

# Factors affecting use of magnesium sulphate for pre-eclampsia or eclampsia: a qualitative evidence synthesis

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**Background** Hypertensive disorders account for 14% of global maternal deaths. Magnesium sulphate (MgSO<sub>4</sub>) is recommended for prevention and treatment of pre-eclampsia/eclampsia. However, MgSO<sub>4</sub> remains underused, particularly in low- and middle-income countries (LMICs).

**Objective** This qualitative evidence synthesis explores perceptions and experiences of healthcare providers, administrators and policy-makers regarding factors affecting use of MgSO<sub>4</sub> to prevent or treat pre-eclampsia/eclampsia.

**Search strategy** We searched MEDLINE, EMBASE, Emcare, CINAHL, Global Health and Global Index Medicus, and grey literature for studies published between January 1995 and June 2021.

**Selection criteria** Primary qualitative and mixed-methods studies on factors affecting use of MgSO<sub>4</sub> in healthcare settings, from the perspectives of healthcare providers, administrators and policy-makers, were eligible for inclusion.

**Data collection and analysis** We applied a thematic synthesis approach to analysis, using COM-B behaviour change theory to map factors affecting appropriate use of MgSO<sub>4</sub>.

**Main results** We included 22 studies, predominantly from LMICs. Key themes included provider competence and confidence

administering MgSO<sub>4</sub> (attitudes and beliefs, complexities of administering, knowledge and experience), capability of health systems to ensure MgSO<sub>4</sub> availability at point of use (availability, resourcing and pathways to care) and knowledge translation (dissemination of research and recommendations). Within each COM-B domain, we mapped facilitators and barriers to physical and psychological capability, physical and social opportunity, and how the interplay between these domains influences motivation.

**Conclusions** These findings can inform policy and guideline development and improve implementation of MgSO<sub>4</sub> in clinical care. Such action is needed to ensure this life-saving treatment is widely available and appropriately used.

**Keywords** Eclampsia, health systems, hypertension, magnesium sulphate, pre-eclampsia, pregnancy, qualitative evidence synthesis, systematic review.

**Tweetable abstract** Global qualitative review identifies factors affecting underutilisation of MgSO<sub>4</sub> for pre-eclampsia and eclampsia.

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## Introduction

Pre-eclampsia and eclampsia are hypertensive disorders of pregnancy experienced by 4.6% and 1.4% of women, respectively, during pregnancy and childbirth.<sup>1</sup> They are characterised by high blood pressure, proteinuria and (once progressed to eclampsia) seizures, which can be fatal to both woman and baby.<sup>2,3</sup> Hypertensive disorders are the

second leading direct cause of maternal mortality, accounting for 14% of maternal deaths.<sup>4</sup> However, the precise contribution is unknown for many low- and middle-income countries (LMICs) because of suboptimal detection and reporting of these conditions.

Magnesium sulphate (MgSO<sub>4</sub>) is recommended by the World Health Organization (WHO) for women with severe pre-eclampsia/eclampsia,<sup>5</sup> and has been proven to be

effective in major trials<sup>6,7</sup> and meta-analyses.<sup>8–11</sup> Administering MgSO<sub>4</sub> to women who have pre-eclampsia halves their risk of developing eclampsia,<sup>10</sup> and more than halves their risk of death.<sup>4</sup> MgSO<sub>4</sub> is cost-effective<sup>12</sup> and safe,<sup>13–17</sup> and has been on the WHO Essential Medicines List since 1996.<sup>18,19</sup> The current WHO recommendation for severe pre-eclampsia/eclampsia is the administration of a full intravenous/intramuscular regimen, including an initial loading dose and maintenance doses over 24 hours.<sup>5</sup> Women must be monitored for signs of magnesium toxicity between doses, therefore it is recommended that MgSO<sub>4</sub> be administered in health facilities with adequate staffing and clinical resources for monitoring.<sup>20</sup> Alternative dosage regimens of MgSO<sub>4</sub> are also being evaluated.<sup>21,22</sup>

Despite strong evidence of effectiveness and cost-effectiveness, MgSO<sub>4</sub> is often underused for these indications,<sup>13,23–25</sup> particularly in LMICs.<sup>26</sup> Previous research has explored factors affecting MgSO<sub>4</sub> guideline implementation, identifying system and market failures that restrict drug availability, absence of clinical protocols and staff reluctance.<sup>18,27–29</sup> However, to our knowledge, no systematic review has synthesised evidence on factors affecting use of MgSO<sub>4</sub> for women with pre-eclampsia/eclampsia. A qualitative evidence synthesis (QES) may help to understand why MgSO<sub>4</sub> is not more widely adopted in practice. The aim of this QES is to explore the perceptions and experiences of healthcare providers, administrators and policy-makers regarding factors affecting use of MgSO<sub>4</sub> to prevent or treat pre-eclampsia/eclampsia administered globally, and to develop a conceptual understanding of how these factors influence MgSO<sub>4</sub> use.

## Methods

We followed the Cochrane Effective Practice and Organisation of Care (EPOC) QES guidance<sup>30</sup> and report our findings according to the ‘Enhancing transparency in reporting the synthesis of qualitative research’ (ENTREQ) statement (Appendix S1); the review protocol is registered with PROSPERO (CRD42020167185).<sup>31</sup> There was no patient or public involvement, and a core outcome set was not applicable in this review.

### Inclusion criteria

Eligible studies considered factors affecting use of MgSO<sub>4</sub> (any dosage regimen) for pre-eclampsia/eclampsia prevention or treatment during the antenatal, intrapartum and postpartum periods. Eligible studies included participants who were health system stakeholders (policy-makers, administrators, health workers and lay health workers). Eligible studies were conducted in healthcare facilities of any level (e.g. hospitals, clinics and primary health care) in any country. Home or community settings were excluded as MgSO<sub>4</sub> is not recommended for use outside

healthcare facilities. Eligible studies were primary studies using qualitative methods for data collection and analysis.<sup>30</sup> Conference abstracts, posters and clinical case studies were excluded. Mixed-method studies were eligible if they used qualitative data collection and analysis methods.

### Search methods

We searched MEDLINE, EMBASE, Emcare, CINAHL, Global Health and Global Index Medicus for studies from 1 January 1995 (when the Eclampsia Collaborative study definitively established MgSO<sub>4</sub> as an effective treatment for eclampsia<sup>6</sup>) to 28 June 2021. Search strategies were developed using MgSO<sub>4</sub>, anticonvulsant, pre-eclampsia/eclampsia and hypertension terms (Table S3). We did not use a methodological filter.<sup>30</sup> We searched OpenGrey, AHRQ, NICE, Jhpiego, Population Council, WHO international and Google Scholar for grey literature, and reviewed reference lists of included studies.<sup>8–11,21</sup>

### Study selection and data extraction

Two reviewers (from KEE, RIZ, MAB, JPV) independently reviewed each title and abstract for eligibility. We retrieved full texts for potentially relevant studies and two reviewers independently assessed eligibility (from KEE, RIZ, MAB). Disagreements at either stage were resolved by discussion, involving a third reviewer if necessary. We used Google Translate to translate titles and abstracts published in languages other than English; where translation indicated possible inclusion, we planned to list as ‘studies awaiting classification’ (no articles met these criteria). Where more than one paper reported the same study (using the same sample and methods), the papers were collated to ensure the study was the unit of interest.<sup>30</sup> A data extraction form was developed and used to extract data on context and design, and qualitative data (author themes, interpretation and participant quotes).<sup>30</sup>

### Methodological limitations of included studies

Critical appraisal of included studies was conducted by two reviewers independently (KEE, RIZ) using an adaptation of the Critical Skills Appraisal Programme (CASP) tool.<sup>32</sup> Consensus was reached through discussion. We assessed study aims, methodology, design, recruitment, data collection, data analysis, reflexivity, ethical considerations, findings and research contribution.<sup>33</sup> We did not exclude studies based on this assessment, but used the assessments in GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) assessments.<sup>34</sup>

### Data management, analysis and synthesis

We used an inductive ‘thematic synthesis’ approach<sup>35</sup> to synthesise themes emerging from the data (KEE, RIZ, MAB).

We began by free line-by-line coding results of five highly relevant studies covering different health system levels and stakeholder types. Codes were organised into a hierarchy, grouping related codes under descriptive themes. Results from included studies were coded line-by-line in NVIVO<sup>36</sup> using the codebook, which developed iteratively throughout analysis. Text assigned to each code was checked for consistency and further division into sub-codes. We developed higher-order analytical themes to identify health system factors affecting use of MgSO<sub>4</sub>. We then used COM-B behaviour change theory<sup>37</sup> to explore and categorise health system stakeholders' Capability, Opportunity, Motivation to appropriately use MgSO<sub>4</sub>.

### Confidence in the review findings

Two review authors (KEE, RIZ) used the GRADE-CERQual approach to assess confidence in each review finding,<sup>38</sup> based on methodological limitations,<sup>34</sup> coherence,<sup>39</sup> adequacy<sup>40</sup> and relevance.<sup>41</sup> We assessed each component by levels of concern (no or very minor/minor/moderate/serious), then made a judgement about the overall confidence in the review finding (high/moderate/low/very low).<sup>42</sup> All findings started as high and were downgraded where concerns about GRADE-CERQual components were identified. We present summaries of findings and GRADE-CERQual assessments in a summary of qualitative findings table (Table S1) and evidence profile (Table S2).

### Reflexivity

We maintained a reflexive stance throughout the review process and regularly discussed and critically reflected on our positionality.<sup>30,43</sup> At the outset of this review, the

review team considered that MgSO<sub>4</sub> is an effective intervention that should be used for prevention and treatment of pre-eclampsia/eclampsia, and that health system barriers probably limit the implementation in practice. The review team has expertise in public health (KEE, RIZ, JPV, MAB), women's health (KEE, RIZ, JPV, MAB), health economics (KEE), social science (MAB), medicine (JPV) and epidemiology (KEE, RIZ, JPV, MAB). We remained mindful of our presuppositions to minimise the risk of these skewing our analysis or interpretation.<sup>30,43</sup> Specifically, we used refutational analysis techniques, such as exploring and explaining any contradictory findings between studies.<sup>33</sup>

## Results

We included 25 papers from 22 studies (Figure 1, Table 1), published between 2005 and 2021. One global study was conducted in 24 countries,<sup>44</sup> the remaining 21 studies were conducted in 12 countries: Bangladesh, Brazil, Ethiopia, India, Kenya, Malawi, Mexico, Mozambique, Pakistan, Nigeria, South Africa and Zimbabwe. All but the global study were from LMICs. Studies included perspectives of facility administrators,<sup>13,14,27,28,44–54</sup> health researchers,<sup>29,44,50,55</sup> policy-makers,<sup>29,44–49,51,52,55</sup> doctors,<sup>13,27,29,44,48–50,56–58</sup> midwives/nurses,<sup>29,44,47–49,52,56,59–61</sup> and community health workers.<sup>48,58,60</sup>

Studies primarily used in-depth interviews and/or focus group discussions. Detailed critical appraisals are provided (Table S3); the primary reasons for downgrading were limitations in recruitment/sampling strategies, reflexivity, informed consent and ethics approval, data analysis, and insufficient evidence to support findings. Explanations for

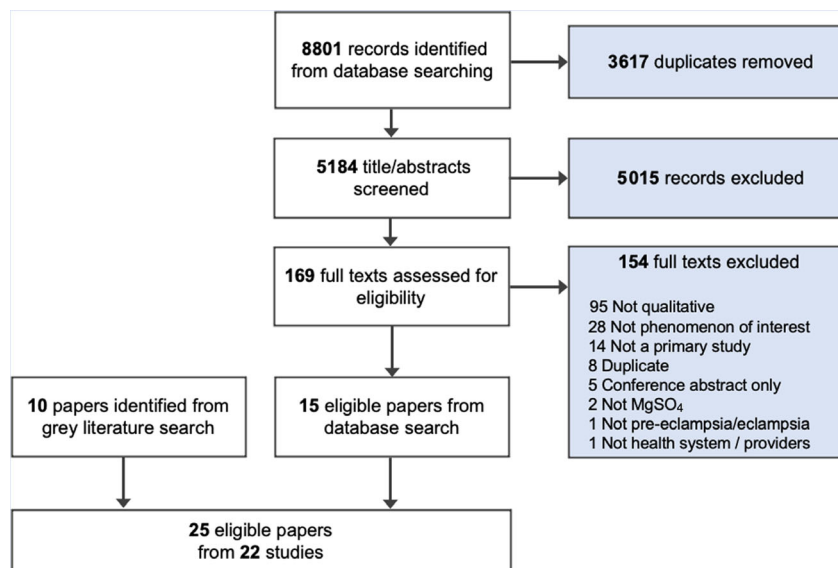


Figure 1. PRISMA diagram.

**Table 1.** Characteristics of included studies

Author and year	Country	Type and number of participants	Data collection	Data analysis
Aaserud 2005	Multiple	Doctors, midwives, researchers, health managers	Observations, 5 group discussions	Thematic and policy framework analysis
Alabintei 2021a,b	Nigeria	Health-facility managers	29 key informant interviews	Thematic analysis
Barua 2011	India	Nurses, clinicians, obstetricians and gynaecologists	7 FGDs	Grounded theory
Bigdeli 2013	Pakistan	Healthcare providers, policy-makers, academics	Document review, 48 IDIs, unknown number of FGDs, observation	Deductive content analysis
Charanthimath 2018	India	Community leaders, doctors, administrators	14 FGDs and 12 IDIs	Thematic analysis
Chaturvedi 2013	India	Doctors, administrators, district health officials, and programme managers	39 IDIs, observation, record analysis	Thematic analysis
Chikalipo 2020	Malawi	Nurses, midwives, technicians	1 FGD and 10 IDIs	Thematic analysis
Danmusa 2014 & 2016	Nigeria	Global experts, local key informants and stakeholders	23 IDIs	Not specified
Hossain 2019	Bangladesh	Policy-makers and programme managers	37 IDIs	Content and thematic analysis
Ishaku 2019	Nigeria	Policy-makers and programme stakeholders	64 IDIs	Content and thematic analysis
Lotufo 2016	Brazil	Healthcare managers	Document analysis, observation, interviews	Deductive content analysis
Lotufo 2017	Brazil	Obstetricians	30 IDIs	Content analysis
Ndwiga 2018	Kenya	Policy-makers, midwives, doctors, community health workers, and traditional birth attendants	98 IDIs	Thematic analysis
Oguntunde 2015	Nigeria	Healthcare facility manager	30 IDIs, survey, observational checklists	Thematic analysis
Ramadurg 2016	India	Nurses, Auxiliary Nurse Midwives, accredited social health activist (ASHAs)	8 FGDs, surveys	Thematic analysis
Raney 2019	India	Nurse mentors	12 IDIs	Thematic content analysis
Sheikh 2016	Pakistan	Lady health workers, lady health supervisors, traditional birth attendants, doctors	7 FGDs and 26 IDIs	Thematic analysis
Sripad 2018	Ethiopia	Policy-makers, health officers, representatives from MoH and professional associations	62 IDIs	Thematic analysis
Van Dijk 2013	Mexico	Maternal health researchers, doctors	13 IDIs	Content analysis
Warren 2015a	Nigeria	Policy-makers and programme stakeholders	72 IDIs	Content analysis
Warren 2015b	Bangladesh	Policy-makers and programme manager stakeholders	50 IDIs	Content and thematic analysis
Woelk 2009 and Sevene 2005	Mozambique, South Africa, Zimbabwe	Policy-makers	Document review, 49 IDIs	Thematic analysis

Danmusa 2014 and Danmusa 2014 are from a single study; Woelk 2009 and Sevene 2005 are from a single study; Alabintei 2021 and Alabintei 2021 are from a single study.

FGD, focus group discussion; GD, group discussion; IDI, in-depth interview; MoH, Ministry of Health.

GRADE-CERQual assessments are in Table S2: of 28 review findings, we graded ten as high confidence, 17 as moderate confidence and one as very low confidence. The primary reason for downgrading was for relevance – this was a global review with almost all evidence from LMICs.

### Qualitative synthesis findings

We developed nine overarching themes under three domains: provider competence and confidence, health system capability and knowledge translation (Figure 2). Table S1 presents the summary of qualitative findings and CERQual assessments.

Domain	Themes
Provider competence and confidence	<ol style="list-style-type: none"> <li>1. Attitudes and beliefs about MgSO<sub>4</sub></li> <li>2. Complexities of administering MgSO<sub>4</sub></li> <li>3. Provider knowledge and experience of MgSO<sub>4</sub></li> </ol>
Health system capability	<ol style="list-style-type: none"> <li>4. Availability of MgSO<sub>4</sub></li> <li>5. Supply chain issues: manufacturing, marketing, logistics and procurement</li> <li>6. Adequate resourcing: equipment, supplies, facilities and staffing</li> <li>7. Pathway to care for pre-eclampsia/eclampsia: antenatal care, referral systems and loading dose administration</li> </ol>
Knowledge translation	<ol style="list-style-type: none"> <li>8. Availability and use of appropriate policies and clinical practice guidelines</li> <li>9. Research dissemination and advocacy by 'champions' can facilitate uptake</li> </ol>

Figure 2. Domains and themes.

## Provider competence and confidence

### 1. Attitudes and beliefs about MgSO<sub>4</sub>

**Finding 1.1:** MgSO<sub>4</sub> is often perceived by providers, administrators and policy-makers as useful and effective, and acknowledged as the preferred treatment for pre-eclampsia/eclampsia. In Latin America, some believe that MgSO<sub>4</sub> is overused for women with mild pre-eclampsia (moderate confidence).<sup>13,27,29,44,50,52,53,55,56,60</sup> Providers in two studies were more aware of MgSO<sub>4</sub>'s effectiveness for eclampsia than severe pre-eclampsia,<sup>13,29</sup> potentially because effectiveness was first demonstrated for eclampsia.

**Finding 1.2:** Some providers preferred alternative drugs (particularly diazepam and phenytoin) because of past training, less cumbersome protocols for use, perceived safety or familiarity. Providers' decisions to use alternatives may be based on positive attitudes towards the alternative, or negative perceptions of MgSO<sub>4</sub> (moderate confidence).<sup>29,50,55,56,58,60,62</sup> Many providers were trained and comfortable in using diazepam; for some, familiarity outweighed 'newer' and less familiar MgSO<sub>4</sub> regimens.<sup>29,55,62</sup> Compared with diazepam, MgSO<sub>4</sub> was considered more difficult to administer and less safe.<sup>29,62</sup> Phenytoin was considered an alternative treatment in India and Mexico, where some believed it to be superior.<sup>50,56</sup>

**Finding 1.3:** Fear of complications or adverse events from MgSO<sub>4</sub> can undermine beliefs about its safety and can create barriers to its use. Some providers felt fearful, cautious or concerned when using MgSO<sub>4</sub> based on a perceived likelihood of adverse events (e.g. maternal respiratory arrest, death). This fear was exacerbated when providers were at risk of being blamed for adverse events (high confidence).<sup>13,18,29,48–50,56–59,61</sup> Providers' fear, caution and concern were most commonly due to their

perceived risk that complications may cause harm or death.<sup>13,18,29,48–50,56–59,61</sup> Some providers held persisting beliefs about the "toxicity" of MgSO<sub>4</sub>.<sup>29,48,57,58</sup> For some, fears were based on lived experiences.<sup>29,55</sup> Fears can lead providers to feel inadequate or stressed using MgSO<sub>4</sub>,<sup>13,29,57</sup> resulting in hesitation or avoidance.<sup>13,56</sup>

### 2. Complexities of administering MgSO<sub>4</sub>

**Finding 2.1:** Providers may be less likely to administer MgSO<sub>4</sub>, or may administer it incorrectly, because of confusion about when and how to administer, perceived difficulty of administering and a fear of incorrect use. However, some providers think the difficulty of administering MgSO<sub>4</sub> is overstated (moderate confidence).<sup>29,48–50,56,57,59–61</sup> Some providers were unsure about recognising disease severity (mild versus severe pre-eclampsia) and indications for MgSO<sub>4</sub> use.<sup>49,56,61</sup> Providers also experienced confusion about methods for administration,<sup>49,56,60,61</sup> and believe that administration is difficult.<sup>48,50,59</sup> However, some felt those not using it are 'lazy'.<sup>59</sup>

**Finding 2.2:** Difficulties identifying and preparing the correct dose undermine providers' willingness, confidence and competence to administer MgSO<sub>4</sub> (high confidence).<sup>29,48–50,57,59,61</sup> Training may be inadequate or incorrect,<sup>29</sup> and requirements are harder to remember when pre-eclampsia/eclampsia is encountered relatively infrequently.<sup>57</sup> Variability in local dosage regimens causes confusion,<sup>29,59</sup> and MgSO<sub>4</sub> packaging sizes differ from recommended dose amounts.<sup>59,61</sup> Difficulties with dosing lead to providers delaying or avoiding MgSO<sub>4</sub> use.<sup>48,59</sup>

**Finding 2.3:** The need to monitor women after administering MgSO<sub>4</sub> increases the perceived burden and riskiness of using it, which can contribute to underutilisation (moderate confidence).<sup>29,44,48,50,56,57,59</sup> Monitoring is



considered resource and labour-intensive, contributing to a perception that MgSO<sub>4</sub> can only be used in higher-level facilities.<sup>44,48,56,57,59</sup>

**Finding 2.4:** Determining the appropriate cadre of healthcare provider to administer MgSO<sub>4</sub> (e.g. through task-shifting or task-sharing) can be a barrier or facilitator to appropriate use, especially in resource-constrained settings where higher cadre providers are unavailable or have limited capacity (moderate confidence).<sup>28,46–48,51,53,58–60</sup>

There were diverse views about what cadres of provider should administer MgSO<sub>4</sub>.<sup>28,46–48,58–60</sup> Some considered that it can only be administered by doctors,<sup>28,48,53,58,60</sup> whereas others felt that trained nurses and midwives can administer it.<sup>47,48,51,60</sup> Concerns included that lower cadres may not have sufficient skills or motivation to monitor women post-administration,<sup>59</sup> and allowing them to administer could result in abuse or harm.<sup>51</sup>

### 3. Provider knowledge and experience of MgSO<sub>4</sub>

**Finding 3.1:** Knowledge about the benefits and risks of MgSO<sub>4</sub>, its indications for use and how it should be administered (including appropriate regimens) is a facilitator for appropriate use, whereas insufficient knowledge can reduce providers' confidence and competence (moderate confidence).<sup>29,48–50,53,56–58,60,62</sup> Limited knowledge can lead to inappropriate practice, such as sending a woman home after administering the loading dose.<sup>62</sup>

**Finding 3.2:** Effective and practical training can increase providers' knowledge and (simulated) experience of MgSO<sub>4</sub>, thereby improving their capability and motivation to use it. Training does not guarantee use, but is seen by some as a pre-requisite to use (high confidence).<sup>14,29,44,46,48,49,52,53,55–59,61,62</sup> Training increases perceptions that providers can administer MgSO<sub>4</sub> correctly.<sup>27,44,52,56,57</sup> Training is more likely to be effective if it is practical<sup>48,49,59,61</sup> and recent.<sup>29,49,59</sup>

**Finding 3.3:** Practical, first-hand experience administering MgSO<sub>4</sub> (including clinical experience and simulation or practical skills training) encourages providers to use MgSO<sub>4</sub> appropriately. Conversely, the absence of recent, frequent experience can undermine providers' confidence, competence and willingness to administer MgSO<sub>4</sub> (moderate confidence).<sup>29,48,50,55,57–62</sup> Observing the positive effects of MgSO<sub>4</sub> influenced providers' attitudes, becoming 'convinced' and advocating for its use.<sup>55,62</sup>

## Health system capability

### 4. Availability of MgSO<sub>4</sub>

**Finding 4.1:** MgSO<sub>4</sub> is often unavailable in some facilities (particularly rural or lower-level facilities in LMICs), and stock-outs are an obstacle to its use. MgSO<sub>4</sub> is also not consistently available in many LMICs at country, regional and district levels, suggesting that facility-level stock-outs may reflect system-level unavailability (high

confidence).<sup>13,14,18,28,29,44–49,51,53,56,57,62</sup> Stock-outs occur across different facility levels, including primary care settings, secondary and tertiary hospitals, and rural facilities.<sup>13,29,48,56,57</sup> Even in settings where MgSO<sub>4</sub> is available there can be a disconnect between perceptions of system-level and facility-level availability, with those in administrative or policy roles unaware that stock-outs are occurring, or those at facility-level unaware that it is available to procure.<sup>18,46–48,51</sup> Access is less likely to be a problem in high-income countries.<sup>44</sup>

### 5. Supply chain issues: manufacturing, marketing, logistics and procurement

**Finding 5.1:** Registration, licensing and inclusion of MgSO<sub>4</sub> on national Essential Medicines Lists are acknowledged to be important pre-requisites, although they will not alone guarantee MgSO<sub>4</sub> use (high confidence).<sup>18,28,29,44,48,52</sup> MgSO<sub>4</sub> may not be registered for use in all settings.<sup>18,28,44</sup> Reasons include that policy-makers may be unconvinced it is necessary, with some believing diazepam is equally effective.<sup>18</sup>

**Finding 5.2:** MgSO<sub>4</sub> is generally perceived as cheap and affordable. However, in some settings, affordability is undermined in practice by higher retail prices and families' low incomes (moderate confidence).<sup>13,14,18,29,44,51,52</sup>

**Finding 5.3:** Limited local production, a relatively small market for MgSO<sub>4</sub> compared with other drugs with multiple indications and problems with distribution and storage all contribute to unavailability of MgSO<sub>4</sub> in some LMIC settings. The low price of MgSO<sub>4</sub> price can contribute to these availability issues, as the financial returns available to pharmaceutical companies are low and consequently the incentive to produce and market MgSO<sub>4</sub> is limited (moderate confidence).<sup>18,29,44–46,49,51,52,55,62</sup> Several studies note the importance of distribution and logistics for MgSO<sub>4</sub> access,<sup>18,46,49,62</sup> and the presence of bottlenecks and problems in distribution.<sup>18,49,55</sup> Providers described expiration of MgSO<sub>4</sub> because of relatively infrequent use, particularly at lower-level facilities.<sup>49,51</sup>

**Finding 5.4:** MgSO<sub>4</sub> availability at health facilities relies on effective national and local procurement systems; even where MgSO<sub>4</sub> is available, failures in complex and fragmented procurement systems in some settings contribute to facility-level stock-outs. Facility-level managers may seek to bypass official procurement channels that are perceived as ineffective, which can increase fragmentation and undermine centralised systems (moderate confidence).<sup>13,18,29,46–49,53,62</sup> Problems with procurement included: mismatched demand from hospital departments and national medicines lists,<sup>29</sup> clinicians failing to request MgSO<sub>4</sub>,<sup>18,29</sup> exclusion of MgSO<sub>4</sub> from central procurement,<sup>18,52</sup> and complex, unreliable requisition processes.<sup>13,49,52</sup> Failures can occur at central or local government levels,<sup>46,48</sup> or facility-level.<sup>18,53</sup> Primary and

community health facilities are more likely to experience problems obtaining MgSO<sub>4</sub>.<sup>46,47</sup> If pre-eclampsia/eclampsia is not encountered often or is considered uncommon at a facility, administrators may choose not to procure MgSO<sub>4</sub>.<sup>53</sup> Failures in national procurement systems contribute to stock-outs.<sup>13,18,29,46–49,62</sup> Procurement could be more effective with improved supply monitoring,<sup>62</sup> transparency regarding quantities required,<sup>46</sup> and facility-level coordination to match supply and demand.<sup>49</sup>

**Finding 5.5:** Women or their relatives may be required to privately purchase MgSO<sub>4</sub> from hospital pharmacies or retail outlets in some settings where medicines cannot be sourced from the facility directly. For some families, this may cause financial hardship or they may not have money readily available to purchase it, which can cause delays or barriers to use (high confidence).<sup>14,29,47–49,56,62</sup>

Private purchase may be required because of facility stock-outs,<sup>14,48,49,56</sup> or as standard practice to manage demand.<sup>29,47,49,62</sup> Retail outlets generally charge higher prices.<sup>14,48,49</sup>

#### 6. Adequate resourcing: equipment, supplies, facilities and staffing

**Finding 6.1:** Providers' capability and confidence to safely administer MgSO<sub>4</sub> is undermined if the necessary equipment and supplies are missing and facilities are inadequate. MgSO<sub>4</sub> is considered safer to use in well-equipped facilities, with access to sphygmomanometers, urine dipstick tests, laboratory and diagnostic equipment, medications such as calcium gluconate, and sufficient rooms and beds for monitoring (high confidence).<sup>28,29,48,49,53,56,57,59,61,62</sup>

**Finding 6.2:** Insufficient staffing, competing clinical duties, workload pressure and inflexible work schedules restrict the use of MgSO<sub>4</sub>, especially given that administration requires ongoing monitoring for toxicity. Staffing constraints are especially problematic for women experiencing severe pre-eclampsia or eclampsia outside usual hours (high confidence).<sup>14,28,48,49,53,55–59,61</sup> Staff shortages occurred across multiple levels, involving nurses,<sup>49,56,61</sup> midwives,<sup>14,49,59</sup> doctors<sup>18,28,53,56–58,61</sup> and paramedics,<sup>56</sup> at primary and community health centres<sup>28,48,49,57,58,61</sup> or hospitals.<sup>18,29,48,49,56,59</sup>

**Finding 6.3:** Perspectives varied on appropriate facility level(s) for administration of MgSO<sub>4</sub>. Its use in hospitals is generally accepted, but some consider that MgSO<sub>4</sub> should not be administered at lower-level facilities. As a result, women seeking care at lower-level facilities may not receive treatment. Reasons for preferring higher-level facilities include the availability of equipment, a particular cadre of provider and access to intensive care facilities (high confidence).<sup>28,29,44,46,49,52,53,57,58,60,61</sup> Some suggested that MgSO<sub>4</sub> could be used at primary health facilities or emergency mobile health services with training

and resourcing,<sup>28,29,52</sup> others felt use in primary health settings was inappropriate.<sup>52,57,58,60</sup> Use of MgSO<sub>4</sub> may not always occur at lower-level hospitals.<sup>28,29,46</sup>

#### 7. Pathway to care for pre-eclampsia/eclampsia: antenatal care, referral systems and loading dose administration

**Finding 7.1:** MgSO<sub>4</sub> use relies on identifying women with symptoms of pre-eclampsia or eclampsia. Timely identification relies on women accessing quality antenatal care that includes regular blood pressure checks, preventive treatment of hypertension, detection and classification of pre-eclampsia/eclampsia symptoms, and prompt treatment or referral (moderate confidence).<sup>46,51,53,58,60</sup>

**Finding 7.2:** Prompt, successful referral to higher-level facilities enables timely and effective MgSO<sub>4</sub> treatment, especially for women in remote or rural areas. Challenges to effective referrals in some settings include lack of capability at referral and referring sites, problems with transport, costs and complex inter-facility communication processes. Timeliness of treatment can be improved where a loading dose is given at a lower-level healthcare facility before referral (moderate confidence).<sup>46,48,52,53,58,61,62</sup>

**Finding 7.3:** Administration of a loading dose of MgSO<sub>4</sub> by lower-cadre providers before referral is considered beneficial, safer and less complicated to administer than the full regimen; attitudes toward task shifting its administration to lower-cadre healthcare workers (including paramedics, community health workers, skilled birth attendants, midwives and nurses) were generally positive. However, some were concerned about the knowledge and capability of these providers (moderate confidence).<sup>13,27,29,46–49,58,60–62</sup> Loading dose administration is considered less complicated than the full regimen, described by some as 'easy' and 'safe'.<sup>27,46</sup> Administration of a loading dose was considered necessary because of barriers for women from rural areas accessing higher-level care<sup>27,46,47,49</sup> and skilled staff shortages.<sup>46,47</sup> However, a loading dose may not be given even where permitted because of perceived safety issues,<sup>29,49</sup> inadequate resourcing<sup>13,29,46,58,61</sup> or providers being unaware of its importance.<sup>46,58</sup>

#### Knowledge translation

#### 8. Availability and use of appropriate policies and clinical practice guidelines

**Finding 8.1:** Policies and guidelines should clearly recommend MgSO<sub>4</sub> for eclampsia and severe pre-eclampsia and describe indications and administration methods in detail appropriate to the intended audience and context. Policy should specify those settings in which administration is recommended. Translating higher-level policy into local protocols including algorithms and job aids can be useful. Inconsistent and ambiguous policy or guidance creates confusion for healthcare workers and may

undermine MgSO<sub>4</sub> use (high confidence).<sup>18,28,29,44,48,50</sup> Guidelines should specify indications for MgSO<sub>4</sub> use,<sup>44,48</sup> and how to administer it, including dosage and administration methods.<sup>29,48,53,54,62</sup>

**Finding 8.2:** The process for developing policies, guidelines and protocols varies. Processes that are consultative and include diverse stakeholders are perceived by some to increase ownership and uptake of guidelines. Stakeholders may include clinicians, governments and non-governmental organisation representatives (very low confidence).<sup>44,50,53,55,62</sup> It is unclear whether including local clinicians or administrators to create ownership and increase uptake is effective.<sup>18,50</sup> Governments' receptiveness to input from clinicians is considered an important facilitator in policy development.<sup>55</sup>

**Finding 8.3:** For policy and guidelines to influence clinical practice, guidance must be disseminated and available to administrators and healthcare providers at all facility levels where MgSO<sub>4</sub> is to be used. There is confusion in some settings about whether national policy exists, and concern that national and regional policies are not properly disseminated to intended audiences (moderate confidence).<sup>18,29,46–48,50,51,53,54,56,58,59,62</sup> Policies should be translated into clinical practice guidelines and made available at facility-level<sup>18,29,46,48,50,56</sup> in wards.<sup>48,59,62</sup>

**Finding 8.4:** In practice, guidelines are sometimes not followed. Although some providers are interested in guidelines and believe that they are useful, others are resistant to change, unaware or disinterested. At facility-level, the protocols used are sometimes inconsistent with national and international guidelines. Increased monitoring and obligations are perceived to improve compliance (moderate confidence).<sup>18,29,44,46–48,50,55,58,59,62</sup> A lack of interest or awareness about guidelines and updates is noted particularly among older physicians.<sup>50,55,58</sup> Facility administrators and providers are not obligated to follow policies or guidelines.<sup>18,44,50,55</sup> Variable protocols at facility-level can leave staff confused and result in practice that is not consistent with national or international recommendations.<sup>44,50,56,59</sup>

## 9. Research dissemination and advocacy by 'champions' can facilitate uptake

**Finding 9.1:** Evidence from research, such as clinical trials of effectiveness, can influence clinical practice and improve MgSO<sub>4</sub> use if key results are properly disseminated and translated for the local setting. Local experience may be more persuasive for some than international research. Accordingly, MgSO<sub>4</sub> uptake may be more likely where local researchers have participated in trials, because they advocate its use and enhance credibility of findings for the local setting (moderate confidence).<sup>29,44,50,55,62</sup> Local participation in international trials

may increase the uptake of MgSO<sub>4</sub> by developing local champions<sup>29</sup> and increasing the local credibility of findings or providing local complementary evidence.<sup>55,62</sup> Dissemination of research findings may be via journal publication<sup>44</sup> and participation by researchers in policy formulation.<sup>55</sup>

**Finding 9.2:** Stakeholders can act as 'champions' of MgSO<sub>4</sub> use by raising awareness of its effectiveness, issuing guidelines or policies for use, and encouraging uptake at both policy and implementation levels. This role can be performed by individuals (including policy-makers and clinicians) and organisations (including medical associations, non-profit organisations and international agencies) (moderate confidence).<sup>29,44,49,55,62</sup> Champions' influence may increase 'political will' and put the issue 'on the policy agenda'.<sup>44,49,55,62</sup>

Figure 3 depicts abbreviated findings using the COM-B model to understand how addressing factors affecting implementation may influence behaviour change toward appropriate use of MgSO<sub>4</sub>. Within each COM-B domain, we mapped facilitators and barriers to physical and psychological capability, and physical and social opportunity, and how the interplay between these domains influences motivation (reflective and automatic). When these facilitators are reinforced, and barriers are addressed, we expect behaviour (appropriate use of MgSO<sub>4</sub> for pre-eclampsia/eclampsia) to improve. In turn, positive experience using MgSO<sub>4</sub> reinforces providers' capability, opportunity and motivation to continue its use.

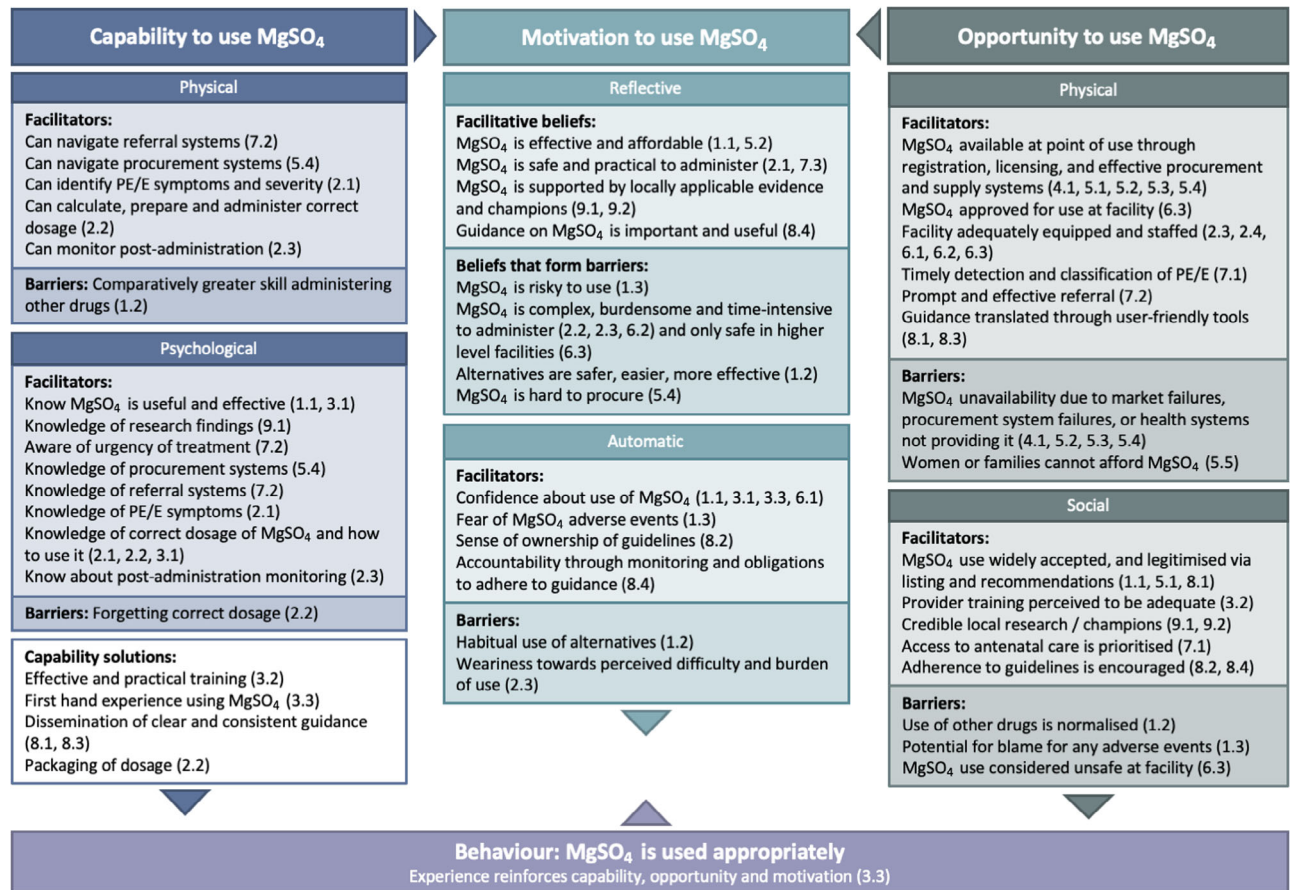
## Discussion

### Main findings

This QES revealed a broad range of factors affecting MgSO<sub>4</sub> use operating across multiple health system levels. First, whether providers will use MgSO<sub>4</sub> appropriately depends on their competence and confidence, which may be undermined by MgSO<sub>4</sub>'s unfamiliarity and perceived riskiness, and strengthened through training and experience. Second, appropriate MgSO<sub>4</sub> use depends on the capability of health systems to ensure that it is consistently available at facilities that are adequately resourced and accessible to women. Finally, appropriate MgSO<sub>4</sub> use depends on effective knowledge translation through research dissemination, clear guidelines and protocols, and local champions.

The COM-B model shows how factors may be addressed to improve the implementation of MgSO<sub>4</sub>. Appropriate MgSO<sub>4</sub> use depends on the collective behaviour of policy-makers promoting MgSO<sub>4</sub> and ensuring its availability, administrators translating policy into practice by creating an enabling environment<sup>63</sup> for MgSO<sub>4</sub> use, and providers making appropriate clinical decisions to administer MgSO<sub>4</sub> for individual women. The model can be used to inform





**Figure 3.** COM-B model of appropriate use of MgSO<sub>4</sub>.

development of interventions for particular settings by providing a framework to consider the full range of options and select the best option to target specific barriers.

### Interpretation

The factors identified in this QES are consistent with those found in other studies, such as Ridge et al. who used a case study to develop a 'fishbone diagram' of requirements for rational use of MgSO<sub>4</sub> at a health facility in Zambia.<sup>64</sup> Our QES furthers this understanding, by combining evidence from a global synthesis of qualitative evidence with the COM-B model to explore how such factors affect behaviour. Many of our findings align with evidence from quantitative studies, including providers' preference for diazepam<sup>65–67</sup> and desire for simplified dosing regimens,<sup>25,26,68</sup> concerns about availability of MgSO<sub>4</sub>,<sup>25,64,65,69,70</sup> and the impact of inadequate resourcing.<sup>67,71–73</sup> Task-shifting has been proposed as a solution to address staffing shortages and barriers to accessing higher-level facilities; WHO guidelines currently allow for nurses and midwives to administer MgSO<sub>4</sub> under certain circumstances (e.g. as a loading dose, or where higher-cadre staff are unavailable).<sup>74</sup>

### Implications for practice

We developed the following questions based on our findings to assist health system administrators, policy-makers and other stakeholders. When developing interventions and policies to identify and address barriers to appropriate use of MgSO<sub>4</sub> for pre-eclampsia/eclampsia in a given context, these individuals could consider the following:

#### *Increasing provider competence and confidence*

1. Are providers aware of the benefits of MgSO<sub>4</sub> compared with alternatives?
2. Do providers have pre-existing fears regarding adverse events that need to be addressed?
3. Do providers receive regular and refresher in-service training that is sufficiently practical (including clinical simulations)?
4. Can MgSO<sub>4</sub> administration processes be simplified, including through simpler, lower-dose regimens and improving calibration of how MgSO<sub>4</sub> is packaged and administered (e.g. through ready-to-use doses)?
5. Are resources and training adapted for the local context?

*Improving health system capability*

6. Is MgSO<sub>4</sub> consistently available at all health facilities in which it is recommended for use? If not, how can bottlenecks in supply chains or procurement systems be removed?
7. Is MgSO<sub>4</sub> supplied free-of-charge or at an affordable price for women and families?
8. Is MgSO<sub>4</sub> supplied in a form that is appropriate for the recommended dosage regimen?
9. Is the health facility sufficiently well-equipped to facilitate MgSO<sub>4</sub> administration?
10. In lower-resource settings with staffing shortages, can MgSO<sub>4</sub> be safely administered by lower-cadre health-care workers?

*Ensuring effective knowledge translation*

11. Are national policies consistent with international guidelines, translated into local guidelines and tools (including algorithms or job aids), and disseminated effectively?
12. Are local stakeholders equipped to 'champion' use of MgSO<sub>4</sub>?

**Strengths and limitations**

A limitation of this QES is that data regarding system-level issues (e.g. procurement and supply) were often specific to particular local contexts – only high-level, generalised conclusions could be drawn. System-level constraints and bottlenecks are likely to vary between countries and regions, and should be assessed for each implementation context. All relevant qualitative evidence since effectiveness of MgSO<sub>4</sub> for pre-eclampsia/eclampsia was demonstrated (2002 and 1995, respectively) was included, and factors affecting use may have changed over time. However, over 90% of included studies were published after 2010, so available evidence probably reflects current practices. Finally, six grey literature reports were linked to work by the Population Council's Ending Eclampsia projects in four countries,<sup>46–49,51,52</sup> and the issues explored in these projects (specifically, policy awareness and task-shifting of loading dose) may be somewhat overrepresented. This was mitigated during analysis by exploring these issues within themes identified across all included studies, and considering evidence from pre- and post-intervention reports concurrently. Although a comparison of views of different cadres of health workers would provide interesting insight into factors affecting MgSO<sub>4</sub> use from different perspectives, we were unable to explore this in our analysis, as most included studies did not report this level of detail.

Despite these limitations, this QES presents the first global review of factors affecting implementation of MgSO<sub>4</sub> to treat pre-eclampsia/eclampsia from the perspective of health system stakeholders. Taking a health systems

approach encompasses supply-side barriers at all levels, enabling a full picture of things that can 'go wrong' in the chain of events required to get MgSO<sub>4</sub> to all women who need it.

**Conclusion**

This QES identified a range of factors affecting use of MgSO<sub>4</sub> for pre-eclampsia/eclampsia relating to provider competence and confidence, health system capability and knowledge translation. Policy-makers and researchers should consider these findings when designing and implementing policies and interventions to increase appropriate use. Contrary to some providers' beliefs about the riskiness of MgSO<sub>4</sub>, in practice adverse events from MgSO<sub>4</sub> are uncommon and translation of this knowledge could improve uptake.<sup>75,76</sup> Practical training for providers, translating knowledge into clear clinical practice guidelines adapted for local contexts, and addressing systematic problems in supply chains and procurement mechanisms may improve MgSO<sub>4</sub> uptake. Studies are also exploring the efficacy of simpler, lower-dose regimens<sup>21,22,77</sup> that may be easier and safer to administer. As this review did not find evidence regarding specific dosage regimens, further primary research is needed to understand provider perspectives on specific regimens and whether some are easier to use than others.

Further research is also needed to explore the experiences, attitudes and beliefs of women and their partners or families regarding use of MgSO<sub>4</sub> for pre-eclampsia/eclampsia – including, for example, experience of pain or adverse effects. Context-specific research on facility-level stock audits or surveys of providers' knowledge and preferences could complement insights from this QES to inform local implementation strategies. Ultimately, action by policy-makers, administrators and providers across multiple health system levels will be crucial to improve uptake of this life-saving treatment.

**Disclosure of interests**

None disclosed.

**Contribution to authorship**

KEE designed this study with input from JPV and MAB. KEE, RIZ, MAB and JPV conducted study screening, data extraction, critical appraisal and GRADE-CERQual assessments. KEE led the analysis and manuscript writing, with input from RIZ, JPV and MAB. All authors reviewed and approved the final manuscript.

**Details of ethics approval**

Not applicable, this is a systematic review of published qualitative studies.

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## Data availability

Data sharing not applicable to this article as no data sets were generated or analysed during the current study.

## Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Table S1.** Summary of qualitative findings.

**Table S2.** Evidence profile.

**Table S3.** CASP assessments of included studies.

**Appendix S1.** Search strategies.

**Appendix S2.** ENTREQ statement. ■

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