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SPECIAL COMMUNICATION

Scale-up of magnesium sulfate for treatment of pre-eclampsia and eclampsia in Nigeria☆

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1. Background

Pre-eclampsia/eclampsia is a serious condition that complicates 5%–10% of pregnancies globally [1] and, together with other hypertensive diseases of pregnancy, is responsible for approximately 14% of maternal deaths every year [2]. Because treatment requires early and careful monitoring of the pregnancy, the negative impact of these diseases is felt more in low-income countries where health-system factors often cause delay in reaching appropriate care [3]. In Nigeria, which has the second highest number of maternal deaths in the world [4], the prevalence of eclampsia/pre-eclampsia is reported at 163 per 10 000 deliveries [5]. One facility-based study [6] attributed 46.1% of maternal deaths to pre-eclampsia and eclampsia in Jigawa state in Northern Nigeria, where there is a high prevalence of early marriage (young age is a risk factor for pre-eclampsia) [7].

Although there is little understanding of what causes pre-eclampsia/eclampsia, there is an effective treatment for this condition. In 1994, WHO recommended magnesium sulfate as the standard treatment for pre-eclampsia and eclampsia, and within 2 years, it was placed on WHO's Essential Medicines List. Treatment of pre-eclampsia with magnesium sulfate has been shown to significantly lower the risk of eclampsia (by 58%) and the risk of mortality (by 45%) [8–10].

Despite its known efficacy, this inexpensive drug is often underused, partly because the diffusion of an innovation takes time, but also because it requires a strong and effective referral system, often a challenge in under-resourced health systems. Although the treatment of eclampsia seems simple—introduce magnesium sulfate into the woman's blood stream and deliver the fetus as soon as possible—doing so in time and correctly is complicated and involves many steps and many players [11–14].

The substantial contribution of pre-eclampsia/eclampsia to maternal mortality in Nigeria—along with the promise of magnesium sulfate as a solution—caught the attention of the John D. and Catherine T. MacArthur Foundation in 2005, when a program officer overheard a conversation between two Nigerian doctors who were lamenting the failure of a piece of equipment in their hospital laboratory that was used in the manufacture of magnesium sulfate. Without it, one was saying to the other, they would have no supply of the drug to treat pre-eclampsia/eclampsia and no way to save women's lives.

In 2007, the MacArthur Foundation began funding a series of grants to expand the use of magnesium sulfate for pre-eclampsia/eclampsia in Nigeria. The impact of this work on maternal mortality was significant: the case fatality rate due to eclampsia dropped from 20.9% to 2.3%, and the findings encouraged the government to scale up the intervention to other states [15]. In 2014, the Foundation commissioned a process evaluation of this work to help to determine what factors facilitated uptake and expansion of magnesium sulfate services, the challenges encountered while implementing the projects, and existing opportunities for future scaling up of the services across the country. The present paper reports on the findings of that process evaluation.

2. Methods

The process evaluation was conducted by a team of experts from the Public Health Institute, Oakland, CA, USA, between June and November 2014. It included a desk review of literature and grantee reports, interviews with global experts and local key informants and stakeholders, and visits to program sites. Most of the data were gathered using qualitative methods: interviews with key stakeholders and evaluator observations during site visits. Additionally, available quantitative data were reviewed, with a focus on training records and hospital and health center service statistics gathered by grantees. The Public Health Institute's institutional review board approved the research protocol and interview guides before the research was performed (IRB # I14-012).

☆ The present report is an abbreviated version of one previously published by the MacArthur Foundation (Expanding Use of Magnesium Sulfate for Treatment of Pre-eclampsia and Eclampsia—Building Toward Scale in Nigeria; published December 2014). It is published by permission of the MacArthur Foundation.

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3. Overview of activities evaluated

Beginning in 2007, the MacArthur Foundation made a series of grants to both public (Federal Ministry of Health) and private organizations (Population Council, Society of Gynaecology and Obstetrics of Nigeria [SOGON], EngenderHealth, and Ipas) to integrate the use of magnesium sulfate into the Nigerian health system. Recognizing that drug supply alone would not guarantee successful access, the Foundation supported a comprehensive set of activities that also included constituency building, public advocacy, research and evaluation, and community outreach and capacity building.

Work initially focused on drug supply, which was perceived to be the biggest issue in Nigeria preventing use of magnesium sulfate. In 2007, the Foundation brought together stakeholders from the Federal Ministry of Health and the United Nations Children's Fund (UNICEF) with an initial plan of using the well-established and secure UNICEF supply chain to distribute magnesium sulfate and an ultimate goal that state governments would put in place good and sustained procurement, supply, and tracking policies to avoid stockouts and pilferages.

In 2008, an introductory pilot project in Kano State, Northern Nigeria, trained doctors and midwives from 10 state health facilities to administer magnesium sulfate using a simplified protocol (modified Pritchard regimen). Concurrently, the project conducted community sensitization efforts focused on helping women and their families to identify the signs and symptoms of pre-eclampsia, and worked with community health extension workers and traditional birth attendants to address the need for recognition of the danger signs, treatment, and referral. The substantial drop in mortality and the cost-effectiveness of the magnesium sulfate intervention encouraged the Kano State Government to scale up the intervention to the remaining 26 hospitals in the state [15].

Building on the compelling evidence generated by the pilot project in Kano, the MacArthur Foundation funded SOGON to expand the magnesium sulfate work in Kano and to five other states (Plateau, Enugu, Borno, Cross River, and Lagos), with a goal of introducing the drug in one hospital in each state. SOGON engaged with state governments to raise awareness and advocate for state policies, using its members to visit health officials throughout each of the designated states. Once again, the substantial case fatality drop across the six state hospitals (unpublished data) lent local legitimacy to the use of the drug to treat pre-eclampsia and eclampsia. The snowball effect from these results allowed for the scale-up and expansion of magnesium sulfate into other states.

A 2008 grant enabled the Federal Ministry of Health to focus on institutionalizing delivery of magnesium sulfate throughout the healthcare system, including development of national service delivery guidelines and training curricula. The Ministry allied itself with the Nigerian Medical Association and the National Association of Nigerian Nurses and Midwives, as well as with obstetrics and gynecology department heads and chief pharmacists of selected tertiary health institutions in each state to integrate magnesium sulfate into existing clinical services. The Ministry also conducted trainings—both in-service and pre-service—in 170 institutions across all 36 states and the Federal Capital Territory; through a process of step-down trainings, more than 1800 doctors were trained. Fig. 1 shows the incremental process to scale-up of services.

As the expansion progressed, it became clear that efforts to initiate treatment at the primary-care level were also needed; by the time women reached the hospital, the condition had often progressed past the point of effective treatment. A continuing grant to the Population Council in 2011 enabled operations research in 20 primary-care facilities—10 with a task-shifting intervention and 10 without the intervention—to assess how best to involve traditional birth attendants, community health extension workers, and nurses in identification, immediate clinical care, and referral. The work also involved ethnographic research to determine the factors influencing the observed delay in women seeking treatment and to develop ways to facilitate more successful referral for further care.

Year	2008	2009	2010
States	1	11	36
Hospitals	10 (then 36)	48	400+

Fig. 1. The expansion in the number of states and facilities offering magnesium sulfate for treatment of pre-eclampsia and eclampsia in Nigeria. Although all states had received some level of training by 2010, the progress to scale up of services ranges from training only in some states to integration into multiple hospitals in others.

4. Findings

The Foundation's multifaceted strategy enabled grantees to collectively make substantial progress toward the full integration of the use of magnesium sulfate into the Nigerian healthcare system. Of particular note is that the Foundation and grantees incorporated recognized strategies for successful scale-up [16] into project planning and implementation. Fig. 2 provides an overview of how the specific approaches used in Nigeria aligned with the recommended steps for scale up. The evaluation findings support the use of this intentional scale-up approach, particularly in the areas of building legitimacy through the effective use of research and evaluation, strategically engaging stakeholders to build a supportive constituency, and modifying structures (including task shifting, institutionalizing information and training, and managing drug supply).

4.1. Using research and evaluation to legitimize change

The evaluation found that documenting and proving the utility and success of magnesium sulfate was instrumental to the legitimization of its use and the continued engagement of health ministries and institutions. The rigorous research led by the Population Council helped to seat the work within wider international evidence on the topic and helped stakeholders to realize and understand the dynamics of the complexities of administering the correct doses of magnesium sulfate, and to recognize that midwives, nurses, and community health extension workers could safely administer the loading dose of the drug and then provide accurate referral information and action.

4.2. Building a constituency

Diligent engagement with the government at every step of the program combined with clinical successes helped to achieve the necessary support, including at top levels of the government. The part played by SOGON was judged by key informants as particularly important in the legitimization of the intervention and gaining acceptance of the project by government officials at the national level; SOGON members and other health professionals engaged by them became the loudest advocates of magnesium sulfate to the government.

4.3. Task shifting and referral

The operations research that demonstrated successful task shifting to include the community health extension workers in the administration of the treatment protocol was a key element of project success. The Population Council's research at the hospital and community level showed that the women in need of the life-saving drug resided mostly in rural areas, prompting a pilot study and program to train community health extension workers to administer the first loading dose and then

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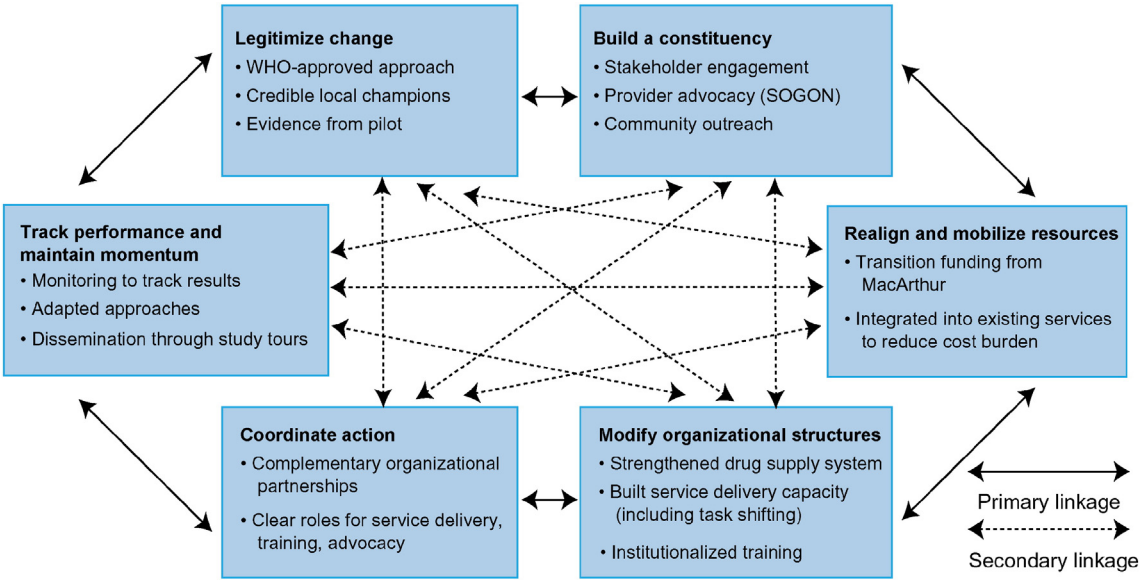

Fig. 2. Alignment of project approaches with steps in the scale-up process. Adapted from Cooley and Ved [14]. Abbreviation: SOGON, Society of Gynaecology and Obstetrics of Nigeria.

refer the patient. The results of that study led to a change in national health policies so that community health extension workers are now allowed to administer the drug and refer cases for continued care. This proved critical to better addressing the needs of rural women.

The evaluation identified two significant problems with the referral system. First, referral from primary healthcare facilities to magnesium sulfate intervention sites was not timely, resulting in deaths at the referral site (it was noted that most fatal cases of eclampsia were those referred from the primary healthcare level). Because most primary healthcare facilities have not benefited from the intervention and scale-up efforts, major problems remain in terms of timing and effectiveness of referral from these locations.

Second, stakeholders reported that many patients who received a loading dose failed to complete the referral process to a higher level facility for delivery. This finding is consistent with other studies: in one study [17], 90% of women who received the loading dose did not complete the referral process.

4.4. Developing guidelines, curricula, and job aides

The development of national service delivery guidelines and training curricula for the use of magnesium sulfate to treat pre-eclampsia and eclampsia, and their subsequent integration into the national healthcare system, was found to be another key factor supporting scale-up efforts. Clear protocols (including guidelines and algorithms for the administration of magnesium sulfate) for training of all levels of service providers (including community health extension workers) were collaboratively produced by the Federal Ministry of Health, EngenderHealth, the Population Council, SOGON, State Health Commissioners, and other partner organizations. With the assistance of state-level actors and community stakeholders, these protocols permeated down to local government areas, including at the health facility and community levels. Job aides helped to solidify correct practice.

Nevertheless, continuing the advocacy and engagement with policymakers as well as with new medical and nursing staff will be critical to build on the achievements and maintain the momentum that has been developed. The evaluation found that full integration of magnesium sulfate into the curricula and standards of care in Nigeria is still very vulnerable. One stakeholder commented: "Within just few months of its introduction, mortality from eclampsia fell to zero in all intervention facilities. However, after [the pilot], mortality from eclampsia returned to its pre-pilot period in all the facilities. It was then we realized how important advocacy is to the introduction of a drug or service, no matter how good it is. If we had done good advocacy, the government would have taken over and we may not have had a return to the pre-magnesium sulfate period in terms of mortality from eclampsia in those facilities."

4.5. Addressing drug supply issues

The evaluation found that the Population Council's focus on effective monitoring, requisitioning, and distribution of drugs at program facilities is beginning to address magnesium sulfate supply problems in Nigeria. Key informants noted that the enhanced monitoring of magnesium sulfate supplies had a positive effect on reducing stockouts not only of magnesium sulfate, but also of other medicines. In Kano State, the increased focus on effective monitoring, requisitioning, and distribution of drugs at engaged facilities and at the administrative level was believed to have positively affected other aspects of the health system.

The general state of the government's free maternal health medical services program—which was designed to improve access to health services including essential health commodities—was, however, frequently mentioned by informants as a key reason why the government's magnesium sulfate scale up has not been fully realized. This is because the supply of magnesium sulfate as part of the free medical services is now being affected by the irregularity of the free medical supplies.

Most informants did not freely admit to lack of magnesium sulfate in the facilities where they work. However, many service providers interviewed maintained that the reason magnesium sulfate supply was never exhausted at the general hospitals was because health workers in the hospitals would only provide the loading dose of the drug, requiring patients to purchase the additional doses needed for treatment from the private sector (magnesium sulfate appears to be readily available through hospital pharmacies). According to one study conducted in 2013 [17], 62.2% of the cases required families of the women to purchase the drug for use after the loading dose.

5. Discussion

By successfully implementing the MacArthur Foundation's multifaceted strategy and paying attention to the necessary steps in the scale-up process, grantees have collectively made substantial progress toward the full integration of the use of magnesium sulfate into the Nigerian

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healthcare system. In less than a decade, use of magnesium sulfate has gone from sporadic use by a handful of providers to use in more than 400 of Nigeria's 1042 secondary and tertiary hospitals across the country. This transition is particularly remarkable given the general challenges faced by the health infrastructure in Nigeria and the fact that magnesium sulfate involves a complicated clinical protocol.

Numerous challenges still remain as the country continues to scale up the program. Correct use of magnesium sulfate is very inconsistent and there is the need to address the underlying factors that prevent health workers from providing magnesium sulfate according to acceptable standards. These factors include: continued provider hesitancy about the complexity of the dosing protocol; inadequate number of trained staff as a result of transfers, retirements, and attrition; inadequate drug supply; and failure to follow the protocol to refer and/or deliver the pregnancy (sometimes even sending the woman home), mainly because of the misperception that the loading dose of magnesium sulfate (which effectively stops convulsions) has treated the problem.

Continued monitoring will be important to ensure that the new guidelines and curricula are included in the training of all new healthcare workers. Although work with the regulatory agencies at the national level and selected training institutions has provided evidence of workability, there is a critical need to include magnesium sulfate in the curricula of all institutions that train midwives and community health extension workers. Until the curricula are viewed as integral to medical and nursing training, monitoring and advocacy will be required.

There is also an ongoing need for community-based education on the symptoms of pre-eclampsia/eclampsia and on the importance of medical care even beyond the initial relief of the loading dose of magnesium sulfate. The rates of institutional births and births attended by a skilled birth attendant are still low throughout Nigeria and especially in the north [7]. Because the full regimen of magnesium sulfate must be completed at the hospital level, channels must be explored to ensure a continuum of care from home to hospital. Practical ways to improve the effectiveness of the home-to-hospital continuum of care include: helping households to identify the danger signs of pregnancy and understand need for referral through training of community resource persons (e.g. traditional birth attendants) and by involving women's advocacy groups in the community; capitalizing on the recent policy changes on task shifting to devolve the administration of the loading dose of magnesium sulfate to the community health extension workers at primary health centers; helping communities to solve their referral transport challenges; improving the quality of prenatal care services by ensuring that needed supplies are available and using a checklist that will help improve the detection of pre-eclampsia at prenatal care visits; and improving the quality of the care women receive in the health facilities so they will trust the services and not avoid using them.

Mistrust of health services, and of hospitals particularly, poses an almost insurmountable barrier to reducing the risk of eclampsia. A model that recognizes the pregnant woman as a consumer who will make choices on the basis of personal, societal, and structural influences can help to identify barriers and suggest possible interventions. Enlisting the support of women's advocacy groups to generate demand for quality maternal health services while improving the quality of the interpersonal care provided in facilities will help to build trust in the delivery services. Generating a public demand for woman-friendly delivery services is an approach that could be conducive in Nigeria, given the predominance and strength of women's advocacy groups in the country.

6. Conclusion

The story of how Nigeria introduced and scaled up use of magnesium sulfate to treat eclampsia—one of its most prevalent causes of maternal mortality—can provide important information and insight to other countries struggling with the same problem. The MacArthur Foundation led this scale-up by bringing together and supporting a complementary group of players to implement a multifaceted approach. The approach recognized that incorporating a new clinical practice into a healthcare system takes careful planning, policy support, resources, and time. Through sustained funding, and by paying attention to all the components necessary for the scale-up of a new technology such as magnesium sulfate, the MacArthur Foundation and the Federal Ministry of Health of Nigeria, working in concert with professional societies and key research institutions, have demonstrated a successful path to expanding access to this lifesaving treatment that can be adapted and replicated in other countries.

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Conflict of interest

The authors have no conflicts of interest.

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