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ENTERING NEW FIELDS OF SIMULATION APPLICATION - CHALLENGES FACED IN SIMULATION MODELLING OF STROKE SYSTEMS

Dr. Durk-Jouke van der Zee

University of Groningen
P.O. Box 800, 9700 AV, Groningen
THE NETHERLANDS
d.j.van.der.zee@rug.nl

Dr. Thomas Monks

NIHR CLAHRC Wessex
University of Southampton
Southampton SO17 1BJ
UNITED KINGDOM
thomas.monks@soton.ac.uk

Dr. Maarten.M.H. Lahr,
Dr. Gert-Jan Luijckx,
Prof. dr. Erik Buskens

University Medical Center Groningen
P.O. Box 30001, 9700 RB, Groningen
THE NETHERLANDS
m.m.h.lahr@umcg.nl,
g.j.luijckx@umcg.nl,
e.buskens@umcg.nl

ABSTRACT

Stroke is a major cause of death and long-term disability world-wide. To improve functional outcome 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. Unfortunately, tPA remains substantially underutilized. Acute 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 a number of pioneering simulation studies challenges in simulation application and simulation methodology are identified. The definition of a domain specific modelling framework for acute stroke care is advocated to master system complexities, facilitate joint team work in solution finding, organize model data collection and make a further entrance to the field.

Keywords: Simulation modelling methodology, ischemic stroke, stroke systems, hyper acute pathway

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; WHO, 2012). The acute brain infarction is caused by a blood clot. As a result of the blocked blood vessel downstream brain tissue is deprived from oxygen and starts to mortify. The longer the blood clot is existent the more damage is done, resulting in (severe) disability and possibly death.

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 at the root of 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. The sooner the treatment is started the better functional outcome is i.e. TIME = BRAIN.

Main causes of undertreatment found are the narrow therapeutic time window, patient and bystander unfamiliarity with stroke symptoms and how to act, and stroke care organization. Notably, the benefit of tPA depends strongly on time since stroke onset (The National Institute of Neurological Disorders and Stroke rtPA Stroke Study Group, 1995; Hacke et al., 2008; Lees et al., 2010; Wardlaw et al., 2012; Emberson et al., 2014), which in turn negatively affects the chance of administering tPA treatment as time since onset increases (Hamann, 2004).

In recent years many researchers made proposals for improving stroke care organization, thereby attempting to reduce patients' delay along the stroke pathway, and – hence – increase their chances for favourable outcomes. Respective research efforts have primarily relied on the use of Randomized Controlled Trials (RCTs) as a main research vehicle. RCTs are meant to establish potential benefits of alternative set-ups of the stroke pathway, by comparing 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. Although the merits of RCTs for use in health research concerning simple or solitary interventions such as pharmaceuticals or devices are clearly established, complexity of the acute stroke pathway – entailing a sequence of interrelated care services, spanning both the pre-hospital and the hospital phase – may hinder its applicability. For example, two recently proposed improvement programs reported disappointingly low nonsignificant increases in tPA treatment rate of 1.0–1.5% (Dirks et al., 2011; Scott et al., 2013). Clearly, disadvantages of real-life testing in terms of time, costs and efforts involved in study set-up and experimenting, and project organization, management and lead time become apparent here (Law, 2007).

Recently, several studies have shown how simulation may be used as an efficient alternative or precursor to clinical trials (Monks et al., 2012; Pitt et al., 2013; Churilov et al., 2013; Lahr et al., 2013a; Lahr et al., 2013c; Jacobson et al., 2015; Komenda et al., 2015). 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 to be put to test at minimum efforts and means. Moreover, where efforts in setting up clinical trials often restrict studies to just a part of the stroke pathway, simulation can easily cope with interventions addressing the entire stroke pathway. Furthermore, simulation efficiency does not only allow for redesigning existing stroke pathways but also rethinking the way care chains may be set-up for a region. For example, should stroke care be offered at every community hospital (i.e. decentralize facilities), or should care be concentrated in a comprehensive stroke center (i.e. centralize facilities)?

Apart from aforementioned efforts simulation hardly made an entrance in the field. In this article we identify and study modelling challenges faced in addressing the field, thereby relying on our experiences in doing some of the pioneering studies for the field (Monks et al., 2012; Pitt et al., 2013; Lahr et al., 2013a; Lahr et al., 2013c). Our findings are meant to accelerate studies in the field (i) by identifying hurdles – and ways to overcome these – for those who consider undertaking simulation studies, and (ii) reveal research requirements for simulation modelling methodology.

The remainder of the paper is organized as follows. In Section 2 we shortly typify the hyper acute stroke pathway. In Section 3, we address challenges faced in simulation application, concerning complexities in system design, innovations impacting future system design, and project organization. Next, in Section 4 we address methodological challenges faced in simulation use for stroke system optimization. Finally, we will discuss and summarize main findings (Section 5 and 6).

2 STROKE SYSTEMS – THE HYPER ACUTE PATHWAY

Stroke is categorized in two sub types: ischemic and hemorrhagic, relating to about 85% and 15% of the patient population respectively. Ischemic strokes occur when a blood vessel is blocked due to a clot and disrupts blood circulation to the brain, whereas hemorrhagic strokes boil down to a bleeding. Only ischemic strokes are eligible for tPA treatment, see Section 1.

The stroke pathway entails several phases. Here we only consider the initial phase, the so-called hyper acute (emergency) phase, see Figure 1. The hyper acute phase spans care services from stroke onset to tPA treatment. Patients either arrive at the hospital by Emergency Medical Services (EMS) after making a call to their GP or the emergency number (112) or by self-referral. Next, a patient's eligibility for tPA treatment depends on his/her delay along the pathway (treatment must be administered within < 4.5 hours of the onset of symptoms) together with the results from the

neurological examination, laboratory evaluation (blood testing) and neuroimaging examination (CT-scanning). tPA treatment influences patient outcomes in terms of the severity of their disabilities, ranging from no disabilities, to major disabilities or death. Note that a small number of the patients faces a stroke while being hospitalized.

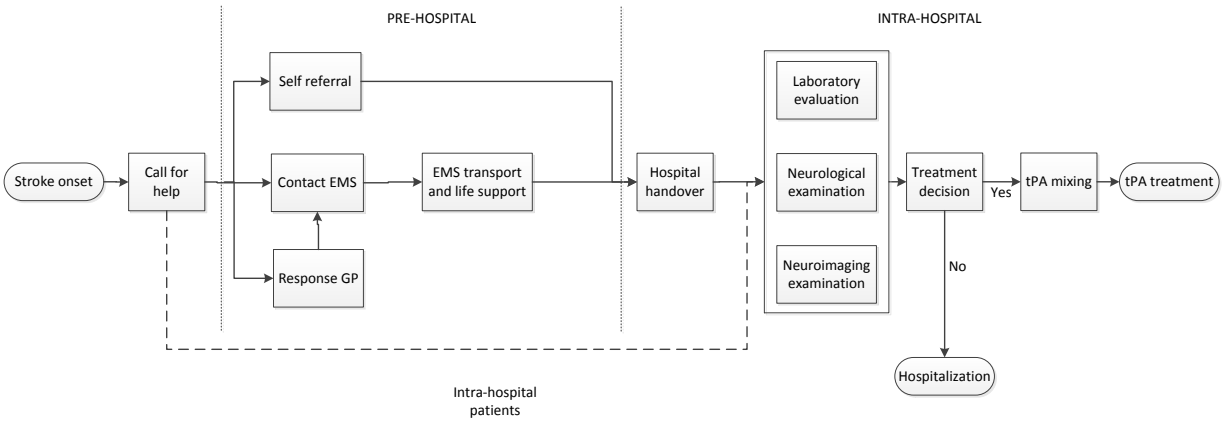

Figure 1 *Hyper acute stroke pathway – dominant set-up*

3 CHALLENGES IN SIMULATION APPLICATION

Until a few years ago hardly any simulation study had been performed for optimizing the hyper acute stroke pathway. Below we address modelling challenges encountered in our recent studies (Monks et al., 2012; Pitt et al., 2012; Lahr et al., 2013a; Lahr et al., 2013c). Challenges will be linked to system complexities, system innovation, performance measurement and project characteristics.

3.1 System Design

Where RCTs only allow for studying a small set of interventions along the stroke pathway, simulation efficiencies enable elaborate testing of more complex systems. Observed opportunities for simulation use are in decision support for operational decision making – focusing at the overall chain optimization of existing treatment chains, and strategic decision making – concerning the choice of the regional stroke system network topology. The first opportunity is in line with a growing awareness in the field that a concerted effort of all parties involved in the hyper acute pathway results in best chain performance, i.e., highest treatment rates and best outcomes. Whereas earlier research efforts concentrated on optimizing the intra-hospital phase, relevance of including the pre-hospital phase in overall chain optimization has been widely acknowledged in recent years (Fassbender et al., 2013). The second opportunity relates to the observed need for a regional organization of care, for reasons of health economics and health quality, i.e., patient outcomes. For example, it has been shown how concentrating treatment of acute stroke in comprehensive stroke centres, instead of attending to patients in the nearest community hospital may benefit patients (Lahr, 2013; Lahr et al., 2013b). Clearly, such choices with respect to regional organization of stroke care suggest a trade-off between transport delays in the pre-hospital phase vs. potentially better care and shorter lead times for the comprehensive stroke centre (Monks et al,. 2014).

3.2 System Innovation

Whereas opportunities sketched in Section 3.1 essentially do not question pathway set-up in terms of the nature of care services, recent innovations do so. We observe two avenues of future change, concerning health technology employed in patient diagnosis, and new treatments. As far as technology is concerned we mention the following examples:

- The Point of Care device, allowing for a quick analysis of patient blood samples – as a replacement of classic blood testing as done in a lab (Rizos et al., 2009).

- Telemedicine, suggesting to exploit communication devices for, for example, consulting stroke expertise at a distance for use on scene or in a hospital lacking suchlike expertise, or pre-notifying patient arrivals at the hospital (Levine and Gorman, 1999).
- Mobile scanning technology available in the ambulance, allowing for CT-scanning at the patient scene. Note that this concept is exploited by so-called Mobile Stroke Units, i.e., dedicated ambulances that allow for tPA treatment at the patient scene (Wendt et al., 2015).

Note that all aforementioned examples stress reduction of delays along the stroke pathway.

Furthermore, we mention emerging new treatments for acute stroke. Recently, the use of endovascular thrombectomy (mechanical clot retrieval using a medical device) has been shown to improve patient outcomes (Berkhemer et al., 2014). Although its benefits are clear, it comes at a price, by setting specific demands concerning stroke expertise, and scanning technology (CTA-scanning). This may imply that in the near future it may only be offered by comprehensive stroke centres.

3.3 Performance Measurement

Interestingly, recent stroke studies have shown the linkage of treatment effectiveness in terms of patient outcomes and logistic performance, i.e., patient delay from stroke-onset to his/her treatment. 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 treatment lead time. In turn, patient outcomes may be used to assess cost-effectiveness of alternative set-ups of the hyper acute stroke pathway.

3.4 Project Characteristics

Simulation studies on stroke systems tend to put high requirements on project team composition. Typically, the team hosts parties involved in the pathway, i.e., neurologists, EMS and GPs, health economists, health system engineers and simulation modellers. Profound insights on the way (interlinked) care services influence patient outcomes and the way chain logistics may be best organized, modelled and analysed are the key stones of a successful simulation study. Project efforts should be concentrated on creating a mutual understanding of stroke system set-up to facilitate its joint (re)engineering. Such an understanding is not guaranteed as parties, and disciplines represented in the team, may not be familiar with such co-operation.

4 CHALLENGES IN SIMULATION MODELLING METHODOLOGY

How to facilitate the simulation modeller and his team in setting up and doing the study? Here we explore methodological issues as they relate to the problem situation, and current means for addressing them.

4.1 Problem Situation

Optimization of the hyper acute stroke pathway is considered a world-wide issue. This is due to the number of patients involved (estimated at 15 million per year worldwide), and the severity of health consequences faced by those patients not being treated (as they arrive not within the therapeutic time window or the hospital is unable to treat them within 4.5 hours of onset) or who could have been treated earlier within the therapeutic time window – thereby improving their chances on favourable outcomes. In principle, care services along the hyper acute pathway required for effective tPA treatment are rather well-known. However, their implementation and facilitation (staffing, resources, and their co-ordinated use) may differ from country to country or even from region to region, due to the way local health infrastructures have been set-up. Nevertheless, world wide similarities in both choice of care services and system set-up suggest a high potential for simulation model re-use.

The hyper acute pathway is a complex system. Relevant parties in set-up and operation of the hyper acute stroke pathway include not only care givers, such as GPs, EMS, and neurologists, but also those who fund or regulate stroke care, such as insurance companies, (local) governments, and professional societies, and – last but not least – (representatives of) patients. This clarifies the need for problem structuring, to get a joint hold of system set-up and problems faced in optimizing it. In turn, this may

also provide initial guidance on (conceptual) modelling – by revealing possibilities for model simplification.

For a simulation study to be successful (historical) data on patient lead times, diagnostic results, and their treatment and its outcomes are crucial, both to facilitate model set-up and its validation. Ideally, the build up of patient lead time along the hyper acute pathway since stroke onset can be explained by sufficient data on relevant care services. In turn, diagnostic results, like patient's choice of first responder, EMS urgency level etc. will inform patient routings. Finally, data on patient treatment captures their likeliness of being treated, and their expected outcomes. Unfortunately, in many cases respective categories of data may (i) not be easily accessed as they are dispersed over separate parties involved in the hyper acute pathway or (ii) may not be available altogether, and have to be obtained at high costs.

Typically, as simulation is new for the field, aforementioned parties involved in optimizing stroke systems are not familiar with simulation. This implies a need to familiarize them with the tool, its application, and its potential for decision support on stroke system design.

4.2 Guidance Available

How should we address the challenges faced in the problem situation, as identified in Section 4.1? Many challenges link to the initial phases of a simulation study, i.e., conceptual modelling. So far, model coding, and its analysis, seem to be less of an issue. Note that this does not imply that they may not become a future issue.

Three basic approaches may be distinguished for guiding the analyst in specifying a conceptual model for simulation (Robinson, 2008a). Principles of modelling advocate the benefits of aiming for simple models through incremental modelling. Their application may, among others, entail the good use of metaphors, analogies, and similarities in model creation (Pidd, 1999). Methods of simplification work the other way around by suggesting a reduction of model scope and detail. Gains with respect to modelling efforts or computational efficiencies in doing experiments may be realized by, for example, combining model elements, leaving them out or adapting their attributes (Innis and Rexstad, 1983). Modelling frameworks suggest a step wise approach for detailing the conceptual model in terms of its elements, their attributes and their relationships. Typically, proposed steps are supported by guidelines, methods, and good practices.

The main differences among modelling frameworks concern their intended field of application, scope, and process support. Modelling frameworks developed so far tend to address rather broad fields of application, like operations systems (Robinson, 2008b), supply chains (Van der Zee and Van der Vorst, 2005), health systems (Kotiadis, 2007), and the military (Pace, 1999; Pace, 2000). Whereas some frameworks restrict scope to the specification of model content only (Arbez and Birta, 2011), other frameworks include problem understanding, modelling objectives, experimental factors and model responses (Kotiadis, 2007; Robinson, 2008b). Chwif et al. (2013), and Kotiadis et al. (2014) address process support by suggesting formats for workshops, conceptual model documentation and the way model data are to be collected. For overviews of modelling frameworks, see Robinson (2008a), Karagoz and Demirors (2011), and Van der Zee et al. (2011).

Clearly, aforementioned approaches indicate relevant support for simulation conceptual modelling. However, they usually do not inform and guide the analyst in addressing modelling needs that are specific for a branch of industry or a domain of health care.

5 DISCUSSION

Challenges faced in simulation-based optimization of the hyper acute stroke pathway indicate that developing conceptual frameworks may be worthwhile, in an attempt to master system complexities, facilitate joint team work in solution finding, organize model data collection and make a further entrance to the field. Problem scale, and similarities in system set-up suggest that efforts put in defining such frameworks are relevant and feasible. Moreover, a domain specific framework would present an interesting – potentially viable – example of simulation model re-use. Re-use would build on the identification of generic model components, solution directions (model inputs), and relevant performance measures (model outputs), and ways of exploiting such means in process set-up and data

collection. Clearly, defining such a framework is no easy job, already because it involves the involvement of many parties and disciplines.

6 CONCLUDING REMARKS

In this article we identify and study simulation modelling challenges faced in addressing the hyper acute stroke pathway. In doing so, we rely on our experiences in performing some of the pioneering studies for the field. We found how many challenges seem to address simulation conceptual modelling. The definition of a domain specific modelling framework for acute stroke care is advocated in an attempt to master system complexities, facilitate joint team work in solution finding, organize model data collection and make a further entrance to the field. Apart from being highly relevant for the field, given patient numbers, and potential for improving their health, the framework may present an interesting example of simulation model re-use. In our future work we will address the definition and use of such a framework.

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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.

THOMAS MONKS is a Senior Research Fellow in Operational Research in the Faculty of Health Sciences, University of Southampton where he leads NIHR CLAHRC Wessex's methods research group. He holds a BSc in Computer Science and Mathematics, MSc in Operational Research and PhD in Simulation Modelling. He has worked as both a Software Engineer in the private sector and an Operational Research Analyst within the public sector. His specialty is simulation of healthcare systems

of unscheduled and emergency care. He is co-chair of the UKs Simulation Workshop 2016 and co-chair of the UKs simulation special interest group. His webpage is http://www.southampton.ac.uk/healthsciences/about/staff/tm3y13.page

MAARTEN M. H. LAHR is a postdoctoral researcher at the HTA unit of the Department of Epidemiology, and member of the Healthy Ageing Team, 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.