 19 patients completed the study • One patient had recurrent convulsion within 30 mins of initiative treatment and was given an additional 2g IV to stop the seizure. • None of the patients experienced loss of deep tendon reflex or respiratory depression; no signs of MgSO4 toxicity • Mean serum magnesium level at baseline was 1.96mmol/L; subsequent serum levels (2.1mmol/L) remained within suggested therapeutic level of 2.0-3.5mmol/L. • Based on this small study, the authors conclude that serum magnesium levels in eclamptic patients receiving only MgSO4 to manage their seizures remained within therapeutic range; recommend more widespread use of magnesium sulphate without the need to estimate serum magnesium.
Ezugwu, E. C., Agu, P. U., Nwoke, M. O., & Ezugwu, F. O. (2014). Reducing maternal deaths in a low resource setting in Nigeria. Nigerian Journal of Clinical Practice, 17(1), 62–66.	Retrospective pre/post intervention study	Enugu State University Teaching Hospital, Nigeria Jan. 2005—Dec. 2007 & Jan 2008—Dec. 2009 59 maternal deaths		Reviewed files of all maternal deaths over a six year period (three years before the adoption of guidelines aimed at maternal mortality reduction and three years after)	• 91% retrieval rate, MMR of 645 per 100,000 live births. • Evidence based guidelines were identified through PubMed and Google scholar and were adapted to the local context. • For this study, resident doctors and nurses were then trained on the guidelines, which included using the Pritchard regimen for the management of severe PE/E. • After adoption of the guidelines, there was a 43.5% reduction in MMR (488 vs 864 per 100,000 live births) • CFR for eclampsia fell by 80% (15.8% to 2.7%)

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of methods/intervention	Main findings/ limitations Conclusions/ Recommendations
Igwegbe. AO, Eleja, GU, Ugboaia, JO, & Ofiaeli, RO. (2012). Improving maternal mortality at a university teaching hospital Nnewi, Nigeria. International Journal of Gynecology & Obstetrics, 116(3), 197-200.	Retrospective evaluation study	Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi January 1, 2004—December 31, 2010 4,916 live births		This study compared maternal mortality at the facility during the pre-SERVICOM and post-SERVICOM periods.	• As a result of Federal proclamation of a social contract with all Nigerians to provide "basic services to which each citizen is entitled in a timely, fair, honest, effective and transparent manner," all government establishments were required to prepare a "Service Compact" (SERVICOM) contract with all Nigerians. • NAUTH launched a SERVICOM charter in May 2005 to improve service delivery to patients including: elimination of fee-for-service for all emergency services (including obstetric services); prompt and appropriate treatment, monitoring of services and record keeping and penalties for "errant staff" • Overall MMR 1098 per 100,000 livebirths over the six year period. In 2004, MMR was 1,567 per 100,000 and in 2010, the MMR 691 per 100,000. • PE/E was most common direct cause of maternal death (25%) • Introduction of SERVICOM reduced the delay at the facility to receive treatment (change in intake and waiver procedures led to reduction in presentation-intervention interval)
Ishaku, S., Ahonsi, B., Tukur, J., & Ayodeji, O. (2013). Attrition from care after the critical phase of severe pre-eclampsia and eclampsia : Insights from an intervention with magnesium sulphate in a primary care setting in northern Nigeria. Health, 5(9), 1461–1466.	Case-control	PHC facilities in Kano State, Nigeria September 2010—August 2011 10 PHCs, 150 patients recruited		10 PHCs were included, 5 were in an experimental arm and 5 were controls; all facilities received severe PE/E patients and performed stabilizing treatment (anti-hypertensives) before sending patient to referral centers. The health workers at the experimental PHCs were trained to recognize patients with severe PE/E and were trained to administer loading dose of MgSO4 (10g IM) before referral. They also received training on detecting MgSO4 toxicity and how to administer the antidote, calcium gluconate. Health workers at control PHCs did not give MgSO4 and either gave diazepam or no anticonvulsant.	• 75% of the women referred to hospitals defaulted; default rate was higher among those who had been at experimental PHCs and received the loading dose of MgSO4 • It is possible that the immediate, yet temporary, effect of MgSO4 gave the false idea that the patients were cured and that follow up was unnecessary; contributing somewhat to the higher attrition among the experimental group; the community needs to be educated about the continuing dangers of severe PE/E • "With appropriate training and supervision, lower-cadre health care professionals can safely administer MgSO4 to treat severe pre-eclampsia and eclampsia without significant toxic effects in primary care settings in developing countries."
Nkwocha, G. C., Anya, S. E., & Anya, A. E. (2006). Obstetric mortality in a	Retrospective review of births and	Federal Medical Centre, Umuahia, Abia State.		This study used hospital records to compare mortality rates from the period before the 1990 launch of the "Safe Motherhood	• Overall, puerperal sepsis, hypertensive disorders of pregnancy (pre-eclampsia and eclampsia), hemorrhage and uterine rupture, together, accounted for 88% of maternal deaths.

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of methods/intervention	Main findings/ limitations Conclusions/ Recommendations
Nigerian general hospital. *Nigerian Journal of Medicine : Journal of the National Association of Resident Doctors of Nigeria*, *15*(1), 75–76.	maternal deaths 'before-and-after' study	January 1, 1981—December 31, 1998 21,244 deliveries		Programme" in Nigeria which aimed to reduce maternal mortality by 50% before 2000.	• MMR decreased 8% from 4942 per 100,000 before 1990 and 4545 per 100,000 from 1990-1998 • Deaths due to PE/E increased after the launch of the Safe Motherhood Programme: In 1981-1989, pre-eclampsia caused 4.4% of maternal deaths and eclampsia caused 13.9%. From 1990-1998, PE caused 10.5% and eclampsia caused 17.9%
Okereke, E., Ahonsi, B., Tukur, J., Ishaku, S. M., & Oginni, A. B. (2012). Benefits of using magnesium sulphate (MgSO(4)) for eclampsia management and maternal mortality reduction: lessons from Kano State in Northern Nigeria. *BMC Research Notes*, *5*, 421.	Retrospective study; before-and-after	Bayero University/Aminu Kano Teaching Hospital, Kano Baseline: 2006—2007 Intervention: February 2008—January 2009 Baseline: 1,233 patients Intervention: 1045 patients (49 severe PE, 996 eclampsia)		Data for the study was obtained from obstetric records for eclamptic patients. For baseline: patients were treated using diazepam, which was commonly available Intervention: doctors and midwives were trained to use $MgSO_4$ following protocol and detect and treat $MgSO_4$ toxicity (using calcium gluconate)	• 52% of the patients were teenagers, 60.4% were primigravidae, 74.1% were illiterate, 71% were in monogamous relationships • This study found a reduction in case fatality among eclampsia patients from 20.9% (95% CI: 18.7, 23.2) at baseline to 2.3% (1.4, 3.2) during intervention period. • 92.5% of patients treated with MgSO4 did not have recurrent convulsions • This study found that training providers on protocol for treating severe PE/E with MgSO4 is effective to reduce CFR due to eclampsia and there is no significant difference in cost of MgSO4 vs. diazepam.
Okonofua, FE et al. "Training Health Workers for Magnesium Sulfate Use Reduces Case Fatality from Eclampsia: Results from a Multicenter Trial." *Acta obstetricia et gynecologica Scandinavica* 92 (2013): 716–720.	Multicenter trial 'before-and-after'	Kano, Lagos, Calabar, Jos, Maiduguri, Enugu Baseline: January—May 2008 Training: April-June 2009 Intervention: August 2009	Incidence of eclampsia baseline: 1.5% intervention: 1.4% CFR	Baseline: review of hospital records and in-depth interviews with providers to inform development of training curriculum. Training: mandatory 3-day workshop on epidemiology of maternal mortality, clinical features of eclampsia, ways to overcome limitations in the healthcare system in managing eclampsia, protocols on $MgSO_4$. Intervention: use of Pritchard regimen to treat $MgSO_4$ and guidelines on use and timing of anti-hypertensives and monitoring patient.	• Aminu Kano Teaching Hospital, Lagos State University Teaching Hospital, University of Calabar Teaching Hospital, University of Jos Teaching Hospital, University of Maiduguri Teaching Hospital, University of Nigeria Teaching Hospital • Multi-professional trainings included: Ob/Gyns, doctors in training, nurses, midwives, nurses/midwives in training, staff from related departments and senior management • The results from pre- and post-tests at the training sessions indicate a significant increase in knowledge related to eclampsia management • During one year after the intervention, 219 eclampsia cases were treated; compared to baseline, a similar incidence of eclampsia was seen but maternal mortality was significantly reduced

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of methods/intervention	Main findings/ limitations Conclusions/ Recommendations
		Six teaching hospitals in Nigeria	Baseline: 15.1% endline: 3.2%	Endline: clinical records of cases of eclampsia for one year after the intervention were reviewed and analyzed	• Perinatal mortality rate reduced slightly, but the difference was not significant (141.5 per 1,000 at baseline, 129.8 per 1,000 after intervention, p=0.32). • 13.5% of newborns had low birthweight after the intervention • "Key message: building the capacity of healthcare providers to use magnesium sulfate for the treatment of eclampsia is an effective intervention for reducing the number of deaths due to eclampsia in low-income countries"
Okusanya, B O, K D Garba, and H M Ibrahim. "The Efficacy of Intramuscular Loading Dose of MgSO4 in Severe Pre-Eclampsia/ Eclampsia at a Tertiary Referral Centre in Northwest Nigeria." *The Nigerian postgraduate medical journal* 19.2 (2012): 77–82.	Descriptive comparative study	Federal Medical Centre Katsina 10g dose: April 1, 2008—April 30, 2009 14g dose: May 1, 2009—October 25, 2009 10g dose 54 women 14g dose: 49 women		All women presenting with severe PE/E were prospectively enrolled during two periods; the first receiving a 10g loading dose of $MgSO_4$ and the second period using a 14g loading dose. Severe PE: BP 116/110 mmHg and proteinuria of at least 2+ Eclampsia: occurrence of convulsions in women with severe PE	• 55 women had severe PE (25 were in 10g group. 30 in 14g group) • 48 had eclampsia (29 in 10g group and 19 in 14g group) • Two (7%) of the women in the 10g group had recurrent convulsions and none who were in the 14g group experienced recurrent convulsions (difference is not significant). • Rates of vaginal delivery, onset of convulsion/recurrent convulsion, maternal death and neonatal Apgar score did not have statistically significant rates between the two groups. • 10g IM loading dose prevented eclampsia in 80% of women with severe PE and prevented recurrent convulsions in 93% of women with eclampsia. • Using 10g did not increase chances of caesarean section or severe birth asphyxia at 5 minutes. • The six perinatal deaths observed were all in women in the 10g groups, but these women were admitted with intrauterine fetal demise before treatment was delivered. • RCT is needed to confirm efficacy and safety of lower loading dose for potential use at lower level facilities.
Onah, H., & Iloabachie, G. (2002). Conservative management of early-onset pre-eclampsia and fetomaternal outcome in Nigerians. *Journal of Obstetrics and Gynaecology*, *22*(4), 357–362.	Prospective case control	University of Nigeria Teaching Hospital, Enugu May 5, 2005—June 30, 2000 175 study group 574 controls	CFR among early onset: 33.3% CFR among late onset: 7.1%	749 consecutive cases of PE were recruited. The early-onset cases (PE manifested before 30 weeks gestation) formed the study group and the remaining cases were the controls. Demographic and obstetric details were recorded including gestational age at onset of disease as well as BP and urine test. After being admitted, patients were routinely tested for :full blood count, serum electrolytes, urea and creatinine, liver function tests, clotting profile, urinalysis and ultrasonography, they were put on bed rest,	• 'Pure' PE: hypertension associated with proteinuria in previously normotensive women. • Superimposed PE: significant aggravation of preexisting hypertension associated with sustained proteinuria • Alpha-methyldopa and hydrallazine were used to control high BP above 160/110 mmHg (methyldopa was used antepartum and hydrallazine used to manage hypertensive crises, eclampsia and during peripartum). • Seizures were controlled using diazepam (MgSO4 was unavailable). • Early onset group experienced 14 maternal deaths (7 due to eclampsia, 3: renal failure, 2: HELLP syndrome, 1: anesthetic accident, 1: septicemia from AIDS) –80% of early onset group gained two weeks gestation.

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of methods/intervention	Main findings/ limitations Conclusions/ Recommendations
				given diazepam and anti-hypertensives as deemed necessary by the physician.	• Causes of death in the late onset group were: eclampsia=7, renal failure=6, abruptio placentae=5, anesthesia-related causes=4, cerebrovascular accident=2, HELLP syndrome=2, associated diabetic ketoacidocis=1, septicaemia from AIDS=1 • Based on the high CFR among early onset cases, the authors recommend that these cases be managed conservatively to improve fetal and maternal outcomes
Tukur, J., Ahonsi, B., Ishaku, S. M., Araoyinbo, I., Okereke, E., & Babatunde, A. O. (2013). Maternal and fetal outcomes after introduction of magnesium sulphate for treatment of preeclampsia and eclampsia in selected secondary facilities: a low-cost intervention. *Maternal and Child Health Journal*, *17*(7), 1191–1198.	Before and after	Kano, Bichi, Wudil, Gwarzo, Rano, Minjibir, Tudun Wada, Doguwa, Rano, Rogo February 1, 2008—January 31, 2009	baseline CFR: 20.9% post intervention CFR: 2.3%	Five hospital officials from the Hospitals Management Board and one doctor and one midwife from each of the ten facilities were invited to participate in a training. The two-day training provided didactic lectures on evidence-based management of hypertensive disorders of pregnancy and use of $MgSO_4$. Participants were taught to administer 4g $MgSO_4$ IV and 10g IM followed by 5g IM every 6 hours until 24 hours after delivery or the last seizure and also to monitor for toxicity by checking deep tendon knee reflex. Data was then collected on maternal sociodemographics, pattern of severe PE/E, and fetomaternal outcomes at the ten facilities and compared to baseline survey from three general hospitals	• Baseline surveys showed that 1,233 patients with severe PE/E, 258 died : baseline CFR: 20.9% • 25 master trainers participated in the training and subsequently trained 160 health workers (doctors, midwives, and community health extension workers) • During the project period, 49 cases of severe PE and 996 cases of eclampsia were treated at the facilities out of a total of 22, 502 deliveries • 322 cases of eclampsia manifested antepartum, 430 were intrapartum, and 244 developed postpartum • After the intervention, only 24 of the 1045 cases died, significantly reducing the CFR associated with severe PE/E. • Perinatal mortality was 12.3% (129 of 1045); perinatal mortality was significantly higher among patients who experienced three or more convulsions (there was no baseline perinatal mortality rate, but another facility that uses diazepam reported a 35.3% stillbirth rate). • Introducing MgSO4 for severe PE/E is a low-cost and replicable intervention that has a positive effect on maternal and fetal morbidity and mortality and should be scaled up.
Tukur, J., Ogedengbe, C., Nwanchukwu, E., Araoyinbo, I. A., Yakasai, I. A., Adaji, S. E., & Ajala, B. (2011). Introduction of an innovation for the reduction of maternal mortality in Kano State, northern Nigeria: a case study of magnesium		Kano State Feb—December 2008 1045 patients treated with $MgSO_4$	CFR: 2.3%	$MgSO_4$ was introduced to ten general hospitals and data was collected from the facilities to monitor the intervention. A workshop on $MgSO_4$ use and monitoring was conducted and 25 master trainers took the knowledge they acquired and conducted step down trainings to 160 clinical providers.	• 60.4% of the patients treated with MgSO4 were primigravida and 44.1% had no form of ANC • 23 women (2.2%) experienced toxic effects associated with MgSO4 but they were treated with calcium gluconate and no morbidity or mortality resulted • 24 mothers died, and 129 (12.3%) of the babied were delivered dead • The 24 deaths in this study made up 4.9% of all maternal deaths during the 12 month period of the project

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of methods/intervention	Main findings/ limitations Conclusions/ Recommendations
sulphate. *Tropical Doctor*, *41*(4), 197–200.				Prior to these trainings, a pilot survey was conducted to assess the use of $MgSO_4$ in general hospitals. Advocacy visits were then necessary to explain to health officials the evidence for the effectiveness of $MgSO_4$.	• Compared to maternal deaths due to eclampsia during the 12 months prior to the intervention (268/567; 47.3%), the attributable deaths from eclampsia reduced by 42.4% • This project was successful because it was evidence-based, sustainable through stakeholder involvement, and replicable.
Tukur, J., Umar, N. I., Khan, N., & Musa, D. (2007). Comparison of emergency caesarean section to misoprostol induction for the delivery of antepartum eclamptic patients: a pilot study. Nigerian Journal of Medicine : Journal of the National Association of Resident Doctors of Nigeria, 16(4), 364–367.	Randomized pilot study	Federal Medical Centre Azare, Bauchi 50 eclamptic patients		Primigravida patients with singleton pregnancies presenting with antepartum or imminent eclampsia and a closed cervical os were randomized for delivery by CS or by induced labor using misoprostol.	• Misoprostol failure rate was 4 patients (16%); these four were subsequently delivered by CS. • The CS group spent an average 10.1 days in the center compared to 6.08 days spent on average in the center by the misoprostol group. • Maternal complications and admissions of babies were frequent in the CS group. • Maternal mortality in each group was 4% • Given the findings of this pilot study, the authors recommend using misoprostol (cheap, available, and safe for delivery of antepartum eclamptics) in the event of a delay for CS. A larger, multi-center study is also suggested.
Ugwu, E. O. V, Dim, C. C., Okonkwo, C. D., & Nwankwo, T. O. (2011). Maternal and perinatal outcome of severe pre-eclampsia in Enugu, Nigeria after introduction of Magnesium sulfate. *Nigerian Journal of Clinical Practice*, *14*(4), 418–421.	Retrospective case review Before-and-after	University of Nigeria Teaching Hospital Enugu January 1 2005—December 31, 2008 Diazepam: 47 women $MgSO_4$: 30 women	Prevalence of severe PE: 3.3% CFR before: CFR after:	This retrospective case review looked at cases of severe PE and the maternal and perinatal outcomes for two years before and two years after the introduction of $MgSO_4$ as standard treatment for severe PE in 2007 (previously diazepam).	• 77 cases of severe PE over the four year period; 49.4% were primigravidae • One woman from the diazepam group experienced tonic-clonic seizures, none of the women in the MgSO4 group experienced seizures after the initiation of the treatment; no maternal death occurred in either group. • Women in the diazepam group were more likely to experience prolonged hospital stay compared to the MgSO4 group. • 25 of the 79 babies died within the perinatal period (2 sets of twins) giving a perinatal case fatality rate of 32.5%–but there was not a significant difference in perinatal mortality between the groups. • This study showed that MgSO4 is the most effective and safest drug to manage convulsions in severe PE and results in reduced maternal and perinatal morbidity when compared to diazepam.

Appendix IV:

SUMMARY TABLES OF DEMONSTRATED AND POTENTIAL RISK FACTORS FOR PE/E

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Abubakar, A., Abdullahi, R., HZ, J., Dauda, M. H., & MA, P. (2009). Maternal Ethnicity and Severity of Pre-Eclampsia in Northern Nigeria. *Asian Journal of Medical Sciences*, *1*(3), 104–107.		Primary Health Centers in Katsina, Adamawa and Borno States February—August 2009 61 cases of severe PE	N/A	Blood pressure measured and monitored. BMI calculated. Total serum cholesterol, triglyceride, high and low density lipoproteins were determined from a blood sample taken after overnight fasting. Urinalysis began. -22 in Group A (Hausa) -20 in Group B (Kanuri) -19 in Group C (Fulani)	• No significant difference in the severity of pre-eclampsia between the Hausa and Kanuri, though they demonstrated elevated levels of triglyceride, serum cholesterol, pathological edema, increase in blood pressure, and higher levels of urine protein. • The Fulani group showed higher levels of the above and were more likely to progress to eclampsia than the other two tribes.
Ademuyiwa, O., Odusoga, O. L., Adebawo, O. O., & Ugbaja, R. (2007). Endogenous antioxidant defences in plasma and erythrocytes of pregnant women during different trimesters of pregnancy. *Acta Obstetricia et Gynecologica Scandinavica*, *86*(10), 1175–1182.	Case-Control	Obstetrics Departments of Sacred Heart Hospital Abeokuta, Nigeria and Olabisi Onabanjo University Teaching Hospital, Sagamu Nigeria 97 pregnant women, 7 with new onset of PE Controls (n=20) female students from University of Agriculture, Abeokuta, Nigeria and Olabisi		Blood samples taken from all participants for exzymatic determinations. The study looked at: enzymic antioxidants (SOD, CAT, GST), non-enzymic antioxidant (GSH), and a heme biosynthetic enzyme, aminolevulinic acid dehydratase (ALAD) to determine characterize the profiles of antioxidant response in pregnant women.	• This study showed an increased plasma activity of Mn-SOD and statistically significant low values of erythrocyte CAT, SOD and ALAD activities in PE compared to healthy pregnant women • Other antioxidants in plasma and erythrocytes remain unchanged • The data from this study supports hypothesis that 'oxidative stress' (OS) occurring secondary to impaired oxidant defenses, might be one mechanism underlying the pathophysiology of pre-eclampsia (small sample size, needs further studies)

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
		Onabanjo University, Ikenne, Nigeria.			
Adeyinka, D., Oladimeji, O., Adekanbi, T., Adeyinka, F., Falope, Y., & Aimakhu, C. (2010). Outcome of adolescent pregnancies in southwestern Nigeria: A case control study. *Journal of Maternal-Fetal and Neonatal Medicine*, *23*(8), 785–789.	Retrospective case control	University College Hospital, Ibadan, Nigeria January 2007—November 2008 45 cases, 90 controls	Incidence of PE/E among cases: 20% Incidence of PE/E among controls: 3.33%	Cases were women aged <18 years and controls were between 20 and 35 years	• Defined pre-eclampsia as hypertension (> 140/90mmHg on two occasions 4 hours apart) and proteinuria (>0.3g/dl) in the second half of pregnancy. Eclampsia = associated with convulsions, oliguria (>400ml/24h), increased tendon reflex, pain in the right hypochondriac region. • Adolescents were significantly more likely to develop PE/E than their non-adolescent counterparts.
Adokiye, E., Isreal, J., C, H. T., & Levi, W. O. (2015). Factors influencing the prevalence of Preeclampsia-eclampsia in booked and unbooked patients: 3 years retrospective study in NDUTH, Okolobiri. *World Journal of Medicine and Medical Science*, *3*(1), 1–14.	Retrospective case review	Department of Obstetrics and Gynaecology, Niger Delta University Teaching Hospital, Okolobiri, Nigeria January 1, 2011—December 31, 2013 1,667 deliveries	Incidence of PE/E: 5.69% Eclampsia only: 2.16%	Review of medical records for all pregnant women admitted and managed to delivery during the study period.	• Seven (7.37%) of PE/E cases were teenagers, 48 (48.42%) were 20-29 years, 40 (42.11%) were 30+ years old • 89.5% live in rural areas • 66.32% had either primary or post primary education • 60% had more than two previous deliveries • Perinatal mortality was 36.84%; 41.05% were preterm deliveries (29-36 weeks) • 77.68% were unbooked, 69.47% had visited TBAs • Proteinuria in PE/E patients: 3+ = 30.53%; 2+= 40.00%; 1+ 27.37%; no proteinuria = 1.05% • 85.79% treated with Pritchard regime for MgSO4 • 81.10% received Aldomet (Methyldopa); 97.89% were given Hydralazine • 21.05% were given diazepam
Afolabi, B. B., Iwuala, N. C., Iwuala, I. C., & Ogedengbe, O. K. (2009). Morbidity and mortality in sickle cell pregnancies in Lagos, Nigeria: a case control study. *Journal of Obstetrics and Gynaecology : The Journal of the Institute of Obstetrics and Gynaecology*, *29*(2), 104–106.	Retrospective case control	Department of Obstetrics and Gynaecology, Lagos University Teaching Hospital, Idi-Araba, Lagos, Nigeria		Examination of delivery records for all pregnant HbSS women delivering during study period and the case notes of the next two delivering age-and parity-matched HbAA women were retrieved.	• Among HbAA women 5.6% developed PE and 1.3% developed eclampsia; among HbSS women, 6.7% developed PE and none developed eclampsia • This study did not find that HbSS women were at a higher risk of developing PE; the power of this study is not enough to make conclusions

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
		January 1996—December 2000 75 women with HbSS and 150 women with HbAA			
Airede, L., & Ekele, B. (2003). Adolescent maternal mortality in Sokoto, Nigeria. *Journal of Obstetrics and Gynaecology*, *23*(2), 163–165.	Retrospective, cross-sectional study	Usmanu Danfodiyo University Teaching Hospital, Sokoto January 1990 to December 1999		Information relating to age, parity, literacy level, booking status, duration and outcome of labour, mode of delivery and cause of death were obtained from casenotes and data were reviewed and analyzed	• MMR 4863 per 100,000 livebirths • 46 (23.4%) of all maternal deaths were adolescents (12-19 years old) • Eclampsia causes 21 (46%) of the adolescent maternal deaths
Akerele, J., Abhulimen, P., & Okonofua, F. (2001). Prevalence of asymptomatic bacteriuria among pregnant women in Benin City, Nigeria. *Journal of Obstetrics and Gynaecology*, *21*(2), 141–144.	Semi-quantitative screening	ANC clinics in Benin City 500 pregnant women	N/A	Semi-quantitative culture of midstream urine from pregnant women to screen for asymptomatic bacteriuria in first trimester. Samples with significant bacteriuria (10^5 or more bacteria per ml) were examined under the light microscope for: presence and number of red blood cells, white blood cells, epithelial cells, and casts.	• "Rational therapy of asymptomatic bacteriuria in pregnant women may prevent associated risks such as pyelonephritis and pre-eclampsia." • Of the 500 women screened, 433 specimens showed significant bacteriuria. • [note: this study did not report the number of participants who developed PE/E)]
Akiibinu, M. O., Kolawole, T. O., Ekun, O. A., & Akiibinu, S. O. (2013). Metabolic dysfunctions in Nigerian pre-eclamptics. *Archives of Gynecology and Obstetrics*, *288*(5), 1021–1026.	Case-control	32 pregnant women with pre-eclampsia (cases) 5 months		Pre-eclamptic women were recruited after 20 weeks. Total antioxidant potential (TAP), total plasma peroxides (TPP), total cholesterol (TC), total protein (TP), albumin, globulin, nitric oxide (NO), C-reactive protein (CRP), total tri-iodotyronine (TT3) and thyroid	• Cases were defined as having hypertension (systolic BP = 169 + 26.0 mmHg, diastolic = 102 + 11.0 mmHg), significant proteinuria (368 + 39 mg/24h, severe headache, abdominal pain and vomiting. • Weight, BMI, mean values of sBP, dBP urinary protein, TSH, T3-CHOL, TPP, OSI,

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		40 normal pregnancies (controls)		stimulating hormone (TSH) were determined. Oxidative stress index (OSI) was calculated as the percent ratio of TPP and TAP.	MDA and CRP in pre-eclamptics were significantly higher than in the controls. • Mean values of plasma TT3, albumin, TP TAP and NO were significantly lower among cases when compared with controls. • Globulin showed no significant difference between cases and controls • Results indicating that pre-eclamptics had hypothyroidism, hypercholesterolemia, oxidative stress and deranged inflammatory responses. • Conclusion: hypercholesterolemia, oxidative stress, deranged inflammatory responses and lower thyroid function are possible features of PE
Akinloye, O., Oyewale, O. J., & Oguntibeju, O. O. (2010). Evaluation of trace elements in pregnant women with pre-eclampsia. *AFRICAN JOURNAL OF BIOTECHNOLOGY*, *9*(32), 5196–5202.	Case control study* *the paper itself claims to be a 'cross-sectional randomized study'	Ladoke Akintola University of TechnologyTeaching Hospital, Osogbo, Osun State, Western Nigeria 49 pre-eclamptic patients (cases) 40 age-matched non pre-eclamptic women (controls)		Blood collection was done using a sterile needle and syringe into appropriate tube, each sample was analyzed and zinc, copper, selenium, manganese and magnesium levels were determined	• All elements evaluated (zinc, copper, selenium) were significantly lower in the PE group when compared to the control group. • Dietary supplementation of these elements may help prevent PE • Mean BMI, systolic blood pressure and diastolic blood pressure were all significantly higher among cases than controls • Mean serum concentrations of zinc, copper, selenium, manganese and magnesium were all significantly lower among cases than controls • Suggests that PE is associated with oxidative stress
Anorlu, R. I., Iwuala, N. C., & Odum, C. U. (2005). Risk factors for pre-eclampsia in Lagos, Nigeria. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, *45*(4), 278–282	Case-control	Lagos University Teaching Hospital February 2001 to August 2002 1803 women who delivered during study period	137 of 1803 had PE/E (128 were analyzed) Incidence: 7.6%	Socio-demographic characteristics, pre-pregnancy weight, medical history and previous obstetric history, and level of stress at home and at work was collected during face-to-face interviews	• 91 (71.1%) were primigravidae • Risk factors associated with increased risk of pre-eclampsia were: nulliparity (OR 4.77; 95% CI 2.90–7.78), stressful work during pregnancy (OR 2.10; 95% CI 1.20–3.71), stressful home environment (OR 1.97; 95% CI 1.27–3.69), previous pre-eclampsia (OR 11.68; CI 3.81–37.61), history of chronic hypertension (OR 2.21; 95% CI 1.17–6.20), a body weight greater than 80 kg (OR 2.01; 95% CI 1.05– 3.87); and multiple pregnancy (OR 2.71; 95% CI 1.27—6.13)

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Arinola, G., Arowojolu, A., Bamgboye, A., Akinwale, A., & Adeniyi, A. (2006). Serum concentrations of immunoglobulins and acute phase proteins in Nigerian women with preeclampsia. *Reproductive Biology*, 6(3), 265–27		Obstetrics and Gynaecology Clinic of the University College Hospital, Ibadan, Oyo State, Nigeria 92 women 15-30 years old		Participants divided into three groups: --32 pregnant women in 3rd trimester with preeclampsia --36 pregnant women in 3rd trimester without preeclampsia --24 non-pregnant women with no history of abortion as controls Blood and urine samples were taken and analyzed for: immunoglobulin classes (IgA, IgG, and IgM) and acute phase proteins (alpha-2-macroglobulin, haptoglobin and transferrin). Mean of two readings for each specimen were taken as actual value	• Diagnosis of PE was done based on: significant proteinuria (>100mg/day) and high blood pressure (>130/90 mmHg) on at least two occasions 6 hours apart or more. • Mean level of IgG was significantly lower in subjects with preeclampsia and significantly higher in patients with normal pregnancy when compared to non-pregnant controls. • Mean level of IgA was significantly reduced in pre-eclamptic subjects vs. controls • Mean levels of transferrin and alpha-2-macroglobulin were significantly lower and among PE group compared with other two groups. • Haptoglobin was significantly higher in women with PE compared to normal pregnancy, but both pregnant groups had lower levels compared with non-pregnant women.
Atiba, A. S., Abbiyesuku, F. M., 'Niran-atiba, T. A., Oparinde, D. P., Ajose, O. A., & Akindele, R. A. (2014). Free radical attack on membrane lipid and antioxidant vitamins in the course of pre-eclamptic pregnancy. *Ethiopian Journal of Health Sciences*, *24*(1), 35–42.	Longitudinal prospective cohort	Ladoke Akintola University of Technology Teaching Hospital, Osogbo and Egbedore Local Government Health Centre, Awo, Osun state, Nigeria May 2011–January 2012 118 pre-eclamptic and 115 apparently normal pregnant women were recruited		100 women for each of the three study groups (PE, normal pregnancy (NP), nonpregnant (NoP)) participated in baseline and follow up eight weeks later. Venous blood was collected from pregnant participants and nonpregnant controls. Plasma was separated and used for malondialdehyde (MDA) and vitamins C and E analysis.	• Pre-eclamptic women were defined as having elevated BP of 140/90 mmHg on two consecutive recordings 4 to 6 hours apart, minimum proteinuria of 300gm in 24 hour urine sample or 1+ on dipstick. • Highest levels of MDA were in PE patients and lowest in NoP patients; MDA among PE patients was also higher than NP during the second and third trimesters. • No change in plasma levels of vitamins C and E was found as pregnancy advances • Studies needed to identify the specific antioxidant to counteract lipid peroxidation (free radical injury) which may help reduce PE.

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
		Age matched non pregnant women			
Attahir, A., Sufiyan, M. B., Salihu, A., & Rabiu, a M. (2010). Association between Maternal Socio – economic Status , Polygamy and Risk of Pre – eclampsia in Rural Areas of Northern Nigeria. *Journal of Family and Reproductive Health*, *4*(1), 47–52.	Case control	Primary Health Centers in Katsina, Adamawa and Borno states Two groups of 50 each: A--Pregnant non-hypertensive women B—women with pre-eclampsia		BP was measured and questionnaire was administered to each patient to assess the association between various social factors and risk of PE	• If PE progresses to eclampsia, characterized by malignant hypertension and epileptiform convulsions, caesarian section is required. • Known risk factors: nulliparity, history of pre–eclampsia in previous pregnancy, extremes of maternal age, multi fetal gestation, chronic hypertension, diabetes mellitus, chronic kidney disease, vascular or connective tissue disease, thrombophilia, high Body Mass Index (BMI), and obesity. • Family history of hypertension, diabetes or kidney disease was more common among women with PE • Seclusion and polygamy were not found to have an effect on risk of developing PE • The women with PE were more likely to be uneducated, lack income, which could lead to low ANC attendance among this population
Awodu, O. A., Shokunbi, W. A., & Ejele, O. A. (2003). Lupus anticoagulant in Nigerian women with preeclampsia. *West African Journal of Medicine*, *22*(3), 240–242.	Case control	University of Benin Teaching Hospital 26 pregnant women, 18-45 years old with PE 50 apparently healthy pregnant women, 18-45 years old		Blood samples were collected and platelet poor plasma was prepared and preserved for testing/analysis. Kaolin clotting time (KCT) was done to test coagulation Lupus anticoagulant was determined to be present if the KCT ratio at 20% test plasma to KCT at 100% normal control plasma $\geq$ 1.2	• This study found 15.4% prevalence of lupus anticoagulant in women with PE which is statistically higher than the prevalence of LA in apparently healthy pregnancies. (it is controversial as to whether LA presence is causal or consequence of clinical manifestations with which it has been associated) • This study recommends that LA in PE in Nigeria is significant and all women should be screened for LA.
Chigbu, C. O., Okezie, O. A., & Odugu, B. U. (2009). Women in southern Nigeria with change in paternity do not have increased incidence of pre-eclampsia. *Journal of Obstetrics and Gynaecology : The Journal of the Institute of Obstetrics and*	Prospective cohort	Catholic Maternity Hospital, Moniaya, Ogoja, Cross River State, Nigeria September 2006—August 2007		Women attending ANC clinic of the hospital for their second pregnancy were recruited, sociodemographic and obstetric data was collected including paternity of index and previous pregnancies, outcome of previous	• The “exposure” for this cohort study was change in paternity • PE was defined as hypertension (>140/90 mmHg on at least two occasions at least 6h apart or dBP of 110mmHg at any time or an increase of 30mmHg and 15mmHg in sBP and dBP respectively or mean arterial pressure of

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Gynaecology, *29*(2), 94–97.		779 women were recruited and 732 were included in the final analysis due to loss to follow up		pregnancy and duration of sexual cohabitation with present partner. Urine protein was measured using dipstick testing and ANC follow up was every four weeks until 28 weeks gestation and every two weeks after that until 37 weeks.	greater than 105 mmHg) with proteinuria after 20 weeks of pregnancy • 312 (group A) had change in paternity; 420 had no change in paternity (group B) • The rate of PE was not significantly different between the two groups, within Group A, duration of cohabitation did not show significant difference between those who developed PE and those who did not. • "the findings of this study call for a re-examination of the 'change in paternity theory of pre-eclampsia'"
Enaruna, N., Ande, A., & Okpere, E. (2013). Clinical significance of low serum magnesium in pregnant women attending the University of Benin Teaching Hospital. *Nigerian Journal of Clinical Practice*, *16*(4), 448–53.	Prospective cohort	University of Benin Teaching Hospital, Benin City June—December 2011 160 patients		Participants (included antenatal women recruited in 2nd trimester and followed up until 1 week postpartum) had blood drawn at recruitment to measure serum magnesium and were followed up until delivery when repeat serum magnesium assay was done	• Primary outcome measure was prevalence of hypomagnesemia in pregnancy • Magnesium deficiency was detected in 16.25% of the patients and was significantly correlated with occurrence of PE, leg cramps, and preterm birth. • Recommends magnesium supplementation (or eating magnesium-rich diet)
Familoni, O. B., Adefuye, P. O., & Olunuga, T. O. (2004). Pattern and factors affecting the outcome of pregnancy in hypertensive patients. *Journal of the National Medical Association*, *96*(12), 1626–1631.	Retrospective cohort	Olabisi Onabanjo University Teaching Hospital, Sagamu January 1997—December 2002 2,393 deliveries	HDP incidence: 5.3%	Medical records of pregnant patients were analyzed, 127 were identified as having a hypertensive disorder of pregnancy (HDP). Based on hypertension type, patients were categories as "high-risk" or "low-risk" the groups were compared	• 26.2% had gestational hypertension, 19.7% had pre-eclampsia superimposed on chronic hypertension and 54.1% had PE/E. • Those with PE/E had the worst maternal and fetal outcomes (6.1% maternal mortality, 18.2% target organ damage, 36.4% fetal mortality, 66.7% fetal respiratory distress) • 62 (50.8%) were high-risk and 60 (49.2% were low-risk • High-risk group had higher rates of: illiteracy, maternal death, stroke, abruptio, fetal death, and caesarean section and lower rates of regular ANC. • Parity had no effect on whether the patient was high- or low-risk •
Glew, R. H., Cole, D. M., Mehla, G. S., El-Nafaty, A. U., Crossey, M. J.,	Case control	Federal Medical Centre, Gombe and	N/A	Pregnant women were placed into one of four groups: Group 1: PE; Group 2:	• PE was defined as BP 140/90 mmHg or greater and proteinuria (>190mg/g creatinine)

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Tzamaloukas, A., & VanderJagt, D. J. (2005). Lysosomal enzymes in preeclamptic women in northern Nigeria. *Clinica Chimica Acta; International Journal of Clinical Chemistry*, *353*(1-2), 95–101.		Specialist Hospital, Gombe June-August 2001 Group 1: 41 women Group 2: 31 women Group 3: 44 women Group 4: 52 women		hypertensive aproteinuric; group 3:normotensive proteinuric; group 4: healthy pregnant women (controls) Urine specimens were collected and underwent biochemical analyses. Results were statistically analyzed	• The goal was to assess whether lysosomal enzyme concentrations in women with PE were due to the hypertension or proteinuria, or both. • This study found that low levels of β-hexosaminidase in pre-eclamptic women is associated with proteinuria and not hypertension; it is not likely, therefore, that screening for lysosomal enzymes would be useful in predicting or monitoring PE.
Glew, R. H., Melah, G., El-Nafaty, A. I., Brandt, Y., Morris, D., & VanderJagt, D. J. (2004). Plasma and urinary free amino acid concentrations in preeclamptic women in northern Nigeria. *Clinica Chimica Acta; International Journal of Clinical Chemistry*, *342*(1-2), 179–185.	Case control	Federal Medical Centre, Gombe and Specialist Hospital, Gombe 37 pre-eclamptic women 16 controls		Urine and blood samples were taken and analyzed for amino acids. Statistical analyses were performed to compare variables between patients with PE and controls	• Defined “pre-eclamptic” as: cerebral or visual disturbances, epigastric pain, pulmonary edema or cyanosis, sBP > 140mmHg or dBP >90 mmHg and proteinuria (190mg total protein/g creatinine or more) • Serum concentrations of common amino acids (including serum arginine) were not significantly different between study groups, except phenylalanine. • Phenylalanine concentration was significantly higher among PE group
Guerrier, G., Oluyide, B., Keramarou, M., & Grais, R. F. (2013). Factors associated with severe preeclampsia and eclampsia in Jahun, Nigeria. *International Journal of Women's Health*, *5*(1), 509–513.	Hospital-based case control study	Jahun Hospital October 2010—May 2011 2,835 pregnant women 1,257: normal pregnancy (controls) 419: Severe PE/E (cases)	16% had severe PE/E (175: severe PE, and 244: eclampsia)	Participants were selected from the emergency obstetric program in the rural Jahun hospital, patients were interviewed and gave demographic information, medical history, social history, current history, use of traditional treatments, delivery details and neonatal outcome.	• Eclampsia is the occurrence of seizure and/or altered level of consciousness not caused by epilepsy or other convulsive disorders, with signs of severe preeclampsia. • Severe PE : new hypertension with blood pressure of 160 mmHg systolic or diastolic BP of 110 mmHg or greater, after 20 weeks of gestation in a woman who was normotensive before 20 weeks, associated with proteinuria • Of 244 eclamptic cases, 194 were ante- and intra-partum, and 50 were admitted postpartum; 11% experienced no signs of severe hypertension (headache, blurred vision) • The groups were similar except for: the cases were younger (mean age 21 vs mean age 25 among controls), a higher

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					proportion attended fewer than four ANC visits (79% vs 73%) • 63% used traditional treatments during their pregnancy (herbal medicines to treat bleeding, ease abdominal pain, or for rupture of the amniotic sac) • Cases were statistically more likely to have cesarean section, longer hospital stay, stillbirth or neonatal death. • Use of herbal treatment was not found to increase the risk of developing severe PE/E.
Idogun, E. S., Imarengiaye, C. O., & Momoh, S. M. (2007). Extracellular calcium and magnesium in preeclampsia and eclampsia. *African Journal of Reproductive Health*, *11*(2), 89–94.	Cross sectional	University of Benin Teaching Hospital, Nigeria 11 patients 23 controls,	N/A	Patients were randomly selected from among hospital attendees, "patients" were women presenting with PE (or PE/E) in their third trimester who were going for caesarean section; those on $MgSO_4$ and calcium lactate drugs were excluded. Controls were normotensive pregnant women, also going for CS. Blood was taken from participants, and plasma was harvested and analyzed for calcium, magnesium and electrolyte and urea estimations; cerebrospinal fluid (CSF) was taken during lumbar puncture for spinal anaesthesia and calcium and magnesium estimations were made.	• Plasma calcium was significantly higher in controls vs. patients but there was no significant difference between groups for plasma magnesium levels. • Calcium CSF and magnesium CSF were significantly lower in patients than in controls • Lower levels of magnesium and calcium may have an effect on PE/E
Ikechukwu, I. C., Ojareva, O. I. A., Ibhagbemien, A. J., Okhoaretor, O. F., Oluwatomi, O. B., Akhalufo, O. S., … Chigaekwu, M. N. (2012). Blood lead, calcium, and phosphorus in women with preeclampsia in Edo State, Nigeria. *Archives of Environmental & Occupational Health*, *67*(3), 163–169.	Cohort	Irrua Specialist Teaching Hospital Irrua, Edo State, Nigeria November 2006—September 2008		Women aged 20-35 attending ANC clinic at the hospital. Women with history of any chronic disease and glycosuria were excluded. Medical histories were taken and recorded in duplicate by doctors who were unaware of the goal of the study.	• PE was defined as SBP > 140 mmHG and/or DBP > 90 mmHg and proteinuria during at least two visits after 22nd week of gestation. • 150 normal pregnant women and 59 with preeclampsia • Blood lead levels were significantly higher in women with PE than normal pregnant women and serum calcium and inorganic phosphorus were significantly lower than in normal pregnant women. • A possible explanation for the increase in blood lead in PE women vs normal

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		283 pregnant women, 74 excluded for noncompliance 209 nonpregnant controls		BP was measured, protein and sugar levels tested in urine. Blood samples were taken from each participant at delivery and analyzed for calcium and phosphorus determination and blood lead determination.	pregnant women is a possible increase in maternal bone lead mobilization. • Elevated blood lead levels may contribute to the development of PE
Ikpen, M. A., Eigbefoh, J., Eifediyi, R. A., Isabu, P. A., Okogbenin, S., Okogbo, F. O., … Ekwedigwe, K. C. (2012). Determination of antioxidant status of pre-eclamptic and normotensive sub-rural Nigerian pregnant women at the Irrua Specialist Teaching Hospital, Irrua, Edo State. *The Journal of Maternal-Fetal & Neonatal Medicine*, *25*(10), 2046–2050.	prospective case—control study	Antenatal clinics, antenatal and labour wards, Accident and Emergency unit of Irrua Specialist Teaching Hosptal, Irrua, Edo State.		Eighty cases and 80 matched controls were recruited into the study. Cases: booked pregnant women with PE Controls: gestational age and parity matched normotensive pregnant women Blood samples were taken from all participants and analyzed for vitamins C and E.	• Two consecutive BP measurements of >140.90 mmHg 4 hours apart after 20th week and significant proteinuria (>2+) or 1+ if the specific gravity was < 1.030 and pH was <8. • Plasma vitamin C and E levels were significantly lower in cases than in controls. • Role of antioxidants in pathogenesis of PE is inconclusive, but may be an opportunity to prevent PE
Isezuo, S. A., & Ekele, B. A. (2004). Eclampsia and abnormal QTc. *West African Journal of Medicine*, *23*(2), 123–127.	Prospective case control	Usman Danfodiyo University Teaching Hospital, Sokoto, Nigeria August 2001 and July 2002 30 patients		30 consecutive patients with intrapartum eclampsia were included in the study. General information was obtained as well as medical history. BP was measured three times at rest and the average of the last two were taken as the BP. Electrocardiogram (ECG) was recorded during the intrapartum period to measure QT interval	• Eclampsia is characterized by generalized convulsion, elevated BP and proteinuria with or without oedema occurring after 20 weeks gestation. • QT interval is the "total time from the onset of ventricular depolarization to the completion of repolarization" • Cases had higher mean heart rate, higher frequency of sinus tachycardia and significantly higher QTc. • This study found that eclampsia is associated with hypocalcaemia, abnormal QTc and T-axis deviation; serum magnesium did not differ significantly between study groups
Leone, S., Res, J. B., No, V., O, O. V., S, A. A., Adewumi, A., & Olalekan, A. (2009). Homocysteine Levels in Nigerian Women with Pre-eclampsia / Eclampsia. *Sierra Leone Journal of Biomedical Research*, *1*(1), 55–60.	Case control	Lagos University Teaching Hospital, Idi-Araba January—October 2006		"all participants were to strictly maintain the drug regimen prescribed for routine antenatal use only" Venous blood was collected and plasma levels of homocysteine were determined	• Rising homocysteine level in eclamptics was significantly associated with blood pressure levels. • Plasma homocysteine levels in the 3rd trimester of pregnancy is significantly higher among eclamptic women than those who have a normal pregnancy.

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		100 primigravidae women (60 lost to follow up, or incomplete data) 25 eclamptic women 25 non pregnant women		at registration, at 26 weeks and at 34 weeks gestation for all participants.	• Mean corpuscular volume, plasma homocysteine level and rising blood pressure during pregnancy may help predict development of PE/E.
Nwobodo, E. I., Panti, A., & A, N. E. P. (2012). Adolescent maternal mortality in North-west Nigeria. *West African Journal of Medicine*, *31*(4), 224–226.	Review of hospital case records	Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto January 2000—December 2009 2,047 live births among adolescents		Case reports of live births for women 15-19 years old were collected and reviewed. Demographic and other health data were extracted and analyzed.	• 165 maternal deaths among adolescent mothers: MMR = 5415 per 100,000 live births • Main cause of death was eclampsia: 53.9% • ANC allows for early detection of PIH which can prevent the progression to eclampsia
Okafor, U. V, & Ezegwui, H. U. (2010). Cesarean delivery in preeclampsia and seasonal variation in a tropical rainforest belt. *Journal of Postgraduate Medicine*, *56*(1), 21–23.	Retrospective record review	University of Nigeria Teaching Hospital, Enugu July 1996—June 2006 6798 deliveries, 1579 CS deliveries 196 had toxemia of pregnancy (166: PE and 30: eclampsia)		Records for patients presenting for CS with PE/E during rainy and dry seasons were reviewed, and demographics and obstetric history and outcome were extracted and analyzed.	• The primary objective of this study was to assess whether or not seasonality in a tropical rainforest belt had an effect on the presentation of preeclamptics undergoing cesarean section. • Among preeclampsia, 115 had CS during rainy season, 52 during dry season. • Among those with eclampsia, 26 presented during rainy season and 4 during dry season • This study found a "systemic seasonal variability in the need for cesarean delivery for preeclamptics with a peak during the rainy season"
Olayemi, O., Strobino, D., Adedapo, K., Aimakhu, C., Odukogbe, A.-T., & Salako, B. (2010). Influence of previous abortions and new paternity on the risk of hypertension in nulliparous parturients in Ibadan:	Prospective cohort	University College Hospital (UCH) and Adeoyo Maternity Hospital (AMH), Ibadan	Hypertension in pregnancy incidence: 33%	Nulliparous women were recruited before 20 weeks gestation. For the baseline data, participants were interviewed about: sociobiological variables, history of previous abortions, sexual history, and family history of	• At AMH, 76.5% of the participants reported a prior abortion, but only 20.4% reported same paternity abortion • At UCH, 64.9% reported prior abortion, and 31.5% reported same paternity abortion

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
a cohort study. *The Journal of Obstetrics and Gynaecology Research*, *36*(5), 965–969.		2000 patients (1000 at each site)		hypertension and BP and urine protein were also measured. Within 48 hours of delivering the final interview was conducted, BP measured and urine tested.	• "There was no statistical difference in the incidence of hypertension among participants with previous abortion (32.98 vs 33.10 P=0.962)" • Nor was there a statistical difference in the development of hypertension regarding change in paternity; 30.12% of women reporting same paternity abortions and 34.10% without same paternity abortions developed hypertension (p=0.164) • The authors suggest researching presentation of human leukocyte antigen (HLA) from semen prior to conception to reduce incidence of eclampsia.
Olayemi, O., Strobino, D., Aimakhu, C., Adedapo, K., Kehinde, A., Odukogbe, A.-T., & Salako, B. (2010). Influence of duration of sexual cohabitation on the risk of hypertension in nulliparous parturients in Ibadan: A cohort study. *The Australian & New Zealand Journal of Obstetrics & Gynaecology*, *50*(1), 40–44.	Prospective cohort	University College Hospital (UCH) and Adeoyo Maternity Hospital (AMH), and Oluyoro Catholic Hospital (OCHH), Ibadan AMH: 900 women UCH: 950 women OCH: 780	Gestational hypertension incidence: 28.93% PE incidence 4.13%	Nulliparous women were recruited before 20 weeks gestation. For the baseline data, participants were interviewed about: sociobiological variables, history of previous abortions, sexual history, and family history of hypertension and BP and urine protein were also measured. Within 48 hours of delivering the final interview was conducted, BP measured and urine tested.	• 29.64% reported having had previous abortion, and 25.92% were same paternity abortions • This study found that incidence of hypertension was higher among those who had had abortions (29.40%) than those who had not (28.52%) • Change in paternity did not have a significant impact on incidence of hypertension • Multivariate analysis found that length of sexual cohabitation was protective against hypertension (4% decline in risk of developing hypertension for every month increase in cohabitation). • This multivariate model controlling for age, BMI, educational attainment and family history of hypertension found that same paternity abortions were protective (HR 0.46, CI 0.22—0.96) but previous abortion alone was not. • The early timing of previous abortions (first trimester) would account for no observe protective feature of abortions in this study (when other studies have shown abortions to be protective
Olusanya, B. O. (2011). Perinatal outcomes of multiple births in southwest Nigeria. *Journal of Health,*	Retrospective cross-sectional review of	Island Maternity Hospital, Lagos		Participants were included in this study from a prospectively recruited cohort of	• This study's primary objective was determine perinatal outcomes that may influence neurodevelopment adversely among multiple gestations; the relevance

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Population, and Nutrition, *29*(6), 639–647.	hospital records	May 2005—December 2007		newborns under a separate program on universal newborn hearing screening. This study defined "hypertensive disorders" as pre-eclampsia, eclampsia and pregnancy-induced hypertension	for our study is that Olusanya's study indicated that multiple gestation is associated with an increased risk of hypertensive disorders. • This study found that mothers with multiple gestations (twins or triplets in this case, no higher-order births occurred during the study period) were significantly more likely to have had hypertensive disorders. • 268/4,416 (6%) of singleton births were associated with hypertensive disorders compared to: 26/157 (16.5%) multiple gestations
Onah, H. (2002). Prognostic value of absolute versus relative rise of blood pressure in pregnancy. *African Journal of Reproductive Health*, *6*(1), 32–40.	cohort	Department of Obstetrics and Gynaecology, University of Nigeria Teaching Hospital, Enugu December 17, 1997—March 31, 1999 515 women (7% incomplete: 478 participants)		Longitudinal measurement of BP, anthropometric data and MMR in study population (heathy ANC subjects). Participants were recruited prior to 16 weeks gestation. Fundal height, weight, height, BP, and presence or absence of proteinuria were recorded Participants were categorized into groups: A: relative diastolic blood pressure (DBP) rise from the averaged 16-20 weeks readings until delivery < 15mmHg and absolute DBP<90mmHg B: relative DBP rise $\geq$ 15mmHg and absolute DBP < 90mmHg C: absolute DBP$\geq$ 90mmHg no matter the relative rise in BP Analysis was also done with groups based on systolic BP (using 140mmHg as the threshold rate and 30mmHg as the relative rise amount)	• 478 of the 515 women completed the study. • Diagnosing hypertension from a relative rise in DBP of 15mmHg included 48% of subjects who had normal pregnancies. These relative rises in BP could indicate that closer surveillance is required. • This study found that maternal and fetal outcomes were not significantly affected by the relative rise in DBP (as long as DBP <90mmHg) • Strict eligibility criteria meant many were excluded (women booked after 16 weeks, delivered preterm, etc) • The data in this study suggest that absolute blood pressure (140/90 mmHg) is a better predictor of feto-maternal outcome than relative rise measurements in systolic or diastolic pressures. •

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Osungbade, K., Oginni, S., Olumide, A., K, O., Oginni, S., & Olumide, A. (2008). Content of antenatal care services in secondary health care facilities in Nigeria: implication for quality of maternal health care. *INTERNATIONAL JOURNAL FOR QUALITY IN HEALTH CARE*, *20*(5), 346–351.	Cross-sectional	Osun state N/A 390 ANC clients		Antenatal care exit interview forms from the Safe Motherhood Needs Assessment package was used to collect information from 390 pregnant women leaving ANC visits.	• All of the women in this study had their blood pressure checked which is an important screening tool for detecting hypertension and toxaemia (now called PE) • At the hospitals, 48.6% of the 284 women and 28.3% of 106 at Health Centers had their urine checked for protein levels • This study concluded that the screening services and care were reasonably capable of addressing pre-eclampsia and early detection of some fetal problems but they were insufficient for detecting long-standing pre-eclampsia and other conditions (detecting and treating severe anemia and preventing complications of malaria in pregnancy).
Owolabi, A., AO, F., Kuti, O., Adeyemi, A., Faturoti, S., & Obiajuwa, P. (2008). Maternal complications and perinatal outcomes in booked and unbooked Nigerian mothers. *Singapore Medical Journal*, *49*(7), 526–531.	Prospective case control	Wesley Guild Hospital Unit, Ilesa, Nigeria (Obafemi Awolowo University Teaching Hospitals Complex) August 2004—May 2006 1,154 deliveries		Outcomes of pregnancies booked for ANC were compared to outcomes of women who were unbooked	• 29% (n=336) were unbooked • Unbooked mothers were more likely to be younger, unmarried, have lower education and social status, higher proportion of multipara, experience antepartum haemorrhage, anemia and PE/E • 7.9% of unbooked women developed PE/E compared to 2.1% of booked mothers (OR 1.71, 1.15—2.55)
Salako, B. L., Olayemi, O., Odukogbe, A.-T. A., Adedapo, K. S., Aimakhu, C. O., Alu, F. E., & Ola, B. (2003). Microalbuminuria in pregnancy as a predictor of preeclampsia and eclampsia. *West African Journal of Medicine*, *22*(4), 295–300.	Cohort	University College Hospital (UCH) Ibadan 93 healthy normotensive pregnant women (		During initial booking, BP and urinalysis was conducted and 100 women who were normotensive were recruited and had urinalysis completed. PE: BP of 140/90 mmHg or more or a rise of 30mmHg in systolic BP or 15mmHg in diastolic BP (measured two times, six hours apart, at rest) associated with proteinuria.	• Ninety-three delivered at UCH, two had spontaneous abortion and five delivered elsewhere. • At booking 61.3% (57 patients) had normal albumin excretion and 22 (23.7%) had microalbuminuria and 12 (15%) had gross microalbuminuria. • This study found that there was a statistically significant difference in incidence of PE with an increase in albumin excretion. • Microabuminuria was found to predict preeclampsia with high sensitivity but with low positive predictive value (overestimated the number of cases)

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence / Incidence/ CFR	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Salako, B., Odukogbe, A., Olayemi, O., Adedapo, K., & Aimakhu, C. (2003). Serum albumin, creatinine, uric acid and hypertensive disorders of pregnancy. *East African Medical Journal*, *80*(8), 424–428.	Cohort	University College Hospital (UCH) Ibadan 23 healthy normotensive primigravidae singleton pregnant women		59 women were recruited into the study when they booked for ANC prior to 20 weeks gestation at the facility and were included in analysis if they delivered at the facility as well. These women were followed throughout their pregnancies. All participants gave complete clinical history, had BP measured and urinalysis done. Analysis of serum samples was performed as well (at a lab)	• Of the 59 women recruited, two had abortions, 13 did not attend the minimum required number of prenatal clinic visits and 21 did not deliver at UCH. • 23 completed the study; five (21.7%) had PE, two (8.7%) had pregnancy-induced hypertension and 16 (69.6%) remained normotensive. • Oedema and proteinuria were mild in all cases of PE, one of the cases of PE died. • This study found that there was no significant difference in uric acid and creatinine levels between the groups, but mean serum albumin concentration was significantly higher in the PE group. • Based on the findings of this study: serum uric acid and creatinine concentrations early in pregnancy are not useful to predict subsequent development of PE/E • Mean serum albumin levels early in pregnancy could be useful in predicting subsequent PE—further research is needed. To define the value of estimation.
Vanderjagt DJ, Patel RJ, El-Nafaty AU, Melah GS, Crossey MJ, Glew RH. High-density lipoprotein and homocysteine levels correlate inversely in preeclamptic women in northern Nigeria. Acta Obstet Gynecol Scand. Denmark; 2004 Jun;83(6):536–42.	Case control	Federal Medical Center or the Specialist Hospital, Gombe June—August 2001 43 cases with PE/E 130 controls	N/A	Participants were recruited while attending the facilities. The cases were diagnosed with PE/E if they had systolic BP greater than 140 mmHg, diastolic BP greater than 90mmHg, proteinuria in excess 190 mg total protein/g creatinine, and edema. Blood samples were taken from all participants and serum cholesterol concentration, serum HDL-cholesterol concentration, and serum triacylglycerol concentration were measured.	• Mean serum total homocysteine concentration was greater among the women with PE/E than compared to the controls. • HDL-cholesterol concentration was found to be higher among the healthy women vs. those with PE/E • There was not a difference between the two groups for LDL-cholesterol and triacylglycerols. • Conclusion: this study found a significant negative correlation between the level homocysteine and the concentration of HDL-cholesterol in women with PE/E in northern Nigeria

Appendix V:

SUMMARY TABLES OF OTHER HEALTH OUTCOMES ASSOCIATED WITH PE/E

Citation	Study Design	Location, Timeframe, and Sample size	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
ADEBAMI, O. J., OYEDEJI, G. A., OWA, J. A., & OYELAMI, O. A. (2007). Maternal factors in the etiology of fetal malnutrition in Nigeria. *Pediatrics International*, *49*(2), 150–155.	Prospective	Neonatal and Maternity Units of the Wesley Guild Hospital Ilesa, Nigeria, a unit of Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife January – August 2001 473 consecutive, singleton, live birth, term (37-42 weeks gestation) neonates"	Maternal prenatal records were reviewed, additional history collected from mother. Babies were classified into 'babies with FM' and 'babies without FM' and the two groups were compared.	• The study found that 27% of babies with FM were born to mothers with PIH/eclampsia compared to 3.6% of babies without FM from mothers with PIH/eclampsia • "Hypertension and pre-eclampsia induce fibrinoid degeneration of arteriolar media with resultant intimal thickening and decreased luminal diameter. It causes permeability of essential nutrient across the placental barrier to the fetal and has, therefore, been implicated as a causative factor of FM"
Adekanle, D., & Akinbile, T. (2012). Eclampsia and Pregnancy Outcome at Lautech Teaching Hospital, Osogbo, SouthWest, Nigeria. Clinics in Mother and Child Health, 9(1).	Descriptive, cross-sectional retrospective review	Ladoke Akintola University of Technology Teaching Hospital, Osogbo, South West, Nigeria January 1, 2005—December 31, 2010	Review of case notes of women who had eclampsia Eclampsia defined as: "systolic blood pressure of ≥ 140mmHg, diastolic blood pressure of 90 mmHg, proteinuria of at least 1 plus and convulsions in patients with no background history of seizure disorder were retrieved.	• MMR was 1,981 per 100,000 live births • 83 cases of eclampsia of 3952 deliveries, incidence = 2.1%, CFR: 8.3 • Eclampsia accounted for 9.9% of maternal deaths (n=7) • Almost half of referrals (48.2%) were from private health facilitates and 2.4% were from TBAs • 54.2% had antepartum eclampsia, intrapartum and postpartum eclamptic were each 22.9% • 48.2% were booked in private health facilities and 21.7 were booked in primary health facilities and then referred to this tertiary center. • 71.1% of the cases were treated with MgSO4 and experienced CFR of 8.3% • Most common maternal morbidity recorded was acute renal failure • 54.2% of patients had caesarean section which was significantly associated with neonatal survival • Documented improvements in maternal and neonatal outcome due to use of MgSO4 rather

Citation	Study Design	Location, Timeframe, and Sample size	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
				than diazepam, unavailability of MgSO4 supplies—often due to cost—is likely a contributor to poor outcome
Adeyemo, W. L., Rabiu, K. A., Okoturo, T. M., Adebanjo, A. A., Adewunmi, A. A., & Adeyemi, M. O. (2012). Orofacial injuries associated with eclampsia in patients presenting at a Nigerian Tertiary Hospital. *Journal of Obstetrics and Gynaecology*, *January 20*(32), 54–57.	Prospective case review	Lagos State University Teaching Hospital December 2008—November 2009 107 patients presented with eclampsia	For women arriving at the facility with eclampsia, a proforma was designed to collect: age, parity, history of ANC, # of eclamptic fits, presence/absence of orofacial injuries and morbidity/mortality associated with eclampsia. In cases of orofacial injury, further details were collected as to the nature and cause of the injury	• 45 patients (42%) with eclampsia presented with orofacial injuries. Injuries were most often on the tongue and/or lips • Injury in most cases (n=16) was caused by relatives forcing hard objects into patient's mouth or biting down during convulsions. • Six patients were injured due to a fall. • 98% were not booked for ANC at this facility and were only referred after developing eclampsia • Patients who received ANC from TBAs and at churches were significantly more likely to have orofacial injuries
Alhassan, M., Anyiam, C., Bosan, I., Danbauchi, S., David, S., & Isa, M. (2008). Role of pre-eclamptic toxaemia or eclampsia in hypertensive women attending cardiac clinic of Ahmadu Bello University Teaching Hospital Zaria, Nigeria. *Annals of African Medicine*, *7*(3), 133–137.	Cross-sectional	Cardiac Clinic of Ahmadu Bello University Teaching Hospital, Zaria, Nigeria 50 consecutive adult female hypertensive patients	all patients provided demographic and clinical characterization from history and physical examination 49 of the 50 patients recruited were studied.	• Those who had PE in a previous pregnancy developed hypertension an average of 8.42 + 7.69 years after the pregnancy and for those without PE, 12.76 + 8.90 years. (no statistically significant difference) • Of the 49 participants, 32.7% had previous PE • Of those who had previous PE, 43.8% had complications of hypertension including: hypertensive heart disease, hypertensive heart failure, cerebrovascular accident, and peripartum cardiac failure.
Faponle, A., & Makinde, O. (2007). Caesarean section: Intra-operative blood loss and its restitution. *East African Medical Journal*, *84*(1), 31–34.	Prospective study	Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria January 1, 2005—December 2005 641 patients who underwent caesarean section	The following was collected for all caesarean sections at the facility during the study period: Demographics, American Society of Anaesthesiologists grading, coexisting conditions, presence of clinical anaemia, indication for Caesarean section, pre-operative packed cell volume, surgical details.	• PE/E were cited as indication for 9.4% (n=60) of the caesarean sections • Pre-eclampsia "carried the expected increased transfusion and major blood loss risk"
Geidam, A. D., Audu, B. M., Kawuwa, B. M., & Obed, J. Y. (2009). Rising trend and indications of caesarean section at the university of	Retrospective review	University of Maiduguri Teaching Hospital	Retrospective analysis of caesarean sections performed.	• 1,192 caesarean sections were performed during the study period, 79.4% of which were emergency C/S

Citation	Study Design	Location, Timeframe, and Sample size	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Maiduguri teaching hospital, Nigeria. *Annals of African Medicine*, *8*(2), 127–132. http://doi.org/10.4103/1596-3519.56242		January 2000 to December 2005 10,097 deliveries		• Eclampsia caused 7.2% and severe pregnancy-induced hypertension caused 4.8%
Igwegbe, A., & Udigwe, G. (2001). Teenage pregnancy: still an obstetric risk. *Journal of Obstetrics and Gynaecology*, *21*(5), 478–481.	Retrospective and comparative study	Nnamdi Azikiwe University Teaching Hospital, Nnewi. June 1 1995—November 31, 1997 1465 deliveries	Reviewed hospital records of 28 teenage deliveries and 30 records of mothers aged 20-24 were randomly selected to be used as controls	• 32 teenage deliveries, 21.8 per 1000 deliveries • This study found no significant difference between the teenagers and the control group with regard to PE/E
Makinde, O. N., Adegoke, O. A., Adediran, I. A., Ndububa, D. A., Adeyemi, A. B., Owolabi, A. T., … Salawu, L. (2009). HELLP syndrome: the experience at Ile-Ife, Nigeria. *Journal of Obstetrics and Gynaecology : The Journal of the Institute of Obstetrics and Gynaecology*, *29*(3), 195–199. http://doi.org/10.1080/01443610902753945	(cohort)	Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria January 1—December 31, 2006 34 consecutive cases of severe PE/E	Cases of severe PE/E were recruited and bloodwork and other biochecmical studies done (platelet count, peripheral blood smear, serum bilirubin lactate dehydrogenase, and aspartate transaminases estimation) HELLP syndrome was diagnosed in those who developed: haemolysis, abnormal liver function and thrombocytopenia (platelet count $\leq$90,000mm^3) were	• Each patient was categorized into three categories: 1) 12 cases Severe PE: hypertension after 20th week, dBP$\geq$110mmHg on admission, proteinuria $\geq$30mg/dl in random urine specimen or $\geq$ 300mg in 24hr 2) 10 cases Imminent eclampsia: all parameters in (1) plus headache, blurring of vision and upper abdominal pain 3) 12 cases Eclampsia: all parameters in (1) and seizures. • Six (17.6%) of the cases developed HELLP syndrome. 4 had eclampsia, 1 had imminent eclampsia and 1 had pre-eclampsia • CFR: 11.8% The only fatalities were the four eclamptic patients who also had HELLP syndrome. • There were 38 infants delivered, and six (15.8%) perinatal deaths.
Ndukwe, K., Ugboko, V., Ogunlola, I., Orji, E., & Makinde, O. (2004). Orofacial injuries in eclamptic Nigerians. *African Journal of Reproductive Health*, *8*(3), 147–151.	Retrospective case review	Department of Obstetrics and Gynaecology Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria January 1994 to July 2002 173 patient records	Cases from patients with eclampsia during the study period were identified, and data extracted and analyzed.	• 21 of the 173 cases (12.1%) sustained orofacial injuries (mostly lacerations and bruises to soft tissues including the tongue). Dislocation of the lower jaw (temporomandibular joint dislocation) occurred in one case. Two patients died due to complications related to uncontrolled bleeding, acute renal failure and septicemia. • "antibiotics were prescribed in all the cases as part of the treatment regimen for eclampsia" • Recommend a campaign to ensure ANC attendance and against the forceful insertion of unpadded objects into the mouth during seizure.

Citation	Study Design	Location, Timeframe, and Sample size	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Okafor, U., & Efetie, E. (2006). Cerebrovascular accident with quadriplegia following postpartum eclampsia. ACTA ANAESTHESIOLOGICA SCANDINAVICA	Case report	National Hospital, Abuja One, 26 –year-old woman	The patient diagnosed with postpartum eclampsia was referred from a peripheral hospital, she delivered a live baby vaginally and experienced a tonic/clonic seizure just after delivering and became unconscious. After seizing, her Glasgow Coma score was determined to be 3, meaning she was deeply unconscious. She had a fever (38˚C), mild pedal oedema, puffy eyes and 'grunting respiration," a BP of 130/80 mmHg on presentation.	• There had been no history of elevated BP during ANC. • Her case was managed with magnesium sulphate, IV 5% dextrose/salinje, 50% dextrose and Zinacef (antibiotic). • She remained in the ICU for 42 days and was discharged from the Hospital after 169 days. BP had normalized, but she was still quadriplegic. • This is the only known case of quadriplegia resulting from postpartum eclampsia in sub-Saharan Africa. • This study reinforced the thought that neurological effects of PE/E are more common when eclampsia presents postpartum; this patient had cerebral oedema
Okafor, U., & Efetie, E. (2009). Anaesthetic management of patients with pre-eclampsia/eclampsia and perinatal outcome. Journal of Maternal- Fetal and Neonatal Medicine, 22(8), 688–692.	Retrospective record review	University of Nigeria Teaching Hospital (UNTH), Enugu. July 1998—June 2008 6798 total deliveries, 285 cases PE/E, 196 cases of PE/E delivered by CS	Hospital records for patients with PE/E who had caesarean delivery were reviewed and demographics, obstetric outcomes, and type of anaesthesia administered was recorded and analyzed.	• 12.4% (n=196) of all CS were for patients with PE/E. (59: mild PE, 107: severe PE, 30: eclampsia) • This group experienced 38 perinatal deaths, 180 per 1000 births (19 stillbirths and 19 early neonatal deaths). • 157 were delivered under general anaesthesia; 34 under spinal anaesthesia and 5 under epidural block. • 79% of the perinatal deaths were delivered by general anaesthesia. • Indications for CS among PE/E patients included: severe PE/E with unfavorable cervix, fetal distress/intrauterine growth retardation, previous CS, failed induction/failed vacuum extraction, prolonged labor and others • 25.6% of perinatal deaths occurred in cases of severe PE, 21.2% occurred in cases of eclampsia and only 4.9% occurred in cases of PE. • 89% of neonatal deaths occurred <36 weeks; 52% were <32 weeks • The increase to 20% use of regional anaesthesia (vs 1.3% in an earlier study) did not seem to have an impact on perinatal death.

Citation	Study Design	Location, Timeframe, and Sample size	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Okafor, U., & Okezie, O. (2005). Maternal and fetal outcome of anaesthesia of caesarean delivery in preeclampsia / eclampsia in Enugu, Nigeria: a retrospective observational study. *International Journal of Obstetric Anesthesia*, *14*(2), 108–113.	Retrospective survey of hospital records	University of Nigeria Teaching Hospital (UNTH), Enugu. July 1998—June 2002 3926 total deliveries, 898 CS deliveries 125 cases of PE/E delivered by CS	176 of 3926 (4.5%) deliveries were complicated by PE/E CFR: 5.2%	• This facility was using methyldopa to control hypertension in these patients and nifedipine and beta-blockers added at the physicians' advice. Hydralazine was also used to manage hypertensive crises. • Due to cost and unavailability of MgSO4, diazepam is often used prophylactically and also to treat eclamptic fits • 82.4% (n=103) of the cases of PE/E delivered by CS were emergency procedures. • Six maternal deaths all of whom received general anaesthesia. • General anaesthesia was used for 116 (92.8%) of the patients, spinal anaesthesia was used in the other nine cases. • 13 stillbirths and 10 neonatal deaths • Recommend using spinal anaesthesia for better health outcomes and also reduced cost.
Oladapo, OT, JO Sotunsa, and AO Sule-Odu. "The Rise in Caesarean Birth Rate in Sagamu, Nigeria: Reflection of Changes in Obstetric Practice." *Journal of Obstetrics and Gynaecology* 24.4 (2004): 377–381.	Retrospective comparative study	Olabisi Onabanjo University Teaching Hospital, Sagamu Two periods: January 1, 1989—December 31, 1991 July 1, 2000—June 30, 2003	Data were collected from theatre records, labor ward records, and case files on deliveries during the two study periods.	• This study found that hypertensive disorders in pregnancy (severe PE/E) was cited as the indication for CS in 20 (8.9%) of caesareans during from 1989—1991 • This increased to 13.4% (n=44) of CS due to severe PE/E in 2000-2003. • This finding is in line with other papers that report better maternal and fetal outcomes when a woman with severe PE/E is delivered via caesarean.
OLADAPO, O. T., ADEKANLE, D. A., & DUROJAIYE, B. O. (2007). Maternal risk factors associated with fetal death during antenatal care in low-resource tertiary hospitals. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, *47*(5), 383–388.	Case control study	Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State (OOUTH) and Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Osun state (LAUTECHTH) January 1, 2002 and December 31, 2006 at OOUTH	Cases: booked singleton pregnancies who experienced fetal death during ANC Controls: booked pregnancies who had live births Four controls selected for each case (two immediately before and two after each case). Cases and controls were compared.	• After multivariate logistic regression analyses, the following were found as predictors for fetal death among women receiving ANC: pregnancy induced hypertension (adjusted OR: 8.24, CI 3.01—22.51), proteinuria (adj. OR 4.23, CI: 1.57—11.42) and perceived reduction of fetal movements (adj OR 7.17, CI: 1.57—45.76). • % of cases and controls with: • proteinuria: Cases: 41.9%, controls, 11.0% • PIH: cases: 43.5%, controls: 7.6% • previous hypertension: cases: 10.9%, controls: 2.2% • PE: cases 24.4%, controls: 0.0%

Citation	Study Design	Location, Timeframe, and Sample size	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
		January 1, 2003—December 31, 2006 LAUTECHTH Cases: 46 Controls: 184		
Olagbuji, B., Ezeanochie, M., Ande, A., & Okonkwo, C. (2012). Prevalence and risk factors for persistent hypertension after the puerperium in pregnancies complicated with hypertensive disorders. *Journal of Obstetrics and Gynaecology : The Journal of the Institute of Obstetrics and Gynaecology*, *32*(6), 529–532.	Prospective cohort study	University of Benin Teaching Hospital (UBTH), Benin City, Nigeria December 2009—November 2010. 198 women	Women who were managed for new-onset gestational hypertensive disorders who had received ANC, intrapartum and postpartum care at the facility were recruited during the prenatal period. "new-onset gestational hypertensive disorders" = gestational hypertension, or PE/E after 20 weeks gestation in previously normotensive, non-proteinuric women with no history of chronic hypertension.	• "Persistent hypertension" was diagnosed if hypertension remained during the postpartum visit, six weeks after delivery. • 51 (25.8%) were discovered to have persistent hypertension at the 6th week postnatal follow up visit. • Persistent hypertension was significantly higher among women with maternal age > 35 years old and also among HIV-positive women. • Serum uric acid and creatinine levels were also significantly higher among the women who developed persistent hypertension
Olusanya, B. O., & Solanke, O. A. (2012). Perinatal outcomes associated with maternal hypertensive disorders of pregnancy in a developing country. *Hypertension in Pregnancy*, *31*(1), 120–130.	Retrospective study	Island Maternity Hospital (IMH), Lagos May 15, 2005—2007 216 mothers with HDP	Mothers with HDP were recruited and their cases reviewed for: fetal distress, prematurity (<37 weeks gestation), low birth weight (<2500g), fetal growth restriction, birth asphyxia, admission to special baby care unit, and lack of exclusive breastfeeding as well as maternal factors. Hypertensive disorders of pregnancy (HDP): chronic hypertension, pregnancy-induced hypertension, pre-eclampsia and eclampsia	• 216 HDP/ 3491 mother-infant pairs = 6.2% incidence of HDP • 10 (4.6%) were chronic hypertension, 120 (55.6%): pregnancy-induced hypertension, 86 (39.8%): PE/E • After adjusting for maternal factors and some relevant infant confounders, this study saw that HDP increased the odds of preterm birth (OR 3.30), fetal growth restriction (OR 2.94), low birth weight (OR 4.68) and birth asphyxia (OR 2.99). • Recommends greater collaboration between obstetricians and pediatricians to address HDP and its effects beyond maternal and perinatal mortality.

Citation	Study Design	Location, Timeframe, and Sample size	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Olusanya, B. O., & Solanke, O. A. (2012). Maternal and neonatal profile of late-preterm survivors in a poorly resourced country. *The Journal of Maternal-Fetal & Neonatal Medicine*, *25*(4), 346–352.	Cross-sectional study	Island Maternity Hospital, Lagos May 2005—December 2007 4176 Surviving late preterm and full-term live births	Infants were recruited under 24 hours after birth, before being discharged from the hospital. Late preterm was defined as: $34^{0/7}$ to $36^{6/7}$ weeks gestation. Gestational age was based on number of days between LMP (last menstrual period) and delivery	• 89 (38.4% of women with hypertensive disorders: PE/E and PIH) had PE/E and 41 (46.1%) of them were late-preterm • Univariate analysis showed that having a hypertensive disorder was significantly associated with late-preterm delivery • Multivariate analysis revealed that late-preterm delivery was independently associated with hypertensive disorders (OR 3.66, CI 1.97—6.84).
Onuh, S., & Aisien, A. (2004). Maternal and fetal outcome in eclamptic patients in Benin City, Nigeria. *Journal of Obstetrics and Gynaecology*, *24*(7), 765–768.		University of Benin Teaching Hospital 1995—2002 103 cases of eclampsia	Patient data for cases of eclampsia was retrieved from case notes and summary sheets and analyzed.	• Incidence of eclampsia: 1.32%; The incidence of eclampsia among nullipara was 2.4% which is significantly higher than the incidence among multipara (0.9%). CFR: 11.7% • Only 13, (12.6%) of the patients came for ANC at UBTH while 90 (87.4%) either were referred from other facilities or did not attend ANC (“unbooked”) • 58.4% (n=59) of the patients were delivered by caesarean section. • Complications included: cerebrovascular accident (n=6), transient blindness (n=6), abruptio placentae (n=6), HELLP syndrome (n=4), Acute renal failure (n=3), disseminated intravascular coagulation (n=2), aspiration pneumonia (n=1); 26.2% of cases experienced a complication • Fetal outcome: there were 117 births (14 sets of twins, and 1 set of triplets); 25 perinatal deaths (9 stillbirths, and 16 early neonatal deaths) prematurity was the cause of death for 17 (68%) and birth asphyxia 6 (24%) and sepsis 2 (8%). •
Onyearugha, C. N., & Ugboma, H. A. A. (2012). Fetal outcome of antepartum and intrapartum eclampsia in Aba, southeastern Nigeria. *Tropical Doctor*, *42*(3), 129–132.	Retrospective review of hospital registers	Department of Obstetrics and Gynaecology, Abia State University Teaching Hospital, Abia January 1, 2002—December 31, 2007 48 babies delivered to eclamptic mothers	Relevant information (gestational age, birthweight five-minute Apgar score and mother’s age, booking status parity, number of fits and mode of delivery) was obtained from delivery registers for 48 babies delivered to eclamptic mothers; data analyzed.	• Hospital incidence of eclampsia- 0.80%; CFR: 20.8% • Women only come to this facility for treatment as a last resort; tradition treatment for fitting is “crude oil pushed into their mouths and eyes” • 13 babies were <1500g, 15 were 1500g-2499g, 19 were 2500g—4000g, and 1 was >4000g • Five-minute Apgar sore: 29 (60%)= 0 [stillborn], 4 (8.3%)= 1-3 [severely asphyxiated], 9 (18.8%)= 4-6, 6 (12.5%) >7 • Poor Apgar scores could be partly explained by asphyxiogenic effect in utero during maternal convulsions.

Citation	Study Design	Location, Timeframe, and Sample size	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
Onyiriuka, A. N., & Okolo, A. A. (2007). Neonatal morbidity pattern in infants born in Benin City to Nigerian mothers with hypertensive disorders in pregnancy. *Nigerian Journal of Clinical Practice*, *10*(4), 294–299.	Case control study	University of Benin Teaching Hospital (UBTH) January 1, 1992—June 30, 1994 Cases: 256 live newborns of hypertensive mothers Controls: 804 infants of normotensive mothers	For each hypertensive mother recruited, three normotensive pregnant mothers were recruited as controls. All participants came for clinical visits every 2 weeks and had BP measured and urine tested HDP= documented history of hypertension (140/90 mmHg) before pregnancy, an increase in either SBP (by 30mmHg) or DBP (by 15mmHg) above the booking BP, an intrapartum blood pressure = 140.90 mmHg obtained on at least two occasions not less than six hours apart during delivery	• Comparing the outcomes of the infants born to hypertensive vs. normotensive women, this study found that 39.5% vs 17.9% were low birth weight, 29.3% vs. 12.% were preterm • Caesarean delivery rate was significantly higher among hypertensive women. • This study concludes that "pregnancies complicated by hypertension are associated with an increase in neonatal morbidity" and that these infants are a high-risk group that need close attention and treatment of these specific outcomes.
Osinubi, A., Ajayi, G., & Adegbola, O. (2009). Effect of normal and pre-eclamptic pregnancies on plasma cholinesterase in Nigerian women. *African Journal of Endocrinology and Metabolism*, *8*(1), 1–3.	Case control study	Antenatal Clinic and Prenatal Diagnostic and Therapy Center, College of Medicine of the University of Lagos/Lagos University Teaching Hospital 30 women: mild PE 27 women: severe PE 30: normal pregnancy 30 healthy non-pregnant women	Patients were recruited and categorized into four groups: healthy non pregnant, healthy pregnant, mild PE and severe PE Mild PE: pregnancy-induced sBP >160mmHg or diastolic BP $\geq$ 110mmHg with proteinuria 2+ Severe PE: any two of the following signs were present: (1) systolic blood pressure >160 mmHg or diastolic blood pressure >110 mmHg; (2) proteinuria (>3+ on dipstick [500 mg/dL]); (3) facial oedema.	• Plasma cholinesterase concentrations: **Healthy, non-pregnant** (controls) 3594 $\pm$ 422 m/L Healthy pregnant: 2135 $\pm$ 330 [postpartum: 3212 $\pm$ 346. **Mild PE:** 1781 $\pm$330 [postpartum: 3157 $\pm$ 75] **Severe PE:** 1630 $\pm$ 326 [postpartum: 2864 $\pm$ 700] • This study found that pregnancy reduced plasma cholinesterase concentrations when compared to healthy non-pregnant women; PE further reduced concentrations when compared to normal pregnant women. • Reduced plasma cholinesterase activity leads to prolonged succinylcholine effect. • It was also noted, that cases of severe PE did not see concentrations of serum cholinesterase return to normal within six weeks after delivery. • Recommendations: cases of severe PE should be monitored beyond six weeks postpartum, consider using peripheral nerve stimulator when

Citation	Study Design	Location, Timeframe, and Sample size	Brief summary of Methods	Main findings/ limitations Conclusions/ Recommendations
			Serum cholinesterase concentrations were measured by collecting blood and separating the plasma for cholinesterase assays between 28—41 weeks for pregnant women and 6 weeks postpartum	succinylcholine is administered in PE/E, further research targeting cholinesterase activity as diagnostic tool and prognostic marker in PE/E pregnancies.
Ozumba, B. C., & Anya, S. E. (2002). Maternal deaths associated with cesarean section in Enugu, Nigeria. *International Journal of Gynaecology and Obstetrics: The Official Organ of the International Federation of Gynaecology and Obstetrics*, *76*(3), 307–309.		University of Nigeria Teaching Hospital, Enugu January 1994—December 1999 1,684 cesarean section deliveries		• Overall CS rate of 25.6% • Hypertensive disorders of pregnancy (HDP) was cited as indication for 27% of CS (behind prolonged/ obstructed labor, 31%). • There were 26 deaths following CS, 23% of which were associated with HDP
Waziri-Erameh, M. J., Omoti, a E., & Edema, O. T. (2003). Bilateral total loss of vision following eclampsia--a case report. *African Journal of Reproductive Health*, *7*(2), 106–108.	Case report	Benin City	31 year old patient, para-5 who suffered bi-lateral total loss of vision for four weeks. She had been successfully treated for eclampsia and lost vision during the convulsion, this progressively became worse and she was referred for ophthalmological consultation	• Eclampsia was treated using Hydrallazine to reduce the blood pressure and diazepam to stop the convulsions. • Upon referral, she had a blood pressure of 130.90, which may indicate that she had underlying hypertension during pregnancy • Steroids were given and within a few weeks, her vision was restored.

Appendix V:

SUMMARY TABLES OF PROGRAM DESCRIPTIONS AND LITERATURE REVIEWS

Citation	Paper Type	Summary
Abalos, E., Cuesta, C., Grosso, A., Chou, D., & Say, L. (2013). Global and regional estimates of preeclampsia and eclampsia: a systematic review. European Journal of Obstetrics & Gynecology and Reproductive Biology, 170(1), 1–7.	Systematic Review	11 datasets found on PE/E in Nigeria (4 on PE, 7 on E). Total population covered by these datasets = 54,144 women. Crude incidence of PE among the four datasets = 4.6% and crude incidence of E among the 7 datasets = 4.0%
Ameh, C., & van den Broek, N. (2015). Making It Happen: Training health-care providers in emergency obstetric and newborn care. *Best Practice & Research Clinical Obstetrics & Gynaecology*, 1–15.	Program description	The Making It Happen multi-country programme (implemented in Nigeria during Phase II) aims to build the capacity of health-care providers to recognize and manage complications during pregnancy, childbirth and the post-partum period through 'skills-and-drills' competency-based training in skilled birth attendance, emergency obstetric care and early newborn care (EmONC). Key interventions under MiH programme are: 1) in-service training of healthcare providers working in maternity areas (including management of severe PE/E) 2) quality improvement using audit methodology 3) improved monitoring and evaluation.
Ekele, B. A. (2009). Use of magnesium sulfate to manage pre-eclampsia and eclampsia in Nigeria: overcoming the odds. *Annals of African Medicine*, *8*(2), 73–75.	Editorial	Even though $MgSO_4$ has been shown to be the safest and most effective method for managing convulsions in pregnant women and to prevent recurrence, many providers and facilities have been unable to adjust to the new standard and still stock and use diazepam to manage eclampsia. Other barriers to using $MgSO_4$ include: fear of toxicity (which is detectable and treatable using calcium gluconate), no local manufacturer making availability more difficult and more expensive, and the dosage itself.
Garba, J., & Umar, S. (2013). etiology of maternal mortality using verbal autopsy at Sokoto, North-Western Nigeria. Etiologie de la mortalité maternelle en utilisant l'autopsie verbale à Sokoto, Nigeria du Nord-Ouest. *African Journal of Primary Health Care and Family Medicine*, *5*(1), 6 p	Descriptive, cross-sectional study	Interviews using a verbal autopsy questionnaire with relatives of a women 15-49 years old who had died of pregnancy-related condition in the preceding two years. Sixty-two maternal deaths were identified and **58** questionnaires for the verbal autopsy were completed. Eclampsia was the cause of death for 18.97% (second most common after Haemorrhage, 48.28%) Among primipara, eclampsia was the cause of death for 29.2%
Hlimi, T. (2015). Association of anemia, pre-eclampsia and eclampsia with seasonality: A realist systematic review. *Health & Place*, *31*(0),	Systematic review	Hlimi conducted a systematic literature review of studies that look at the effect of weather/rainfall/seasonality might have on the development of anemia and PE/E. This review included three studies from Nigeria, one was

Citation	Paper Type	Summary
180–192.		published in 1970, one in 1981 and one in 2009. The study from 2009 (Okafor et al.) is included in this current literature review on PE/E in Nigeria. Overall, Hlimi found that there are often observed seasonal patterns for anemia and PE/E and that PE/E might follow similar seasonal variation to malaria, but more research is needed.
Lalonde, A., & Grellier, R. (2012). FIGO saving mothers and newborns initiative 2006–2011. *International Journal of Gynecology & Obstetrics*.	Summary of FIGO funded projects under Safe Motherhood and Newborn Health (SMNH) Committee	One of the projects described was implemented in Nigeria: Saving mothers and newborns in Edo, Amambra and Kaduna States; this project aimed to improve data collection and use, through improved birth register records, fatal outcome records and clinical audits. The project also trained providers on EmONC and strengthened capacity of national professional societies (midwifery and obstetric) through development of protocols and advocacy activities. Three achievements of the project were: supplying $MgSO_4$ to all state hospitals by the Kaduna state government, reduced cost of $MgSO_4$ by manufacturers and four obstetric protocols were introduced.
McDonald, S., Lutsiv, O., Dzaja, N., & Duley, L. (2012). A systematic review of maternal and infant outcomes following magnesium sulfate for pre-eclampsia/eclampsia in real-world use. *International Journal of Gynecology and Obstetrics*, *118*, 90–96.	Systematic review	A systematic review of studies conducted looking at the effectiveness of magnesium sulfate. The authors searched MEDLINE and EMBASE for studies published from January 7, 1990 to July 20, 2010 and included 'before-and-after' studies, cohort studies, and serial cross-sectional studies which reported outcomes of women receiving $MgSO_4$ compared to a group of women who did not. Studies looking at a sample <10 were excluded. Primary outcomes were: maternal death, infant death, eclampsia or recurrent seizure. Secondary outcomes included: pulmonary edema, pneumonia, cardiac arrest, coagulopathy, renal failure, liver failure, cerebral hemorrhage, respiratory depression or arrest, toxicity (calcium gluconate required to stop toxic effect of $MgSO_4$), length of stay in ICUs. From 754 citations, 156 full text articles were reviewed and 150 were excluded for sample size, study design or failure to report outcomes of interest. The six studies included were all cohort studies, included 536 women with eclampsia treated with $MgSO_4$ and 698 who were treated with another anticonvulsant. The results from the six studies included, seem to indicate that the improvements demonstrated in RCTs are comparable to those observed in real-world use of $MgSO_4$ and result in reduction in recurrent seizures, morbidity and mortality.
Mohammed, S., Ahonsi, B., Oginni, A., Tukur, J., & Adoyi, G. (2015). Obstetric knowledge of nurse-educators in Nigeria: Levels, regional differentials and their implications for maternal health delivery. *Health Education Journal*.	Cross-sectional survey	This paper aimed to assess the knowledge of nurse-midwife educators on the major causes of maternal mortality in Nigeria by administering a survey. The authors found that 57.2% of 292 educators could diagnose pre-eclampsia. 86% knew about $MgSO_4$ but only 16.8% knew about using calcium gluconate as an antidote to $MgSO_4$ toxicity. Nearly two thirds (63.7%) were unable to describe the steps of active management of third stage labor. In addition to these, other knowledge gaps were identified relating to oxytocic use for hospital delivery, when to perform episiotomies, and causes of postpartum haemorrhage. The authors propose scale up of quality obstetric care by updating pre-service curricula in addition to in-service appraisals and continuing education on these issues.
Okafor, U. (2009). Maternal and perinatal outcome after caesarean delivery in preeclampsia or eclampsia in Enugu, Nigeria: four years on. *International Journal of Obstetric*	Correspondence	This correspondence from Okafor provides a brief update on health outcomes following caesarean delivery of women with PE/E and their babies. Based on a retrospective review of hospital cases of PE/E deliveries via CS (1998—2002), the author previously recommended a multidisciplinary approach to management and increased

Citation	Paper Type	Summary
Anesthesia.		use of spinal anaesthesia. Here, the author looks at records from July 2002 to June 2006 to assess whether the outcomes have improved for women with PE/E undergoing CS. During the recent four year period, three eclamptics (2 spinal, 1 epidural), 17 severe PE (15 spinal, two epidural) and 10 mild PE (8 spinal, 2 epidural) were delivered via CS. Maternal outcomes were improved when compared to the prior study period; possibly due to the preference of spinal anaesthesia (general anaesthesia is known to be associated with higher rates of maternal mortality and morbidity). Perinatal mortality was unchanged. Definitions: Mild preeclampsia: BP between 140/90 and 160/110 mmHg on two occasions six hours or more apart, or a rise from midtrimester values of 3mmHg in systolic or 15mmHg in diastolic BP, more than).3g/L proteinuria on two consecutive specimens and significant non-dependent oedema. Severe PE: BP persistently above 160/110 mmHg, proteinuria above 5g/24 hours and headache, blurred vision, epigastric pain and oliguria.
Okereke, Ekechi, Babatunde Ahonsi, et al. "Benefits of Using Magnesium Sulphate (MgSO(4)) for Eclampsia Management and Maternal Mortality Reduction: Lessons from Kano State in Northern Nigeria." *BMC research notes* 5 (2012).	Project description	In 2012, 33 heath workers in five facilities in Jigawa state were selected and recruited to be mentors for junior medical officers, nurses, midwives, CHOs and CHEWs to improve MNCH service delivery. In February of 2013, this study conducted interviews with stakeholders (mentors, mentees, facility managers and state government health officials) to assess perceptions about clinical mentoring as a strategy to improve MNCH service delivery. The clinical mentors and the healthcare workers in-charge of obstetrics saw changes regarding the introduction and updating of treatment guidelines for basic emergency health services including using magnesium sulphate to manage PE/E. This study concludes that clinical mentoring improved worker capacity to deliver quality MNCH services and that by integrating mentorship into the district health system, it has the potential to promote government ownership and sustainability.
Olamijulo, J., Ogedengbe, O., & Giwa-Osagie, O. (2008). Availability and use of obstetric guidelines in Nigeria. *International Journal of Gynaecology and Obstetrics*, *102*(3), 242–245	Cross-sections survey	This survey was meant to assess the availability and use of obstetric guidelines by asking Ob/Gyns (at SOGON Annual General Meeting and Scientific Conference) to respond to a self-administered questionnaire. One hundred and seventy-eight responses were completed, but only 176 were able to be analyzed. Most (83.5%) of the respondents had over ten years' experience. The results showed that 55.9% of respondents reported that guidelines for severe PE/E were in place, but only 38.8% said that they were used regularly.
Osungbade, K., & Ige, O. (2011). Public health perspectives of preeclampsia in developing countries: implication for health system strengthening. *Journal of Pregnancy*.	Review Article	Literature review of papers published on PE/E in developing countries between 2000 and 2010. Based on the papers identified that reported numbers for Nigeria, prevalence of PE ranged from 2-16.7%. Challenges identified include: managing PE, three delays to care, health policies. Recommend: risk assessment and clinical management, society and community interventions, and health system strengthening

Citation	Paper Type	Summary
Tukur, J. (2009). The use of magnesium sulphate for the treatment of severe pre-eclampsia and eclampsia. *Annals of African Medicine*, *8*(2), 76–80.	Literature review	Tukur discusses the severity of maternal mortality due to PE/E in Nigeria and describes key issues related to using magnesium sulphate He explains that while $MgSO_4$ was introduced in 1925 to manage convulsions it wasn't until 1995 that its efficacy was confirmed by the Collaborative Eclampsia Trial (Magpie Trial). Despite its now known efficacy, $MgSO_4$ remains mostly unavailable in developing countries where it is most needed. Tukur goes on to describe the two predominant dosing regimens: Pritchard and Zuspan as well as the importance of monitoring for toxicity. Choice of regimen depends on various factors including expertise and availability of staff to administer the drug, (Pritchard is often preferred in low resource settings because it is a simple IM injection that can be administered by lower cadre providers and doesn't require infusion pump). Pritchard involves administering a loading dose bolus of 4g of $MgSO_4$ via IV over 5-10 minutes and is followed immediately by 10g (5g in each buttock) and subsequent maintenance doses of 5g in alternate buttocks every four hours. Zuspan involves an initial IV dose of 4g of $MgSO_4$ over 5-10 minutes followed by 1-2g every hour by infusion pump(a gravity fed infusion set can be used) It is necessary to train providers on $MgSo_4$ use and ensure that protocols for its use are in place. Ensuring the involvement of important stakeholders is essential to ensure availability and utilization of $MgSO_4$

Appendix VI:

SUMMARY TABLES OF DESCRIPTIVE PAPERS ON HOSPITAL REPORTS

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
Abe, E., & Omo-Aghoja, L. O. (2008). Maternal mortality at the Central Hospital, Benin City Nigeria: a ten year review. *African Journal of Reproductive Health*, *12*(3), 17–26.	Retrospective review of hospital records.	Obstetric unit of Central Hospital, Benin City, Nigeria January 1, 1994 – December 31, 2003 28,186 deliveries	N/A	• 146 maternal deaths over the 10 year period, overall maternal mortality ratio of 518/100,000 total deliveries. • PE/E was fourth leading direct cause of maternal mortality, contributing 15.6% of overall maternal deaths. • Training, retraining and continuing medical education on emergency obstetric care, making maternal health care free, and reducing poverty and increasing female education to reduce the burden of maternal mortality.
Aboyeji, A., Ijaiya, M., & AAFawole. (2007). Maternal mortality in a Nigerian teaching hospital -- a continuing tragedy. *Tropical Doctor*, *37*(2), 83–85.	Retrospective review of hospital records.	University of Ilorin Teaching Hospital, Ilorin, Nigeria January 1, 1997— December 31, 2002 13,092 live births		• 108 maternal deaths during the period, overall maternal mortality ratio of 825/100,000 live births • Severe PE/E was most common cause of death (27.8%) • "The emergence of severe pre-eclampsia/eclampsia as the common most clinical cause of maternal death is not entirely surprising. […] it is also possible that this is so because more of the patients with the condition are elderly and they may have other medical conditions such as hypertension as an underlying disease. This will carry more mortality than the straightforward eclampsia associated with primigravidity." • MMR may be overestimated since this is a referral center and often sees complicated, high risk cases. • Recommendations: train TBAs to recognize obstetric emergencies,
Adamu, A., & Ekele, B. (2012). Pregnancy outcome in women with eclampsia at a tertiary centre in northern Nigeria. *African Journal of Gynecology & Obstetrics*, *119*(S3), S531–S867.	Retrospective analysis of demographic and clinical data of patients with eclampsia	Obstetrics & Gynecology department of Usmanu Danfodiyo University Teaching Hospital. January 2000—December 2009. 1035 eclamptics	Incidence: 1035/23,266 = 4.4% CFR = 18%	• Maternal mortality Ratio = 2670/100,000; 26.7% of which were eclamptic deaths. • Intrapartum: 62.6% • Delivery method: spontaneous vaginal= 45.2%; instrumental deliveries= 28.7%, destructive operations= 6.5%, Caesarean section was performed in 19.6% of the cases, 6.1% of eclamptic women died undelivered. • Women were more likely to die if they had not received antenatal care. • Complications among women who died included: Aspiration pneumonitis, pulmonary edema, hyperpyrexia, cerebral edema, acute renal failure, disseminated intravascular coagulopathy, abruption placentae, HELLP syndrome, and anesthetic complication • Over half of the maternal deaths occurred in the first 24 hours after hospital admission.

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
				• Fetal outcome: alive at discharge=59.2%; fresh stillbirth=18.3%' macerated stillbirth= 14.7%; early neonatal death=7.7%
Adamu, Y. M., Salihu, H. M., Sathiakumar, N., & Alexander, G. R. (2003). Maternal mortality in northern Nigeria: a population-based study. *European Journal of Obstetrics and Gynecology and Reproductive Biology*, *109*(2), 153–159.	Retrospective on vital statistics register	Kano State, Research and Statistics Department of the Ministry of Health in Kano State	Eclampsia causes 31.3% of all maternal deaths	• 4154 maternal deaths out of 171,621 Maternal mortality ratio: 2420 per 100,000 • Eclampsia was found to be the most important cause of maternal deaths • "Phase I delay (delay in seeking appropriate treatment), in particular, appears to be the rate-determining step along the non-biologic pathway through which death precipitated by eclampsia occurs." • Recommend training staff in detecting and referring women at risk for eclampsia (as well as anemia and ruptured uterus) during pregnancy.
Adelaja, L. M., & Olufemi Taiwo, O. (2011). Maternal and fetal outcome of obstetric emergencies in a tertiary health institution in South-Western Nigeria. *ISRN Obstetrics and Gynecology*, *2011*.	Retrospective study of case records	Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Nigeria Jan 2005—December 2007 262 obstetric emergencies out of1420 deliveries	Severe PIH: 8.8% of obstetric emergencies Eclampsia: 8.0% of obstetric emergencies	• Obstetric emergencies accounted for 70.6 of the 17 maternal deaths • Prevention and effective management through ANC, personal financial planning for pregnancy, development of adequate blood banking system, regular training of doctors and nurses can go a long way to reduce maternal and perinatal mortality in Nigeria.
Ade-Ojo, I., & Loto, O. (2008). Outcome of eclampsia at the Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife. *Nigerian Journal of Clinical Practice*, *11*(3), 279–284.	Rerospective review of case records	Obafemi Awolowo University Teachin Hospital Complex, Ile-Ife, Nigeria January 1, 1994—December 31, 2003 124 cases of eclampsia	Incidence of elcampsia: 0.91%	• Eclampsia was highest among young adults <25 years of age, those women carrying their first pregnancy, those who were unbooked. • 62.5% of cases occurred after 36 weeks gestation • Common symptoms included: headache (100%), hypertension (75%) and fever (20.2%) • Antepartum eclampsia (56.5%) • Maternal mortality = 8.0% and Perinatal mortality = 19.1% • Morbidities include: acute renal failure, pulmonary edema, and aspiration pneumonitis • 55.3% (n=69) had emergency abdominal delivery • Recommendations include: strengthening essential obstetric care
Adeoye, I. A., Onayade, A. A., & Fatusi, A. O. (2013). Incidence, determinants and perinatal outcomes of near miss maternal morbidity in Ile-Ife Nigeria: a prospective case control study. *BMC Pregnancy and Childbirth*, *13(93)*, 8-10.	Case-control	Maternity units of Obafemi Awolowo University teaching Hospitals Complex, Ile-Ife, Nigeria July 2006—June 2007 *w/periods of interruption	Hypertensive disorders of pregnancy = 37.3% (n=28) of near miss cases [severe	• Maternal near miss was defined as "any woman who experienced a life-threatening complication and who nearly died but for the hospital care she received" and included cases of: haemorrhage, hypertensive disorders in pregnancy, dystocia, infection, severe anemia. • Majority of near miss cases were not booked for ANC at tertiary facility (70.7%) which was significantly different from proportion of controls not booked for ANC at tertiary level (27. 0%) • 37.3% of near miss morbidities caused by hypertensive disorders in pregnancy

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
		75 near miss, 300 controls	PE=19(25.3 %), eclampsia= 9(12.0%)]	• Chronic hypertension found to have strongest association as a risk factor for near misses (7 fold increase in risk). • Key determinants of near miss: phase I delay, chronic hypertension, emergency caesarean section, and assisted vaginal delivery.
Adinma, E. D. (2012). Pattern of clinical presentation of eclampsia at Nnamdi Azikiwe University Teaching Hospital, Nnewi, Southeastern Nigeria. *Nigerian Journal of Medicine*, *21*(3), 313–316.	Retrospecti ve study of cases of eclampsia	Nnamdi Azikiwe University Teaching Hospital, Nnewi, Southeastern Nigeria January 1, 2000—December 31, 2009 6,262 cases reviewed	Prevalence of 0.91%	• 57 cases of eclampsia, but only 46 case files were complete and included in the analysis. • Antepartum eclampsia= 35 (76.1%); intrapartum = 7 (15.2%); postpartum = 4 (8.7%) • 21 cases experienced three or more convulsions before treatment was started, 9 cases had two convulsions, and 16 experienced one convulsion prior to treatment. • Patients presented with: headache (74%), edema (71%), severe hypertension (dBP >110mmHg) (69%), Blurring of vision (65%) and unconsciousness (26%) • 60.9% were nulliparous and 89% were unbooked
Adinma, E. D. (2013). Maternal and perinatal outcome of eclampsia in tertiary health institution in Southeast Nigeria. *Journal of Maternal-Fetal and Neonatal Medicine*, *26*(2), 211–214.	Retrospecti ve study of cases of eclampsia	Nnamdi Azikiwe University Teaching Hospital, Nnewi, Southeastern Nigeria January 1, 2000—December 31, 2009 6,262 cases reviewed	Prevalence of 0.91% CFR: 8/46= 17.4%	• 57 cases of eclampsia, but only 46 case files were complete and included in the analysis. 71.7% of which were delivered by caesarean section • Morbidities include: pulmonary edema (n=6), acute renal failure (n=4), coagulopathy (n=3) aspiration pneumonitis (n-2), cardiovascular accidents (n=2) and HELLP syndrome, septicemia and cerebral edema occurred in 1 each. • Eight maternal deaths • Perinatal outcomes: 46 women delivered 51 babies (1 set triplets and three sets twins). 82.5% were premature, and 70.6 had low birth weight • 13 perinatal deaths (25.5%)
Agida, E. T., Adeka, B. I., & Jibril, K. A. (2010). Pregnancy outcome in eclamptics at the University of Abuja Teaching Hospital, Gwagwalada, Abuja: a 3 year review. *Nigerian Journal of Clinical Practice*, *13*(4), 394–398.	Retrospecti ve review of case notes	University of Abuja Teaching Hospital, Gwagwalada, Abuja Case note review, of patients with eclampsia from May 1, 2005 and April 30, 2008 4471 deliveries, 59 eclampsia cases, 46 case notes available	59 cases of eclampsia; incidence of 13 per 1,000 deliveries CFR: 8.5% Stillbirth rate: 2 per 1,000 deliveries	• At the time, this facility used the Zuspan regimen • Eclampsia was most common among 20-24 year olds (34.8%). 60.9% of eclampsia cases were in women 20-29 years old • 60.9% were primigravidae • 22 (47.8%) had proteinuria of 3+, 3 (6.5%) had no proteinuria • 20 were managed with diazepam and 19 were managed with MgSO4; only three patients had recurrent seizures • 39 were delivered by caesarean, 5 vaginally (1 of whom delivered elsewhere and was referred when she developed eclampsia postpartum), and 1 died undelivered. • Complications included: acute renal failure (6 patients) 3 of whom died (though 5 maternal deaths due to eclampsia were recorded, the case notes were only available for three).

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
				• 37 babies were delivered alive, (6 of whom were <1500g; 14 were 2500g> but >1500g; and 16 were >2500g) 8 stillbirths
Alabi, O. O., Olarunfemi, G., & Onile, T. G. (2012). The trend in maternal mortality in an upgraded tertiary facility in North Central Nigeria. *Nigerian Journal of Medicine : Journal of the National Association of Resident Doctors of Nigeria*, *21*(3), 282–289.	Retrospective review of case records	Federal Medical Centre, Lokoja, Kogi Jan 1, 2005 – December 31, 2009 44 maternal deaths reviewed	Hypertensive disorders causes 31.8% of maternal deaths	• MMR during this period at the facility was 463 per 100,000 live births • PE/E accounted for 14 of the 44 maternal deaths • During the study period, MgSO4 was unavailable at the facility; since its introduction at the center in Oct 2009, no one has died from PE/E
Bukar, M., Kunmanda, V., Moruppa, J., Ehalaiye, B., Takai, U., & Ndonya, D. (2013). Maternal mortality at federal medical centre yola, adamawa state: a five-year review. *Annals of Medical and Health Sciences Research*, *3*(4), 568–571.	Retrospective study of maternal deaths	Federal Medical Centre Yola. January 2007—December 2011 28 case files of maternal deaths	N/A	• 54 maternal deaths among 8497 deliveries: MMR= 636 per 100,000 deliveries; 33 files were retrieved and 28 were complete for analysis. • Leading cause of maternal death was PE/E (32.1% of 28)—all of those who died of PE/E had not attended ANC, were Muslim and Hausa or Fulani.
Buowari, Y. (2013). Pattern and Outcome of Eclampsia Managed at a General Hospital in North-West Nigeria. *Nigerian Health Journal*.	Retrospective study of eclampsia patients	General Hospital Aliero, Kebbi state, Nigeria December 2004 to November 2006 58 records		• 47 antepartum or intrapartum; 11 postpartum eclampsia • Of those 47, 31 (66%) were delivered by caesarean and 44 (75.86%) survived and were discharged • 37 babies survived, 6 were fresh stillbirths and 4 were caveated stillbirths. • At the time of the cases, diazepam was the only anticonvulsant available
Chigbu, B., Onwere, S., Kamanu, C., Aluka, C., Okoro, O., & E, A. (2009). Pregnancy outcome in booked and unbooked mothers in South Eastern Nigeria. *East African Medical Journal*, *86*(6), 267–271.	Hospital based retrospective study	Abia State University Teaching Hospital, Aba, Nigeria January 1, 2005—December 31, 2007 3,734 mothers who delivered	Incidence (unbooked): 7.9% Incidence (booked): 2.0% Overall incidence: 3.0%	• Unbooked mothers had statistically higher incidence of PE/E (OR 3.88; 95% CI 2.61-5.77) • Eclampsia caused 9 deaths among unbooked women and 6 among booked women • Unbooked mothers in this study were generally younger, with lower educational status and higher probability of being unmarried.
Ebeigbe, P., & Aziken, M. (2010). Early onset pregnancy induced hypertension/eclampsia in Benin City, Nigeria. *Nigerian Journal of Clinical Practice*.	Retrospective study of hospital cases	University of Benin Teaching Hospital, Benin City, Nigeria		• Early onset pregnancy induced hypertension/eclampsia contributed 6.3% of all HDP cases (1 per 141 deliveries) • 58.7% of HDP cases were delivered by caesarean section • Perinatal survival rate was 34.0%,

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
		March 1, 2000 –February 28, 2005		• This study suggests that aggressive management (stabilization and early delivery) of early onset severe PE is associated with good outcomes for mother but poor perinatal outcomes. Conservative management should be only used in well-equipped facilities that have the resources and capacity for close monitoring and urgent response.
Efetie, E. R., & Okafor, U. V. (2007). Maternal outcome in eclamptic patients in Abuja, Nigeria--a 5 year review. *Nigerian Journal of Clinical Practice*, *10*(4), 309–313.	Retrospective analysis of medical records	National Hospital, Abuja March 1, 2000—February 28, 2005	Incidence 7.8 cases of eclampsia per 1000 deliveries CFR= 28.3%	• Eclampsia occurred most often in unbooked, nulliparous mothers, 71.5% of cases were delivered by caesarean due to 'unfavourable cervix' • 58.7% of cases occurred antepartum, 26.1% were postpartum and 15.2% were intrapartum • Diazepam was used to control fits, MgSO4 was only used in two cases. • Hydrallazine was used to control hypertensive (particularly in ICU) while Nifedipine and Methyldopa were used when BP was better controlled • 19 developed complications including (HELLP syndrome, acute renal failure, disseminated intravascular coagulation, septicaemia, lobar pneumonia, pulmonary edema, cerebral hemorrhage, cerebral damage and quadriplegia. • 13 maternal deaths, 46.2% due to HELLP syndrome
Eke, A. C., Ezebialu, I. U., & Okafor, C. (2011). Presentation and outcome of eclampsia at a tertiary center in South East Nigeria–a 6-year review. *Hypertension in Pregnancy*, *30*(2), 125–132.	Retrospective study of case notes	Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra state, Nigeria 2004-2009 212 case notes of eclampsia patients	Prevalence= 1.57% CFR 7.5%	• 24.5% of eclamptic patients were unbooked • Most commonly affected women were nulliparous teenagers (60.4%). Cesarean delivery accounts for 75.5% of all eclamptic deliveries • 12 neonatal and 8 perinatal deaths
Ekele, B., Bello, S., & Adamu, A. (2007). Clusters of eclampsia in a Nigerian teaching hospital. International Journal of Gynecology *and Obstetrics*, *96*(1), 62–66.	Retrospective cohort	Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria Jan 1, 1995—December 31, 2004 Reviewed files of 15,318 deliveries over the period	Overall prevalence: 4.29% Incidence at the beginning of the study period: 0.39% (1995) and increased to 7.0% (2004)	• Cases were defined as "maternities that presented with fitting or fitted while on admission, had blood pressure equal to or greater than 140/90 mmHg at least 2+ proteinuria with or without edema, and had no past history of epilepsy." • 26.3% were antepartum, 67.3% were intrapartum and 6.4 were postpartum. 95.4% patients were unbooked. 75.8% were primigravida • Incidence increased significantly over the study period with peaks identified in 1996, 2001 and 2004. (Each is twice about twice the expected/projected rate for that time.) • Factors that may have caused UDUTH to receive more cases of eclampsia: it is the only tertiary facility in the area and would receive more difficult cases and the facility's participation in the Magpie Trial meaning they had MgSO4 and clinicians in nearby facilities were aware which might have encouraged selective referral of women PE/E

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
				to UDUTH. Also many of the risk factors for PE/E are common in this area.
El-Nafaty, A., Melah, G., Massa, A., Audu, B., & Nelda, M. (2004). The analysis of eclamptic morbidity and mortality in the Specialist Hospital Gombe, Nigeria. *Journal of Obstetrics and Gynaecology*, *24*(2), 142–147.	Retrospective case review	Specialist Hospital Gombe January 1, 1997—December 31, 1999 302 cases of eclampsia	Incidence of 3.9% CFR= 11.6%	• Eclampsia occurred intrapartum in 55% of the patients • 90% of cases experienced headache, blurred vision, and epigastric pain prior to first seizure • dBP > 110 mmHg was recorded in 33.8% • 66.9% were teenagers, 73.5% were primigravidae, spontaneous vaginal delivery occurred in 52.6% (40.4% were caesarean section) • 111 perinatal deaths (36.8%) (108 were due to eclampsia, the other 6 had congenital anomalies) • Of the 216 live births, 40% were preterm • Morbidities included: pyrexis (7.3%), postpartum hemorrhage (4.6%) abruption (2.7%), and others at lower frequency
Fabamwo, A., Akinola, O., Tayo, A., Gbadegesin, A., Kushemiju, O., & Oyedele, Y. (2007). Socio-Demographic Characteristics of Eclamptic Patients at a Tertiary Institution in Lagos Nigeria. *Nigerian Medical Practitioner*, *52*(4).	Retrospective review	Department of Obstetrics and Gynaecology, Lagos State University Teaching Hospital, Ikeja, Lagos State January 1, 1999— December 31, 2003 12,875 deliveries	Incidence = 1.66% eclampsia	• 65.4% of cases were nulliparous, incidence was highest for women under 30 • Unbooked, young, nulliparous women were found to be most prone to developing eclampsia, recommend targeting this group to attend ANC regularly.
Igberase, G., & Ebeigbe, P. (2006). Eclampsia: Ten-years of experience in a rural tertiary hospital in the Niger delta, Nigeria. *Journal of Obstetrics and Gynaecology*, *26*(5), 414–417.	Descriptive review of hospital cases	Baptist Medical Centre (BMC), Eku, Delta State January 1, 1994—December 31, 2003 123 cases of eclampsia	Incidence of eclampsia: 2.3%	• 17 (13.8%) of women with eclampsia were unbooked. Teenagers accounted for 21.1$ of cases. • Most common symptoms were: headache (78%), blurring of vision (57.7%), vomiting (29.3%), epigastric pain (19.5%), and dizziness (55.3%) • 68% of the patients began experiencing seizures antepartum, 23.6% intrapartum, and 8.2% postpartum
Igberase, G., & Ebeigbe, P. (2007). Maternal mortality in a rural referral hospital in the Niger Delta, Nigeria. *JOURNAL OF OBSTETRICS AND GYNAECOLOGY*, *27*(3), 275–278.	Maternal death audit	Baptist Medical Centre (BMC), Eku, Delta State January 1, 1994—December 31, 2003 5,153 deliveries, 115 maternal deaths	CFR: 15.4%	• MMR= 2,232 per 100,000 live births (booked: 420 per 100,000; unbooked 4,123 per 100,000) • PE/E caused 20 (17.4%) of maternal deaths during this period, the third most significant cause after puerperal sepsis (33%) and abortions (22.6%). • Two thirds were delivers by CS, 25.2% by spontaneous vaginal delivery and 8.1% (n=10) by instrumental delivery. • Mean systolic BP at presentation was 174 + 29.7 mmHg and mean diastolic BP was 111.8 + 18.1 mmHg • 19 maternal deaths • Perinatal mortality was 195 per 1,000 births • Recommend: community-based health education programs to encourage667777654 early ANC, train TBAs and integrate them into

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
				primary healthcare team, improve referrals and capacity of tertiary institutions to provide intensive care for eclamptic patients.
Ikechebelu, J., & Okoli, C. (2002). Review of eclampsia at the Nnamdi Azikiwe University teaching hospital, Nnewi (January 1996-December 2000). *Journal of Obstetrics and Gynaecology*, *22*(3), 287–290.	Retrospective case review	Nnamdi Azikiwe University Teaching Hospital, Nnewi January 1996—December 2000 43 cases of eclampsia	Incidence of eclampsia: 0.75% CFR 9.3%	• 65% were primigravidae, 83.7% were unbooked, 81.4% were under 30 years of age, mean age was 23.5 years • 24 (55.8%) had eclamptic fits antepartum, 11 (25.6%) intrapartum and 8 (18.6%) postpartum. • No fits occurred below BP of 150/90mmHg • 100% were treated with diazepam; break-through seizures were controlled with diazepam, and IV paraldehyde was used in one patient who was not responding well to diazepam. • All 43 patients received Hydrallazine to control blood pressure • Rate of caesarean section was 85.7%, • Seven fetal deaths occurred (two due to low birth weight and asphyxia and the other five were stillborn before arriving at the facility) • Health education, ANC, women's awareness of obstetric services, early diagnosis and treatment, protocols for management of fluid balance, antihypertensive, and anticonvulsive therapies are necessary to reduce morbidity, mortality and high rates of CS.
Jido, T. (2012). Ecalmpsia: maternal and fetal outcome. *African Health Sciences*, *12*(2), 148–152.	Prospective hospital case review	Aminu Kano Teaching Hospital, Kano, Nigeria 120 cases of eclampsia	Incidence of eclampsia 1.2% CFR: 11.7%	• Maternal complications in eclamptic patients: prolonged unconsciousness: 13 (10.8%); acute renal failure: 6 (5.0%), cerebrovascular accident 5 (4.2%); HELLP syndrome: 5 (4.2%) and others including: pulmonary oedema/pneumonia, coagulopathy, abruptio placenta, cortical blindness, cardiomegaly, vesicovaginal fistula • 14 maternal deaths due to eclampsia • Perinatal outcomes in eclamptic mothers: stillbirth: 27 (22.5%), birth asphyxia: 47 (39.1%); low birth weight: 31(25.8%); admission to nursery: 19 (15.0%) •
Kullima, A. A., Kawuwa, M. B. M., Audu, B. M., Geidam, A. D., & Mairiga, A. G. (2009). Trends in maternal mortality in a tertiary institution in Northern Nigeria. *Annals of African Medicine*, *8*(4), 221–224.	Retrospective review hospital files	Federal Medical Centre, Nguru January 1, 2003—December 31, 2007 112 case notes from maternal deaths	N/A	• MMR 2,849 per 100,000 deliveries • Eclampsia persistently was the leading cause of death (46.4% of all deaths during the period) • Grandmultiparas, illiteracy and lack of prompt ANC were significant contributors in this study
Mairiga, A., & Saleh, W. (2009). Maternal mortality at the State Specialist Hospital Bauchi, Northern Nigeria. *East African Medical Journal*, *86*(1), 25–30.	Prospective analysis of	State Specialist Hospital, Bauchi, Nigeria	N/A	• MMR= 1,732 per 100,000 live births • 81% of maternal deaths were in unbooked deliveries • Severe PE/E accounted for 31.9% (n-245) of maternal deaths (followed by obstetric haemorrhage and sepsis)

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
	maternal mortality	January 1, 2001—December 31, 2007 767 maternal deaths		• Updating management policy for eclampsia and focus on increasing quality of emergency obstetric care can help reduce maternal death as well as use of magnesium sulphate and training providers from referring facilities on how to use it. Improving blood banking and transfusions can also help women in this community survive.
Makinde, O. N. (2011). The Contribution of Severe Pre-Eclampsia and Eclampsia to Perinatal Mortality in a Nigerian Teaching Hospital. In D. O. Ezechi (Ed.), *Perinatal Mortality*.	cohort	Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria January 1, 2006—January 31, 2007 39 cases of severe PE/E		• Each patient was categorized into three categories: • 16 (41.02%) Severe PE: hypertension after 20th week, dBP>110mmHg on admission, proteinuria >30mg/dl in random urine specimen or > 300mg in 24hr • 11 (28.2%) Imminent eclampsia: all parameters in (1) plus headache, blurring of vision and upper abdominal pain • 6 (15.4%) Eclampsia: all parameters in (1) and seizures. • Six perinatal deaths (13.95%) (among four cases), three early neonatal deaths were a set of triplets. Overall perinatal mortality rate attributable to a single disease entity (severe PE/E) was 5.84 per 1000 births • The author recommends that in this setting, the Pre-eclampsia community Guidelines (PRECOG) would minimize incidence and complications of 'SPEE" (severe PE/E)
Mbachu, I. I., Udigwe, G. O., Okafor, C. I., Umeonunihu, O. S., Ezeama, C., Eleje, G. U., & GU, M. I. U. G. O. C. U. O. E. C. E. (2013). The pattern and obstetric outcome of hypertensive disorders of pregnancy in Nnewi, Nigeria. *Nigerian Journal of Medicine*, *22*(2), 117–122.	Descriptive retrospecti ve review	Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria January 2004—December 2008 4026 deliveries	3.7% incidence of hypertensive disorders in pregnancy. CFR: 5.6%	• 148 women managed for hypertensive disorders in pregnancy; 138 complete folders were available for analysis • 64 (46.4%) had PE, 50 of whom had "severe" PE; 28 (20.3%) had eclampsia; 7(5.1%) had Chronic hypertension; 14 (10.1% had chronic hypertension with superimposed preeclampsia; 17 (12.3%) had unclassified hypertension. • Booking status and severity of disease were important determinants of maternal and neonatal outcome in this study •
Melah, G., Massa, A., & El-Nafaty, A. (2006). Pregnancy outcomes of women with eclampsia in Gombe, Nigeria. *International Journal of Gynecology and Obstetrics*, *92*(3), 251–252.	Review of hospital records	Specialist Hospital Gombe January 1, 1997—December 31, 2000 11,985 deliveries	Incidence of eclampsia: 3.7%	• MMR 2058 per 100,000 deliveries • 438 cases of eclampsia, 67.8% were teenage mothers, 79.8% were primigravidas; 51.0% delivered vaginally • 64.7% were live births and 35.3% stillbirths. Among women with eclampsia, perinatal mortality was 2023 per 100,000 live births (due to prematurity, intrauterine fetal death, and low birth weight)
Nwagha, U. I., Nwachukwu, D., Dim, C., Ibekwe, P. C. P., & Onyebuchi, A. (2010). Maternal mortality trend in South East Nigeria: less than a decade to the millennium developmental goals. *Journal of Women's Health (2002)*, *19*(2), 323–327.	Retrospecti ve study	Federal Medical Centre (FMC), Abakiliki and Ebonyi State University Teaching Hospital (EBSUTH), Abakiliki and two mission hospitals: Mile 4 Hospital, Ishieke and Mater		• 134 maternal deaths of 14, 884 live births: MMR= 902.7 per 100,000 live births • 30% of all deaths were 20-29 years old and 35.1% were grand multiparous; overall 12 maternal deaths (12.4%) from PE/E • Most common cause of death at FMC was PE/E (30%)(n=3) • EBSUTH saw 2 (6.5%) maternal deaths from PE/E, Mile 4 Hospital had 2 (7.7%) and Mater Misericordiae Hospital had 5 (16.7%) maternal deaths from PE/E

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
		Misericordiae Hospital, Afikpo January 2003—December 2005 14,884 live births		
Nwobodo, E., & Ahmed, Y. (2011). Maternal mortality associated with eclampsia in Sokoto, Nigeria. *Orient Journal of Medicine2*, *23*.	Retrospective hospital record review	Usmanu Danfodiyo University Teaching Hospital, Sokoto January 2005—December 2009. 277 maternal deaths	CFR: 31.7%	• 117 (42.2%) of maternal deaths were caused by eclampsia • CFR was slightly higher for women <20 years (36.2%), first delivery (33.8%), no formal education (32.4%) no prenatal care (32.3%), and Glasgow coma score of <5 at presentation (46.1%) (only Glasgow coma score had a significant difference) • 24.7% of perinatal deaths were due to eclampsia (61.5% of which were from mothers who also died). • Educating women, promoting FP, ANC and delivery services, and health education on feature of severe PE are measures that can help reduce maternal death from eclampsia
Okafor, U. V, & Aniebue, U. (2004). Admission pattern and outcome in critical care obstetric patients. *International Journal of Obstetric Anesthesia*, *13*(3), 164–166.	Retrospective review of hospital records	University of Nigeria Teaching Hospital, Enugu. January 1997—December 2002 6,544 deliveries		• 816 patients admitted to ICU during period, rate of 2.8 per 1000 deliveries. • Nine were preeclamptic or eclamptic (which made up 50% of the obstetric admissions) other obstetric admissions included: obstetric haemorrhage, gestational diabetes. • Four of the PE/E cases admitted to the ICU died (44%) due to cardiovascular collapse following multiple organ failure (n=3) and cerebral haemorrhage (n=1). • This and other studies show that PE/E and obstetric haemorrhage are the most common causes of obstetric admissions to the ICU • This study suggests that PE/E might benefit from preoperative admission to ICU and invasive monitoring could help reduce mortality
Okafor, U. V, & Efetie, R. E. (2008). Critical care management of eclamptics: Challenges in an African setting. *Tropical Doctor*, *38*(1), 11–13.	Retrospective study of records	ICU of the National Hospital, Abuja November 2001—April 2005	CFR: 29%	• 40 eclamptics presented at the ICU during the study period, but records for two were incomplete and not included in analysis; ICU admission rate of 8.2 per 1000 live births. 32 (84.2%) of these patients were unbooked for ANC. • 4,857 deliveries, 4,854 live births, (5,051 total births, including multiple births). • 20 (52.6%) had antepartum eclampsia, 12 (31.6%) had postpartum eclampsia, and six (15.8%) had intrapartum eclampsia • 29 (76.3%) were delivered by caesarian section • Major complications included: HELLP syndrome, disseminated intravascular coagulation, acute renal failure, and quadriplegia. • MgSO4 was unavailable at the time, ant all expect for one of the patients received diazepam to control fitting.

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
				• To lower BP, Hydrallazine was the preferred antihypertensive. • The main cause of death in this study was HELLP syndrome (n=5, 45%)
Okeh, U. (2009). Statistical analysis of the maternal death rate at the Ebonyi State University Teaching Hospital, Abakaliki, for the year ending 31 December 2007. *African Journal of Primary Health Care and Family Medicine*, *1*(1), 3 p.	Retrospective review of case notes	Ebonyi State University Teaching Hospital, Abakaliki January 1—December 31, 2007 1,646 deliveries		• MMR=2735.6 per 100,000 deliveries • Severe PE/E accounted for 35.6 (n=16) maternal deaths (haemorrhage caused 28.9% and sepsis caused 13.3% of maternal deaths) • 88.9% (n=40) of all maternal deaths were unbooked; improving ANC attendance an help prevent development of severe PE/E and reduce maternal death by detecting and managing pre-eclampsia early
Okogbenin, S A et al. "Eclampsia in Irrua Specialist Teaching Hospital: A Five-Year Review." *Nigerian Journal of Clinical Practice* 13.2 (2010): 149–153.	Retrospective review	Irrua Specialist Teaching Hospital, Edo state 5 year period 78 cases of eclampsia		• (no full text available, but was able to extract relevant details from Abstract) • Eclampsia accounted for 2.52% of admissions to the labor ward; case notes available for 74 cases. • All except four were unbooked and over half (54.29%) of those unbooked cases had not received any ANC. • Patients experienced: headache (74.32%), blurred vision (21.62%), restlessness (16.22%), nausea (10.81%) and vomiting (10.81%). • Perinatal mortality = 28.38%, maternal mortality= 22.97%
Okusanya, BO et al. "Maternal Deaths: Initial Report of an on-Going Monitoring of Maternal Deaths at the Federal Medical Centre Katsina, Northwest Nigeria." *Journal of Maternal - Fetal and Neonatal Medicine* 26.9 (2013): 885–888.	Review of hospital reports on maternal death	Department of Obstetrics and Gynaecology, College of Medicine, University of Lagos June 1, 2008—May 31, 2012 68 maternal deaths		• MMR = 827 per 100,000 live births, PE/E was the second most common direct cause of maternal death (n=14, 18.9%) • Among teenagers (23.5% of deliveries), PE/E was the most common cause of maternal death, accounting for 37.5% •
Oladapo O, Adetoro O, Ekele B, Chama C, Etuk S, Aboyeji A, et al. When getting there is not enough: a nationwide cross-sectional study of 998 maternal deaths and 1451 near-misses in public tertiary hospitals in a low-income country. BJOG An Int J Obstet Gynaecol [Internet]. 2015	Prospective review of hospital cases Cross sectional	Nigeria June 1, 2012—August 14, 2013 42 hospitals in six geopolitical zones 2,449 SMO cases		• Identified all cases of severe maternal outcome (SMO): maternal near-miss (1451) or maternal death (998). • 91, 724 live births, MMR at participating facilities was 1088 per 100,000 live births, maternal near-miss was 15.8 per 1,000 live births, and SMO ratio was 26.7 per 1,000 live births. • Hypertensive disorders (chronic hypertension and PE/E) were the most common complication and caused 24% of SMOs • Eclampsia was the most frequent complication and accounted for 1/5 maternal deaths. • About half women experiencing organ dysfunction due to hypertensive disorders in pregnancy, died—effort is needed to reduce maternal mortality by promptly managing organ dysfunction resulting from HDP. • Overall, the median time interval to initiating "definitive treatment/intervention' was 60 minutes, but in 47.4% of SMO cases,

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
				the delay was over an hour and in more than 1/5 cases it was over four hours • The research team identified deficiencies in management of almost half SMO cases (1215, 49.6%) • Contributors to substandard care included: late presentation to hospital, inability to pay/no insurance, unavailability of blood products
Oladapo, O., Lamina, M., & Fakoya, T. (2006). Maternal deaths in Sagamu in the new millennium: a facility-based retrospective analysis. *BMC Pregnancy and Childbirth*, *6*, 6.	Retrospective descriptive analysis	Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria January 1, 2000—June 30, 2005 75 maternal deaths	N/A	• 75 maternal deaths and 2509 live births; MMR= 2989.2 per 100,000 live births • Hypertensive disorders in pregnancy (severe PE/E) caused 28% of the maternal deaths, (eclampsia: 24%, severe PE, 4%) • Nine women died from complications due to severe PE/E before delivery; these complications were: cerebrovascular accident (n=8) and acute renal failure (n=1). • Up to the end of the study period, MgSO4 had not been adopted for treating severe PE/E and was unavailable
Olapade, F., & Lawoyin, T. (2008). Maternal mortality in a Nigerian maternity hospital. African Journal of Biomedical Research, 11(3), 267–273.	Retrospective case control	Adeoyo Maternity Hospital, Ibadan, January 2003—December 2004 84 maternal deaths		• MMR= 963 per 100,000 live births • 14 (16.7%) maternal deaths caused by eclampsia; 64.2% of these were among women under 25 years old • 71.4% of deaths due to eclampsia were in nulliparous women, 85% occurred within 24 hours of being admitted, 71.4% were unbooked, and more deaths due to eclampsia were seen during the rainy season
Olatunji, A. O., & Sule Odu, A. O. (2006). Maternal mortality from eclampsia. *Journal of Obstetrics and Gynaecology*, *26*(6), 542–543.	Retrospective review	Olabisi Onabanjo University Teaching Hospital, Sagamu 1988—1997 93 cases of eclampsia	Incidence 1.7% CF ratio: 0.2 (20%, CFR)	• 5,423 deliveries over the study period and 92 maternal deaths, 19 of which were caused by eclampsia. • 82 cases were antepartum, eight were intrapartum and three were postpartum, 94.7% of deaths were in antepartum cases.
Olatunji, A., & Sule-Odu, A. (2007). Presentation and outcome of eclampsia at a Nigerian University Hospital. *Nigerian Journal of Clinical Practice*.	Retrospective review	Olabisi Onabanjo University Teaching Hospital, Sagamu January 1988—December 1997 93 cases of eclampsia	Incidence 1.7% CFR: 20.4%	• 93 cases of eclampsia, all patients received diazepam to control convulsions and hydralazine (antihypertensive) when needed. • 96.8% were unbooked, 60.2% were delivered by caesarean section, and 78.5% were nulliparous • Nulliparous teenagers were the most at risk of dying from eclampsia n=38) • 87 were antepartum, 4 were intrapartum and 2 were postpartum (*conflicts with previous paper published on these data, above)
Olowonyo, T., Oshin, S., & Obasanjo-Bello, I. (2005). Registering in a health facility for delivery protects against maternal mortality in a developing country setting. *Journal of Obstetrics*	Prospective cross-sectional study	Primary, secondary and tertiary facilities and 123 private facilities in Ogun State	N/A	• Using a one-page form, researchers collected the data elements they required to calculate various neonatal, perinatal, infant, under-five and maternal mortality rates. • MMR= 177.6 per 100,000 live births • Eclampsia accounted for 9 of the 37 maternal deaths

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
and Gynaecology, *25*(7), 638–641.		November 2003—July 2004 37 maternal deaths		• 8 of the 9 deaths caused by eclampsia were unbooked/unregistered patients •
Omo-Aghoja, L., Aisien, O., Akuse, J., & Okonofua, F. (2010). Maternal mortality and emergency obstetric care in Benin City South-south Nigeria. *Journal of Clinical Medicine and Research*, *2*(4), 55–60.	Retrospective review of hospital records	University of Benin Teaching Hospital, Benin City, Edo state January 1, 2005—December 31, 2007 3,681 deliveries	CFR: 15.9%	• 84 maternal deaths, MMR= 2,282 per 100,000 deliveries, • 113 cases of eclampsia were managed • 18 (21.4%)(*there was a typo in the table, it says 12.4%) of the maternal deaths were due to "severe pregnancy induced hypertension/eclampsia" • Recommends improved emergency obstetric services
Onah, H., Okaro, J., Umeh, U., & Chigbu, C. (2005). Maternal mortality in health institutions with emergency obstetric care facilities in Enugu State, Nigeria. *Journal of Obstetrics and Gynaecology*, *25*(6), 569–574.	Retrospective maternal death analysis	Enugu State December 1, 2003—April 30, 2004 141 maternal deaths		• Five facilities were included: University of Nigeria Teaching Hospital (UNTH), the Mother of Christ Specialist Hospital (MOCSH), Parklane Specialist Hospital (PSH), Bishop Shanahan Hospital (BSH), and Ntasiobi Ndi No N'afufu Hospital • Overall MMR= 772 per 100,000 (UNTH was the worst with an MMR of 2,283 per 100,000 and MOCSH had only 192 per 100,000) • Only complete folders were retrieved for 89 (63.1%) of the maternal deaths. • PE/E caused 15 of the 89 maternal deaths (16.9%)
Onakewhor, J. U. E., & Gharoro, E. P. (2008). Changing trends in maternal mortality in a developing country. *Nigerian Journal of Clinical Practice*, *11*(2), 111–120.	Retropective review of case notes	Mission hospital, Benin City January 1, 1996—December 31, 2000 32 maternal deaths	N/A	• 32deaths out of 7,055 deliveries, MMR= 454 per 100,000 • 34.4% (n=11) of maternal deaths were due to eclampsia; this was the most significant cause of maternal death followed by sepsis and PPH at 18.8% each • This study presents some case scenarios of maternal deaths, two related to PE/E: • --One woman, 32 years old, para 2, with PE arrived at the UBTH after being referred from a private maternity home, after two convulsions, she died before she could deliver • --A 25 year old woman with severe PE (BP 181/130mmHg) declined admission, went home to update her husband and returned later but died shortly after re-admission
Onwuhafua, P. I. (2002). Dying undelivered. *Journal of Obstetrics and Gynaecology : The Journal of the Institute of Obstetrics and Gynaecology*, *22*(2), 155–158.	Retrospective review of hospital records	Ahmadu Bello University Teaching Hospital, Kaduna January 1, 1990—December 31, 1997 15 women who died undelivered		• 53 maternal deaths out of 10,572 deliveries; MMR= 501 per 100,000 • Incidence of dying undelivered = 141 per 100,000 deliveries • Severe PE/E contributed six (40%) of the undelivered deaths, followed by ruptured uterus (n=4, 26.7%) • Two of the eclampsia patients were grandmultiparae, poor, and illiterate. • Seven of the fetuses survived and six of them were in patients with eclampsia.

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
				• Recommendations include: health education for would-be clients, improve content of ANC, improve obstetric emergency capability at facility, establish materno-fetal medicine unit and awareness and policy relating to postmortem caesarean section
Onwuhafua, P. I., Onwuhafua, A., & Adze, J. (2000). The challenge of reducing maternal mortality in Nigeria. *INTERNATIONAL JOURNAL OF GYNECOLOGY & OBSTETRICS*, *71*(3), 211–213.	Retrospective review of hospital records	Ahmadu Bello University Teaching Hospital, Kaduna 1990—1997 53 obstetric deaths 16 abortion deaths		• MMR= 652 per 100,000 (including abortion deaths) • Nulliparity and unbooked had the highest rates of maternal mortality. • Eclampsia contributed 17 maternal deaths (36.95%)
Onwuhafua, P. I., Onwuhafua, A., Adze, J., & Mairami, Z. (2001). Eclampsia in Kaduna State of Nigeria–a proposal for a better outcome. *Nigerian Journal of Medicine : Journal of the National Association of Resident Doctors of Nigeria*, *10*(2), 81–84.	Retrospective review of hospital records	Ahmadu Bello University Teaching Hospital, Kaduna 1990—1997 45 cases of eclampsia	Incidence of eclampsia= 0.42% CFR: 42.22%	• Antepartum eclampsia occurred in 60% of cases, 31.3% had intrapartum and 8.7% postpartum • The most common symptoms were: headache (100%), hypertension (88.88%) and fever (42.22%). • Diazepam successfully controlled fits in 66.6% of patients • 19 maternal and 20 perinatal deaths • Recommendations include: standard plan for managing eclampsia and distributed as guides to all hospitals, ANC and delivery services must improve and provide quality surveillance of women and identification of women at risk of eclampsia, intensive care facilities are needed to treat women experiencing acute renal and cardiopulmonary complications.
Orji, E., Ogunlola, I., & Onwudiegwu, U. (2002). Brought-in maternal deaths in south-west Nigeria. *Journal of Obstetrics and Gynaecology*, *22*(4), 385–388.	Prospective review at hospital	Ife State Hospital, Ile-Ife and Wesley Guild Hospital, Ilesa (part of the Obafemi Awolowo University Teaching Hospitals Complex) 1995—1999 24 brought-in maternal deaths		• Eclampsia was determined to be the probable cause of death in 8 (33.3%) of the brought-in maternal deaths • Common reasons for late presentation to the hospital include: inability to obtain transit (41.7%), inability of health care staff to detect problems early enough (33.3%), inability of referring hospital to perform emergency C-section (25%), unavailability of blood for transfusion(25%), unwillingness of drivers to travel at night (25%), and no money to pay for hospital fees (16.7%) • One woman had suffered from eclampsia at 38 weeks gestation and it took her husband some time to collect the money for transit and hospital fees. She was carried on a motorcycle for 10km to the closest place to get on a vehicle to the facility. She had to wait for the vehicle to arrive and died on the way before arriving at the hospital.
Sule-Odu, A. (2000). Maternal deaths in Sagamu, Nigeria. *International Journal of Gynecology and Obstetrics*, *69*(1), 47–49.	Review of hospital records	Ogun State University Teaching Hospital, Sagamu 1988—1997		• MMR= 1936.1 per 100,000 = 103 maternal deaths out of 5320 deliveries, 86.4% of which were due to obstetric causes • Eclampsia accounted for13 (12.6%) of all maternal deaths and pregnancy induced hypertension caused 5 (4.9%) • Blood banking, improved access to healthcare services and empowering women can reduce maternal deaths.

Citation	Study Design	Location, Timeframe, and Sample size	Prevalence/ Incidence/ CFR	Main findings/ limitations Conclusions/ Recommendations=
		103 maternal deaths		
Tukur, J., Umar, B. A., & Rabi'u, A. (2007). Pattern of eclampsia in a tertiary health facility situated in a semi-rural town in northern Nigeria. *Annals of African Medicine*, *6*(4), 164–167.	Retrospective review of case records	Federal Medical Centre, Birnin Kudu, Jigawa State 207 cases of eclampsia	Incidence of eclampsia: 9.42%	• Eclampsia contributed to 43.1% (n=22) of all maternal deaths and 27 (13%) perinatal deaths • 56% of patients experienced delay before reaching hospital. • 58.5% were <20 years old, 78.3% were primigravida, and 51.7% were delivered by cesarean section • Eclampsia manifested antepartum in 32.9% (n=69), intrapartum in 54.1% (n=112) and postpartum in 12% (27). • Recommends health education for community members to increase awareness of the importance of ANC
Ujah, I. A. O., Aisien, O. A., Mutihir, J. T., Vanderjagt, D. J., Glew, R. H., & Uguru, V. E. (2005). Maternal mortality among adolescent women in Jos, north-central, Nigeria. *Journal of Obstetrics and Gynaecology*, *25*(1), 3–6.	Retrospective case file review	Jos University Teaching Hospital, Jos, Plateau State January 1991—December 2001 4,564 adolescent deliveries	N/A	• Adolescent= 10-19 years old • 25 maternal deaths among study population, Adolescent MMR= 547 per 100,000 deliveries • Eclampsia and Sepsis each caused 5 deaths, accounting for 26.3% each of the overall adolescent maternal deaths.
Ujah, I., Aisien, O., Mutihir, J., Vanderjagt, D., Glew, R., & Uguru, V. (2005). Factors contributing to maternal mortality in north-central Nigeria: a seventeen-year review. African Journal of Reproductive Health, 9(3), 27–40.	Review of case files	Jos University Teaching Hospital, Jos, Plateau State 1985—2001 267 maternal deaths		• 267 maternal deaths out of 38,768: MMR 740 per 100,000 deliveries • Eclampsia accounted for 75 (23.6%) of all maternal deaths. Eclampsia ranked third most common direct cause of maternal death after Haemorrhage (34.6%) and sepsis (28.3%) • An indirect cause of maternal mortality was acute renal failure (8%) which is a complication of eclampsia. •
Yakasai, I., & Gaya, S. (2011). Maternal and fetal outcome in patients with eclampsia at Murtala Muhammad specialist Hospital Kano, Nigeria. *Annals of African Medicine*.	Case record review	Murtala Muhammad Specialist Hospital (MMSH) Kano April 2008—May 2009 688 cases of eclampsia	Prevalence of eclampsia: 5% CFR= 5.2%	• 127 women died out of 13,943 deliveries ; MMR= 904 per 100,000 • Eclampsia contributed 28.57% of all maternal deaths. • Perinatal mortality among eclamptics was 132 per 1000 eclamptic deliveries. 6.2% were fresh stillbirths, 3.5% were macerated stillbirths, and 3.5% were not delivered. • 50.14% of the patients were teenagers (10-19 years old) • 82.3% were primigravidae, 48.5% received some ANC (mostly from primary health centers) • 44.9% developed convulsions antepartum • 83.3% presented within 12 hours of the first convulsion and outcomes are made worse by delay in presentation.