

Developing a Model of Care for Home Infusions of Natalizumab for People With Multiple Sclerosis

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ABSTRACT

Natalizumab is an effective treatment for multiple sclerosis that requires 4-weekly infusions that are usually provided in hospital outpatient clinics. In this study, a model of care (MOC), an overarching design for the provision of a health care service, was developed to permit home infusions of natalizumab. The proposed new MOC comprised 9 dimensions, in addition to the central concept of patient-centered care at home. The new MOC is responsive to patient needs and prioritizes the nurse–patient therapeutic relationship. It provides practical examples of patient-centered care to guide clinical practice for this patient population in the home setting.

Key words: home care, home infusion therapy, model of care, multiple sclerosis, natalizumab, patient-centered care

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All authors participated in the meetings to develop the model of care. Dr Schultz led the literature review work. Ms Thomas led the development of home infusion processes. Mr Georgiou, Ms Simon, Ms Juaton, Mr Webb, and Dr Ravindran provided feedback on hospital infusion processes. Dr Cusack provided input into nursing workforce requirements and Prof Karnon provided input on health economics. Dr Schultz drafted the first version of the manuscript; all authors read and approved the final manuscript.

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Ms Thomas is director of Post-Op Care at Home (Pty Ltd). This organization was subcontracted to deliver the home care nursing. Therefore, if the outcome of the project is positive and home delivery of natalizumab becomes a new model of care, this could lead to commercial gain for Ms Thomas.

Ms Naidoo is an employee of Biogen, manufacturer of natalizumab. Therefore, if the outcome of the project is positive and home delivery of natalizumab becomes a new model of care, this could lead to commercial gain for Biogen if it leads to more patients receiving natalizumab than would otherwise have been the case.

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Multiple sclerosis (MS) is a chronic autoimmune disorder causing inflammation, demyelination, and degeneration of the central nervous system and affecting some 2 million people worldwide.¹ Natalizumab is a disease-modifying therapy that reduces the relapse rate, number of lesions, and progression of disability for people with relapsing-remitting MS.² A monoclonal antibody, natalizumab is delivered as a 1-hour intravenous (IV) infusion of 300 mg every 28 days.³ It is generally well tolerated by patients through peripheral IV administration, although adverse drug events include hypersensitivity reactions (eg, anaphylaxis), infections (eg, urinary tract infection), and less serious infusion-related reactions occurring during or up to 1 hour after the infusion (eg, fatigue and headache).⁴ Acute hypersensitivity reactions (eg, urticaria) occur in 3% to 4% of patients, with serious hypersensitivity anaphylaxis reactions occurring in 1% of patients.^{2,5} Infusion-related reactions are typically nonspecific and, in addition to fatigue and nausea, may also include weakness, dizziness, sweating, fever, rash, rigors, diaphoresis, slow pulse, and/or a moderate drop in blood pressure, dyspnea, chest pain, and leg bruising.^{3,6,7}

The safety of natalizumab in the long term is consistent with shorter-use safety profiles.^{8,9} For long-term use the most significant safety concern with natalizumab is progressive multifocal leukoencephalopathy (PML). PML is an opportunistic central nervous system infection that has been associated with John Cunningham virus.¹⁰ First identified in 2005,^{11,12} the incidence of PML in patients who had received natalizumab is 4.2 cases per 1000.^{12,13} Anti-John Cunningham virus antibody index testing, regular magnetic resonance imaging monitoring, and testing for clinical manifestations are recommended to reduce the risk of PML from natalizumab.^{10,12,14}

Natalizumab infusions are conventionally delivered in hospitals, physicians' offices, MS clinics with infusion centers, and free-standing infusion centers with physician supervision.¹⁵ In South Australia, patients receive natalizumab infusions in hospital-based outpatient clinics.¹⁶ However, for people with chronic disease, home care can lead to better outcomes through avoidance of travel times and out-of-pocket expenses.^{17,18} This reflects a growing trend worldwide toward delivery of health care in the home rather than hospital.^{19,20}

Home care is defined as "the care provided by professionals to people in their own homes with the ultimate goal of not only contributing to their life quality and functional

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health status, but also to replace hospital care with care in the home for societal reasons."^{21(p861)} In parallel to the broader provision of health care at home, home infusion therapy is the administration of medications using IV, subcutaneous, and/or epidural routes in the home setting.²² Beginning with home parenteral nutrition in the late 1970s²³ and home IV immunoglobulin therapy,²⁴ the move to home infusions has extended into a range of diseases and treatments. For example, home-based chemotherapy has recently been shown to be feasible, safe, and valued as an alternative to treatment at an outpatient clinic.²⁵

There has been little progress in delivering monoclonal antibody treatments at home, although home infusions of infliximab for people with Crohn's disease was trialed for 29 adults in the Netherlands²⁶ and 10 children in the United States.²⁷ Similarly, the first at-home natalizumab infusion service in which 34 patients received nearly 500 doses in total at home was recently described in a conference abstract.²⁸ No specific details were published about the protocol for home infusions or how it was developed and approved.

Providing patients with choice and flexibility about where they are able to receive their treatment and who can provide it is a central tenet of patient-centered care.^{29,30} To support the provision of patient-centered care and provide home care as a safe option to people with MS, it is necessary to develop a new model of care. A *model of care* is defined as "an overarching design for the provision of a particular type of health care service that is shaped by a theoretical basis, evidence-based practice and defined standards."^{31(p47)} The aim of this study was to develop a patient-centered MOC for home infusions of natalizumab for people with MS.

METHODS

The concept of home infusion therapy was applied to people receiving natalizumab for MS. The research team drew on extant literature and evidence-based practice, clinical and research experience, and existing standards and policies to develop a patient-centered MOC.

Definitions and Framework for the New MOC

To guide the new MOC, the Institute of Medicine's definition of patient-centered care was used: "Providing care that is respectful of, and responsive to, individual patient

preferences, needs and values, and ensuring that patient values guide all clinical decisions.”^{30(p6)} This definition provided the foundation for many of the dimensions of the MOC, which naturally placed patients at its center and incorporated 8 key components of patient-centered care: (1) respect for patients’ preferences and values, (2) emotional support, (3) physical comfort, (4) information, communication, and education, (5) continuity and transition, (6) coordination of care, (7) the involvement of family and friends, and (8) access to care.²⁹

This study was guided by the United Kingdom Medical Research Council framework for developing and evaluating complex interventions.³² A search for relevant evidence (“preclinical or theoretical phase”) was first conducted in March 2016 and updated in June 2018. PubMed, Scopus, Cochrane Library, Joanna Briggs Institute, and Cumulative Index to Nursing and Allied Health Literature databases were searched using search terms and medical subject headings including “home infusion”; “home care”; “natalizumab”; “monoclonal antibody”; “adverse events”; “IV infusion”; “multiple sclerosis”; and “home care services.” The search identified 35 published studies relevant to the aims of this study, including studies in 5 main topics: safety and adverse effects of natalizumab,^{2,4-13} home care,^{19-22,33-36} home infusions,^{18,24-28,37-41} infusion guidelines and standards,^{15,42} and medication management.⁴³ In addition to relevant published studies, product information,³ training guides,⁴⁴ Australian health care standards,⁴⁵ and organizational protocols¹⁶ were included, and US infusion therapy standards⁴⁶ were reviewed for applicability in the Australian setting. Critical appraisal of studies was not conducted.

Key findings from the included studies were extracted and discussed during regular (4–6 weekly) research team meetings in 2016–2017. The discussions focused on the 5 main topic areas and involved all members of the research team, representing home care nursing, nurse education and regulation, day unit clinicians, health policy and economics, neurology, pharmaceutical industry, evidence synthesis, and patient safety research. In phase 1 modeling, which involved modeling to improve understanding of the components of an intervention,³² the components of the MOC to safely deliver home infusions of natalizumab were developed inductively from the literature and research discussions. Decisions were made by consensus during meetings, and draft minutes were circulated for discussion and confirmation at subsequent meetings.

The resulting MOC was to be used to design a phase 2 exploratory trial,³² testing the feasibility of delivering home infusions and providing preliminary data about safety and effectiveness.⁴⁷ As the MOC was designed to be formally evaluated, it included components related to data collection and documentation of adverse events.

Setting

The study was set in Adelaide, South Australia, as a collaboration among a university, a major public metropolitan

acute care hospital, a private provider of home nursing, and a pharmaceutical company. Meetings occurred at the day-infusion service within the hospital outpatient area. The MOC was intended to replicate care provided in the day-infusion service; therefore, other hospital medical and nursing staff were also consulted, and the perspectives of patients with MS were gained opportunistically by staff delivering infusions in the hospital clinic.

Ethics

As the development of the model of care involved review of literature, policy and current practice, and discussions by researchers, formal ethical approval was not required for phase 1 modeling. The phase 2 study protocol, based on the MOC developed here, was subsequently reviewed and approved by the Royal Adelaide Hospital Human Research Ethics Committee (HREC/16/RAH/192).

RESULTS

The new MOC developed for home infusions of natalizumab is summarized in Figure 1. The MOC was composed of 9 dimensions, in addition to the central concept of patient-centered care at home for people with MS. Each dimension is described in more detail in the Figure.

Home Nursing Care Provider

The hospital does not provide a home nursing service; therefore, a private provider of home nursing care (Post-Op Care at Home Pty Ltd [POCaH]⁴⁸) was contracted to deliver the home infusions. Three registered nurses, each with more than 10 years of experience, were employed to deliver infusions. Appropriate insurance coverage (ie, professional indemnity, public liability, and work injury) was in place. Equipment used by the home nursing provider included an infusion stand, consumables, and vital signs monitoring (temperature, blood pressure, and respiration). The home care provider was represented on the research team and led much of the developmental work required to operationalize the model of care. The hospital lacked funding for home nursing; therefore, the home nursing care and consumables were funded by Biogen Australia and New Zealand, manufacturers of natalizumab.

Competency of Nurses

Clinical competency is essential to maintaining patient safety; for infusion nursing, such competencies include clinical management of special populations, anatomy and physiology, safety considerations, vascular access device planning, and management and infusion administration.⁴⁶ Sound patient assessment, documentation, and patient education skills are essential for home infusion nursing as well.³⁷

The registered nurses delivering home care were required to undertake the following: (1) a half-day orientation to home infusions, (2) a full-day orientation to POCaH,

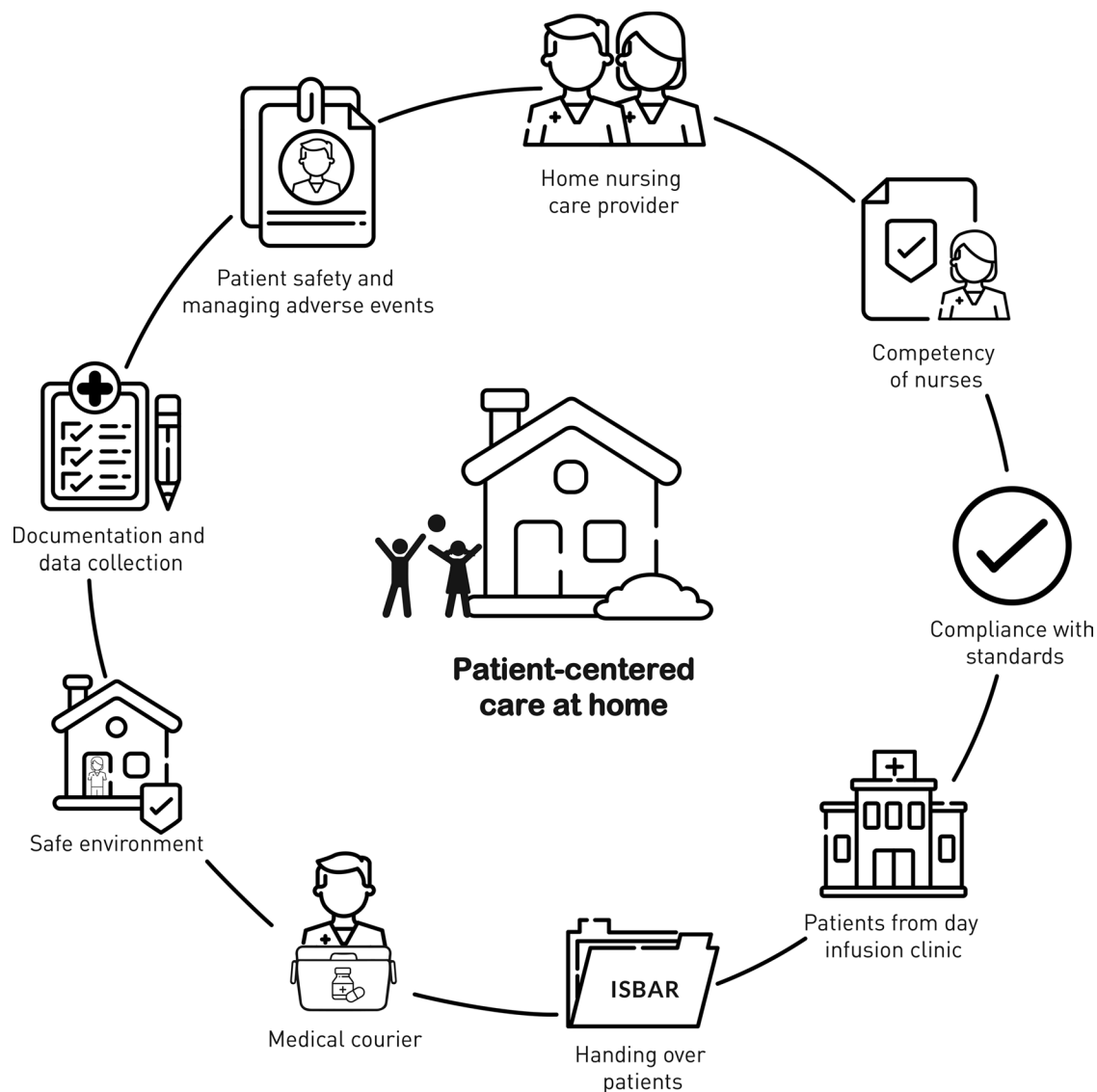


Figure 1 The new model of care developed for home infusions of natalizumab. Abbreviation: ISBAR, Identify, Situation, Background, Assessment, and Recommendation. © Timothy Schultz.

and (3) a 2-hour online training about prescribing and delivering natalizumab.⁴⁴ In addition, nurses undertook a half-day placement in the hospital clinic to familiarize themselves with the clinic's processes and to provide similar care to the infusion clinics. Because some patients experience difficulty with IV access,^{7,27} a refresher course in cannulation was also undertaken to ensure currency of practice.

Compliance With Standards

The 2011 National Safety and Quality Health Service Standards cover high-prevalence adverse events, such as health care-associated infections, medication safety, and clinical communication.⁴⁵ The National Safety and Quality Health Service Standards and the Infusion Nurses Society's 2016 *Infusion Therapy Standards of Practice*⁴⁶ were used to inform the development of the POCaH Safe Quality Health Service Manual. Some of the practices built into the model

of care that were derived from these standards include the following:

1. Patient identification: patient name, birth date, and address were used as the 3 identifiers required for treatment to proceed;
2. Signed consent from the patient and the physician to proceed with home treatment; and
3. Signed treatment order from the physician used to clarify the 9 steps for accurate medication delivery.

Patients From the Day Infusion Clinic

As some patients had been receiving natalizumab infusions at the hospital clinic for ≥ 5 years, strong therapeutic relationships between clinic staff and patients were noted. The involvement of patients and clinic staff, as well as the MS clinical nurse specialist, in the development of the MOC

helped to manage existing therapeutic relationships in the clinic. Ensuring that the patients' neurologist approved their participation in the trial was another strategy to manage this challenge. As part of the consent process, patients were also clearly informed that, after the conclusion of the research, their usual care would revert back to the clinic.

Handing Over Patients

Ensuring continuity is an essential nursing factor for home infusions.³⁷ Home infusion nurses met the project participants in the clinic before their first home infusion, facilitating patient preferences (eg, preferred vein for cannulation, timing, and location of the next infusion), sharing of contact details, and initiation of a nurse–patient therapeutic relationship. Patients were encouraged to contact nurses directly for any scheduling changes.

To facilitate consistency in the handover of patients between the public (clinic) and private (POCaH) settings, the Identify, Situation, Background, Assessment, and Recommendation (ISBAR) handover tool (as used in the public setting) was also adopted. The ISBAR mnemonic improves safety in the transfer of critical information and facilitates effective communication.^{34,49} A handover form was developed to assist in the transfer of patients into POCaH care. This form captured patient contact details, general practitioner details, other medications, allergies, pain management, and signatures of the neurologist and patient.

Medical Courier

Natalizumab is provided in single-use 15-mL vials, which, like most pharmaceuticals, must be at 2°C to 8°C (36°F–46°F).⁴³ Vials should also be protected from light and not shaken or frozen.³ Given these restrictions and air temperatures that readily exceed 40°C in the Australian summer, medical couriers were employed to transport the medication. Additionally, couriers were on hand to assist in the evaluation of the safety of the environment for the nurse and to intervene if required.

To ensure compliance with “cold chain” handling requirements, medical couriers used a Coolpac 15 Pre-Qualified Insulated Shipper (Coolpac; Doveton, Victoria, Australia). These are certified to maintain 2°C to 8°C for up to 72 hours in a Mediterranean summer and were piloted for use in an Australian context. As an additional safety measure, a temperature logger (LogTag; Northcote, Auckland, New Zealand), accurate to 0.5°C, was included with the natalizumab in the Coolpac Shipper. The temperature logger was set to visually alert if the 8°C threshold was crossed, and data for each infusion were recorded. Data about each natalizumab transfer (eg, date, time, location, patient details, and temperature) were recorded on a data collection document.

Safe Environment

Hazards in the home environment include bloodborne pathogen exposures, demanding patient mobilization and

transfer tasks, threat of violence and other personal safety issues, and the presence of pets.³⁹ The importance of a safe environment for both home care nurses and patients^{28,37} was addressed in POCaH orientation, including strategies for improving safety in home care and use of an environment checklist. The checklist included items relating to parking, patient's health status, presence of family members, cleanliness and suitability of the environment, and other issues, such as the presence of pets.

Documentation and Data Collection

Effective documentation of care is essential within health care,⁴⁵ and the home infusion environment specifically.^{37,42} Data from each home infusion were recorded to provide a record of home care to add to the clinic's patient records and to collect data as part of the phase 2 trial. A “Clinical Pathway and Report” form was developed. This form captured patient and infusion details, including the method of delivery (eg, port and IV cannula); the presence of any infections, treatments, and outcomes; details about the expiration date and batch numbers; any comments about environmental safety; and observations (eg, temperature, pulse, respiratory rate, or blood pressure) measured before, during, and after the infusion.

Patient Safety and Managing Adverse Events

The author team developed eligibility guidelines for patients to minimize the likelihood of a hypersensitivity reaction. As most hypersensitivity reactions typically occur by the second ever infusion,² as a conservative measure, only patients with a minimum of 6 previous natalizumab infusions were eligible for the new MOC.

In addition to minimizing the likelihood of a hypersensitivity reaction, the new model of care included clear guidelines for managing adverse events and serious adverse events. A total of 9 documents were developed, including a flow chart of actions, definitions, and reporting requirements. In the event of an adverse event, home care nurses were instructed to stop the infusion, apply first aid, and contact the hospital's on-call neurologist. For serious adverse events causing severe discomfort and risk of serious injury or death (eg, anaphylaxis), nurses were instructed to contact an ambulance for immediate medical help. As per usual clinic-based care, a preinfusion questionnaire was administered before all home infusions. Vital signs were measured for 20 minutes postinfusion, with an additional 20 to 40 minutes if required until the patient was stable.

DISCUSSION

This study led to the development of a new MOC for delivering natalizumab infusions in patient's homes. The MOC can be used as a protocol to manage the hand over of patients between hospital and home, transport of medication to patients' homes, the delivery of home infusions, treatment

of any adverse events, and training of home care nurses. The new MOC is responsive to patients' needs and prioritizes the nurse–patient therapeutic relationship through mutual respect, acknowledgment of autonomy, and sharing goals.⁵⁰ The MOC helps to meet Multiple Sclerosis Australia's position statement on Health and Community Services: "People with MS should have access to a range of coordinated and integrated health and community care services, in line with their needs."^{51(p1)}

The proposed new MOC has 9 dimensions in addition to a central component of patient-centered care at home. Most of these map to the 4 key areas identified as predictors of positive outcomes in infusion nursing⁴²: (1) appropriate patient selection: patient safety and managing adverse events; (2) effective patient education: handing over patients; (3) meticulous patient care and comprehensive assessment and monitoring: home nursing providers, competency of nurses, compliance with standards, and documentation and data collection; and (4) interprofessional communication and collaboration: patients from the hospital clinic and medical courier. The one other dimension of the MOC is safe environment, which seeks to manage risks from the home environment to both staff and patients.

The planning for the new MOC has ensured that the preconditions for implementation and evaluation are in place before the commencement of the evaluation.³¹ A recent phase 2 pilot study evaluated the safety, feasibility, acceptability, clinical effectiveness, and costs of the new MOC.⁵² Patient perspectives of the MOC have also been collected to inform its potential further development.⁵³ Future considerations of scale up and sustainability of the home infusion MOC should be informed by the phase 2 trial⁵² and future phase 3 and phase 4 studies.³² Sustainability of funding home nursing is clearly paramount to greater uptake across the Australian health system. Although cost savings are consistently reported for home infusions across a range of therapy indications,⁴⁰ operationalizing funding between different parts of the health system is likely to be challenging.

Patient Centeredness in Home Infusions

The philosophy and practice of patient-centered care should be at the core of the new model of care.⁵⁴ Patient-centered care values the needs of patients, caregivers, and staff and emphasizes the reciprocity of therapeutic relationships and responsiveness to individual patient's needs, values, and preferences.^{29,30} Respect; coordination and integration of care; information, communication, and education; physical comfort; emotional support; and involvement of family and friends are all key dimensions to patient-centered care.⁵⁵ In the new MOC for home infusions, these dimensions are apparent through the greater flexibility and patient involvement in the delivery of care and the timing and location for infusions; for example, infusions can be given after hours, in the patient's home or that of a friend or family member, or in the patient's workplace. The model of care also permits

greater flexibility in rescheduling infusions. These practical examples of patient-centered care can help to embed it into home infusion clinical practice.

Patient Safety and Quality of Care

Maintaining patient safety and preventing complications in the context of delivery of care at home are paramount.⁴² Homes lack specialized equipment available in acute care settings, and care at home may be less structured and less regulated.³³ Patient safety was addressed by restricting patient eligibility to those who had previously received at least 6 natalizumab infusions and were deemed stable by neurologists, developing clear guidance for home nurses to manage an adverse event, replicating the care provided in the clinic setting using appropriate standards of care and ensuring the competency of the home care nurses. It is expected that these measures will ensure the safety of patients with MS at home, although further evaluation of the MOC is likely to be required.⁵²

This proposed model of care reflects other home care initiatives designed to improve efficiency, patient centeredness, safety, and quality, while reducing health care costs and meeting greater demand.²¹ Treatments that have recently been shown to be safe and efficacious when delivered at home include IV antibiotics for cellulitis,⁴¹ enzyme replacement therapy for Gaucher disease⁵⁶ and Fabry disease,¹⁷ and complex chemotherapy in acute leukemia and lymphoma.³⁸ Possible benefits from home care include improved adherence to treatment, better quality of life and clinical outcomes, reduced health system costs, and greater convenience to patients.^{17,18}

LIMITATIONS

The study is limited to a single medication, although it is probable that key learnings can be adapted to other infusion medications and for other types of chronic diseases. Although the team conducted a comprehensive search for literature across multiple databases, it is possible that relevant articles were not included in our search results. Care protocols from only 1 organization were used as the basis for care in the day-infusion clinic.

CONCLUSION

The new MOC has been developed to allow people with MS to receive infusions of natalizumab at home and addresses 9 key dimensions of patient centeredness. The MOC provides practical examples of patient-centered care to guide clinical practice for this patient population in the home setting. The need to ensure patient safety in the home setting is integral to the new MOC. Additional work is required to evaluate the model of care and scale it up to ensure its utility at the health system level across multiple hospital sites.

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