Proceedings of the 2015 Winter Simulation Conference
L. Yilmaz, W. K. V. Chan, I. Moon, T. M. K. Roeder, C. Macal, and M. D. Rossetti, eds.

SIMULATION CONCEPTUAL MODELING FOR OPTIMIZING ACUTE STROKE CARE ORGANIZATION

Durk-Jouke van der Zee

University of Groningen
P.O. Box 800
Groningen, 9700AV, THE NETHERLANDS

Maarten M.H. Lahr
Gert-Jan Luijckx
Erik Buskens

University Medical Centre Groningen
P.O. Box 30001
Groningen, 9700 RB, THE NETHERLANDS

ABSTRACT

Stroke is the second leading cause of death and a leading cause of long-term disability world-wide. Treatment with intravenous tissue plasminogen activator (tPA) is the most effective medical treatment for acute brain infarction within 4.5 hours after the onset of stroke symptoms to improve functional outcome. Unfortunately, tPA remains substantially underutilized. Stroke care organization is among the dominant factors determining undertreatment. Recently, simulation has been suggested and successfully implemented as a tool for optimizing stroke care pathway logistics. Starting from this observation we propose a domain specific simulation conceptual modeling framework, aiming to enhance decision making on acute stroke organization. The modeling framework provides guidance for the analyst, through specifying and structuring key modeling activities, and suggesting good practices and supportive methods for executing them. Relevance of the framework for project success is illustrated by a case example.

1 INTRODUCTION

Acute ischemic stroke is the second leading cause of death and a leading cause of long-term disability world-wide (Truelsen et al. 2005). Treatment with intravenous tissue plasminogen activator (tPA) is the most effective medical treatment for acute brain infarction. Essentially, tPA restores blood flow in the brain by dissolving the blood clot, causing the infarction. tPA has shown to be effective, i.e., improving patient functional outcome, within 4.5 hours after the onset of stroke symptoms. Of all patients worldwide suffering a stroke, 1–8% (Wardlaw et al. 2009; Adeoye et al. 2011; Singer et al. 2012) are currently treated with tPA, whereas 24–31% (Waite et al. 2006; Boode et al. 2007) would be attainable in optimized settings.

Next to the narrow therapeutic time window, and patient unfamiliarity with stroke symptoms and how to act, acute stroke care organization is among the factors determining undertreatment (Kwan et al. 2004; Lahr et al. 2013b). Notably, the benefit of tPA depends strongly on time between stroke onset and start of therapy (The NINDS rtPA Stroke Study Group 1995; Hacke et al. 2008).

In past years many researchers suggested improvements of stroke care organization, thereby seeking to reduce onset-to-treatment-time (OTT), because efficacy of the treatment is time dependent, the sooner, the better or “time=brain”. Their efforts primarily relied on the use of Randomized Controlled Trials (RCTs) as a main research vehicle. Basically, RCTs compare real-life outcomes for two groups of patients: those that traversed the existing pathway and those for whom the pathway has been adapted according to proposed interventions. Recently, several studies have shown how simulation may be used as an efficient alternative or precursor to clinical trials for testing efficacy of tPA treatment for alternative set-ups of the stroke pathway (Monks et al. 2013; Pitt et al. 2013; Churilov et al. 2013; Lahr et al. 2013a).

Whereas clinical trials are limited to testing a seemingly arbitrarily selected set of interventions along the stroke pathway, the efficiency of computer simulation models allows for a far greater set of interventions entailing the overall pathway to be put to test at minimum efforts. Clearly, disadvantages of real-life testing in terms of time, costs and efforts involved in study set-up and experimenting, and project lead time become apparent here (Law 2008).

Potential and interest for simulation as a method for optimizing stroke organization makes guidance for the analyst in specifying, coding, and analyzing simulation models a relevant issue. Here our prime focus is on model specification or conceptual modeling. Conceptual modeling is meant to establish modeling objectives, and the model elements. A good quality conceptual model suggests a well-informed interpreting of stroke pathway characteristics, and the requirements set by those parties involved in the stroke pathway, especially, Emergency Medical Services (EMS), General Practitioners (GPs), and Neurologists. Clearly, qualities of a conceptual model have great impact on the success of the simulation study. In turn this implies a need for guidance for the analyst, in (mastering) his/her creative efforts in capturing stroke pathway essentials, as well as sharing them with parties involved in the simulation study.

In response to the observed need for guidance of the analyst in conceptual modeling for optimizing stroke care organization we propose a domain specific modeling framework. The framework suggests a step wise approach for specifying the simulation model, in terms of key activities capturing model objectives, model inputs and outputs, and model contents. It distinguishes itself from existing frameworks by its tailoring towards the acute stroke pathway. The proposed framework results from extensions of the framework by Robinson (2008b). Use of the new framework is illustrated by a case example concerning the stroke pathway for the province of Groningen, The Netherlands (Lahr et al. 2013a).

The remainder of the paper is organized as follows. In Section 2 we introduce the research methodology underlying set-up and use of the new simulation conceptual modeling framework optimizing acute stroke care organization. In Section 3, the framework is described in detail. Then the use of the framework is illustrated by a case example (Section 4). Section 5 evaluates contributions made by the framework. Finally, in Section 6, major findings are summarized.

2 METHODOLOGY

The new modeling framework is meant to facilitate the specification of a coded simulation model of an acute stroke pathway by identifying, structuring, and supporting conceptual modeling activities. The latter activities entail establishing modeling objectives, model input (experimental factors), model output (responses) and model content (Robinson 2008b).

The acute stroke pathway is characterized by a series of interlinked care services, see Figure 1. Patients arrive at the hospital either by EMS, after a call to the emergency number (112) or the GP, or by self-transport. GPs either visit the patient first or alarm EMS directly. EMS offers basic or advanced life support and transportation services. Initial intra-hospital activities concern several diagnostic activities in parallel (i.e. patient blood testing, examination by a neurologist, and neuroimaging using a CT-scanner). Next, starting from the diagnostic results, and the time elapsed between stroke onset and hospital arrival (i.e. <4.5 hours), the neurologist decides on whether to treat the patient or not. Note that a minority of the patients faces a stroke while being hospitalized.

On a regional level acute stroke care may be organized in various ways, see Lahr et al. (2013b), for an overview. For example, several researchers indicate that for urban regions one may decide to concentrate acute stroke care in a comprehensive stroke center, being tailored towards an adequate and fast response to stroke patients' needs, by offering 24 hours, 7 days immediate access to neurological consultation and neuroimaging at the emergency department. For rural regions, telemedicine solutions may be considered, allowing regional health facilities to benefit from the neurological expertise offered at a distance. A novel concept concerns the Mobile Stroke Unit (MSU), consisting of a neurological team and a specialized ambulance, including CT scanning equipment. The MSU is meant to shorten travel and treatment time for the patient, by allowing for on-scene treatment by a dedicated unit.

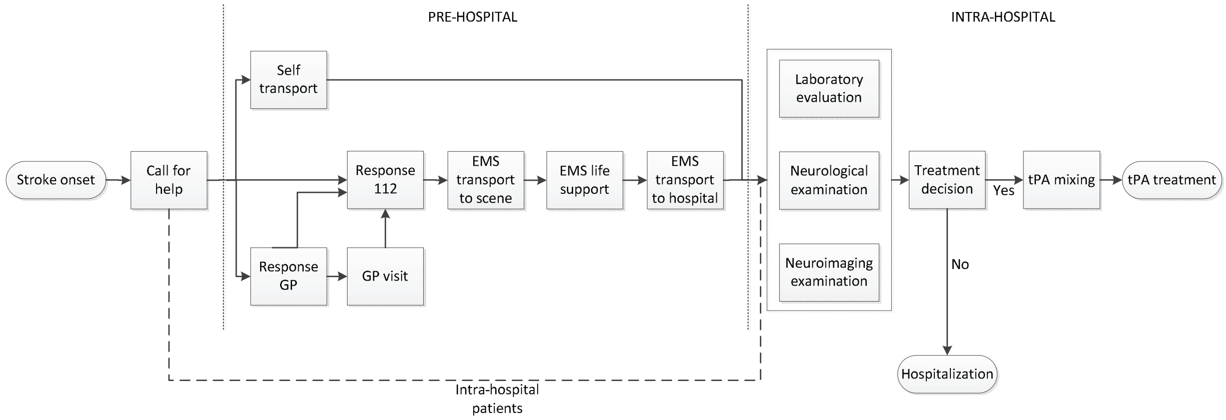

Figure 1: Acute stroke pathway – dominant set-up.

Three basic approaches may be distinguished for guiding the analyst in specifying a conceptual model for simulation (Robinson 2008a). *Principles of modeling* and *methods of simplification* stress the benefits of building simple models in terms of modeling efforts, and model use. Whereas principles of modeling advocate incremental modeling, methods of simplification offer assistance in model pruning. *Modeling frameworks* go beyond aforementioned approaches by also addressing what is to be modeled. They do so by suggesting a step wise approach for detailing the conceptual model in terms of its elements, their attributes and their relationships. Typically, steps to be taken may be supported by guidelines, methods, and good practices. For overviews of modeling frameworks developed so far, see Robinson (2008a), Karagoz and Demirors (2011), and Van der Zee et al. (2011).

Existing modeling frameworks tend to address rather broad domains, by offering some extensions relative to the general case, i.e., discrete event dynamic systems. For example, Kotiadis et al. (2014) show how problem structuring and project management for complex health systems may benefit from the use of their modeling framework. Robinson (2008b) facilitates simulation modeling for a broad class of operations systems building on elementary notions of entities, activities, queues, and resources. Likewise the framework proposed by Van der Zee and van der Vorst (2005) offers support for specifying planning and control systems found in supply chains. While respective frameworks offer clear starting points for defining simulation conceptual models, they usually do not inform and guide the analyst in addressing modeling needs that are specific for a branch of industry or an area in health. In this paper we address this issue by showing how the framework by Robinson may be extended to address such needs in modeling the acute stroke pathway.

3 A CONCEPTUAL MODELING FRAMEWORK FOR OPTIMIZING STROKE CARE ORGANIZATION

3.1 Framework Overview – Key Modeling Activities

The framework distinguishes between five key modeling activities in developing a conceptual model. The first activity links modeling efforts with the *problem situation* by identifying clients, stakeholders and domain experts and last-but-not-least the problem at hand. Starting from the knowledge and insights obtained *modeling objectives* are to be defined, clarifying the purpose of the simulation study. The experimental frame is captured by identifying *inputs*, i.e., experimental factors, and *outputs*, i.e., model responses. Model content is specified in terms of its *scope*, i.e., entities included in the model, and their respective *detail*. The latter specification may build on *assumptions* on the real system and model *simplifications*, assuming model scope or detail being adjusted in the interest of model speed or modeling efficiencies. In Section 3.2 we focus on framework extensions relative to Robinson's (2008b) original framework. See his framework for full details.

3.2 Modeling Activities

3.2.1 Understanding the Problem Situation

In detailing his modeling framework Robinson gives several hints on how to arrive at a good understanding of the problem situation by interviewing relevant parties and/or – in case of ill understood problems – by applying problem structuring techniques. Below we typify the problem situation faced within the acute stroke care domain in general terms.

The problem at hand, i.e., thrombolysis treatment being substantially underused, is widely recognized among those parties involved in acute stroke care. Relevant parties include not only care givers, but also those who fund stroke care, such as insurance companies and (local) governments. Furthermore, acute stroke care organization is acknowledged as a main determinant of patient treatment rates and outcomes for the acute stroke pathway. To improve pathway performance many suggestions have been made, concerning regional set-up of acute stroke care, see Section 2, and expediting of activities along the pathway by speeding them up and/or improving diagnostics, see for example, Fassbender et al. (2013) and Lahr et al. (2013b) .

Although validity of many measures proposed for improving acute stroke care have been shown by many researchers for specific regions, this may not always imply their validity at large, i.e., for a large(r) set of regions. For example, would mobile stroke units be viable solutions for both urban and rural regions, considering their health effectiveness, and associated costs? In case of a limited budget: what measures to consider – that add most to pathway effectiveness? Moreover, next to more research based insights assisting stroke pathway design at large, more precise testing may be required to meet demands to stroke pathway set-up set by specific regions, for example arising from their current care infrastructure, patient characteristics (for example population density, demography, case mix), available budgets, local regulations etc. – typifying *their problem situation*.

Recently, several researchers have shown how simulation may be used as a tool for testing alternative set-ups for the acute stroke pathways, see Section 1. As the tool is new to the field there is a clear need for managing expectations among clients and stakeholders on the nature and contents of the decision support implied by simulation study outcomes, as well as the way they may contribute to the success of the modeling process in terms of joint model validation, and solution creation, thereby relying on an explicit – textual, graphical and/or animated – model. Moreover, due to the complexity of the acute stroke care organization, simulation study success heavily relies on active participation of domain experts, especially care givers offering their services along the pathway. Neurologists tend to play an important role here, possibly acting as a champion in convincing other parties to join efforts. In principle, client roles may be taken by several parties like neurologists, or those that fund or regulate care (for example insurance companies, (local) governments).

3.2.2 Determining the Modeling and General Project Objectives

Modeling objectives clarify the way a simulation study is meant to support client decision making through modeling and analyzing various system configurations according to some pre-specified criterion. Here system configurations relate to alternative set-ups of the stroke pathway, also see Section 3.2.4. Usually, choice of configurations is restricted by, for example, budget, space, regulations etc. Achievements aimed may be further detailed by setting some performance goal, for example, increase tPA treatment rate by 5%.

Modeling objectives are meant to be in line with organizational aims. Organizational aims in health care stress effectiveness of care services in terms of patients' health outcomes. In many cases, health outcomes cannot be estimated using a simulation model, as effects of care services on patients' health cannot be accounted for, i.e., the association between the outcomes monitored and ensuing 'downstream' health effects is not known. Therefore, in acute care, patient lead time is often used as a proxy for estimating health outcomes, assuming a longer lead time to worsen patients' health.

Unlike many other fields in acute care, simulation may be used for estimating effectiveness of stroke care services. Recent research shows how outcomes for acute stroke patient in terms of his/her chances of being treated (Lahr 2013a), disabilities (Lees et al. 2010), and additional life years gained (Meretoja et al. 2014), may be estimated as a function of the patient lead time, i.e., OTT. Lahr et al. (2013a) approximate chances of being treated according to a linear regression model to approximate the chance of tPA treatment set against the overall time delay for all patients arriving < 4.5 hours from the onset of stroke symptoms (i.e. eligible for tPA treatment). Lees et al. (2010) score patient disabilities according to the so-called modified Rankin scale as a function of the patient lead time. The modified Rankin Scale score is a commonly used outcome scale to measure disability and independence in stroke victims (Rankin 1957). The scale consists of six grades, from 0 to 5, with 0 corresponding to no symptoms and 5 corresponding to severe disability. Meretoja et al. (2014) relate reduction of patient lead time to life years gained. In turn, proposed functions allow for defining simulation outputs, aiming to capture, for example, tPA treatment rate, average number of additional life years gained, and functional outcome of patients.

Relying on estimates of acute stroke care effectiveness, also cost-effectiveness criterions may be considered in simulation studies, thereby supporting the client in trading off configuration effectiveness and costs. Operational costs of acute care services may simply be computed by considering resource consumption of each patient traversing the pathway, see Lahr (2013). Costs computations are similar to those used for "classic" logistic simulation modeling and analysis.

Whereas modeling objectives address outcomes of the simulation study in terms of what is to be achieved, general project objectives stress resource availability, and model nature and use. Resource availability is especially linked to the time available for the study. Typically, restrictions on time may impact model detail, and staff and computer resources required. Demands on model nature and use may be detailed in terms of modeling flexibility, run-speed, visual display, ease-of-use, model/component re-use, similar to simulation studies targeting domains other than acute stroke care. In communicating through or about the simulation model the use of proper (medical) jargon should be stressed, to avoid misunderstandings within a multi-disciplinary project team.

3.2.3 Identifying the Model Outputs

Model outputs serve two purposes: (i) to indicate whether achievements aimed for have been realized, and (ii) if applicable - to explain why respective achievements have not been realized. Achievements are easily identified by considering the modeling objectives. See 3.2.2 for various output measures concerning (cost)effectiveness of the stroke pathway. Insights on why achievements aimed for have not been realized, may be obtained by inspecting the build-up of patient lead times and/or operational costs.

3.2.4 Identifying the Model Inputs

Ever since effectiveness of thrombolysis treatment has been established (NINDS rtPA Stroke Study Group 1995) suggestions have been made for improving organization of the acute stroke pathway. Suggestions may be classified according to their nature as being strategic or operational. Strategic measures concern regional stroke network set-up, i.e., parties involved in the stroke pathway and their interlinkages, while operational measures aim for improving diagnostics and expediting care services along the stroke pathway. Obviously, operational measures may supplement strategic measures. So far, a few stroke network topologies for organizing regional stroke care have been considered (Lahr 2013b):

- Decentralized care: acute stroke patients are served at the nearest (community) hospital, i.e., primary stroke center

- Centralized care: acute stroke patients are only served at one or multiple pre-selected hospital, i.e., comprehensive stroke centers.
- Telemedicine solutions: each patient is served at a community hospital; patient diagnosis and treatment is supported by neurologists from hospitals at a distance,
- Mobile stroke units: acute stroke patient are served on scene by a mobile stroke team, and a dedicated ambulance allowing for CT scanning

Typically, a choice for either option is motivated by regional characteristics. For example, telemedicine solutions are suggested for use in rural or remote areas, where stroke incidence is that low that the availability of stroke expertise at local care facilities cannot be afforded. Likewise, in urban areas it may be worthwhile to designate hospitals. For example, stroke patients may be referred to comprehensive stroke centers offering care services dedicated to acute stroke patients, thereby surpassing other (community) hospitals. Suchlike dedication benefits patients in terms of a readily available well-trained stroke team, and access to key-resources, especially CT-scanning equipment (Lahr et al. 2013b). The mobile stroke unit is a very promising approach to reduce delay in acute stroke therapy; however its efficacy still has to be proven.

Many measures for improving diagnostics and expediting care services along the stroke pathway have been suggested over the years, see for example, Fassbender et al. (2013) for a recent overview concerning the pre-hospital phase. Likewise many researchers addressed the intra-hospital phase by suggesting, for example, the use of lean manufacturing principles for speeding up care activities (Ford et al. 2012).

While aforementioned measures may be considered controllable, as clients will have control over their implementation, this is typically not true for measures attempting to increase patient awareness of stroke symptoms and knowledge on how to act. Although, patients' behavior and that of bystanders may be influenced to some degree by educational campaigns, their (lasting) effects in terms of patient delay, i.e., the time lapse from stroke onset to call, are uncertain. Hence their benefits can only be a-priori estimated on the basis of scenarios, trying to capture the range of possible outcomes, on the basis of earlier findings, see Fassbender et al. (2013).

3.2.5 Determining the Model Content

In determining model content a distinction is made in (i) *model scope*, identifying model boundaries, by either including or excluding a representation of elements of the system under study as model components, and (ii) *model detail*, specifying attributes of model components. Choice of model scope and detail builds on *assumptions* and *simplifications*. Assumptions capture beliefs or uncertainties about system elements, whereas model simplifications are meant to enhance model development and use.

Model scope

For capturing model scope Robinson suggests four classes of component types, i.e., entities, activities, queues, and resources, see Table 1. Entities represent movable system elements or flows. Not surprisingly, patients are considered the most important examples of *entities* within the stroke scene. After all, their well-being drives the study.

Activities may easily be linked to care services, also compare Figure 1. Activity subclasses to be distinguished are diagnostics, transportation, basic or advanced life support offered by EMS staff, and tPA treatment. Diagnostic activities are characterized by a set of possible outcomes, and some mechanism or rule for choosing among respective outcomes. As such diagnostic activities cause patients to traverse alternative routes along the acute stroke pathway. Main diagnostic activities are a patient's choice of first responder, appraisal by a GP, a 112 operator's and EMS staff's choice of EMS urgency level (blue lights or not), and three intra-hospital diagnostic activities in parallel. Transportation activities refer to EMS services, and possibly intra-hospital transport (for example, patient transport from the emergency department to the radiology department offering CT-scanning facilities).

The notion of MSUs slightly alters the aforementioned activities, as transportation refers to staff and equipment, instead of patient transport. Furthermore, intra-hospital activities are executed on scene. Important implementations of telemedicine are pre-notifications by either GP, 112 operators or EMS staff on acute stroke patients to arrive at the hospital – allowing for a fast response of the stroke team, and expert support for non-stroke clinicians in community hospitals, see Section 2.

Potential *queues* along the acute stroke pathway may be related to the availability of the 112 call center operator, EMS services or to intra-hospital equipment and staff. Key *resources* for the acute pathway are staff, equipment, and transportation means.

Table 1: Model scope – model components typifying the acute stroke pathway.

Class	Components
Entities	• Patients
Activities	• Diagnostics: Determining EMS urgency, Blood testing, Neuro examination, Neuro imaging, Interpreting diagnostic outcomes • Transportation • Life support (basic, advanced) • tPA Treatment • Telemedicine
Queues	• 112 Call center queue • Intra-hospital queues
Resources	• Staff: 112 operators, GPs, EMS staff, Neurologists, Nurses • Equipment • Ambulances

Level of detail

Each model component may be further detailed in terms of its attributes. For example, patients may be associated with an arrival pattern, clarifying their arrival rate (over the day), and their routing (compare Figure 1). Likewise, care services may be characterized by their cycle times, and in case of diagnostic activities, possible outcomes.

Assumptions and simplifications

Some common assumptions on the stroke pathway are:

- Stroke patients arriving at the hospital within 4.5 hours after stroke onset are high-priority patients. In case of a “competition for resources” stroke patients always have highest priority – as waiting has direct and severe consequences for their health.
- Stroke incidence figures are low on a daily basis. Hence chances of acute stroke patients competing for intra-hospital resources are slim.
- Waiting times at the 112 call center are low. They are expected not to influence patient health.
- In case of 24/7 acute stroke service, care services are not influenced by shift patterns.
- EMS transportation times are not influenced by changes of the acute stroke patient volume, starting from the observations that (i) transport of acute stroke patients concerns a low percentage of ambulance rides in a region and/or (ii) potential increases or decreases of transportation times are compensated for by adjustments of the EMS network.

Obviously, for specific regions aforementioned assumptions should be put to the test. Possible simplifications (partially) building on these assumptions are:

- Include call center waiting times in call center cycle times.
- Omit queues (and resources) from the model; effectively reducing the discrete event simulation model to a Monte Carlo simulation model.
- Replace call center and ambulance network by delay distributions.

3.3 Model Assessment

Each conceptual model is to be judged on its validity, credibility, utility and feasibility. See Robinson (2008b) for definitions and trade-offs among respective requirements.

4 CASE EXAMPLE – ACUTE STROKE PATHWAY GRONINGEN, THE NETHERLANDS

The acute stroke service for the province of Groningen, The Netherlands, services a population of 582,200 inhabitants (250 inhabitants/km^2). Whereas the region is served by 4 hospitals, tPA treatment is centralized by designating a single comprehensive stroke center, i.e., University Medical Center Groningen (UMCG). Acute stroke care service is provided 24/7. Pathway set-up is similar to Figure 1, involving local GPs, EMS, and neurologists at the UMCG.

Recent research indicates good scores on tPA treatment rates for the province of Groningen, i.e., 22.1% (Lahr et al. 2013a). However, several researchers suggest that treatment rates of 24-31% may be attainable in optimized settings (Waite et al. 2006; Boode et al. 2007). Their findings, together with staff ideas on how to improve local pathway performance, motivated the set-up of a simulation study, see Lahr et al. (2013a) for model validation and analysis of simulation results. Whereas the latter study focuses on the analysis of suggested improvements for the Groningen acute stroke pathway, here we will shift focus by considering conceptual modeling aspects of this study. As such this case example is meant to serve as an illustration of the use of the proposed modeling framework. Outcomes of the conceptual modeling activities are summarized in Tables 2-4.

5 DISCUSSION – ADDED VALUE OF THE MODELING FRAMEWORK

In response to the observed potential of simulation for decision support on optimizing acute stroke care organization we defined a domain specific modeling framework for simulation conceptual modeling. The new framework extends the existing modeling framework proposed by Robinson (2008b) by:

- Characterizing the problem situation, in terms of the problem faced (i.e. underutilization of thrombolysis treatment), clients, stakeholders, and domain experts involved, and added value of simulation in problem solving.
- Clarifying how modeling objectives may go beyond the usual logistic performance criterions by stressing the way patient health may benefit from proposed changes to acute stroke pathway set-up.
- Identifying two classes of model inputs: strategic measures aiming to improve stroke network topology, and operational measures, seeking to improve specific care services along the pathway.
- Suggesting (i) a refined set of classes of model components for specifying the coded model, being tailored towards common elements of the stroke pathway, and (ii) common assumptions and simplifications underlying model specification.

The new modeling framework goes beyond the existing frameworks by offering modeling support dedicated towards the domain, taking due notice of the problem situation and system specifics. As such it is meant to benefit both modeling efficiencies, by lessening efforts to be put in model creation, and model effectiveness by building models relying on the jargon in use and solutions accepted by the domain (experts) – thereby facilitating joint communication on model validation and solution engineering.

6 CONCLUDING REMARKS

In this article we address guidance for the analyst in defining a conceptual model for simulation modeling and analysis of regional organization of the acute stroke pathways. Motivation for the development of the new framework is found in that fact that worldwide numerous regions face a similar type of problem, i.e., patient treatment rates are low relative to benchmarks. Apart from the “market potential” for simulation

Table 2: Summary of outcomes for conceptual modeling of the Groningen acute stroke pathway.

Activity	Main results
1. Understanding the problem situation	• Clients: Medical staff involved in the acute stroke pathway, i.e. GPs, EMS services (medical directors), and neurologists. Neurologists act as champions actively promoting improvements along the stroke pathway concerning rapid identification and transport of potential stroke victims among GPs, EMS dispatchers, and ambulance personnel. • Further investigation revealed: - Findings in literature indicate further potential for improving tPA treatment rates, thereby hinting at solution directions. - Observations on current pathway set-up and performance suggest several avenues for its improvement, see model inputs. - Parties involved in the study are keen on learning about the use and benefits of simulation for improving acute stroke pathway design, as this is a new tool for the field.
2. Determining modeling objectives	• Overall aims: The acute stroke service aims for favorable patient outcomes, thereby minimizing patient disabilities. A higher tPA treatment percentage contributes to this aim. • Modeling objective: Assess potential of selected measures for improving the acute stroke pathway for increasing tPA treatment rate. • Expectations (process): - The simulation study facilitates a multi-disciplinary approach towards acute stroke pathway redesign, bringing together a project team of neurologists, epidemiologists, and an industrial engineer. - Adequate solutions build on active participation of project team members in suggesting improvements to the pathway and the way they are modelled. • Expectations (outcomes): Analysis of selected measures for acute stroke pathway improvement.
2. Determining general project objectives	• Project duration: around 6 months for model development and analysis. • Flexibility: Model should allow for easy adaptations to accommodate alternative measures for improving the acute stroke pathway, also see Model reuse. • Run speed: Less important, as only few experiments are considered. • Visual display: Basic iconic display is sufficient. • Model reuse: Model reuse for alternative regions is considered.
3. Identifying the model outputs	• Performance: tPA treatment rate (percentage of population treated with tPA) • Cause and effect: onset-to-treatment time (min.), proportions of patients treated in different time intervals (0-90, 90-180,180-270min.)
4. Identifying the model inputs	• 112 operator diagnosis: Current vs. more liberal policies for assigning high priority EMS transport • Blood testing: Current lab tests vs. use of a Point of Care (POC) device • Protocol used by ambulance personnel for advanced life support on patient scene: current protocol (i.e. stay-and-play) vs. scoop-and-run.
5. Determining the model scope and detail	• Model boundary: Acute stroke pathway, from the initial call for help to the moment of tPA treatment. • Model components and their detail: see Tables 2-4.
5. Assumptions & simplifications	• Given the need for their urgent treatment acute stroke patients always have highest priority in allocation of hospital staff and resource. As acute stroke incidence figures for the UMCG are low (1-2 patients on average on a daily basis) no intra-hospital queues are considered. • Waiting times at the 112 call center are typically low. Therefore no call queueing is modelled. • In hospital services are assumed not to be influenced by shift patterns, as stroke team and required resources are available 24/7. • EMS transportation times are not influenced by model inputs, starting from the observation that transport of acute stroke patients concerns about 2% of the yearly number of ambulance rides in the region.

use, the impact of conceptual model qualities on simulation study success and the highly creative nature of simulation conceptual modeling underpin the need and benefits of guidance for the analyst in conceptual model development. In response to observed needs, we define a domain specific simulation conceptual modeling framework. Extensions of the new framework relative to existing frameworks are in the support offered to the analyst in in specifying modeling objectives, model inputs, and outputs, and model content. Support is offered to the analyst by informing him on the characteristics of the problem situation, i.e., the problem faced, and stakeholders involved, stroke system characteristics in terms of care givers and services, and directions for solution finding. Furthermore, methods for capturing model content are tailored towards their use for modeling acute stroke pathways.

Insights obtained in developing the new framework may also benefit other domains, either in health or in business, by showing what and how to adapt relative to existing modeling frameworks. Furthermore, the definition of domain specific conceptual modeling frameworks may be considered as a well-informed and focused starting point for developing further computer-based support (Ahmed et al. 2014). Main examples of such support concern the embedding of software requirements engineering principles in conceptual modeling, and the (partial) automation of conceptual modeling activities, allowing for a translation of the simulation conceptual model in a coded model, and the generation of project documentation.

Table 3: Groningen acute stroke pathway – model scope.

Component	In/exclude	Justification
Entities		
Patients	Include	Response: patient treatment rate, OTT
Activities		
Call for help, Self transport, Response 112, Response GP, GP visit, EMS transport to scene, EMS advanced life support, EMS transport to hospital, Laboratory evaluation, Neurological examination, Neuroimaging examination, Treatment decision, tPA mixing	Include	Key influence on patient treatment rate, OTT
Hospital registration	Exclude	No impact on patient treatment rate, OTT
Resources		
Ambulances	Exclude	Assume ambulance delays (transportation times) and patient delays coincide
Family car	Exclude	Assume family car delays (transportation times) and patient delays coincide. Applies for self-referring patients only.

Table 4: Groningen acute stroke pathway – model detail.

Component	Detail
Entities	
Patients	Identifier Routing: self referral, intrahospital patient, contact 112, contact GP
Activities	
Call for help	Delay: distribution
Self transport	Delay: distribution
Response 112	Delay: distribution EMS priority: distribution level (A1,A2,B)
Response GP	Delay: distribution Visit: distribution (yes, no) EMS priority: distribution level (A1,A2,B)
GP visit	Delay: distribution
EMS transport to scene	Delay: distribution
EMS advanced life support	Delay: distribution
EMS transport to hospital	Delay: distribution
Laboratory evaluation	Delay: distribution
Neurological examination	Delay: distribution
Neuroimaging examination	Delay: distribution
Treatment decision	Delay: distribution Decision: distribution (yes, no)
tPA mixing	Delay: constant

ACKNOWLEDGMENTS

This project was supported by the Netherlands Organization for Health Research and Development (ZonMw); Ref.: 80-82800-98-104

REFERENCES

Adeoye, O., R. Hornung, P. Khatri, and D. Kleindorfer. 2011. “Recombinant Tissue-Type Plasminogen Activator Use for Ischemic Stroke in the United States: a Doubling of Treatment Rates over the course of 5 Years.” *Stroke* 42:1952-1955.

Ahmed, F., Robinson, S., Tako, and A. A. Tako. 2014. “Conceptual Modelling: Lessons from Computer Science.” In *Proceedings of the Operational Research Society Workshop 2014* (SW14), edited by

B.S. Onggo, C. Heavey, T. Monks, B. Tjahjono and D. J. van der Zee, Birmingham: OR Society.

Boode, B., V. Welzen, C. Franke, and R. van Oostenbrugge. 2007. "Estimating the Number of Stroke Patients Eligible for Thrombolytic Treatment if Delay Could Be Avoided." *Cerebrovascular Diseases* 23(4): 294-298.

Churilov, L., A. Fridriksdottir, M. Keshtkaran, I. Mosley, A. Flitman, and H.M. Dewey. 2013. "Decision Support in Pre-Hospital Stroke Care Operations: a Case of Simulation to Improve Eligibility of Acute Stroke Patients for Thrombolysis Treatment." *Computers in Operations Research* 40:2208–2218.

Fassbender, K., C. Balucani, S. Walter, S. R. Levine, A. Haass, and J. Grotta J. 2013. "Streamlining of Prehospital Stroke Management: the Golden Hour." *Lancet Neurology* 12(6): 585 – 596.

Ford A.L., J.A. Williams, M. Spencer, C. McCammon, N. Khoury, T. R. Sampson, P. Panagos, and J. M. Lee 2012. "Reducing Door-to-Needle Times Using Toyota's Lean Manufacturing Principles and Value Stream Analysis." *Stroke* 43(12): 3395-3398.

Hacke, W., M. Kaste, E. Bluhmki, M. Brozman, A. Davalos, D. Guidetti, V. Larrue, K. R. Lees, R. Kennedy, Z. Medeghri, T. Machnig, D. Schneider, R. von Kummer, N. Wahlgren, and D. Toni. 2008. "ECASS Investigators. Thrombolysis with Alteplase 3 to 4.5 Hours After Acute Ischemic Stroke. *New England Journal of Medicine* 359:1317-1329.

Karagoz, N. A., and O. Demirors. 2010. "Conceptual Modelling Notations and Techniques." In: *Conceptual Modelling for Discrete-Event Simulation*, edited by S. Robinson, R. Brooks, K. Kotiadis, and D.J. van der Zee, 179-210. Boca Raton: CRC/Taylor & Francis.

Kotiadis, K., A. A. Tako, and C. Vasilakis. "A Participative and Facilitative Conceptual Modelling Framework for Discrete Event Simulation Studies in Healthcare". *Journal of the Operational Research Society* 65(2): 197-213.

Kwan, J., P. Hand, and P. A. Sandercock. 2004. "A Systematic Review of Barriers to Delivery of Thrombolysis for Acute Stroke." *Age Ageing* 33:116-121.

Lahr, M. M. H., D.J. van der Zee, G.J. Luijckx, P. C. A. J. Vroomen, and E. Buskens. 2013a. "A Simulation-Based Approach for Improving Utilization of Thrombolysis in Acute Brain Infarction." *Medical Care* 51(12): 1101-1105.

Lahr, M. M. H., G.J. Luijckx, P. C. A. J. Vroomen, D.J. van der Zee, and E. Buskens. 2013b. "The Chain of Care Enabling tPA Treatment in Acute Ischemic Stroke: a Comprehensive Review of Organisational Models." Journal of Neurology 260(4): 960-968.

Lahr, M. M. H., D.J. van der Zee, P. C. A. J. Vroomen, G.J. Luijckx, and E. Buskens. 2013c. "Thrombolysis in Acute Ischemic Stroke: A Simulation Study to Improve Pre-and in-Hospital Delays in Community Hospitals." *PLoS ONE* 8(11) [79049].

Lahr, M. M. H. 2013. "Organizational Models for Thrombolysis in Acute Ischemic Stroke: a Simulation Exemplar.", Phd thesis, University of Groningen, Groningen, The Netherlands.

Lees K. R., E. Bluhmki, R. von Kummer R, et al. 2010. "Time to Treatment with Intravenous Alteplase and Outcome in Stroke: an Updated Pooled Analysis of ECASS, ATLANTIS, NINDS, and EPITHET Trials." *Lancet* 375:1695-1703.

Meretoja A., M. Keshtkaran, J. L. Saver, T. Tatlisumak, M. W. Parsons, M. Kaste, S. M. Davis, G. A. Donnan, and L. Churilov. 2014. "Stroke Thrombolysis: Save a Minute, Save a Day." *Stroke* 45:1053-1058.

Monks, T., M. Pitt, K. Stein, and M. James. 2012. "Maximizing the Population Benefit from Thrombolysis in Acute Ischemic Stroke: a Modeling Study of In-Hospital Delays." *Stroke* 43:2706–2711.

The NINDS rt-PA Stroke Study Group. 1995. Tissue Plasminogen Activator for Acute Ischemic Stroke. *New England Journal of Medicine* 333:1581-1587.

Pitt, M., T. Monks, P. Agarwal, D. Worthington, G. A. Ford, R. Kennedy, R. Lees, K. Stein, and M. A. James. 2012 "Will Delays in Treatment Jeopardize the Population Benefit from Extending the Time

Window for Stroke Thrombolysis?" *Stroke* 43:2992–2997.

Rankin, J. 1957. "Cerebral Vascular Accidents in Patients over the Age of 60. II. Prognosis." *Scottish Medical Journal* 2(5):200-215.

Robinson, S. 2008a. "Conceptual Modelling for Simulation Part I: Definition and Requirements." *Journal of the Operational Research Society* 59: 278-290.

Robinson, S. 2008b. "Conceptual Modelling for Simulation Part II: a Framework for Conceptual Modelling." *Journal of the Operational Research Society* 59: 291-304.

Singer, O. C., G. F. Hamann, B. Misselwitz, H. Steinmetz, and C. Foerch. 2012. Time Trends in Systemic Thrombolysis in a Large Hospital-Based Stroke Registry. *Cerebrovascular Diseases* 33(4): 316-321.

Truelsen, T., M. Ekman, and G. Boysen. 2005. "Cost of Stroke in Europe." *European Journal of Neurology* 12(Suppl 1): 78-84.

Van der Zee, D. J., and J. G. A. J Van der Vorst. 2005. "A Modeling Framework for Supply Chain Simulation – Opportunities for Improved Decision-Making." *Decision Sciences* 36(1): 65-95.

Van der Zee, D.J., R. J. Brooks, S. Robinson, and K. Kotiadis. 2011. "Conceptual Modelling: Past, Present and Future" In: Conceptual Modelling for Discrete-Event Simulation, edited by S. Robinson, R. Brooks, K. Kotiadis, and D.J. van der Zee, 473-490. Boca Raton: CRC Press.

Waite, K., F. Silver, C. Jaigobin, S. Black, L. Lee, B. Murray, P. Danyliuk, and E. M. Brown. 2006. "Telestroke: a Multi-Site, Emergency-Based Telemedicine Service in Ontario." *Journal of Telemedicine and Telecare* 12(3):141-145.

Wardlaw J. M., P. A. Sandercock, and V. Murray V. 2009. "Should More Patients with Acute Ischaemic Stroke Receive Thrombolytic Treatment?" *British Medical Journal* 339:1251-1254.

AUTHOR BIOGRAPHIES

DURK-JOUKE VAN DER ZEE is associate professor of Operations at the Faculty of Economics and Business, University of Groningen, The Netherlands. His research interests include simulation methodology and applications, simulation & serious gaming, manufacturing planning & control, and health care logistics. He is a member of the INFORMS-SIM. His email address is d.j.van.der.zee@rug.nl, and his webpage is http://www.rug.nl/staff/d.j.van.der.zee.

MAARTEN M. H. LAHR is a postdoctoral researcher at the Department of Neurology, University of Groningen, University Medical Center Groningen, The Netherlands. His research interests include organizational models for acute stroke care and discrete-event simulation. His e-mail address is m.m.h.lahr@umcg.nl, and his website is http://www.rug.nl/staff/m.m.h.lahr/.

GERT-JAN LUIJCKX is a neurologist at the department of Neurology, University Medical Center Groningen. He is head of the Cerebrovascular Unit, and Principal Investigator Research School of Behavioural and Cognitive Neurosciences Groningen (BCN). Research topics addressed by him include clinical research prognostic factors acute ischemic stroke therapy, clinical research on neuroprotective determinants in acute stroke and clinical research on organization and implementation of acute stroke care. His email address is g.j.luijckx@umcg.nl.

ERIK BUSKENS is Professor of Health Technology Assessment and program director Healthy Ageing at University Medical Center Groningen, University of Groningen, The Netherlands. His research interests among others encompass the association and mutual dependencies between technological advances and the factual organization of care to attain the desired health and possibly economic benefits. His email address is e.buskens@umcg.nl.