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Review

Epilepsy surgery in low- and middle-income countries: A scoping review

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ABSTRACT

Background: Epilepsy surgery is an important treatment option for people with drug-resistant epilepsy. Surgical procedures for epilepsy are underutilized worldwide, but it is far worse in low- and middle-income countries (LMIC), and it is less clear as to what extent people with drug-resistant epilepsy receive such treatment at all. Here, we review the existing evidence for the availability and outcome of epilepsy surgery in LMIC and discuss some challenges and priority.

Methods: We used an accepted six-stage methodological framework for scoping reviews as a guide. We searched PubMed, Embase, Global Health Archives, Index Medicus for South East Asia Region (IMSEAR), Index Medicus for Eastern Mediterranean Region (IMEMR), Latin American & Caribbean Health Sciences Literature (LILACS), African Journal Online (AJOL), and African Index Medicus (AIM) to identify the relevant literature.

Results: We retrieved 148 articles on epilepsy surgery from 31 countries representing 22% of the 143 LMIC. Epilepsy surgery appears established in some of these centers in Asia and Latin America while some are in their embryonic stage reporting procedures in a small cohort performed mostly by motivated neurosurgeons. The commonest surgical procedure reported was temporal lobectomies. The postoperative seizure-free rates and quality of life (QOL) are comparable with those in the high-income countries (HIC). Some models have shown that epilepsy surgery can be performed within a resource-limited setting through collaboration with international partners and through the use of information and communications technology (ICT). The cost of surgery is a fraction of what is available in HIC.

Conclusion: This review has demonstrated the availability of epilepsy surgery in a few LMIC. The information available is inadequate to make any reasonable conclusion of its existence as routine practice. Collaborations with international partners can provide an opportunity to bring high–quality academic training and technological transfer directly to surgeons working in these regions and should be encouraged.

1. Introduction

About a third of people with epilepsy continue to have uncontrolled seizures despite adequate and appropriate medical treatment [1,2]. Individuals with intractable epilepsy have a poorer quality of life (QOL), increased risk of injury and cognitive decline, poor psychosocial outlook, and an increased risk of premature death compared with their seizure-free counterparts [3–6]. Over the last decades, various epilepsy surgery techniques have evolved to become major treatment options, but they are underutilized [7]. The benefits of these surgeries outweigh the associated risks in achieving seizure freedom, improving QOL, and reducing mortality [8–17]; with about 60% of those who had temporal lobe resective surgery remaining seizure-free in the long-term [18,19].

The extent of epilepsy surgery utilization, outcome, and cost are not well known in low- and middle-income countries (LMIC). A global survey between 1980 and 1990 reported few published literature from LMIC and none from Africa [20]. By the end of 1999, epilepsy surgery was present in only 26 (18.3%) of 142 LMIC [21]. Whether the high 'surgical treatment gap' is due to mere exclusions from international

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surveys or underreporting of surgical practices, it is certain that underutilization is a more serious problem in LMIC than in high-income countries (HIC), with the majority of health centers lacking the capacity to perform neurosurgery or even nonexistent and most health personnel referring surgical candidates elsewhere [22].

Some of the most important factors for the high surgical treatment gap are the lack of organized structured care, lack of infrastructure, shortage of specialists, and the cost of surgery [21,23–25]. A recent review observed that barriers to epilepsy surgery are perpetuated by the uncertainty portrayed by medical practitioners towards surgical treatments, reflecting the knowledge gap, which may be more pervasive in LMIC [26]. With the increasing evidence of surgery as an important treatment option and the higher burden of epilepsy, it is important for healthcare providers and users in LMIC to know that there is more that can be done. At the same time, however, information on the availability of epilepsy surgery is scarce. We aimed the following: i) to identify the availability of epilepsy surgery in LMIC; ii) determine resources available at these centers; iii) determine outcomes and cost of surgical procedures; and iv) discuss the challenges and possible areas for potentially closing the surgical treatment gap in resource poor settings.

2. Methodology

This review was triggered by a growing concern on the standard of care for people with drug-resistant epilepsy in LMIC. We considered various systematic approaches but decided to undertake a scoping review. We proposed that a scoping review will be an appropriate strategy to review and summarize a range of evidence in order to convey the breadth and depth of this less understood treatment option [27]. A scoping study was preferred over a systematic review or meta-analysis as it allows a range of study with varying designs to be incorporated without assessing the quality or using a systematic analytical interpretation of the literature [28]. A scoping review was therefore found to be ideal to help clarify surgical alternatives for people with medically intractable epilepsy in resource poor settings. We adopted the six-stage methodological framework previously suggested [27]. This includes: (1) identifying the research questions; (2) identifying relevant studies; (3) selecting the appropriate studies; (4) charting the data; (5) collating, summarizing, and reporting the results; and (6) a consultation exercise with key stakeholders to inform and validate study findings.

2.1. Identifying the research questions

The primary interest was to map and broadly examine the literature on epilepsy surgery in LMIC. In order to do so, we identified some research questions to guide our scope.

1. What is available regarding epilepsy surgery in LMIC from published literature?
2. What are the types of surgeries and outcomes, QOL, and cost?
3. How important is collaboration and technological transfer between HIC and LMIC?

2.2. Identifying the relevant studies

We identified papers using the following databases: PubMed, Embase, Global Health Archives, Index Medicus for South East Asia Region (IMSEAR), Index Medicus for Eastern Mediterranean Region (IMEMR), Latin American & Caribbean Health Sciences Literature (LILACS), Western Pacific Region Index Medicus (WPRIM), and African Index Medicus (AIM) via the World Health Organization (WHO) Global Index Medicus, and the African Journal Online (AJOL). The search was made using various combinations of the following keywords "epilepsy" and "surgery" or "surgical" or "surgical procedures" or "resecti*" or "disconnecti*", or "neurostimulati*" and individual LMICs according to the World Bank classification (www.worldbank.org). Medical subject headings (MeSH) were used where appropriate, and the references within each article were also reviewed to obtain further information (see Supplement 1 for the detailed search strategy). We included observational studies, clinical trials, case series, and any publication reporting the conduct of epilepsy surgery, outcomes (based on the Engel classification or equivalent), mortality, complication, QOL, or costs. Epilepsy surgery was defined as procedures undertaken mainly to control drug-resistant epilepsy as opposed to removing an acquired structural brain lesion. The surgical procedures include resective, disconnective, or neurostimulative surgical modalities, irrespective of year of publication or language.

Studies reporting neurosurgeries offered exclusively for brain tumors, infections, and other conditions not associated with epilepsy were excluded. Reviews, meta-analysis, single case reports, letters, commentaries, and editorials were excluded, but they were used as a lead to relevant publications.

2.3. Study selection

We used a two-stage selection process. The initial selection process (by MMW) involved the review of title and abstract to determine those likely to be eligible. The second part of the selection process involved two independent reviewers (MMW and FX), who reviewed potentially eligible papers in more details resorting to abstracts and full articles. No study was excluded based on language only as the authors are familiar with the major languages spoken in the regions from which reports originated.

2.4. Charting the data

In order to have a clear focus on the charting process, a form was developed to extract information from the literature (Table 1). The data-charting form was developed from the revised version of quality guidelines for presurgical epilepsy evaluation and surgical epilepsy treatment by the Austrian, German, and Swiss working group [29]. The aim of the guideline is to instruct on the minimum standard requirement for running an epilepsy surgery facility. This served as a guide to understand what is available from LMIC, as what is a minimum requirement in Europe may not be the same elsewhere particularly in LMIC [30].

2.5. Collating, summarizing, and reporting the results

We collected and sorted key information from the eligible articles and summarized them in tables. The key information in addition to the minimum standard requirements includes author, year of publication, name of center and country, period of recruitment, types of surgeries, number operated, follow-up duration, outcome measures, mortality, complications, collaborations, QOL, and cost. Where available, the outcomes from neurostimulative procedures like vagus nerve stimulation (VNS) were recorded. A narrative review was also used to report other information. We recognize the inherent challenges with retrieving data from LMIC due to varying methodologies of the papers and their reporting guidelines, therefore, some of the information we report have been derived from multiple articles and sources.

Various outcome measures are being used by surgeons, but we retrieved those reporting either the Engel or International League Against Epilepsy (ILAE) outcome classifications. The differences and their utility have been discussed in the ILAE commission report on classification of outcome following epilepsy surgery [31]. The Engel classification is widely used, but results from different centers may not be easily compared, while the ILAE classification is easier to use. The ILAE and the Engel classifications, however, have a good inter-rater reliability and significant correlation between the two [32] (Supplement 2 shows details of the outcome scores).

Table 1
The data-charting form[a].
Data of interest [To be reported as: Present (✓); Absent (×); Not mentioned (NA)].

1.	Bibliometric	Author, year of publication, country, period (year) of recruitment, type of surgery, number operated, follow-up duration, outcome measure, mortality, complications, QOL, and cost
2.	Sufficient staffing of qualified personnel	Epileptologist, neurosurgeon, neuropsychologist, and neuroradiologist, psychiatrist, nursing, and technical staff
3.	Technical equipment (minimum)	Video-EEG monitoring (VEM) unit (≥64-channel EEG, 1.5-Tesla MRI), at least two of any epilepsy-specific imaging (single-photon emission computed tomography [SPECT], positron emission tomography [PET], functional MRI [fMRI], MRI postprocessing, magnetoencephalography [MEG], and 64–256-channel EEG with source imaging [ESI]).
4.	Training of staff	A certain period of training at an epilepsy center is required.
5.	Intensive monitoring/VEM evaluation	24-Hour continuous supervision during VEM is required in case of AED reduction and for immediate recognition of emergency situations.
6.	Follow-up, quality assurance, and data acquisition	Appropriate minimum data capture. Recording of relevant pre- and postoperative data at regular intervals to ensure patient's course is documented.
7.	Cooperation/Collaboration	Close and collegial contact with leading epilepsy centers.

[a] Charting form developed from the revised version of quality guidelines for presurgical epilepsy evaluation and surgical epilepsy treatment by the Austrian, German, and Swiss working group by Rosenow et al. [29]. Serial number 2 to 7 is based on the recommendation. QOL – Quality of Life, MRI – Magnetic Resonance Imaging, AED – Antiepileptic drug, EEG – Electroencephalography.

2.6. Consultation with key stakeholders

The optional stakeholder meeting was not conducted because of the lack of funding. This work is an iterative work in progress, and findings should guide stakeholders on action areas and determine where in-depth analysis is required.

3. Results

The initial search identified a total of 1365 publications, 158 duplicates were removed while 201 full texts articles were assessed for eligibility. During the review, 53 potentially eligible studies were excluded. These included neurosurgical procedures for tumors, infections, and others that cannot be classified as epilepsy surgery. In addition, some were conference abstracts that had incomplete information and were difficult to extract (Fig. 1 shows flowchart of the selection process).

A total of 148 publications from 31 countries met the eligibility criteria; representing 21.7% of the 143 LMIC as shown in Table 2 [33–180]. The information retrieved was from published journal articles and some website sources. The publications were mainly longitudinal studies, case series, case–control studies, and one randomized controlled study. They include nine publications from six African countries [33–42], 52 publications from 12 Latin American and the Caribbean countries [43–94], 85 publications from 13 Asian countries [83, 94–176,180], and three publications from two Eastern European

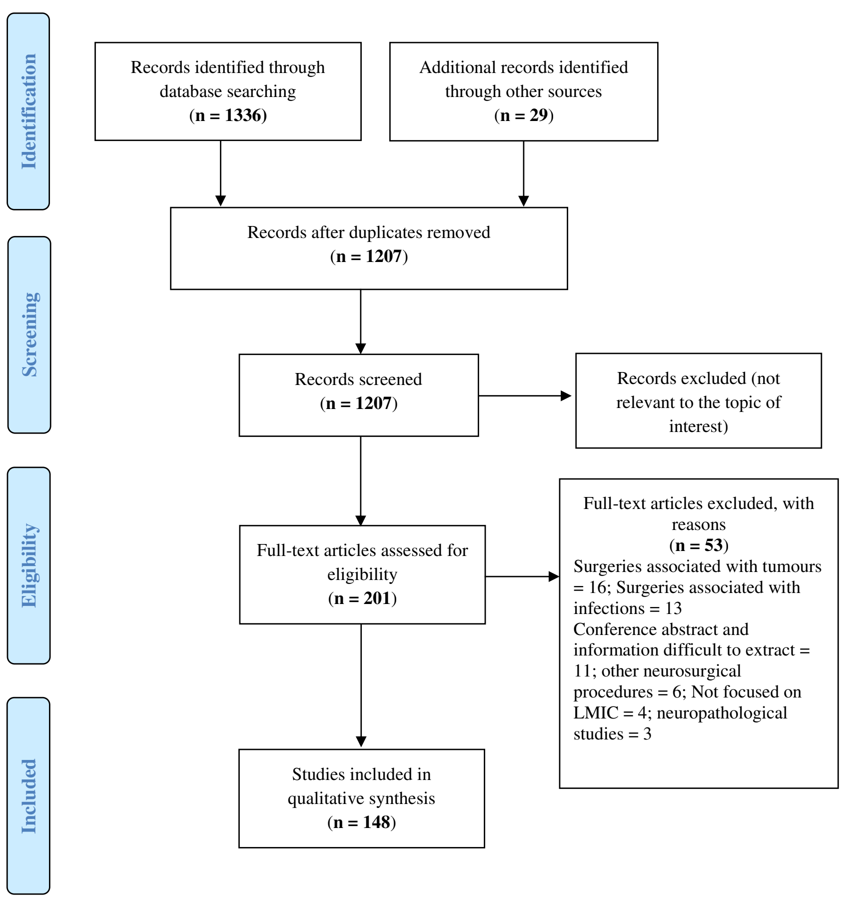

Fig. 1. Flowchart of the selection process.

Table 2
Countries and centers reporting epilepsy surgery and available resources.

Region	Country	Authors/Dates	Center/Hospital	Sufficiently qualified personnel	Minimum technical equipment	Staff training	Intensive monitoring VEM	Follow-up, quality assurance, and data acquisition	Cooperation and collaboration
Africa	South Africa	Krynauw 1950 [33]	Johannesburg Hospital	×	×	NA	×	×	NA
	South Africa	Butler 2005 [34]	Two university neurology departments and a private epilepsy center	✓	✓	NA	NA	NA	NA
	Kenya	Ruperti 1997 [35]	African Neurological Diseases Research Foundation	×	×	NA	NA	NA	NA
	Uganda	Boling et al. 2009 [36], Fletcher et al. 2015 [37], Mandell et al. 2015 [38]	CURE Children's Hospital of Uganda (CCHU)	✓	×	✓	✓	✓	✓ASHA, USAID, ICTEUS, MNI and Stellate Inc.
	Morocco (Rabat)	Lahjouji et al. 2009 [39]	Hôpital des Spécialités, CHU Rabat	NA	✓	NA	✓	✓	×
	Morocco (Fez)	Souirti et al. 2016 [40]	Hassan II University Hospital of Fez	×	✓	NA	✓	✓	✓
	Tunisia	Khiari et al. 2010 [41]	Charles Nicolle Hospital Tunis	×	✓	✓	✓	✓	✓Charles Nicolle Hospital, Rouen EUMEDCONNECT network project
	Egypt	Kassem et al. 2013 [42]	Cairo University Hospital	✓	✓	NA	✓	✓	×
Latin America and the Caribbean	Brazil	Alonso et al. 2006 [43], Araújo Filho et al. 2012 [44], Jardim et al. 2012 [45]	Universidade Federal de São Paulo, (UNIFESP)	✓	✓	NA	✓	✓	×
	Brazil	Amaral et al. 2014 [46]	Universidade Federal de Minas Gerais (UFMG)	NA	✓	NA	✓	NA	×
	Brazil	Frayman et al. 1999 [47], Cukiert et al. 2000 [48], Baldauf et al. 2006 [49]	Epilepsy Surgery Program, Hospital Brigadeiro, São Paulo	NA	✓	NA	✓	✓	×
	Brazil	Zanni et al. 2009 [50], Meguins et al. 2015 [51], Meguins et al. 2015 [52]	Faculdade de Medicina de Sao Jose do Rio Preto (FAMERP)	✓	✓	NA	✓	✓	NA
	Brazil	Paglioli et al. 2004 [53] Almeida et al. 2010 [54], Hemb et al. 2013 [55]	Epilepsy Surgery Center, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre	✓	✓	NA	✓	✓	NA
	Brazil	Meneses et al. 2005 [56], Meneses et al. 2013 [57], Nascimento et al. 2016 [58]	Universidade Federal do Paraná (UFPR), Curitiba	✓	✓	NA	✓	✓	×
	Brazil	Guimarães et al. 2003 [59], Bonilha et al. 2004 [60], Yasuda et al.2009 [61], Gagliardi et al. 2011 [62]	UNICAMP Campinas Sao Paulo	✓	✓	NA	✓	✓	×
	Brazil	Sales et al. 2006 [63], Terra et al. 2010 [64], Bianchin et al. 2014 [65]	Center for Epilepsy Surgery at Ribeirao Preto (CIREP), University of São Paulo	✓	✓	✓	✓	✓	×
	Chile	Campos et al. 2000 [66]	Catholic University of Chile, Santiago Chile.	×	✓	NA	✓	✓	×
	Chile	Acevedo et al. 2015 [67]	Instituto de Neurocirugia Asenjo (INCA)	×	✓	NA	✓	✓	×
	Costa Rica	Brian et al. 2003 [68]	Hospital Nacional de Niños, Centro Ciencias Médicas “Dr. Carlos Sáenz Herrera”	NA	NA	NA	✓	✓	×
	Ecuador	Fernandez-Concepcion et al. 2018 [69]	Hospital Baca Ortiz in Quito,	✓	✓	NA	✓	✓	×
	Colombia	Fandino-Franky 2000 [70], Tureczek et al. 2000 [71], Benedetti-Isaac et al. 2013 [72], Benedetti-Isaac et al. 2015 [73]	Hospital Neurologico Liga Colornbiana Contra La Epilepsia, Cartagena, Colombia.	✓	✓	NA	✓	✓	✓
	Colombia	Freire et al. 2016 [74]	Fundación cardiovascular of Colombia, Bucaramanga	✓	✓	NA	✓	✓	×
	Bolivia	Jiménez Torres et al. 2014 [75]	Neurología/Neurocirugía del Hospital Materno Infantil de la Caja Nacional de Salud Regional La Paz,	✓	✓	NA	✓	✓	×
	Peru	Mejía-Tupa et al. 2014 [76], Mejía-Tupa et al. 2015 [77]	Hospital Nacional Guillermo Almenara (HNGAI) EsSalud. Lima	✓	✓	✓	✓	✓	×
	Argentina	Pomata et al. 2010 [78], Caraballo et al. 2011 [79], Vázquez et al. 2008 [80], Vázquez et al. 2008 [81]	Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires	✓	✓	✓	✓	✓	×
	Argentina	Donadıo et al. 2011 [82], Zaknun et al. 2008 [83]	Institute for Neurological Research FLENI, Buenos Aires	✓	✓	✓	✓	✓	✓

	Argentina	Oddo et al. 2012 [84]	Epilepsy Center of the Hospital Ramos Mejıa	✓	✓	NA	✓	✓	NA
	Mexico	Velasco Monroy et al. 2013 [85]	Epilepsy Clinic of the General Hospital of México	✓	✓	NA	✓	✓	×
	Mexico	Alonso-Vanegas et al. 2010 [86], Alonso-Vanegas et al. 2016 [87], Alonso-Vanegas et al. 2017 [88]	National Institute of Neurology and Neurosurgery and Centro Neurológico Centro Médico ABC Santa Fe	✓	✓	NA	✓	✓	×
	Uruguay	Surgical Programme of Epilepsy [89], Natola et al. 2011 [90]	Institute of Neurology University Hospital, Montevideo, Uruguay	NA	✓	NA	✓	NA	NA
	Venezuela	Gonzalez et al. 2017 [91],	Hospital Universitario de Caracas	✓	✓	NA	✓	NA	NA
	Cuba	Chacón et al. 2009 [92], Bender del Busto et al. 2010 [93], Morales et al. 2009 [94]	International Neurological Restoration Center (CIREN), Havana	✓	✓	NA	✓	NA	NA
Asia and Europe	India	Bhatia et al. 1999 [95], Shukla et al. 2003 [96], Sarkar et al. 2006 [97], Ahmad et al. 2007 [98], Tripathi et al. 2008 [99], Chandra et al. 2008 [100], Zaknun et al. 2008 [83], Dagar et al. 2011 [101], Chandra and Tripathi 2015 [102], Dwivedi et al. 2017 [103], Malhotra et al. 2016 [104], Barbaro et al. 2018 [105]	All India Institute of Medical Sciences (AIIMS) New Delhi	✓	✓	✓	✓	✓	✓
	India	Daniel and Chandy 1999 [106], Daniel et al. 2001 [107]	Christian Medical College, (CMC) Vellore	✓	✓	✓	✓	✓	NA
	India	Rao and Radhakrishnan 2000 [108], Sylaja et al. 2004 [109], Panda et al. 2005 [110], Radhakrishnan et al. 2007 [111], George et al. 2009 [112], Ramesha et al. 2009 [113], Chemmanam et al. 2009 [114], Chaudhry et al. 2010 [115], Ramesha et al. 2011 [116], Dash et al. 2012 [117], Asranna 2017 [118], Rao et al. 2017 [119]	R. Madhavan Nayar Center for comprehensive Epilepsy Care, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum (SCTIMST), Kerala	✓	✓	✓	✓	✓	NA
	India	Jayalakshmi et al. 2011 [120], Panigrahi et al. 2016 [121]	Krishna Institute of Medical Sciences (KIMS), Secunderabad and Hyderabad	×	✓	✓	✓	✓	NA
	India	Ravat et al. 2016 [122], Ravat et al. 2016 [123], Shah et al. 2016 [124]	Comprehensive Epilepsy care Centre, King Edward VII Memorial (KEM) Hospital, Mumbai	✓	✓	NA	✓	✓	NA
	Bangladesh	Chowdhury et al. 2010 [125]	Department of Neurosurgery, Dhaka Medical College Hospital, Dhaka	✓	×	NA	×	✓	NA
	China	Liang et al. 2010 [126]	Capital Epilepsy Therapy Center in Beijing. First Affiliated Hospital of General Hospital of PLA	✓	✓	NA	✓	✓	×
	China	Guan et al. 2013 [127]	Beijing Sanbo Brain Hospital, Capital Medical University, Beijing	✓	✓	NA	✓	✓	×
	China	Dong et al. 2012 [128]	First Affiliated Hospital Baotou Medical College	✓	✓	NA	✓	NA	×
	China	Wang et al. 2011 [129]	Third People's Hospital Bengbu Anhui	✓	✓	NA	✓	NA	×
	China	Guangming et al. 2013 [130]	Epilepsy Center, Yuquan Hospital Tsinghua University	✓	✓	NA	✓	NA	×
	China	Jia-tang et al. 2008 [131]	The Second Affiliated Hospital of Guiyang Medical College	NA	✓	NA	✓	NA	×
	China	Kuang et al. 2011 [132]	Chengdu General Hospital of Chengdu Military Command.	✓	✓	NA	✓	NA	×
	China	Liang et al. 2015 [133]	Hebei General Hospital, Shijiazhuang	✓	✓	NA	✓	NA	×
	China	Liang et al. 2012 [134]	First Affiliated Hospital of Chinese People's Liberation Army General Hospital (1 of 4 centers)	✓	✓	NA	✓	✓	✓
	China	Luan et al. 2002 [135], Sun et al. 2002 [136], He et al. 2015 [137], Meng et al. 2015 [138]	Beijing Tiantan Hospital	NA	✓	NA	✓	NA	×
	China	Yang et al. 2007 [139], Yang et al. 2008 [140], Yang et al. 2009 [141]	Xinqiao Hospital, Third Military Medical University	NA	✓	NA	✓	NA	×
	China	Yang et al. 2004 [142], Yang et al. 2007 [143]	General Hospital Tianjin Medical University, Tianjin	NA	✓	NA	✓	NA	×
	China	Wu et al. 2011 [144], Zeng et al. 2012 [145], Zeng et al. 2014 [146], Chen and Lei 2014 [147]	West China Hospital of Sichuan University	✓	✓	NA	✓	✓	×
	China	Yang et al. 2014 [148], Yang et al. 2014 [149]	Epilepsy Centre, Fuzhou General Hospital	✓	✓	NA	✓	✓	×
	China	Yu et al. 2014 [150], Wang et al. 2009 [151]	Fourth Neurosurgery Center of the Affiliated Hospital of Harbin Medical University	✓	✓	NA	✓	✓	×
	China	Lin et al. 2001 [152]	First Affiliated Hospital, Fujian Medical	✓	✓	NA	✓	✓	×

(continued on next page)

Table 2 (*continued*)

Region	Country	Authors/Dates	Center/Hospital	Sufficiently qualified personnel	Minimum technical equipment	Staff training	Intensive monitoring VEM	Follow-up, quality assurance, and data acquisition	Cooperation and collaboration
			University						
	China	Zonghui et al. 1997 [153]	General Naval Hospital Beijing	NA	✓	NA	✓	NA	×
	China	Piao et al. 2010 [154]	Beijing Institute of Functional Neurosurgery, Xuanwu Hospital, Capital Medical University	NA	✓	NA	✓	NA	×
	Jordan	Al-Ghanem et al. 2009 [155], Faleh-Tamimi and Qudah 2002 [156]	Jordan University Hospital, Amman	✓	✓	NA	✓	✓	×
	Jordan	Aburahma et al. 2015 [157]	King Abdullah University Hospital and Jordan University Hospital in Jordan	✓	✓	NA	✓	✓	×
	Saudi Arabia	Alsemari et al. 2014 [158]	King Faisal Specialist Hospital & Research Centre (KFSHRC)	✓	✓	NA	✓	✓	×
	Thailand	Locharernkul et al. 2005 [159], Kanchanatawan and Kasalak 2012 [160], Kanchanatawan et al. 2014 [161], Srikijvilaikul et al. 2004 [162], Zaknun et al. 2008 [83]	Chulalongkorn Comprehensive Epilepsy Program (CCEP), Chulalongkorn University Hospital	✓	✓	✓	✓	✓	✓
	Thailand	Visudhiphan 1999 [163]	Ramathibodi Hospital, Bangkok	NA	✓	NA	✓	✓	×
	Thailand	Kitwitee et al. 2017 [164]	Prasat Neurological Institute (PNI)	✓	✓	NA	✓	✓	×
	Lebanon	Mikati et al. 2006 [165], Mikati et al. 2012 [166]	American University of Beirut	✓	✓	NA	✓	✓	✓
	Pakistan	Ahmed et al. 2009 [167], Tahir et al. 2012 [168], Sheerani 2005 [169]	Aga Khan University Hospital	✓	✓	NA	✓	✓	✓University of Alberta Hospital (UAH), West Virginia University
	Iran	Asadi-Pooya et al. 2013 [170], Asadi-Pooya et al. 2014 [171], Asadi-Pooya et al. 2015 [170]	Shiraz University of Medical Sciences	✓	✓	NA	✓	✓	✓Thomas Jefferson University,
	Iran	Pakdaman et al. 2016 [172]	Loghman Hospital Tehran	NA	✓	NA	NA	NA	×
	Turkey	Ozkara et al. 2000 [173], Aydemir et al. 2004 [174]	Istanbul University, Istanbul,	✓	✓	NA	✓	✓	×
	Turkey	Hirfanoglu et al. 2016 [175]	Gazi University School of Medicine	✓	✓	NA	✓	✓	×
	Malaysia	Sayuthi et al. 2009 [176]	Hospital University Sains Malaysia	NA	✓	NA	✓	✓	NA
	Georgia	Kasradze et al. 2015 [177]	Epilepsy Center of Institute of Neurology and Neuropsychology (ECINN), Tbilisi	NA	✓	NA	✓	✓	×
	Georgia	http://www.augusta.edu/mcg/neurology/epilepsy/adult/epsurgery.php [178]	Augusta University Surgical Epilepsy Surgery	✓	✓	NA	✓	✓	×
	Moldova	Matkovskii et al. 2007 [179]	The epilepsy center of the Republic of Moldova	NA	✓	NA	✓	NA	NA

Information from some of these centers was acquired from more than one publication. ✓Available; ×Not available; NA — Not mentioned/unsure. MNI — Montreal Neurological Institute, ASHA — American Schools and Hospitals Abroad, USAID — United States Agency for International Development, ICTEUS — The International Consortium for the Treatment of Epilepsy in Underserved Settings.

countries [177–179]. The bulk of the published literatures are from India, China, and Brazil. The papers retrieved spanned over 60 years, but only seven papers were published before the year 2000. A closer look at some of these papers especially from India, Brazil, and China reveal multiple publications from the same cohort. These publications show that a more recent paper incorporates subjects or is a subset of a cohort reported from older papers.

The results on the minimum standard requirements (Table 2) showed that most centers had the minimum technical equipment. Information on whether they had sufficient qualified personnel or adequate training was mainly not mentioned or difficult to extract. Some papers reported on collaborative work between HIC and LMIC in Uganda [36–38], Tunisia [41], Thailand, India, and Argentina [83,105], Pakistan [168], and Iran [171]. The collaborative epilepsy surgery program between North America and the CURE Children's Hospital of Uganda (CCHU) assessed the feasibility of an epilepsy surgery program in a resource-poor setting using just video-electroencephalography (EEG) and computed tomography (CT) volumetric analysis [38]. The Tunisian epilepsy surgery program at the Charles Nicolle Hospital Tunis and the French hospital at Rouen via the EUMEDCONNECT, is an internet network project where clinical, EEG, and radiological information are transferred from Tunis to France for discussion and evaluation [41].

Detailed illustration of the general characteristics, outcomes measures, complications, and mortality is shown in Supplement 3. Table 3 shows the general characteristics of 98 papers reporting outcome measures of various epilepsy surgeries according to either the Engel or ILAE classifications. The commonest surgeries performed at these centers are temporal and extratemporal resective surgeries, disconnective surgeries like corpus callosotomies, hemispherectomies, and subpial resections. The varying reporting methods, number of candidates, classification of surgery type, and the duration of follow-up made reporting our results on outcome difficult. The majority reported outcome measures based on the Engel classification. The reported outcome measures ranged mostly between 40% and 80% (for Engel Class I) and 50% and 90% (for Engel Classes I and II) in carefully selected subjects. Complications are transient or minor while major complications or mortality is rare. These results appear better for temporal lobe surgeries. Table 4 shows neurostimulative techniques like VNS [57,86,120,138,151,157,172] and deep brain stimulation [73], which reflected that the majority of subjects had more than 50% seizure reduction with follow-ups ranging between one to four years.

Table 5 showed that the indicators of QOL improved after surgery [37,47,50,59,93,98,101,122,126,134,159,160,165,174,176], except in one study [62].

Table 6 reports on the cost of epilepsy surgery [66,70,71,114,117,144,147,164,168,171,180] and VNS [138], the cost of epilepsy surgery at 2014 ranges between US$500 in Iran to approximately US$8000 in China.

4. Discussion

We attempted to assess the situation of epilepsy surgery in LMIC. The current status of published evidence reports epilepsy surgery in about a fifth of LMIC. Our findings suggest that the utilization of epilepsy surgery has evolved considerably in some centers in Asia and Latin America with an increasing trend in India, China, and Brazil [182] but appears embryonic in some other countries, particularly in sub-Saharan Africa. A large proportion of the retrieved articles are case series or experiences using small sample size of carefully selected candidates performed by motivated neurosurgeons and may not necessarily portray that epilepsy surgery is an established current practice in these countries. We observed that epilepsy centers were not evenly distributed but located in bigger more affluent cities. This geographical disparity has been observed in a previous review [21]. A review of epilepsy surgery in India showed that geographical disparity is a common problem, and only 2 centers in big cities contributed to more than 50% of 420 surgeries performed annually, which is far from adequate [183].

The surgeries reported were mainly resective, few disconnective, and much fewer neurostimulative techniques. The commonest procedure was temporal lobe resections as these are more likely to have an impact in terms of seizure freedom [18]. Seizure outcome after surgery was good in the majority of subjects and comparable with those reported from centers in HIC. Similarly, complications and mortalities from surgery did not appear to be significantly different from those in HIC [17,184]. Those that had surgery also had an improved QOL, employability, and lower perceived stigma compared with those who did not, especially for those who were seizure-free [37,50,159]. The similar short-term outcome rates in LMIC compared with HIC may be due to centers performing straightforward cases in carefully selected candidates. It will be important to establish the longer-term outcome of these candidates, but some of the studies had a high loss to follow-up that is a common problem in LMIC [185].

Some of the established centers had adequate infrastructure, manpower, and training, but this is not universal. The Ugandan experience shows that the lack of sophisticated modern equipment should not be a limitation to surgery [36,38]. Their model utilized technology and expertise that was reasonably available and could function sustainably in resource-poor setting. Training was possible through the establishment of collaborations with neurosurgeons in HIC. This form of collaboration where expert skill and knowledge were exchanged with centers in the West was also noted at the Charles Nicolle Hospital in Tunisia [41], the Aga Khan University Hospital in Pakistan [167], and the Shiraz University of Medical Sciences in Iran [171]. The successes of these models were achieved through the tri-facetted approach of technological transfer, twinning, and manpower training [30]. It also shows the role information and communications technology (ICT) can play in intellectual and skills transfer, showing that the model used could be replicated elsewhere. With comparable seizure-free rates with HIC, these surgical experiences give hope that epilepsy surgery can be a routine treatment using the minimum available requirements that are more likely to be available in LMIC in comparison with the myriad of equipment used in more affluent societies for epilepsy surgeries. The Pediatric Epilepsy Surgery Task Force of the ILAE Commissions of Pediatrics and Diagnostics in formulating recommendations for presurgical evaluation in children observed that many of the tests employed are resource intense and that failure to carry out all diagnostic tests possible nor insisting on one particular ancillary test should not hamper the conduct of surgery. They suggested that evaluation should be done according to the needs of the clinical cohorts and country-specific resources [186]. The training of personnel in view of the profound manpower shortages in LMIC can be done through collaborations with experts from HIC [187].

The cost of epilepsy surgery reported is a fraction of what it costs in western countries [71]. The issues of cost and affordability are not straightforward [188], as what is regarded as cheap may not necessarily be affordable to the majority of people in LMIC, as those who access this care are probably city dwellers, more educated, and of higher socioeconomic class [26]. Epilepsy surgery is an expensive venture requiring some of the most expensive technologies in the surgical field. Establishing neurosurgical centers is, therefore, a challenge for most LMIC with an already dysfunctional primary care system and the majority of persons unable to access firstline antiepileptic drugs. In view of the high burden of epilepsy in LMIC, it is debated whether surgery may be a cost-effective long-term investment that may benefit more people in the long run [188]. Studies evaluating the costs of surgical versus medical treatment observed that although surgical treatment requires a large initial expenditure, it was superior because of the greater seizure-free rate, with the long term cost-analysis favoring surgery as the cost–time curves intersect in a few years [189–191]. These cost-analyses comparing medical and surgical therapy of epilepsy should be interpreted with caution since the cost of surgery and benefit gained by seizure reduction are not linear and that measuring just the

Table 3
Epilepsy surgery outcomes from low- and middle-income countries.

Author/Date	Country	Number operated	Follow-up duration	Type of surgeries	Seizure outcome	
					Engel score I	Engel score I and II
Boling et al. 2009 [36]	Uganda	10	1 year	CAH	60%	80%
Fletcher et al. 2015 [37]	Uganda	10	8 years	CAH	70%	
Souirti et al. 2016 [40]	Morocco	7		Hippocampectomy, lesion excision	57%	71.3%
Khiari et al. 2010 [41]	Tunisia	10	2 years	Hippocampectomy	40%	
Kassem et al. 2013 [42]	Egypt	137	1 year	Hippocampectomy		> 70%
Bonilha et al. 2004 [60]	Brazil	30	46 months	Anterior TL resection plus AH	53%	83%
Alonso et al. 2006 [43]	Brazil	35	6 months	CAH	51%	
Araújo Filho et al. 2012 [44]	Brazil	115	4.7 ± 1.66 years	CAH	69.5%	89.5%
Jardim et al. 2012 [45]	Brazil	66	≥6 months	Temporal lobe resection	72.7%	89.4
Amaral et al. 2014 [46]	Brazil	34		Temporal lobe resection		64.7%
Baldauf et al. 2006 [49]	Brazil	41	4.3 ± 1.1 years	CAH	95.1%	100%
Meguins et al. 2015 [51]	Brazil	127	1 year	NCC associated TLE	62.2%	91.3%
Paglioli et al. 2004 [53]	Brazil	135	1 year	Temporal lobe resection	89%	
			2 years		86%	
			5 years		83%	
			10 years		81%	
Almeida et al. 2010 [54]	Brazil	384		Temporal epilepsy and extratemporal epilepsy	91.4%	
Meneses et al. 2005 [56]	Brazil	43		Temporal lobe surgery	83.7%	
Nascimento et al. 2016 [58]	Brazil	67	64 months (median)	ATL and SAH		82%
Yasuda et al. 2009 [61]	Brazil	67		Anterior temporal lobe resection plus AH		85%
Bonilha et al. 2004 [60]	Brazil	30	46 months	Anterior temporal lobe resection plus AH	53%	83%
Terra et al. 2010 [64]	Brazil	267	~5 years	Temporal lobectomy, hemispherectomy, Lesionectomy, multilobar resections, lobectomy, CC, SAH	–	72.6%
Bianchin et al. 2014 [65]	Brazil	191		Anterior temporal resection	74%	
Campos et al. 2000 [66]	Chile	17	29.1 months	ATL	88.2%	94.1%
Pomata et al. 2010 [78]	Argentina	150	1 year	CDM resections, lesionectomy, corticoectomy, ATL, CAH, CC	75.3%	86.6%
Caraballo et al. 2011 [79]	Argentina	45	9.5 years	Hemispherectomy	73.5%	86.8%
Donadıo et al. 2011 [82]	Argentina	84	1 year	Lobectomies, CC, MST, VNS, lesionectomies, hemispherectomies	72.6%	89.2%
		110	1–3 years		68.1%	84.0%
			3–5 years		74%	88.0%
		45	5 years		78%	91.5%
Vázquez et al. 2008 [80]	Argentina	91		TLR	84.6%	94.5%
Vázquez et al. 2008 [81]	Argentina	49		Hemispherectomy	81.6%	89.8%
Oddo et al. 2012 [84]	Argentina		1 year	Temporal lobectomy	85.7%	84.2%
Velasco Monroy et al. 2013 [85]	México	57	1 year	ATL with AH	84%	
Alonso-Vanegas et al. 2016 [87], Alonso-Vanegas et al. 2017 [88]	Mexico	67	5.7 years	SMA resection using subpial/endopial technique	61%	92%
Fandino-Franky 2000 [70]	Colombia	97	35 months	CC		66.3%,
Tureczek et al. 2000 [71]	Colombia	89	6 years	ATL	81%	97%
		11	6 years	Hemispherectomies	45.5%	81.9%
		80	6 years	Corpus callosotomy	30%	71.3%
Benedetti-Isaac et al. 2013 [72]	Colombia	21	6.5 years	Temporal lobectomies		90.5%
Jiménez Torres et al. 2014 [75]	Bolivia	16		TLR and extra-TLR	50%	69%
Mejía-Tupa et al. 2014 [76]	Peru	7		Hemispherectomy, lesionectomy, TR	71%	
Bhatia et al. 1999 [95]	India	20	20.5 months	TL, extratemporal resection, CC	65%	75%
Shukla et al. 2003 [96]	India	25	16.8 months	Extratemporal resection		87%
Ahmad et al. 2007 [98]	India	36	6 months	ATL, subpial-AH, extratemporal lesionectomy	77%	
Tripathi et al. 2008 [99]	India	57	3.0 ± 5.8 years	Resection ± MST Hemispherotomy in one	51%	77%
Chandra et al. 2008 [100]	India	19	6.5 years	Hemispherotomy	95%	100%
Dagar et al. 2011 [101]	India	118	≥1 year	TL, ALTL, extratemporal resections, CC, VNS hemispherotomies	79.5%	88.4%
Chandra and Tripathi 2015 [102]	India	11	8.4 months	Endoscopic hemispherotomy	81.8%	100%
		7	9.2 ± 1.46 months	Endoscopic disconnection for HH	71.4%	85.7%
Dwivedi et al. 2017 [103]	India	57	1 year	TLR, extra-TLR, hemispherotomy, CC, HH	77.2%[a]	84.2%[a]
Daniel and Chandy 1999 [106]	India	80	10 years	Topectomy ± amygdalectomy, TL ± amygdalectomy, hippocampectomy, amygdalectomy, hemispherectomy, stereotactic ansotomy		53%
Daniel et al. 2001 [107]	India	6		Peri-insular hemispherotomy	83.3%	99.9%
Rao and Radhakrishnan 2000 [108]	India	119	1 year	ATL	53.4%	
		68.	2 years	ATL	67.6%	
		29	3 years	ATL	69%	
Sylaja et al. 2004 [109]	Indian	17	≥1 year	ATL	29.4%	
Panda et al. 2005 [110]	India	34	4 years (median)	Lesionectomy, ATL, AH, SAH.	79%	94%
Radhakrishnan et al. 2007 [111]	India	373	4.5 years (median)	ATL ± AH, SAH	70.5%	

Table 3 (*continued*)

Author/Date	Country	Number operated	Follow-up duration	Type of surgeries	Seizure outcome	
					Engel score I	Engel score I and II
George et al. 2009 [112]	India	172	4.9 ± 1.1 years	ATL		78.5%
Ramesha et al. 2009 [113]	India	10	2 years	Hemispherotomy, hemispherectomy or focal resection	70%	
Chemmanam et al. 2009 [114]	India	48		TLR, extratemporal resections, CC, VNS.	78.4% for TLR	
Chaudhry et al. 2010 [115]	India	61	5 years (median)	Lesionectomy, lobectomy, frontal cyst decompression, multilobar resection, MST, AH		62.7%
Dash et al. 2012 [117]	India	71	2.6 years	Extratemporal resective surgery	73.2%	
Jayalakshmi et al. 2011 [120]	India	87	2.6 years	ATL with AH, lesionectomy, and functional hemispherectomy	64.1%	
Panigrahi et al. 2016 [121]	India	697	≥ 1 year	TL, lesionectomy, multilobar resections, hemispherotomy, CC, HH resection, VNS		85.7% for TLE 65.2% for ETLE
Ravat et al. 2016 [122]	India	34	62 months	ATL with AH, lesionectomy	85.3%	91.2%
Ravat et al. 2016 [123]	India	51	33 months	Lesionectomy, lesionectomy ± ATL	84.3%	90.2%
Guan et al. 2013 [127]	China	16	1.6 years	Temporoparietooccipital and parietooccipital disconnection	81%	87.3%
Dong et al. 2012 [128]	China	15	≥6 months	TL, SAH, lesionectomy		80%
Wang et al. 2011 [129]	China	65	6 months–11 years	Resection of degenerative brain tissues, TL, CC, MST	40%	53.8%
Kuang et al. 2011 [132]	China	32	1 year	Microsurgical excision, partial ATL, hippocampectomy, amygdalotomy and bipolar electrocoagulation	84.4%	
Liang et al. 2010 [126]	China	29	1 year 2 years 3 years	Tuber resections, ± lobectomies ± CC	72% 60% 54.5%	88% 80% 72.7%
Liang et al. 2015 [133]	China	14	1 year 3 years	CC	28.6% 22.2%	
Liang et al. 2012 [134]	China	206 children	1 year 2 years 5 years	Lesion resection, ATL and SAH	84.0% 72.3%, 67.5%	94.2% 87.8% 85.0%
Luan et al. 2002 [135]	China	108	1–5 years	Bipolar electrocoagulation on functional cortex	75.9%	
Sun et al. 2002 [136]	China	15	3–12 months	Combined surgeries: CC, hippocampectomy, resections and bipolar coagulation	93%	
Yang et al. 2007 [139]	China	114	1–5 years	TL, extratemporal lobectomy and AH	74.6%	88.6%
Yang et al. 2008 [140]	China	189	1–14 years	ATL, extra-TL, AH	62.4%	77.7%
Yang et al. 2009 [141]	China	236	2–15	ATL, extra-TL, AH; MST	67.4%	81.8%
Yang et al. 2004 [142]	China	45	3–28 months.	MST; epileptogenic zone resection; anterior CC, AH	37.8%	
Yang et al. 2007 [143]	China	16	6–32 months	Stereotactic AH; MST	44%	69%
Wu et al. 2011 [144]	China	143	1–3 years	ATL, lesionectomy, hemispherectomy For FLE	63.8% 61.1%	85.1% 72.7%
Zeng et al. 2012 [145]	China	131	6 months 2 years	TL, extratemporal surgery TL, extratemporal surgery	79.4% 61.0%	 77.8%
Zeng et al. 2014 [146]	China	319	6 months 2 years 5 years	TLE, ETLE and hemispherectomy	71.5% 65.5% 34.2% no AEDs 32.6% with AEDs	
Chen and Lei 2014 [147]	China China	100 100	2 years 3 years		73% 75%	
Yang et al. 2014 [148]	China	133	>2 years	Resections	48.9%	72.2%
Lin et al. 2001 [152]	China	51	3 years	ATL, ETL, AH, MST	64.7%	88.2%
Zonghui et al. 1997 [153]	China	60	6 months	MST	60%	
Alsemari et al. 2014 [158]	Saudi Arabia	502	1 year 3 years 5 years	TLE surgery FLE surgery Parietal and occipital lobe Multilobar surgery Hemispherectomy TLE surgery FLE surgery Parietal and occipital lobe Multilobar surgery Hemispherectomy TLE surgeries	Classes I, II, and III[a]	79.6%[a] 62%[a] 67%[a] 65%[a] 64.2%[a] 74.2% 52% 67% 50%% 63% 67%
Locharernkul et al. 2005 [159]	Thailand	111	3 years	ATL, SAH; Lesionectomy cortical resection.	83.8%	
Kanchanatawan and Kasalak 2012 [160]	Thailand	60	>1 year	ATL, tumors, lesionectomy or cortical resection	66%	
Kanchanatawan et al. 2014 [161]	Thailand	189	6 months 2 years	ATL, tumors, lesionectomy or cortical resection	78.8% 88.3%	
Visudhiphan 1999 [163]	Thailand	14	6 months–5	ATL	70%	

(continued on next page)

Table 3 (*continued*)

Author/Date	Country	Number operated	Follow-up duration	Type of surgeries	Seizure outcome	
					Engel score I	Engel score I and II
			years			
Kitwitee et al. 2017 [164]	Thailand	63	1 year 2 years	ATL, Resection	79.4% 77.8%	
Zaknun et al. 2008 [83]	Thailand India, Italy and Argentina.	74	1 year	TL surgery	89%	96%
Srikijvilaikul et al. 2004 [181]	Thailand.	35	≥1 year	TL surgery	74%	81%
Mikati et al. 2006 [165]	Lebanon	20	33.9 ± 9.1 months	TL	95%	100%
Mikati et al. 2012 [166]	Lebanon	93		TL and ETLE resections, multilobar resections, CC, hemispherectomy and VNS	70%	79%
Ahmed et al. 2009 [167]	Pakistan	3		TL, SAH, lesionectomy	67%	
Tahir et al. 2012 [168]	Pakistan	16	1 year 2 years 4 years	Neuronavigation-guided SAH keyhole technique ATL Hemispherectomy	100% 83% 66%	
Asadi-Pooya et al. 2015 [180]	Iran	22	24.8 ± 7.7 months		68.2%	81.8%
Ozkara et al. 2000 [173]	Turkey	77	17 months	TLR, extra TL, multilobar resections.	75%	90%
Hirfanoglu et al. 2016 [175]	Turkey	61	2 years	TLE ETL	88.9% 50%	93.3% 93.3%
Sayuthi et al. 2009 [176]	Malaysia	7	1 year	Lesionectomy, ATL, AH or combination	71%[a]	

[a] ILAE classification; CAH — corticoamygdalohippocampectomy, CC — corpus callosotomy, TL — temporal lobectomy, ATL — anterior temporal lobectomy, ALTL — anterolateral temporal resections, TLE — temporal lobectomy epilepsy, ETL — extratemporal lobectomy, HH — hypothalamic hamartoma, AH — amygdalohippocampectomy, SAH — selective amygdalohippocampectomy, TLR — temporal lobe resection, MST —multiple subpial transection, VNS — vagus nerve stimulation, NCC — neurocysticercosis.

reduction in seizure frequency in the short-term is inadequate to compare costs. The benefit of epilepsy surgery to a substantial number of persons in LMIC, however, may outweigh the cost with regard to the transformative power of a seizure-free life. The capacity to empower a sufferer and the community, restoration of livelihood, and the contribution to the local economy by freeing the caregiver and family from the economic and social burden may be reasons to prioritize epilepsy surgery [188]. Cost-effectiveness of epilepsy surgery should be an area for further studies, as analyses from HIC may not reflect the situation in LMIC due to the weak economic capacity and regional complexities. The equity proposed for people with epilepsy is usually jeopardized by causes of inequality such as poverty, illiteracy, and the marked urban–rural disparities that are deep-rooted and difficult to control in the poorer regions [192]. Strengthening primary healthcare, improving the referral pathway, and expanding health insurance coverage may help diminish this inequality [193–195]. The provision of epilepsy surgery may sometimes not correlate with a country's socioeconomic status, since the higher the gross domestic product the higher the health expenditure. For example, some Middle Eastern countries may not have a problem with infrastructure but may lack expertise while African countries are more likely to have problems with both.

Lesion-related epilepsies may be higher in LMIC. The high prevalence of febrile seizures, malaria, and other central nervous system (CNS) infestations may act as initial precipitating injury for developing hippocampal sclerosis [196]. An important research priority will be to investigate the burden of lesion-related epilepsy and the number of potential surgical candidates within a geographical context. This could

Table 4
Vagus nerve stimulation or neurostimulation from low- and middle-income countries.

Author/Date	Country	Period	Center	Number	Follow-up period	Outcome
Meneses et al. 2013 [57]	Brazil	2007–2012	Instituto de Neurologia de Curitiba, Curitiba	6	26.6 months	Seizure decreased by 40–50% and ≥ 80% in 67%
Benedetti-Isaac et al. 2015 [73]	Colombia	2010–2014	Colombian Center and Foundation of Epilepsy and Neurological Diseases (FIRE), Cartagena de Indias	9	4 years	DBS of posteromedial hypothalamus (pHyp) led to improvement of aggressiveness and QOL in people with DRE associated with aggressive behavior.
Alonso-Vanegas et al. 2010 [86]	Mexico	2001–2004	NNNI and NCMS	35	>12 months	An overall seizure reduction — 55.7%. >90% seizure-free rate — 11.4%, seizure-free — 5.7%, seizure increased — 5.7%. QOL improved overall.
Jayalakshmi et al. 2011 [120]	India	2003–2009	KIMS Hyderabad	5	≥1 year	3 had remission by >50%, one by 40%, and no significant change in one.
Meng et al. 2015 [138]	China	2008–2014	Beijing Tiantan Hospital and Beijing Fengtai Hospital	94	42.3 months	Engel I — 12.8%, Engel II — 11.7%, Engel III — 39.4%, Engel IV — 36.2%. ≥50% seizure reduction in 63.8% of patients
Wang et al. 2009 [151]	China	2001–2004	Two epilepsy centers (Harbin and Shanghai)	8	55.8 months	Seizure reduction ≥50%
Aburahma et al. 2015 [157]	Jordan	2007–2011	King Abdullah University Hospital and Jordan University Hospital in Jordan	28		54% of patients had ≥50% seizure reduction. QALY gain of 3.78 years for children and 1 year for adolescents per lifetime, and reduced financial burden.
Pakdaman et al. 2016 [172]	Iran		Loghman hospital Tehran	44	5 years	Mean seizure reduction – 57.8% in 1st year, 59.6% in 2nd year, 65% in 3rd year, 65.9% in 4th year, and 67% in 5th year of follow-up

NNNI — National Neurology and Neurosurgery Institute "Manuel Velasco Suarez"; NCMS — Neurosciences Center from Medica Sur Foundation, KIMS — Krishna Institute of Medical Sciences, DBS — deep brain stimulation, DRE — drug-resistant epilepsy, QOL — quality of life, QALY — quality-adjusted life years.

Table 5
Quality of life (QOL) of epilepsy surgery candidates in low- and middle-income countries.

Author/Date	Country	Center	Period	Surgery type	Number	QOL results
Frayman et al. 1999 [47]	Brazil	Hospital Brigadeiro, São Paulo	1997	TL, CC	12	Surgical candidates had better postoperative profile in 70% of questions.
Guimarães et al. 2003 [59]	Brazil	UNICAMP Campinas		TL, resection, hemispherectomy,	9	Overall QOL improved after surgery and correlated with seizure control.
Aydemir et al. 2004 [174]	Turkey	Istanbul University		SAH	20 pre-SAH 21 post-SAH	Better QOL observed in post-SAH compared with presurgery group. Higher seizure frequency, comorbidity, and number of AEDs had a negative influence on QOL.
Locharernkul et al. 2005 [159]	Thailand	Chulalongkorn University Hospital	2002–2004	ATL, SAH; Lesionectomy, resections.	111	Surgery improved employment, working ability and income. Seen best in seizure-free subjects.
Kanchanatawan and Kasalak 2012 [160]	Thailand	King Chulalongkorn Memorial Hospital	2007–2008	Various surgeries	60 each case and control	Surgery group had significantly higher QOL scores than those without surgery.
Mikati et al. 2006 [165]	Lebanon	American University of Beirut		Temporal Lobectomy	20 surgical and 17 non-surgical and 20 controls	QOL was significantly better in the surgery group (85% seizure-free compared with 35% in the nonsurgery groups) and no significant difference with healthy control.
Ahmad et al. 2007 [98]	India	AIIMS Delhi	2004–2006	ATL, AH, lesionectomies	36	Significant improvement reported in all domains of QOLIE-31 especially in those with good surgery outcome.
Dagar et al. 2011 [101]	India	AIIMS Delhi	2000–2011	ATL, SAH, resection, hemispherectomy,	40	Surgery improved QOL and scores correlated with duration of seizures, epileptic encephalopathy, and outcome of surgery.
Ravat et al. 2016 [122]	India	K.E.M. Hospital, Mumbai	2001–2013	ATL + AH	34	Reported significant improvement in QOL scores. No negative impact of surgery on memory and intelligence.
Sayuthi et al. 2009 [176]	Malaysia	Hospital University Sains Malaysia	2004–2007	Lesionectomy, ATL, AH	7	Better postoperative QOL compared with preoperative values. Definite with successful surgery.
Fletcher et al. 2015 [37]	Uganda	CCHU		Temporal lobe surgeries	10 surgical candidates and 9 no treated with AEDs	The QOLIE-31 scores were higher in surgical patients. Child/patient and parent/proxy surveys identified lower stigma in seizure-free patients.
Zanni et al. 2009 [50]	Brazil	Epilepsy surgery center - FAMERP		TL, AH	30	Better postsurgical QOL compared with presurgical period. Improved patients' satisfaction and activities of daily living.
Gagliardi et al. 2011 [62]	Brazil	UNICAMP Campinas		TLE	13	No general improvement in the QOL postoperatively, but improvement in general health issues and adverse effects of AEDs and in relationships
Bender del Busto et al. 2010 [93]	Cuba	Centro Internacional de Restauración Neurológica (CIREN)	2002–2007	Partial temporal lobotomy and transurgical EchoG	20	The median QOLIE-31 score improved from 26.5 before surgery to 89 six months after, it plateaued at 84 after a year.
Liang et al. 2012 [134]	China	4 centres in china	2001–2007	ATL, SAH; lesionectomy, resections.	206 children	Postoperative QOL improved in 65.5% patients, impaired in 4.9%, and unchanged in 29.6%.
Liang et al. 2010 [126]	China	Capital Epilepsy Therapy Center Beijin	2001–2007	TSC: Tuber resections, lobectomies, or CC	25	Significant improvement of overall QOL especially for those who are seizure-free.

TL — temporal lobectomy, CC — corpus callosotomy, SAH — selective amygdalohippocampectomy, AH — amygdalohippocampectomy, ATL — anterior temporal lobectomy, TLE — temporal lobe epilepsy, TSC — tuberous sclerosis complex, CCHU — CURE Children's Hospital Uganda, EchoG — electrocorticography, AED — antiepileptic drugs, QOL — quality of life, QALY — quality-adjusted life years, QOLIE — quality of life in epilepsy.

Table 6
Average cost of epilepsy surgery in some low- and middle-income countries.

Author/Date	Country	Center	Average cost of surgery[a]
Campos et al. 2000 [66]	Chile	Catholic University of Chile, in Santiago de Chile.	US$ 5020 — total cost, including evaluation and surgery
Fandino-Franky 2000 [70]	Colombia	Hospital Neurologico of the Liga Colornbiana Contra La Epilepsia, Cartagena,	US$ 3137 — not requiring invasive methods US$ 3995 — if invasive method is needed (for corpus callosotomies)
Tureczek et al. 2000 [71]	Colombia	Hospital Neurologico, HN-LCE Cartagena,	US$ 2250
Chemmanam et al. 2009 [114]	India	SCTIMST, Kerala	US$1500 — uncomplicated extra-temporal Resective surgery and hospital stay US$ 3400 — if requiring invasive monitoring
Dash et al. 2012 [117]	India	SCTIMST, Kerala	US$ 1500 — combined cost of presurgical evaluation, uncomplicated epilepsy surgery and hospital stay, US$ 3400 — if requiring invasive monitoring
Meng et al. 2015 [138]	China	Beijing Tiantan Hospital and Beijing Fengtai Hospital	US$ 30,000 per patient for VNS Therapy System
Wu et al. 2011 [144]	China	West China Hospital of Sichuan University	US$ 2550 to US$ 4230 — for the entire cost of surgery
Chen and Lei 2014 [147]	China	West China Hospital (WCH) of Sichuan University	US$ 7659 — average cost per patient
Tahir et al. 2012 [168]	Pakistan	Aga Khan University Hospital	US$ 1644 — direct total cost for regular care US$ 3044 — for private care.
Asadi-Pooya et al. 2014 [171], Asadi-Pooya et al. 2015 [180]	Iran	Shiraz University of Medical Sciences	US$ 500 — total cost for presurgical evaluation and surgery. US$ 300 — if on medical insurance
Kitwitee et al. 2017 [164]	Thailand	Prasat Neurological Institute (PNI)	US$ 6.200 — for the costs of VEEG, surgery and 1-year follow-up care

[a] These costs are average approximations. SCTIMST — Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, VNS — vagus nerve stimulation, VEEG — video-electroencephalography.

make a case that epilepsy surgery may have been unfairly neglected compared with surgical treatment of other public health conditions [197]. Healthcare providers also have an ethical obligation to identify and facilitate access to epilepsy surgery for these vulnerable subgroups [198]. Whether minimally invasive surgeries may be a cost-effective or efficacious option is an ongoing discussion, as subjects may be more willing to undergo minimally-invasive procedures because of lower perceived risks [199].

Several limitations are noted. Firstly, this review may not necessarily reflect all epilepsy surgeries performed in LMIC, as we have information from less than a quarter of the countries. Because of the difficulty in retrieving literature from LMICs, we may have excluded relevant information outside of our search. Unfavorable results of epilepsy surgery are also less likely to be published in journal articles. Secondly, it was difficult comparing results across board, based on the varying facilities, differing methodological approaches, lack of uniformity in reporting outcome measures, and different follow-up times. The use of international standardized methods for future work would help improve comparability [29]. International multicenter studies involving some LMIC prove that it is possible to produce an evidence-based practice with good quality data [83,105]. Thirdly, despite attempting to use a consistent clear approach following the framework [27], one of the problems we encountered is that the current available literature does not give holistic information. Some articles were excluded from the final analysis because of lack of access to the full text, although reviewing these abstracts substantiated the findings that some are conference abstracts from previous works. We also excluded articles reporting other neurosurgical procedures; however, these papers may indicate a center's potential technical expertise to perform epilepsy surgery if given the necessary support and improvement. Fourthly, no stakeholder meeting, which is an optional item of the scoping framework, was held. Our experiences have shown that this may be a useful option as it would allow interacting with stakeholders. An alternative to a meeting would have been sending questionnaires to the centers. We did not find, for instance, data on qualified personnel and staff training at the centers. Interaction with stakeholders and visits to centers would have provided full information on facilities available and training, although some of this information could also have been gathered by questionnaires. Lastly, we did not retrieve information on referral pattern and how people with epilepsy (PWE) access surgical options and how long it took, this would have been important to understand barriers from the health user's point of view. Understanding the structural, cultural, financial, and political barriers limiting epilepsy surgery will be an important initial step in prioritizing epilepsy surgery.

5. Conclusion

Surgical treatment for epilepsy is available in some LMIC, with an increasing trend in a few. Some experiences have shown that epilepsy surgery can be performed within the resource-poor settings through collaboration with international partners. Information and communications technology can be an important tool for skill transfer. These collaborations with international partners can provide an opportunity to bring high-quality academic training and technological transfer directly to surgeons and should be encouraged. The high cost of implementing surgery may not be a limitation to some LMIC but rather a problem of deciding how to prioritize and allocate resources [200]. Governments should weigh the immediate large monetary investment with the long-term benefits and sustainability. We acknowledge the limitation of data acquisition in LMIC; therefore, we may not have fully retrieved all the information regarding epilepsy surgery. Even where surgeries are performed, the small number operated and varying reporting methods make any reasonable conclusions regarding its definite continued existence difficult.

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Author contributions

The study was conceptualized and designed by MMW and JWS. Data were acquired by MMW and FW. Data were interpreted by MMW, MRK, AM, AWM, and JWS and analyzed by MMW and MRK. Technical input was provided by MRK, AM, ASW, and AWM. The manuscript was drafted by MMW and FX, and all other authors provided intellectual input and approved the final version.

Conflict of interest

MMW, FX, AM, and ASW have no conflict to report. MRK receives research support from UCB and Eisai and has received unrestricted educational grants from UCB and personal fees from UCB, Sage Therapeutics, and Novartis. AWM has received support from UCB, Baxter, and Cyberonics. JWS has received research support from Eisai, UCB, and GW, personal fees from Eisai, UCB, Zogenix, and Janssen outside of the submitted work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2019.01.001.

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