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Effects of the COVID-19 pandemic on medication adherence: In the case of antiseizure medications, A scoping review

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ABSTRACT

Since early 2020, an unprecedented public global health emergency caused by coronavirus (COVID-19) resulted in national governments' imposing confinement measures. Lockdowns and isolation during pandemics complicate disease management and medication adherence. Chronic conditions, such as epilepsy, require linear adherence patterns to prevent breakthrough seizures and to reduce the risk of sudden unexpected death. Limited access to health care facilities for routine care and medicines management further hampers this. Social isolation exacerbates stress, depression and decreases social support, which may combine to reduce adherence to antiseizure medication (ASM) during the pandemic.

Methods: We conducted a literature scoping review to explore ASM adherence among people with epilepsy, non-infected or infected SARS-CoV-2 or recovered from COVID-19 during the pandemic and explore risk factors for adherence. We search Pubmed for articles up to 16 September 2021. Search terms included the thematic of ASM adherence and COVID-19. We adhered to the PRISMA guidelines for reporting scoping reviews.

Results: Six articles were retained after the screening, which covered four overarching themes: change of ASM compliance and as risk factors, lack of follow-up, difficulties accessing ASM, and behavioural risk factors. Our review underscores the lack of evidence on ASM adherence among people with epilepsy infected or recovered from COVID-19. No study retrieved took place in a low-income setting, warranting a cautionary approach to be employed when extrapolating findings on a global scale.

Recommendations for practice: Missing information on past SARS-CoV2 infections impact people with epilepsy precludes exploring a direct effect of SARS-CoV2 on ASM adherence. A more comprehensive chronic disease model based on the burden of co-cardiovascular and neuro-behavioural comorbidities should be envisaged for this population in preparation for future pandemics. A monitoring algorithm needs to be in place to establish a telemedicine framework and community pharmacists' potential to contribute to the model recognised.

1. Introduction

In December 2019, a novel coronavirus outbreak began in China. This newly described coronavirus, SARS-CoV-2, quickly spread around the world at an exponential rate. In March 2020, the WHO declared COVID-19 a pandemic, prompting measures such as lockdown, self-isolation, and social distancing to slow the spread of COVID-19.

As a result, the medical community faces many practical and ethical challenges requiring rapid response, which leads to the postponement of non-essential care. Whilst the pandemic influences everyone worldwide, it can cause additional concerns for people living with chronic disorders such as epilepsy [1]. In 2019, in high-income countries (HICs), an estimated 49 per 100,000 people develop epilepsy every year, whilst in low- to middle-income countries, estimates are higher at 139 per 100,000 [2].

Akin to other chronic diseases, seizure control requires regular

Abbreviations: ASM, Antiseizure medication; LIC, Low-income country; HIC, High-income country; DM, Diabetes mellitus; SSA, Sub Saharan Africa.

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follow-up and continuous medicine supply [3], challenging to sustain in low-income countries. In these settings, a treatment gap defined as the proportion of people with epilepsy who require treatment but do not receive it [4] prevails due to shortages of trained health workers, limited diagnostic equipment, inadequate drug supplies [5].

Conversely, antiseizure medications (ASMs) nonadherence is the abrupt cessation of drugs in this group. Nonadherence, either a voluntary or involuntary behavior of medication intake, including stopping treatment due to financial constraints, is defined as the inability to follow prescribed treatments' recommendations [6].

Irregular ASM consumption is considered inferior to no therapy because of the risk of withdrawal seizures [7]. It may even trigger sudden unexpected death in epilepsy (SUDEP) [8]. Compounding adherence difficulties, epilepsy is often associated with comorbidities [9,10], resulting in polypharmacy in this population. SARS-CoV-2 infection in people with epilepsy may also be problematic. Many therapies currently used to treat COVID-19 may have significant adverse cardiovascular effects, which may exacerbate the negative cardiovascular impact associated with some ASM [11]. As a result, this may reduce ASM adherence.

Evidence suggests that ASM nonadherence ranges from 29% to 66% [12]. Independent predictors for nonadherence include specific beliefs about medications, being depressed or anxious, poor medication self-administration management, recent uncontrolled seizures, frequent dosage times, poor physician-patient relationship and perceived social support [12].

Past disasters and epidemics, including SARS, have been shown to have an impact on ASM adherence [13,14]. The emotional responses brought on by the pandemic and the enforced lockdown may be exacerbated by pre-existing psychiatric conditions [15].

Evidence is accumulating that the lockdown's social and behavioural consequences may increase seizure frequency in people with epilepsy. Stress was cited as an independent seizure precipitant at the onset of the outbreak in China [16]. In conjunction, managing chronic conditions, including epilepsy, may be compounded by inadequate medical care for chronic diseases.

It is also unknown how ASM adherence is affected by a current or past infection. SARS-CoV-2 may have neurotropic and neuroinvasive properties to enter neural tissue by avoiding an immune response and interacting with the angiotensin-converting enzyme 2 receptors [17]. A systematic review suggested common symptoms among people admitted to hospital for SARS or MERS included confusion [18]. There are suggestions that COVID-19 survivors may be at increased risk of psychiatric sequelae [19], similar to MERS CoV infection [18]. It is hypothesised that the same neurotropic and neuroinvasive SARS- CoV-2 may also be associated with a mental status change [20]. It is unknown whether a change of mental status in COVID-19 survivors may yield an impact on ASM adherence.

We explore ASM adherence among people with epilepsy, non-infected or infected SARS-CoV-2 or who have recovered from COVID-19 during the pandemic. Then, we propose suggestions on how to optimize epilepsy management during this pandemic and future pandemics.

2. Main text

2.1. Methodology

2.1.1. Search strategy

A scoping review was performed on 16 September 2021, to characterize the current understanding ASM adherence during the pandemic. The field of research terms included the thematic of ASM/anti-epileptic drugs adherence and COVID-19 and their related fields. A search was performed in PUBMED without time restrictions. Reference lists from retrieved publications were reviewed to identify additional manuscripts not captured by the search.

2.1.2. Inclusion criteria

Inclusion criteria are as follows: observational prospective, retrospective, and cross-sectional studies.

2.1.3. Exclusion criteria

Studies that did not examine adherence in persons with epilepsy or did not report on adherence were not eligible. Furthermore, commentaries were excluded.

2.1.4. Research question

This scoping review aims to answer the following question: What do we know about ASM adherence among people with epilepsy, non-infected or infected SARS-CoV-2 or who have recovered from COVID-19 during the pandemic? What are the risk factors for ASM adherence?

2.1.5. Study selection

We used the patient/population, intervention, comparison and outcomes model (PICO) [21] to answer our research question.

2.2. Population

Persons (18 years and older) with epilepsy

2.3. Intervention

The use of ASM

2.4. Comparison

Historical or external control

2.5. Outcome(s)

Differences in adherence among persons with epilepsy and risk factors for adherence

2.5.1. Synthesis of findings

Key findings were stratified into specific categories, derived from the articles rather than a predefined framework. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses—Extension for Scoping Reviews (PRISMA-ScR) checklist and guidelines (Annex) (Fig. 1, Table 1).

3. Results

Using the broadest search terms in our Pubmed search and from a search through the references of eligible papers, 17 articles were retrieved. Of these, eleven were excluded as the focus was on caregivers ($n = 2$), epileptologists ($n = 1$), focus on children ($n = 1$), or had outcomes irrelevant to search ($n = 7$). Lastly, six articles were eligible, of which one had a retrospective cohort design [22], two had a prospective cohort design [23,24], one had a case-control study design [25], and two a cross-sectional design [26,27], yielding a total sample of 54,585 people with epilepsy. We identified four overarching aspects: change of ASM compliance, and as risk factors, follow-up, difficulties accessing ASM, and behavioural risk factors found to be associated with adherence [13].

Adherence was measured in different ways. In four studies, it was self reported [24–27], of which one used the modified Morisky scale was used [24], one study provided no definitions [23] and one study used prescription data as a proxy for adherence during the lockdown [22].

Three studies used internal or external control groups. Two studies compared pre-COVID-19 to COVID-19 outcomes [22,25], and one study compared people with epilepsy to people without during COVID-19 [25]. Two studies did not use control groups [26,27].

Three studies took place in HICs [22,25 26], two in an

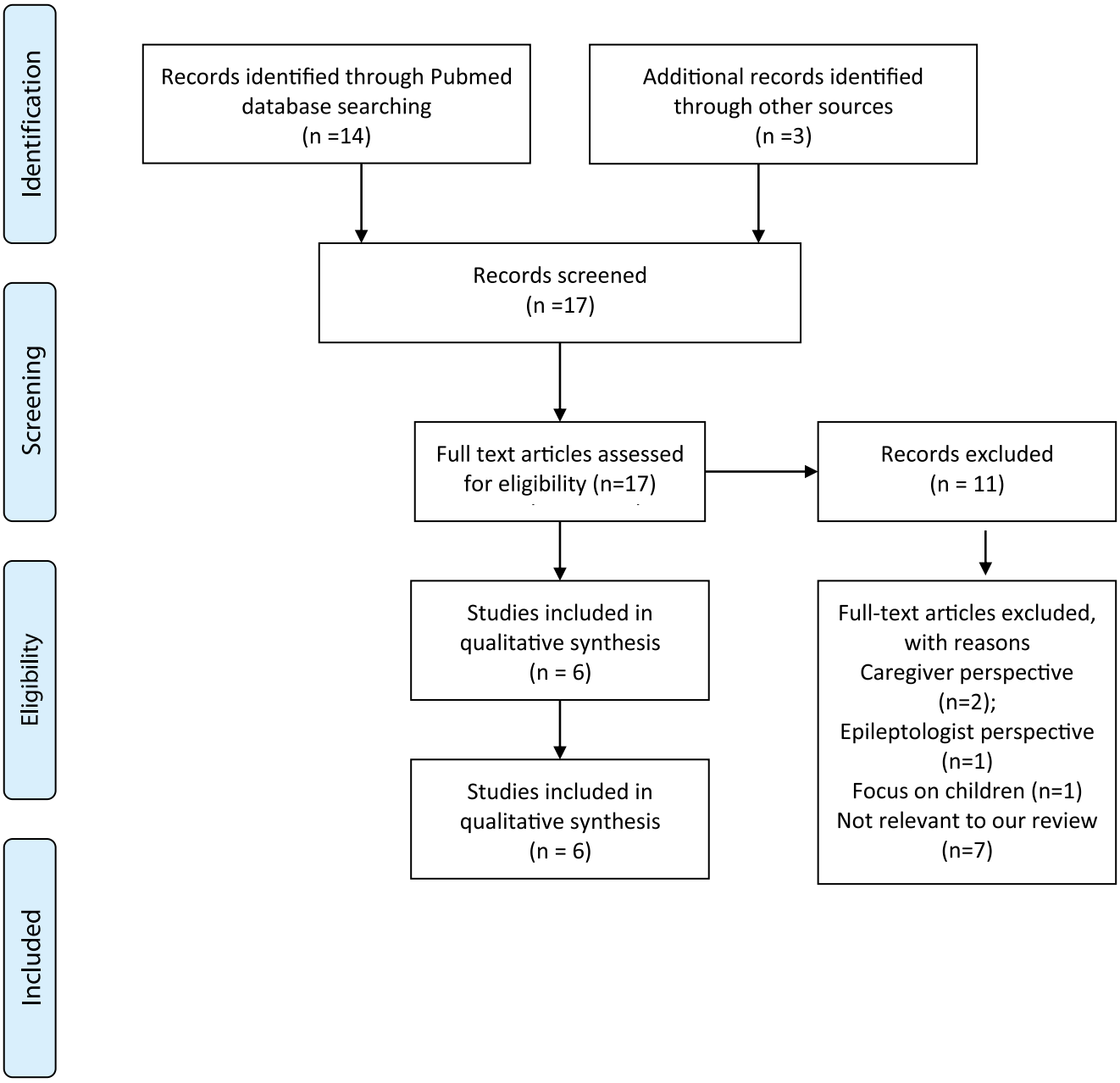

Fig. 1. PRISMA flow diagram.

upper-middle-income country [23,24], one from a middle-lower income country [26] as defined by the World Bank in 2021 [28,29]. No study from a low income country was identified.

No reports on ASM adherence in people with epilepsy infected with COVID-19 are available. In the six studies, it is unknown whether the participants had been infected before the survey. Two studies described whether the participants reported COVID-19 symptoms. In Iran, none reported symptoms [27], and in the Italian study, one person with epilepsy out of 16 who underwent a nasopharyngeal swab for SARS-CoV-2 tested positive [25].

3.1. Change of ASM compliance

In Saudi Arabia, five percent of 156 people with epilepsy reported changes in ASM adherence. Increased stress, self-reported sleep changes and ASM adherence are significant factors associated with increased seizure frequency during the pandemic [26]. In Italy, 32 (7%) people who reported inadequate adherence during the COVID-19 period attributed it primarily to forgetfulness (70%), demotivation (15%), and adverse events (10%) [25]. In contrast, findings from the Turkish study suggested that circumstances made people with epilepsy more motivated and informed about drug compliance than in the preceding months ($p=0.048$) [24].

In Germany and the Netherlands, ASM prescriptions for existing people with epilepsy increased in March 2020 by 36 % (in Germany)and 29 % ($p<0.01$) (in the Netherlands), in anticipation of the lockdown compared to March 2017–2019 [22]. By contrast, a decrease in prescriptions to people with newly diagnosed with epilepsy was observed in March 2020 in Germany (-7%), which further decreased in May 2020 to -22 % and 29% in the Netherlands among all age groups. More granular data suggests a significant decrease in ASM prescriptions issued to newly diagnosed people with epilepsy in April 2020 and May 2020, implying fewer diagnoses or people presenting. This may support the hypothesis that individuals with newly diagnosed epilepsy were underdiagnosed

Table 1
Summary of studies included in the review.

First author, Year	Country	Study design & sample size	Main exposure(s) of interest	Main outcome(s) of interest	Measurement of adherence	Main results and remarks
Mueller T. M. [22]	Germany and the Netherlands	Retrospective cohort study of prescription data ($N = 52,844$)	Persons with epilepsy	Epilepsy care during coronavirus disease during the pandemic	Medication adherence of known persons with epilepsy during the lockdown was calculated using the proportion of patients with a follow-up prescription during the 90 days after their prescription was issued in January or February 2017–2020.	Adherence of known person with epilepsy to ASM treatment appeared to remain stable during lockdown in Germany from March 2020 to May 2020. However, the study suggests reduced care for newly diagnosed persons with epilepsy.
Strizović S. [23]	Serbia	Prospective cohort study ($N = 97$)	Persons with Epilepsy	Quality of life in patients with epilepsy in the era of the COVID-19 crisis using the Serbian Version of Quality of Life Inventory for Epilepsy 31 (SVQOLIE-31) and Neurological Disorders Depression Inventory for Epilepsy scores (SVNDDI-E)	Not defined.	Both scores were significantly lower during the COVID-19 pandemic visit than prior to the pandemic ($p < 0.001$). In the follow-up year, only 8.2% patients reported at least one regular outpatient visit to their neurologist.
Gul Z.B. [24]	Turkey	Prospective cohort study ($N = 110$)	Persons with Epilepsy	Drug compliance and stigmatization during the pandemic	Self-reported (Modified Morisky Scale)	The pandemic made patients more motivated and informed in drug compliance in the patient group and had no effect on stigmatization
Assenza G. [25]	Italy	Case control study design ($N = 453$ persons with epilepsy; $N = 472$ persons without epilepsy)	Persons with epilepsy versus persons without epilepsy.	Impact of COVID-19 lockdown on the care of people with epilepsy and risk factors for seizure worsening	Self-reported	Outpatients appointments were postponed in 95% of cases. 169 people encountered issues related to epilepsy management, of whom 61% had a planned examination delayed. Only 71% were successful in reaching the treating physician.
Alkhotani A. [26]	Saudi Arabia	Cross sectional study ($N = 156$)	Persons with epilepsy	Assessment whether patients with epilepsy experienced an increase in seizure frequency and self-reported stress during the pandemic.	Self-reported	5% of 156 people with epilepsy reported changes in ASM adherence. Of the 156 participants, 15.4% had anxiety and 7.1% depression, with 85 (54.4%) reporting an increase in stress.
Asadi-Pooya A. A. [27]	Iran	Cross sectional study ($N = 100$)	Persons with epilepsy	Factors potentially associated with the perceptions of difficulty in obtaining their drugs	Self-reported	About one-third of patients with epilepsy expressed significant hardship obtaining their drugs after the intensification of the COVID-19 outbreak in Iran. Of the 31 people who experienced hardship in getting ASM, polytherapy with ASM was the leading cause (71%)

and undertreated during the lockdown [22].

In Serbia, a longitudinal study reported full compliance of ASM in people with epilepsy in the follow-up year following the first case of COVID-19 [23].

3.2. Difficulties accessing ASM

About one-third of the 100 people with epilepsy surveyed in Iran stated significant difficulties obtaining medicines. The frequency of seizures increased in 6% of them during the pandemic [27]. Of the 31 people who experienced hardship in getting ASM, polytherapy with ASM was the leading cause (71%) [27].

In an Italian study of 456 people with epilepsy (344 females), 169 (37%) persons reported negative issues related to the management of epilepsy. Of these individuals, 68 (40%) had problems with ASM availability [25].

Conversely, two studies reported no interruptions in access [24,26]. ASM access was ensured in Saudi Arabia, as reported in one study. Most hospitals adopted a medication delivery system to individuals' homes. Thus, people with chronic illnesses were able to access their medications without attending hospitals [26]. This was also the case in Turkey, where prescriptions for epilepsy were extended and specific pandemic hospitals were established [24]. People with epilepsy did not report problems accessing healthcare facilities, and only 1.8% of the 110 surveyed experienced difficulties accessing ASM during the pandemic period [24].

3.3. Lack of follow-up

One Italian study ascertained follow-up in an epilepsy clinic, and a significant proportion of attendees reported having had difficulties [25]. Out-patients appointments were postponed in 95% of cases. Hundred and sixty-nine people encountered issues related to epilepsy management, of whom 61% had a planned examination delayed, and only 71% were successful in reaching the treating physician [25]. Participants also had difficulties in contacting a neurologist when required either by phone, messaging or email.

Only 8 (8.2%) people reported at least one regular outpatient visit to their neurologist in Serbia during the pandemic. Of those who did not make regular outpatient consultations during the COVID-19 epidemic, 70 (72.3%) reported that health system restrictions impeded them from reaching their neurologist [23].

3.4. Behavioural risk factors

None of the six studies examined behavioural risk factors for ASM nonadherence. Three studies described levels of depression and stress [24–26]. In Turkey, a surge in stigmatization due to a COVID-19 diagnosis seemed to comfort people with epilepsy as they were no longer alone in being stigmatised. This feeling seems to have helped counter depression [24]. In Italy, people with epilepsy reported worse depressive and anxiety symptoms (11.6%) than the 472 people without epilepsy (8.1%). Those with epilepsy experienced significantly more mood disorders than participants without epilepsy ($p < 0.001$) [25]. It was impossible to obtain a breakdown by gender from the authors despite polite requests. Whether women with epilepsy were more at risk for moderate or severe depression than their male counterparts is unknown. In Saudi Arabia, of the 156 participants, 15.4% had anxiety and 7.1% depression, with 85 (54.4%) reporting an increase in stress [26].

In Serbia, returns from the Serbian version of Quality of Life Inventory for Epilepsy 31 (SVQOLIE-31) and Neurological Disorders Depression Inventory for Epilepsy scores (SVNDDI-E) in people with epilepsy suggest a significantly lower score during the pandemic than before (during 64.5 ± 14.6;$p < 0.001$ and before 10.5 ± 3.5; $p < 0.001$) [23].

4. Discussion

As underscored by our findings, the evidence on ASM adherence during the COVID 19 pandemic appears to be skewed towards high-income countries. There is a need for an enhanced understanding of the magnitude of ASM nonadherence and its attendant risk factors inherent to the pandemic. Our results also suggest that difficulties in accessing ASM were context-specific and that ASM adherence changes were sub-optimal. The only study that compared people with epilepsy to those without suggests depression and stress to be higher in the epilepsy group [25]. The study also indicated that regular neurological follow-up might avoid unnecessary emergency room visits or outpatient assessments [25]. We were precluded from examining the direct effect of COVID-19 on ASM adherence among people with epilepsy, as only one participant was reported infected. No information was provided on the infection status of the remaining participants.

4.1. Limitations and strengths

The wide breadth of this scoping review captures the evidence and knowledge gaps that had hitherto not yet been synthesized. We acknowledge, however, several limitations. We only found articles addressing the pre-specified target population. This shortage of data should be seen in light of potential limitations inherent to the study designs employed. Firstly, only three out of five studies used comparison groups. Secondly, as four studies relied exclusively on self-reporting, nonadherence may be underestimated. Thirdly, only one large longitudinal study in HIC was identified that enabled us to capture the fluctuations in motivation and availability of ASM that may fluctuate during the pandemic.

We identified some critical clinical and epidemiological research gaps. Indications for ASM have expanded to include neurologic conditions other than epilepsy, including chronic pain, migraine and some psychiatric disorders [30]; there may be a large population whose ASM adherence may be impacted. With the surge of COVID-19 cases globally, it is crucial to assess how interactions with COVID-19 treatments may interact with first-line enzyme-inducing and second-line ASM and how this may impact ASM adherence. It would also be pivotal to elucidate whether the heightened risk of psychiatric sequelae in survivors of COVID-19 may impact ASM adherence.

Our findings also underscore the absence of studies from LICs, where the COVID-19 pandemic may further compound the treatment and diagnostic gap. In sub-Saharan Africa (SSA), past outbreaks, including Ebola and COVID-19 and ensuing school closures, have increased schoolgirls' vulnerability, resulting in child marriage and early pregnancy [30]. As a result, this may bring forth an epidemiological shift, entailing a higher absolute number of pregnant girls with epilepsy in SSA. In this population, epilepsy management during pregnancy constitutes a clinical problem, necessitating an equilibrium between seizure control with enzyme-inducing ASM, management of co-infections in a non-negligible proportion, along with maternal and fetal risk minimisation [31]. The complexity of epilepsy management within this context is likely to put an additional strain on the high treatment and diagnostic gap in SSA. In contrast, in 2007, the median number of neurologists in SSA was estimated at 0.3 per 1 million [32].

5. Recommendation for practice

This pandemic has brought to the fore the ever-greater need for self-management of chronic illness. Self-management, defined as the daily actions that people take to keep their disease under control, minimize its impact on physical health status and functioning, and cope with psychosocial sequelae [33]. If we consider the physician's ability to enable the individuals toward effective self-care a marker of consultation quality [34], then we may deduce that there was a suboptimal adherence to ASM before the pandemic. Prevalences of ASM nonadherence ranging from a quarter to two-thirds [35] suggests an inadequate relationship between physicians and people they attend.

The current pandemic has underscored the urgent need for medical compliance to be reconceptualised [36]. Creating an environment conducive to treating the individual's physical, psychological, behavioural, and social issues will help tackle self-care demand during pandemic times and successfully incorporate future mobile health technology within self-care programs.

COVID-19 is here for the long haul, and intermittent lockdowns should be considered the new norm [37], with infectious disease modellers predicting that future pandemics will be more frequent and deadlier [38]. Pandemics, which have been shown to adversely affect chronic diseases due to decreased access to healthcare facilities, follow-up, and drug access, beg for a blueprint based on a multi-pronged approach.

To ensure ASM's availability during pandemics and reduce the need for clinic attendance, longer supplies and home delivery, as exemplified in a Saudi study [26], may improve adherence and prevent breakthrough seizures, especially in newly diagnosed persons with epilepsy who may be more at risk for undertreatment during lockdowns [22].

The difficulty in obtaining medical advice may also increase anxiety, which may worsen disease management [39]. Concomitantly, as depression and poor sleep hygiene may be linked to compliance, structured training programs for individuals with epilepsy should be designed. These would consist of guidance on care and stress management specific to pandemics. In conjunction, epilepsy helpline and support groups should be tailored to pandemic contexts.

In the context of a pandemic, video consultations through telemedicine should be promoted and expanded with the two-fold objectives of decreasing the risk of disease transmission and improving access to treatment. This may significantly benefit people with epilepsy living in underserved rural areas, for whom it may not be advisable to travel to urban centres and risk exposure.

There is a need to strengthen organised telemedicine assistance in the public health system. Within the current context, wider telemedicine adoption should be envisaged, making all people with epilepsy eligible regardless of whether they test positive. Countries should also adopt a regulatory framework to authorize, integrate, and reimburse telemedicine in their care delivery for all people with epilepsy in emergency and outbreak situations [40].

To define a telemedicine framework for a pandemic, a remote individual monitoring algorithm for an outbreak at local, national, or global scales should be designed. An all-inclusive adherence assessment with

instruments including the Morisky Medication Adherence Scale and Epilepsy Self-Efficacy Scale should be routine practice and undertaken at regular intervals to capture fluctuations. To ensure the maintenance of an optimal concentration of ASM and to monitor short term adherence, an additional strategy may be to collect saliva or blood samples for analysis during mobile ASM deliveries.

Telemedicine may inadvertently exclude the less computer-savvy population, who may also have a more deficient understanding of the application of telemedicine services. In LICs, as a smaller percentage of the population may have internet access, telemedicine may fail to capture this population living in more rural areas, who may already be more at risk for low ASM adherence. Phone calls or text messages may be a more effective follow-up to retain contact with those at risk for low adherence.

Pandemics, including the current one, may exert hardships at individual and societal levels. In this respect, it is paramount to appreciate that not all countries enter a pandemic on an equal footing. Some countries may have felt the destructive effects of natural disasters or have had to incur specific hardships, including economic or political instability. To counter these detrimental impacts on epilepsy care in pandemic times, a task-shifting model consisting of a network linking neurologists to trained local non-physicians and community pharmacists should first be designed to tackle inequalities in care between rural and urban settings [40].

Given the need to enhance sustainability in pandemic times, especially in resource-constrained settings, more than ever, the concept of integrated care for chronic comorbidities for epilepsy may need to be revisited to ensure linear drug adherence.

This requires considering the epidemiology of chronic diseases in people with epilepsy and the shifts in the global chronic diseases landscape. Evidence is mounting that people with DM, and hypertension have a heightened risk of developing epilepsy later in life [41,42]. Evidence suggests that people with HIV+ are more likely to develop seizures due to metabolic disturbances and opportunistic infections [43]. Similarly, neurobehavioral disorders commonly affect people with epilepsy [44], with them at an increased risk for major depressive and anxiety disorders [45] and psychosis [46].

Against a backdrop of a surge of the global prevalence of cardiovascular morbidity, particularly in lower-income populations [47] and a high prevalence of HIV and epilepsy in LICs [48], incorporating epilepsy care into a broader telehealth chronic disease management model may benefit a non-negligible proportion of people in LICs. To support these endeavours and counter limited access by low-income populations, community pharmacists may play a frontline role in promoting adherence to ASM in epilepsy with potential comorbidities, thus easing the burden on health systems [49].

For withstanding a future pandemic and the aftermath of the COVID-19 pandemic, more than ever, a sustainable model will need to be supported by a clearer understanding of ASM adherence during periods of confinement and in persons suffering from long COVID- 19. Knowledge of the comorbidities burden in this population will need to be quantified according to geographical zones to design a tailored enlarged chronic disease management. Capacity-building programs targeting local healthcare workers and community pharmacists to provide integrated care should be developed. Enhanced collaborations between local and international health actors should be sought.

Availability of data and materials

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Competing interests

SM works part-time as a consultant for P95 consulting organization. JWS has received personal fees from Eisai, UCB, GW Pharma, Arvelle and Zogenix and research grants from UCB and GW Pharmaceuticals outside the submitted work. The UK Epilepsy Society endows his current position.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Not applicable.

CRediT authorship contribution statement

Sonia Menon: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Josemir W. Sander:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Supplementary materials

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References

[1] French JA, et al. Keeping people with epilepsy safe during the COVID-19 pandemic. Neurology 2020;94(23):1032–7.
[2] World Health Organization, G., Switzerland. Epilepsy 2019. 2019. https://www.who.int/news-room/fact-sheets/detail/epilepsy.
[3] Newton CR, Garcia HH. Epilepsy in poor regions of the world. Lancet 2012;380(9848):1193–201.
[4] Meyer A-C, et al. Global disparities in the epilepsy treatment gap: a systematic review. Bull World Health Organ 2010;88(4):260–6.
[5] Chin JH. Epilepsy treatment in sub-Saharan Africa: closing the gap. Afr Health Sci 2012;12(2):186–92.
[6] Hugtenburg JG, et al. Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. Patient Prefer Adher 2013;7:675–82.
[7] Reynolds EH. Drug treatment of epilepsy. Lancet North Am Ed 1978;312(8092):721–5.
[8] Kanner AM. To comply with AED therapy ... what patients are not told! Epilepsy Curr 2009;9(5):139–40.
[9] Elliott JO, et al. Comorbidity, health screening, and quality of life among persons with a history of epilepsy. Epilepsy Behav 2009;14(1):125–9.
[10] Téllez-Zenteno JF, Matijevic S, Wiebe S. Somatic comorbidity of epilepsy in the general population in Canada. Epilepsia 2005;46(12):1955–62.
[11] Asadi-Pooya AA, et al. Management of COVID-19 in people with epilepsy: drug considerations. Neurol Sci 2020;41(8):2005–11.
[12] G OR, O.B JJ. Identifying the barriers to antiepileptic drug adherence among adults with epilepsy. Seizure 2017;45:160–8.
[13] Swinkels WA, et al. Influence of an evacuation in February 1995 in The Netherlands on the seizure frequency in patients with epilepsy: a controlled study. Epilepsia 1998;39(11):1203–7.
[14] Lai SL, Hsu MT, Chen SS. The impact of SARS on epilepsy: the experience of drug withdrawal in epileptic patients. Seizure 2005;14(8):557–61.

[15] The L. Redefining vulnerability in the era of COVID-19. Lancet 2020;395(10230):1089.
[16] Huang S, et al. COVID-19 outbreak: The impact of stress on seizures in patients with epilepsy. Epilepsia 2020;61(9):1884–93.
[17] Baig AM, et al. Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host-virus interaction, and proposed neurotropic mechanisms. ACS Chem Neurosci 2020;11(7):995–8.
[18] Rogers JP, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. Lancet Psychiatry 2020;7(7):611–27.
[19] Taquet M, et al. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. Lancet Psychiatry 2021;8(2):130–40.
[20] Hu J, Jolkkonen J, Zhao C. Neurotropism of SARS-CoV-2 and its neuropathological alterations: similarities with other coronaviruses. Neurosci Biobehav Rev 2020;119:184–93.
[21] Schardt C, et al. Utilization of the PICO framework to improve searching PubMed for clinical questions. BMC Med Inf Decis Making 2007;7. 16-16.
[22] Mueller TM, et al. The impact of the coronavirus disease (COVID-19) pandemic on outpatient epilepsy care: an analysis of physician practices in Germany. Epilep Behav 2021;117. 107833-107833.
[23] Strizović S, et al. Influence of COVID-19 pandemic on quality of life in patients with epilepsy - follow-up study. Epilep Behav 2021;121(Pt A). 108026-108026.
[24] Gul ZB, Atakli HD. Effect of the COVID-19 pandemic on drug compliance and stigmatization in patients with epilepsy. Epilep Behav 2021;114(Pt A). 107610-107610.
[25] Assenza G, et al. Epilepsy care in the time of COVID-19 pandemic in Italy: risk factors for seizure worsening. Front Neurol 2020;11. 737-737.
[26] Alkhotani A, et al. The effect of COVID-19 pandemic on seizure control and self-reported stress on patient with epilepsy. Epilep Behav 2020;112. 107323-107323.
[27] Asadi-Pooya AA, Farazdaghi M, Bazrafshan M. Impacts of the COVID-19 pandemic on Iranian patients with epilepsy. Acta Neurol Scand 2020;142(4):392–5.
[28] Bank W. High income countries. 2021.
[29] Bank W. Upper middle income countries. 2021.
[30] UNESCO. Covid-19 school closures around the world will hit girls hardest. 2020.
[31] Menon S, et al. Women with epilepsy in sub–Saharan Africa: A review of the reproductive health challenges and perspectives for management. Seizure 2019;71:312–7.
[32] Owolabi MO, Bower JH, Ogunniyi A. Mapping Africa's way into prominence in the field of neurology. Arch Neurol 2007;64(12):1696–700.
[33] Clark NM, et al. Self-management of chronic disease by older adults: a review and questions for research. J Aging Health 1991;3(1):3–27.
[34] Howie JG, et al. Quality at general practice consultations: cross sectional survey. BMJ 1999;319(7212):738–43.
[35] Farrukh MJ, et al. Use of complementary and alternative medicine and adherence to antiepileptic drug therapy among epilepsy patients: a systematic review. Patient Prefer Adherence 2018;12:2111–21.
[36] Trostle JA. Medical compliance as an ideology. Soc Sci Med 1988;27(12):1299–308.
[37] Scudellari M. How the pandemic might play out in 2021 and beyond. Nature 2020;584(7819):22–5.
[38] IPBES. COVID-19 Stimulus Measures Must Save Lives, Protect Livelihoods, and Safeguard Nature to Reduce the Risk of Future Pandemics. 2020.
[39] Xiao Z, et al. Management of people with epilepsy during the COVID-19 pandemic: a national survey among epileptologists in China. Acta Epileptol 2020;2(1):19.
[40] O'Hare B, et al. Task sharing within a managed clinical network to improve child health in Malawi. Hum Resour Health 2015;13(1):60.
[41] Gaitatzis A, Sisodiya SM, Sander JW. The somatic comorbidity of epilepsy: a weighty but often unrecognized burden. Epilepsia 2012;53(8):1282–93.
[42] Johnson EL, et al. Association between midlife risk factors and late-onset epilepsy: results from the atherosclerosis risk in communities study. JAMA Neurol 2018;75(11):1375–82.
[43] Siddiqi O, Birbeck GL. Safe treatment of seizures in the setting of HIV/AIDS. Curr Treat Options Neurol 2013;15(4):529–43.
[44] Devinsky O. Therapy for neurobehavioral disorders in epilepsy. Epilepsia 2004;45(Suppl 2):34–40.
[45] Hermann B, Seidenberg M, Jones J. The neurobehavioural comorbidities of epilepsy: can a natural history be developed? Lancet Neurol 2008;7(2):151–60.
[46] Clancy MJ, et al. The prevalence of psychosis in epilepsy; a systematic review and meta-analysis. BMC Psychiatry 2014;14. 75-75.
[47] Rosengren A, et al. Socioeconomic status and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study. Lancet Glob Health 2019;7(6):e748–60.
[48] Epilepsy and HIV–a dangerous combination. Lancet Neurol 2007;6(9):747.
[49] Kretchy IA, Asiedu-Danso M, Kretchy JP. Medication management and adherence during the COVID-19 pandemic: perspectives and experiences from low-and middle-income countries. Res Social Adm Pharm 2021;17(1):2023–6.