





BMJ Open Systems approach to improving traumatic brain injury care in Myanmar: a mixed-methods study from lived experience to discrete event simulation

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ABSTRACT

Objectives Traumatic brain injury (TBI) is a global health problem, whose management in low-resource settings is hampered by fragile health systems and lack of access to specialist services. Improvement is complex, given the interaction of multiple people, processes and institutions. We aimed to develop a mixed-method approach to understand the TBI pathway based on the lived experience of local people, supported by quantitative methodologies and to determine potential improvement targets.

Design We describe a systems approach based on narrative exploration, participatory diagramming, data collection and discrete event simulation (DES), conducted by an international research collaborative.

Setting The study is set in the tertiary neurotrauma centre in Yangon General Hospital, Myanmar, in 2019–2020 (prior to the SARS-CoV2 pandemic).

Participants The qualitative work involved 40 workshop participants and 64 interviewees to explore the views of a wide range of stakeholders including staff, patients and relatives. The 1-month retrospective admission snapshot covered 85 surgical neurotrauma admissions.

Results The TBI pathway was outlined, with system boundaries defined around the management of TBI once admitted to the neurosurgical unit. Retrospective data showed 18% mortality, 71% discharge to home and an 11% referral rate. DES was used to investigate the system, showing its vulnerability to small surges in patient numbers, with critical points being CT scanning and observation ward beds. This explorative model indicated that a modest expansion of observation ward beds to 30 would remove the flow-limitations and indicated possible consequences of changes.

Conclusions A systems approach to improving TBI care in resource-poor settings may be supported by simulation and informed by qualitative work to ground it in the direct experience of those involved. Narrative interviews, participatory diagramming and DES represent one possible suite of methods deliverable within an international partnership. Findings can support targeted improvement investments despite coexisting resource limitations while indicating concomitant risks.

Strengths and limitations of this study

- ⇒ This study demonstrates the value of combining discrete event simulation (DES) and narrative-driven participatory diagramming for understanding care pathways in a global health context.
- ⇒ Narrative enquiry provided a participatory method for data creation which balances power between actors, providing robust qualitative data to inform the development of quantitative DES models.
- ⇒ The DES model allowed the exploration of a range of scenarios to help understand the impact of key resources on clinical outcomes.
- ⇒ The combined effects of the SARS-CoV-2 pandemic and the current political climate in Myanmar made it impossible to subsequently validate the model outside of the international research team.
- ⇒ Quantitative simulation models only account for a limited perspective, with the results requiring careful contextualisation before being used to change clinical practice.

INTRODUCTION

Traumatic brain injury (TBI) is a global public health issue, with the 2017 Lancet Commission on Traumatic Brain Injury estimating that over half of the world's population will suffer a TBI within their lifetime.¹ TBI is a particular problem in low-income and middle-income countries (LMICs) where increasing automobile use, poor regulatory frameworks and fragile health systems combine to provide not only an increasing risk of TBI, but an environment in which the prehospital care, intrahospital care and post-hospital care, which TBI requires cannot be provided.²

At the core of TBI management is the provision of surgical intervention, itself a challenge in many LMICs. The 2015 Lancet Commission on Global Surgery found that

over 5 billion of the world's population lack access to safe, affordable, timely surgical care and that surgery itself requires a functional healthcare system to support it.³ In addition, TBI care depends on time-critical investigations, such as CT scans, which can also be a challenge to access without delay in resource poor environments. The effects of delay are consistent with the known pathophysiology of secondary brain injury and experience from other studies which suggest that delay remains a key determinant of outcome in TBI.¹

The management of TBI is complex and difficult to characterise.⁴ While epidemiological studies have been conducted to explore the global picture, mapping practice at the level of the institution to drive service improvement remains a challenge.⁵ This is exacerbated in settings which have low levels of routine data collection, or a lack of established clinical and organisational protocols and care pathways. One conceptual framework which has been advocated to help understand the complex environment of clinical care is systems thinking; either as a standalone device or as part of an established corpus of knowledge such as systems engineering. This has been applied in many settings through a variety of methodological approaches and is advocated by the WHO as an approach for understanding healthcare.⁶ One model for taking a systems approach to healthcare improvement is described in the 2017 report *Engineering Better Care*, which presents a recursive series of questions to be answered as part of such an approach, and which has been explicitly explored within the context of global health.^{7,8}

Accurate and complete quantitative data collection is often considered a prerequisite for operational systems modelling. While data collection and analysis have been shown to be feasible in LMICs, there are significant limitations in data collection associated with resource-limited settings.⁹ This contrasts with high-income settings where electronic health records, implemented to facilitate clinical care, may provide data for operational research and systems analysis.¹⁰ More participatory approaches, such as process mapping, have been described to improve surgical care but these do not have the power of quantitative models.¹¹

Healthcare system modelling using discrete event simulation (DES) is a common approach in operational research, supported by quantitative data in combination with local knowledge. It has been shown to be a useful tool to model a complex system and investigate the potential effects of resource reallocation or improvements.¹² However, extension of this type of modelling into LMIC healthcare systems has been sparse to date, with a few notable exceptions.^{13,14} The success of DES depends on an appropriate representation of the system to be modelled and its applicability can be limited if the system is not well represented or described.

We describe a mixed-methods systems approach to understanding TBI care in a tertiary neurosurgical centre in Myanmar, to demonstrate the feasibility and utility of this approach to a resource-limited tertiary neurosurgical

centre with a significant burden of TBI. This study is the product of an academic institutional health partnership combining the Cambridge Yangon Trauma Intervention Project and the National Institute for Health Research (NIHR) Global Health Research Group on Neurotrauma.¹⁵

METHODS

Setting

The study was conducted across 2019–2020, prior to the SARS CoV2 global pandemic, in Yangon General Hospital (YGH), Myanmar. YGH is a tertiary neurotrauma referral centre in Myanmar receiving both local and regional patients and which functions as both the local and national trauma centre. It has a recently established emergency department and provides a comprehensive array of surgical services. The neurosurgical centre is physically distant from the main hospital campus, with patients requiring transfer between the two sites. We employed an integrated mixed-methods approach based on narrative analysis, participatory diagramming, targeted prospective data collection, model refinement and then model validation and verification. Nested within a wider academic partnership, this work is reported against the Good Reporting of a Mixed Methods Study criteria.¹⁶

Patient and public involvement

This work forms part of a portfolio of research funded by the NIHR Global Health Research Group on Neurotrauma (<https://neurotrauma.world>), who have partnered with patient representatives in both the UK and around the world to understand the consequences of TBI and set research priorities. This partnership informed the initial study design of this project. In Myanmar, we were unable to identify specific patient groups or representatives pertinent to TBI care, and instead chose a participatory research design to include their perspectives within the formal data collection. While this meant patients and the public were not engaged at the outset of the study, the snowball participant sampling allowed them to identify further research participants and shape both the design and findings of the study. Similarly, the choice of narrative methodology allowed patient and public respondents to shape the research data in partnership with the research team. The intention of the research team was to use further patient and public work to understand how the research findings might best be shared with communities, but the cessation of research activity due to the SARS-CoV-2 pandemic and political events in Myanmar made this latter stage unworkable.

Qualitative data

A combination of narrative data supplemented by participatory diagramming was used to understand the lived experience of research participants. This was based on the Soft Systems Methodology (SSM), adapted for use by a multiprofessional, cross-cultural research team.¹⁷

Narrative inquiry and SSM are positioned within a constructivist paradigm in which the data are cocreated by the research team and research participants. The data is a function of the context in which it is created, both on the micro (individual conversation) and macro (society, culture and language) levels. The research team consisted of both UK and Burmese researchers, trained in the Engineering Better Care systems approach, SSM, narrative and diagramming techniques, and with an expert knowledge of the clinical context under study.

A half-day workshop was held in February 2019 at YGH which was attended by 40 participants including neurosurgeons, neurosurgical nursing staff (ward and theatres), anaesthetists, emergency physicians and psychiatrists. All participants provided written informed consent. Participants were grouped by both clinical specialty and seniority to encourage active participation and story-sharing and facilitated in a mixture of Burmese and English by members of the research team. During the workshop, participants were encouraged to create visual maps of their accounts, identifying a mixture of physical structures, clinical processes, patient flow and lines of communication. These visual maps were often supplemented by numerical figures to reinforce particular points.

Subsequently, 2 members of the research team (SW and PPNM) conducted 64 one-on-one interviews with a range of stakeholders including patients and their relatives, physicians, surgeons, nursing and auxiliary staff. Again, participants provided written informed consent and were selected through purposive snowball sampling to explore as wide a range of stakeholders' views as possible. Children and those unable to provide written informed consent were excluded. These interviews were again structured to encourage story-telling and the elicitation of individual narratives, using a combination of audio recording, note-taking and participatory diagramming to capture these accounts. These interviews were conducted in Burmese, anonymised at source and then professionally translated and transcribed.

Both the workshop and subsequent interviews were loosely structured to encourage the elicitation of rich narratives, rather than to address preconceived questions. Facilitators and interviewers referred to the questions posed in Engineering Better Care (figure 1) to help guide the discussions, and sought to explore habitual, exceptional, and hypothetical narratives to gain an understanding of the lived experience of respondents.¹⁸ Prompting questions for these narratives included broad questions such as 'what does a normal day look like?', 'what is the best experience you have had?', 'what was the worst case you have ever seen?'. However, interviewers were encouraged to use a variety of approaches to encourage rich and reflective narratives, including sharing personal stories and observations. No fixed interview schema was used, with an emphasis placed on the quality of the data created, rather than its reproducibility. At the same time, techniques of participatory diagramming and graphical

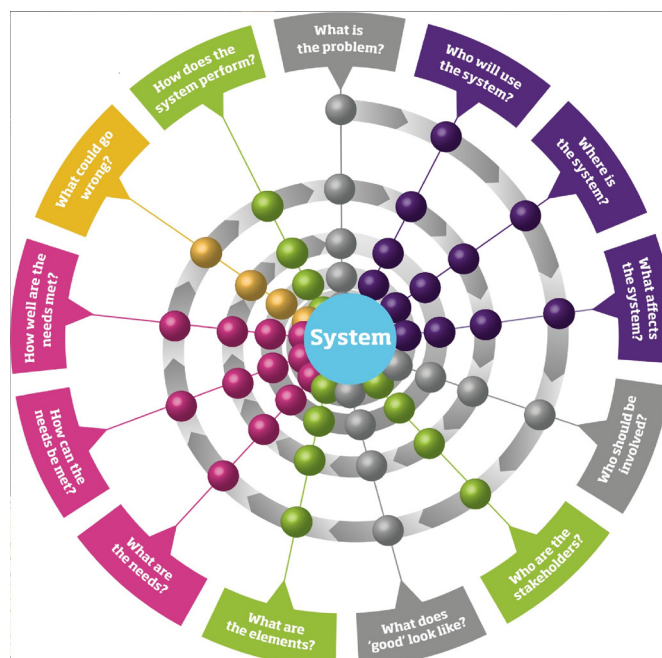


Figure 1 A systems approach to health and care improvement framed as a series of recursive questions reproduced with permission from Engineering Better Care, Royal Academy of engineering, 2017).

elicitation were used to help interviewers and respondents structure this data during the workshop and interviews, with the aim of prompting new insights, clarifying terms and creating a mutual understanding of the narratives being related.¹⁹

The resulting qualitative dataset was imported into proprietary software (ATLAS.ti V.8 Mac, Scientific Software Development). Narratives were analysed to identify key areas of concern, along with the development of a consensus understanding of the system features which were central to these: the boundary of the system under study, its physical components and their orientation to each other, the key clinical processes occurring within the system and the flow of patients through it. A formal thematic analysis of the dataset was not conducted as part of this study.

Quantitative

This qualitative systems model informed the subsequent collection of prospective, targeted, quantitative clinical data. One of the research team (SW) collected a dataset of demographic, inpatient location, discharge destination and outcome data over a 1-month period in February 2020. All neurotrauma admissions to the YGH neurosurgical unit who went on to receive a neurosurgical intervention were included, with collection of initial and subsequent Glasgow Coma Scores (GCS) as a measure of outcome.

Model building

Using a combination of the data from the two initial phases, a DES was developed to represent a simplified

model of the neurotrauma system at YGH. The focus of the model was on the preoperative and postoperative care pathways of the neurotrauma patients including a model of the resource requirements. This focus was grounded in the narrative accounts, which indicated these stages as being the key determinants of overall patient outcome.

The qualitative data were used to structure the care pathway, with the quantitative information used to describe the distributions of resource usage, length of stay (LoS) and discharge destination of patients moving along specific pathways. The model was developed iteratively using the software package Anylogic (university edition, The Anylogic Company, 2016 V.7.3.7). The model was verified through an iterative development process involving the research team members, and critiqued against the existing literature.

RESULTS

Qualitative data

Responses from the 104 respondents (40 workshop participants and 64 interviewees) were supplemented with interview data from workshop facilitators and members of the research team, and combined with field notes and written reflections into a single dataset. The workshops resulted in the creation of meta-narratives constructed as complex images which conveyed a range of information including physical infrastructure, patient flow, clinical decision making, investigations and clinical interventions. These were closely allied to the 'rich pictures' created when using SSM (figure 2). The interview data consisted predominantly of either verbal narratives or cocreated process flow diagrams.

From these, a formal system structure was synthesised, bounded within the neurosurgical unit and focusing on nodes consisting of neurosurgery admissions, the observation wards, the neurosurgery theatres, the CT scanner, the neurointensive care unit and the neurosurgical wards. This boundary was chosen to facilitate targeted quantitative data collection, but also due to the expertise of the Burmese research team being biased toward this area of the hospital. A patient flow logic model was then superimposed on these, with outputs chosen as discharge, referral to another centre or death (figure 3).

Quantitative data

The quantitative data showed 83 admissions with a median age of 33.4 years (range 11–66 years). The median LoS was 3.8 days (range 1–18 days). There was a 18% mortality, 71% discharge to home with an 11% referral rate to another department or hospital on discharge. This population information was used to inform the static distributions of patient flow in the simulation, as shown in figure 3.

The mean admitting GCS was 10.8 (range 3–15) and the mean discharge GCS was 12.6 (range 3–15). Six patients were transferred intubated from ED to the neurosurgery department. Location data collected was consistent with

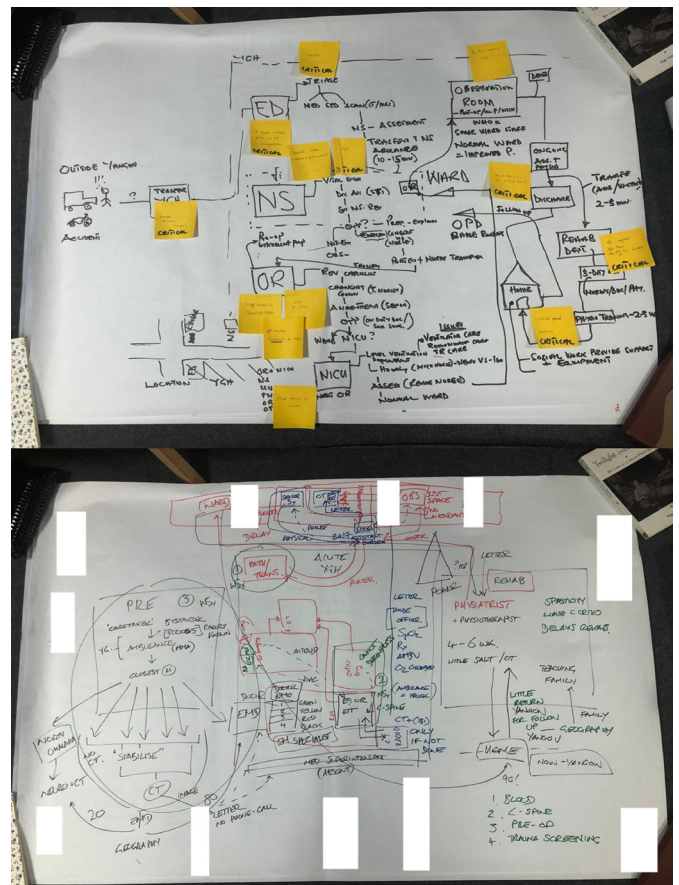


Figure 2 'Rich pictures' generated by workshop data reproduced from Bashford 2021 with permission of the author, with participant names redacted).

the qualitative system mapping, with the most reported locations being the admission unit, observation ward, neurosurgical ward (male and female), neurosurgery theatres and referral destinations. The initial admitting location for the surgical patients was the observation ward with almost all patients (98%) staying for at least 2 days before being transferred to the general neurosurgical ward.

Discrete event simulation

The DES model was structured using the model in figure 3 to explore key activities in a patient's journey from arrival at neurosurgery admissions to discharge home, referral to another hospital or death. All processing times were modelled as triangular distributions to take account of variations and uncertainty in both the process and data. The distributions were developed based on quantitative information and expert experience. Two separate patient groups were identified—surgical and non-surgical treatment streams—that share the same resources but were assigned different distributions and care pathways.

The narrative data identified two key areas as bottlenecks in patient flow: the availability of CT scanning (a time-critical investigation for neurosurgical patients), and the occupancy of observation ward beds. These were subsequently used as the main targets to investigate

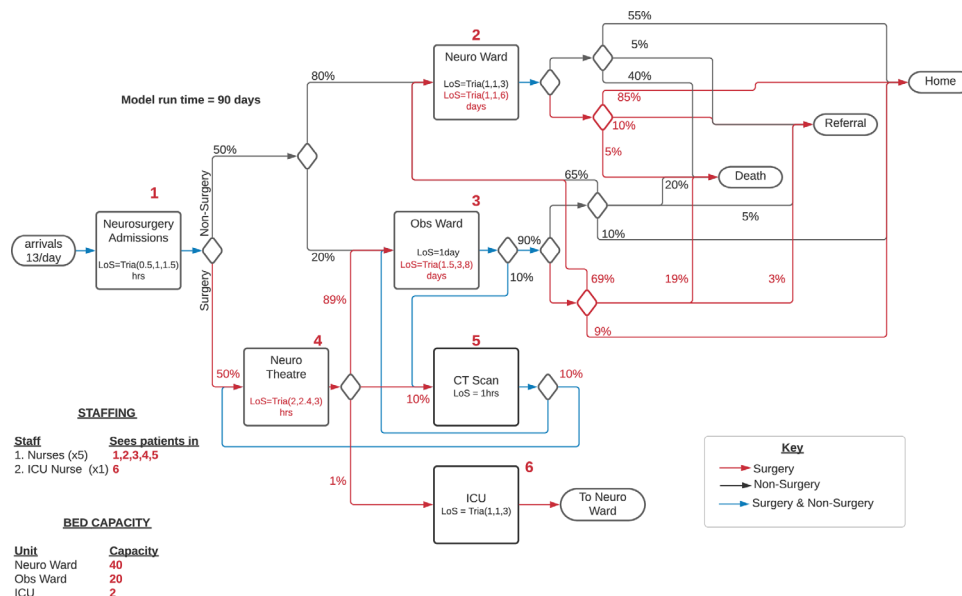


Figure 3 Des model structure showing the variables, patient flow and proportions the surgical patient pathway is denoted in red, the conservative/medical treatment pathway in black. Patients enter the des on the left at ‘arrivals’ and exit on the right into ‘home’, ‘referral’ or ‘death’. LoS, length of stay.

through DES. These were explored across a range of patient flows to explore the resilience of the system to sudden changes in surgical burden.

The simulation was run with a warm-up period of 200 hours and over a period of 90 days. In addition to the three kinds of discharge from the system—home, referral and death—the model reported outputs on queue lengths, waiting times and resource utilisation in selected areas (Scenarios summarised in table 1).

Insights from the narrative data led to a decision to explore the effects of changing the admission rate, the percentage of surgical patients, the capacity of the observation ward, and the availability of CT scanning. CT

availability was explored by both increasing the capacity of available scanners (increasing from one patient per 2-hour time window to two patients per 2-hour time window) and by increasing the priority of access to nursing staff for accompanying CT transfers, observation ward and neuroward. In all, nine scenarios were developed including the baseline. Scenario 9 involved three variations testing different levels of priority access to nursing staff. For model validation, the results of LoS from the model were within the range of 1–21 days estimated by Rock *et al*²⁰ based on empirical data from across Myanmar and consistent with clinical experience and the quantitative dataset.

Table 1 Description of the scenarios used to explore the system

Scenario number	Patient arrival rate	Percentage of surgical patients	Observation ward capacity	Additional changes
0 (baseline)	13	50	20	–
1	8	20	20	–
2	8	80	20	–
3	15	20	20	–
4	15	80	20	–
5	15	80	30	–
6	13	50	30	–
7	15	50	20	–
8	15	80	20	Increased CT capacity to 2/slot
9a	15	80	20	Priority: CT
9b	15	80	20	Priority: CT and observation ward
9c	15	80	20	Priority: CT and observation and neuroward

Three main variables were modified and the effects investigated. Additional improvement possibilities were explored in scenario 8 and 9a–c.

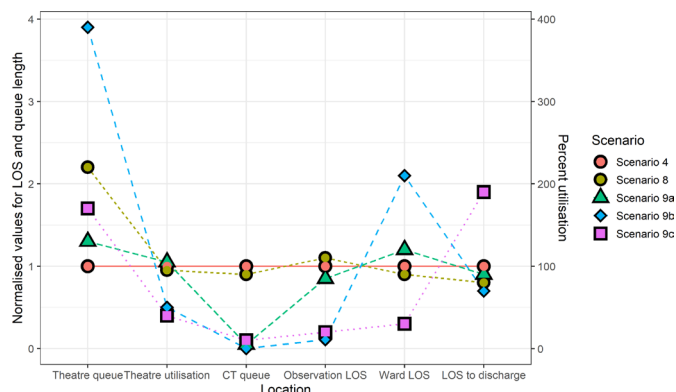


Figure 4 Effects of changing staff priorities on the patient load in different locations to improve CT flow in a high patient volume scenario (scenario 4). We adjusted the CT capacity (scenario 8) or the nursing staff task priorities (scenario 9a—priority to CT, scenario 9b—priority to CT and observation ward, scenario 9c priority to CT, observation and neuroward). The figure shows the queues waiting for theatre, CT and the observation ward, the LoS for neuroward and to discharge with the values normalised to scenario 4. Additionally, we show per cent theatre utilisation. The locations are arranged in the order of patient flow. LoS, length of stay.

The queue to access CT was modelled assuming a 2-hour round-trip based on local experience, with each patient requiring a single nurse escort. In scenario 4—a high patient volume scenario—we found the wait to access a time-critical CT increased to clinically unacceptable levels of several hours in keeping with the narrative accounts. We explored two potential improvement strategies for reducing wait for CT: increasing the number of patients that can go at the same time to 2 (scenario 8) and increasing the priority of CT scanning within the tasks for the available nursing staff (scenario 9a–c).

We found that scenario 8 did not resolve the CT capacity problems with the queue persisting at similar levels to scenario 4. The adjusted prioritisation scenarios where the availability of nurse escorts is increased (9a: CT main priority, 9b: CT and observation ward as priority, 9c: CT, observation ward and neurowards as priority) resolved the CT queuing and allowed for timely CT processing. However, this impacted on other areas of care as illustrated in [figure 4](#), which shows system performance measures (such as LoS and queuing) normalised to scenario 4. As an example, the effect of prioritising CT escorts and observation ward staffing in scenario 9b resulted in a long queue for theatres with reduced theatre occupancy and prolonged neuroward LoS, all due to the lack of available nursing staff to perform the necessary tasks. Similar complex system effects can be seen for scenario 9a and 9c where the delays have been diverted to admissions and theatres.

In addition to the CT bottleneck, the effect of changing patient numbers on the observation ward bed occupancy was investigated. [Figure 5A](#) illustrates the effects of a change in population characteristics by changing the percentage of patients classified as ‘surgical’. Scenario 4

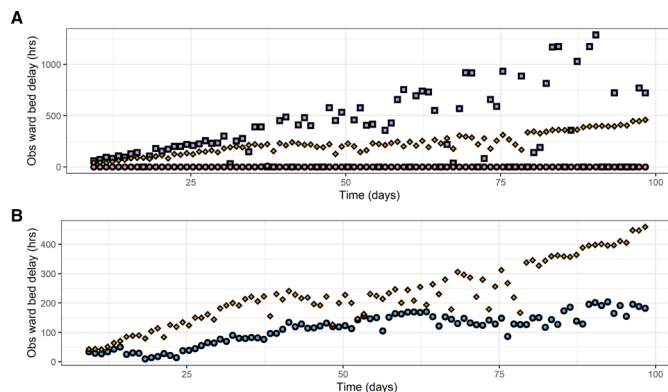


Figure 5 (A) Effect of a change in population by changing the percentage of patients classified as ‘surgical’ the increased length of stay on the observation ward is seen as an increase in delay for observation ward bed access. In yellow scenario 4 (50% surgical patients), in pink scenario 3 (20% surgical patients) and in purple is scenario 7 (80% surgical patients). (B). Effect of varying patient arrival rate with increased arrivals the waiting time for the observation ward bed increases. again, in yellow is the baseline scenario 4 (15 patients/day), in blue we show scenario 7 (13 patients/day).

(50% surgical patients) in black, scenario 3 (20% surgical patients) in blue and scenario 7 (80% surgical patients) in red. The increased number of surgical patients with a longer stay on the observation ward care postoperatively results in an increase in the delay to access an observation ward bed. [Figure 5B](#) illustrates the effect of varying patient arrival rate. With increased arrivals the waiting time for the observation ward bed increases. In black is the baseline scenario 0 (13 patients/day), in blue is scenario 7 (15 patients/day). It is notable that with an increase in the arrival rate of just 2/day, there is a significant increase in the waiting time for a bed, given that the observation ward occupancy is already >90% for the baseline scenario. These results were again consistent with local experience.

Consequently, a possible service change with a moderate expansion of the observation ward capacity from the baseline 20 beds to a potential 30 beds was explored. This was an illustrative change aiming to determine a potential alleviation of a bottleneck. The results are shown in [figure 6](#), with the baseline model (20 beds) shown in purple and scenario 6 (30 beds) in yellow. The delay to access an observation ward bed is shown in the top panel and the percentage occupancy in the bottom panel. The additional bed spaces resolved the near full capacity state of the observation ward and reduced the waiting time for a bed to negligible numbers.

DISCUSSION

We describe a systems approach to understanding the care of neurosurgical patients in a resource-limited setting, based on a combination of qualitative exploration, prospective data collection and DES. The insights gained from this study are both practical and methodological. Practically, we show that changes in staffing

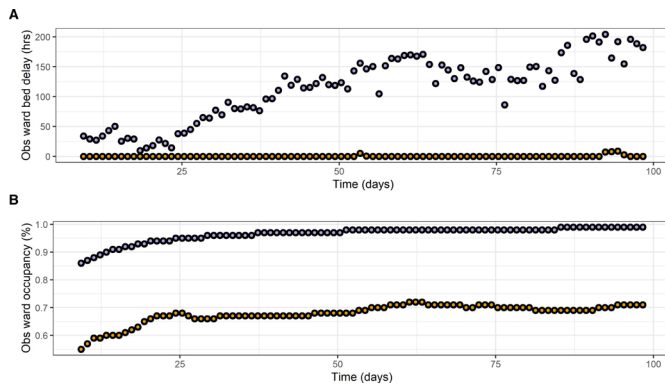


Figure 6 Change in patient load on the observation ward when the capacity is increased in purple is the baseline scenario 0 (20 beds) and in yellow scenario 6 (30 beds). (A) shows the delay to an observation ward bed, (B) shows the observation ward occupancy through the simulation period. The moderate increase in bed capacity clearly reduces the pressure on observation ward beds.

allocation and observation ward capacity may improve patient flow despite coexisting resource limitations. Methodologically, we show how a mixed-methods approach by a cross-cultural multiprofessional research team can deliver high-quality systems modelling which is grounded in both the lived reality of local stakeholders, and in reliable prospectively acquired data.

Understanding healthcare from a systems perspective presents both conceptual and pragmatic challenges. These are best met by marrying robust qualitative and quantitative approaches, however, achieving this in resource limited settings where clinical services are stretched and routine data collection may be impossible is challenging. In addition, much of the systems thinking literature comes from a canon of thought developed in high-income countries, and this may not translate readily to other cultures or languages. Indeed, the Burmese members of the research team found translation of the Engineering Better Care questions very challenging, both linguistically and conceptually. Furthermore, while the project was conceived within the SSM, a constructivist approach grounded in systems thinking which has been applied to healthcare in a range of contexts, this was found to be a barrier to participatory research as the terminology and theory was found to be difficult to translate into Burmese.

As a result, the research approach we describe uses narrative as a tool for understanding lived experience to overcome some of these barriers. Storytelling is common to all human society and is a mechanism for people to both conceive and communicate complex ideas.²¹ Combining this with participatory diagramming provides a natural form of data creation, without requiring local research partners to engage with complex theoretical models. Narrative research also encourages a degree of transformation on the part of the research team, as they elicit and assimilate a variety of stories from widely different viewpoints. In the words of one of the research team:

When we started this research I thought that all of our problems came from a lack of resources. Now I can see so many things we can improve without waiting for more money.

The participatory diagramming also provides a starting point for the DES model which is grounded in the primary experience of the research participants, providing reassurance that the model is close to reality, and that the prospective data collected is parsimonious and of maximum utility. Structuring both of these with the systems approach articulated in Engineering Better Care provides a degree of methodological rigour and ensures that a focus on the function of the system as a whole, rather than discrete processes, remains at the heart of the data collection. Future work might benefit from a more structured interview tool to help combine narrative inquiry with the systems approach.

The DES modelling facilitates the conversion of this rich narrative data into a more abstracted form, which can then be readily manipulated and used to predict changes to system behaviour within specific constraints. Consistent with the experience of the research team, our model explores the resource limitations around access to CT imaging and observation beds. However, the model challenges the narrative data, with access to CT scanning limited less by the access to CT machines, and more by the availability of nurse escorts. The model, however, agrees with the narrative report that nursing provision is stretched when patient volume increases and changing prioritisation of tasks only shifts the resulting delays to another care area. Similarly, the model indicates that while a modest expansion of observation beds improves patient flow, this does not scale indefinitely. Both insights have consequences for real-life improvement opportunities. Ideally, these insights would have been taken back through a process of qualitative exploration to better understand the findings, but both the SARS-CoV-2 pandemic and political events in Myanmar prevented this last phase of the research.

However, it is important to note that our DES model was created to look specifically at patient flow, again grounded in the reported experience that most patient complications arise from a delay to care. TBI, like other specific pathologies, is a time critical condition and it seems reasonable that delay is one of the key drivers of patient outcome.²² However, any number of alternative models could be built to explore communication flow, institutional power or clinical decision making. More complex concepts such as the quality of care are not addressed in our model. The provision of surgery may be considered at the interface of clinical need, access, and quality and our model currently explores only one of these dimensions.²³

The DES model was developed to demonstrate the kinds of insight that are possible when the technique is combined with participatory systems mapping and the rich narrative data from qualitative methods. As a result,

several assumptions were made that may be considered limitations of the model. For example, all LoS durations and processing times were modelled as triangular distributions in the absence of numerical data to allow theoretical curve-fitting. The triangular distribution is pragmatic, intuitive and effective in situations of insufficient numerical data.²⁴ Another assumption made was the absence of priority in the allocation of nurses and beds. Patients were allocated these resources on a first come first served basis.

It is important to note that a variety of other models could have been built based on our qualitative dataset. A different system boundary, such as that of the whole hospital as opposed to the neurosurgical unit, would have required different quantitative metrics and would have been much more complex to build. It would also have required a research team made of different clinical specialties to ground the qualitative and quantitative data within lived expert experience. However, the benefit of good early qualitative work is that it provides the opportunity to explore a variety of different future models, to address a wide range of clinical and operational improvement questions.

CONCLUSION

TBI is a growing burden in the global south, and efforts to improve care in this area are hampered by its complexity, a lack of access to the necessary services, and the delay this engenders.

Our mixed-methods systems approach which combines rigorous qualitative approaches with DES allows for modelling firmly grounded in local context but informed by established mathematical theory. We demonstrate that such research can be carried out by a diverse research team based on the lived experience of a range of stakeholders. The resulting model retains validity when critiqued against this primary qualitative data, provides insights into resource limitations and specific targets for improvement and should be of value across a huge range of clinical and geographical contexts.

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Patient consent for publication Not applicable.

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