# A067 A service innovation in the management of temporary neurological disturbances: a new question for NICE guidance to answer?

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*Note to readers: This is intended as an ‘ideas piece’ and represents early work in progress. Please do not quote without permission.*

### Abstract (note: revised to reflect paper edits)

**Background:** Currently, patients with false positive Transient Ischaemic Attack (TIA) diagnoses fall outside the remit of UK TIA guidance, yet as many as 50% of all suspected TIA cases presenting in Primary Care may be incorrectly diagnosed by their GP. These patients with resolved symptoms are incepted into the TIA service pathway – putting pressure on services – and may potentially discharged without treatment. However, evidence from clinical study settings suggests that this patient group has heightened cardiac risks when compared with the general population of equivalent age. This paper explores whether the focus on TIA overlooks a vulnerable patient population that may presently be under treated and examines the case for service re-design.

**Aims:** (Overarching) To evaluate the implications of alternate service pathway models following temporary neurological disturbances of any origin. (Specific) To examine the feasibility of a potential service innovation in cardiac risk.

**Methods:** Conceptual modelling techniques were employed to identify the problem.

**Results:** We identify the data requirements needed to implement a decision-analytic model and propose methods for closing evidence gaps.

**Conclusions:** This paper provides an important de novo health economic analysis of an important clinical question that was not addressed in the NICE (2008) guidance or elsewhere.  While this preliminary analysis may over-simplify the complex interplay of doctors-patients and treatment decisions, it is hoped that this paper will promote discussion about the need for all to consider the ‘real’ population presenting to TIA services.

## Glossary

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| --- | --- |
| TIA | Transient ischaemic attack (mini stroke). |
| Transient neurological disturbance | Umbrella term for any condition causing temporary neurological symptoms (includes TIA). |
| TIA mimic | False positive TIA (Prescence of disease based on what the stroke specialist identifies). |
| Confirmed TIA | True positive TIA (Prescence of disease based on what the stroke specialist identifies) |
| Suspected TIA | Transient neurological disturbances consistent with a diagnosis of TIA. Sum of true positive and false positive TIA. This is also the total or ‘real’ population presenting to TIA services. |
| PICO | Way of focussing a study question (mnemonic) commonly used in epidemiology. P = Population, I= Intervention, C= Comparators, O= Outcome of interest |

#### Note: Tappenden (2005) provides a good glossary of conceptual modelling terms and is available freely online as part of the HEDS discussion paper series.

#### Conceptual modelling is about moving from a problem situation, through model requirements to a definition of what is going to be modelled and how (Robinson, 2008).

## Introduction

It is well known that TIA can be an early warning signal for an imminent stroke, and there is a strong evidence base identifying the effectiveness of early intervention with medications (antiplatelets, statins and antihypertensives). This evidence led to the development of a National Stroke Strategy in 2007 and NICE guidance in 2008. Subsequent audit confirmed the success of such guidance in expediating initiation of treatments following TIA (NAO, 2010). In this way, the existing service pathway model appears to treat TIA patients efficiently. If it is our desire to prevent stroke following confirmed TIA, the decision-analytic models on which the implemented service pathway models are based appear fit for purpose.

It is much less well known that approximately fifty per cent of patients with GP diagnosed TIA have the wrong diagnosis (also referred to as ‘TIA mimic’) and are incepted into a pathway that is entirely based on the needs of the correctly diagnosed fifty per cent. To date the view of modellers and policy-makers on this issue has been somewhat mute on the issue. One reason for this seems to be that the TIA mimic population is rather protean. Interrogation of referrals to TIA clinics suggests a host of differential diagnoses (Cameron et al, 2011). Modelling all the potential treatment pathways and health states associated with TIA mimic would be an enormous task, which may be unfeasible given the constraints of time and resource. Another reason is that the participants involved in the creation of guidance tend to develop decision-analytic models from appraisal of existing economic evaluations (indeed, this is often a requirement of the HTA body) so there is a kind of historical bias in the evolution of ‘new’ models. A further explanation may be that the cut and thrust of guidelines depends on the treating of diseases not symptoms, isolated conditions and not the reality of multifactorial risk factors, comorbidities and diagnostic uncertainties. If the commissioners demand disease-focussed guidance, it is not surprising that we produce disease-driven decision-analyses. This paper considers whether it is ok for us to forget about the patients who are misdiagnosed by their GP.[[1]](#footnote-1) A more nuanced question would be, ‘Are the service delivery models we produce fit for purpose?’

We therefore undertake to find an answer to the above questions. In operational research there are methods in place for conceptualisation of the decision problem and subsequent modelling. While there are some examples of these having been applied in health-care settings they tend to have been mainly applied to complex systems or processes by simulation modellers (Robinson 2008). Even where the conceptualisation methods do not presume a simulation type model, the focus has typically tended towards structuring of the model as opposed to the structuring of the problem[[2]](#footnote-2) (Robinson, 2010; Roberts et al, 2012). However, more recently there have been practical suggestions for approaches relating to conceptual modelling (Kaltenthaler et al, 2011; Roberts et al, 2012; Tappenden, 2005).

This paper charts the initial development of a conceptual model by way of example in transient neurological disturbances. We start with the ‘problem situation’ and finish with a proposal for a service pathway model that considers patients’ cardiac risk. We conclude by suggesting that there could be unexplored service innovations (both in transient neurological disturbance and possibly in other disease driven models of care) that could be explored using a similar approach.

## A problem situation

**Background to TIA and the relevance of false positives**

All TIA mimics have some other explanation for their symptoms and importantly not all of these other explanations are benign. In particular, there is emerging evidence that the incorrectly diagnosed may face high cardiac and other risks (Bos et al, 2007; Cameron et al, 2011).

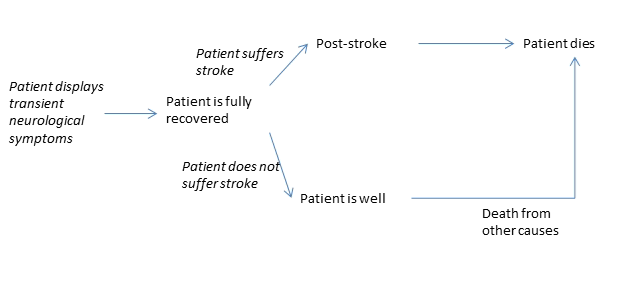
Under the current NICE guidance, all patients with symptoms suggestive of TIA are likely to be offered aspirin and referred to a neurologist for review of treatments (NICE 2008). While this service pathway has proven effectiveness in preventing stroke, there is no evidence base for the false-positive population (Lasserson, 2013). The challenge to the research-active community is to identify a decision-analytic model that is efficient for the total (i.e true- and false-positive) population presenting with the symptomology of TIA.

## Moving from a problem situation

In order to begin to identify the problem, we first examined the methods literature on the conceptualisation of cost-effectiveness models. Guidance from NICE’s Decision Support Unit (DSU) suggests that explicit reporting of the model development process can ensure that models are useful and contextually valid (Kaltenthaler et al, 2011).

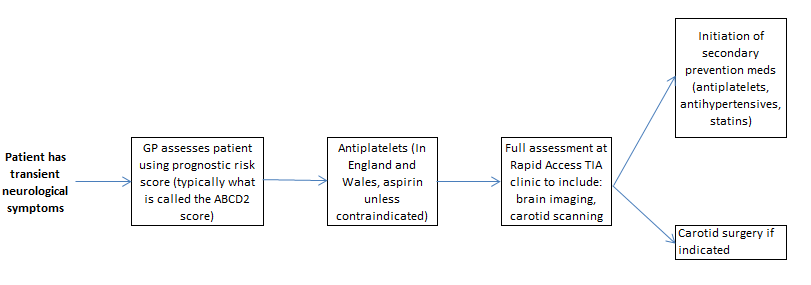
The NICE DSU document also describes two distinct conceptualisation models: problem-oriented models and design-oriented models. Problem-oriented models are defined as ‘those associated with developing, sharing and testing one’s understanding of the decision problem and the system in which it exist’ whereas design-oriented models are ‘those associated with designing, specifying and justifying the model and its structure’. Although distinct, both types of model are useful to the development of the decision-analytic model.

For illustrative purposes we provide an example of a typical problem-oriented model focussing on the disease process (Figure 1). Note that this model is the typical model based on the idea of existing guidance and the premise that TIA is ‘an early warning signal for stroke’ (and nothing else). It may be desirable to include things such as stroke recurrence and recovery, but the diagram nevertheless illustrates the major clinical events which are the sequelae of a confirmed TIA.

**Figure 1: Typical disease process model in TIA**

Note that Figure 1 documents the patients experience in terms of clinical events. This particular model makes the abstraction that the only relevant clinical events are stroke and death. In reality, there may be other relevant clinical events – perhaps too many to reasonably consider in a stylized illustration of the problem-oriented model! However, it seems that it would make sense to ask experts for input on whether they think the current disease focus of the model is a credible model for *all kinds of transient neurological symptoms.* At the very least, it may be possible to expand the current disease-pathway model to include clinical events that are considerably higher in suspected TIA populations than a reference group population (controlling of course for age and sex). Our next step is therefore to engage with experts to identify other relevant events. To this end, we have brainstormed some questions that would help us with the data requirements of a decision-analytic model. But, before we do this, we consider another approach to problem structuring in HTA via a service pathway model.

A distinct but complementary approach following identification of the disease process model is that of the service pathway model. If the disease process model isolates the relevant clinical events of the individual patient, the service pathway model provides the pathway of how that patient is managed by the health system. An example of the service pathway model used in TIA is provided by NICE pathways (NICE pathways [online], 2014). An abridged version of this is presented in Figure 2. One feature of service pathway models and discussed in the DSU guidance is that they can be useful in enabling identification of the resources used to provide services to suspected TIA patients. However, implications in terms of costs and consequences (outputs of the decision-analytic model) will be a combination of both disease process and service pathways: these call on the development of a design-oriented conceptual model.

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**Figure 2: Typical service pathway model in TIA/Stroke (stylised version of NHS pathways)**

Work in progress of a more design-orientated nature by considers the likely evidence requirements of the implemented ‘hard’ model. Before we do this however, we consider whether it is possible to use a simple thought experiment to refine down model options.

The thought experiment goes like this. Imagine that all TIA mimics are benign (let’s assume they have a benign diagnosis and prognosis). Does it matter if these patients are discharged from clinic? Consider the effect on health outcomes and costs. What conclusion do you come to?

Intuition would suggest that patients who are fairly well will not be harmed by a referral to TIA clinic, but there is an opportunity cost in terms of the resources used in the TIA clinic appointment as a consequence of the misdiagnosis.

Now repeat the exercise for TIA mimics who are seriously ill but consider there is no available treatment for this condition. In this case, logic again suggests an earlier diagnosis will not correspond to an improvement in health outcome. Again there are the opportunity costs associated with competing resource use.

In both scenarios so far the rationale for service redesign is non-compelling. There may be some resource implications relating to earlier diagnosis, but in both cases there are not substantial health gains.[[3]](#footnote-3) Yet hopefully by now you will see that there is a scenario where re-design appears to be very valid. If a patient has a serious but treatable condition (and specifically if earlier recognition improves health outcomes), it seems plausible that the additional costs in identification may be offset by the gains in health. In summary then this thought experiment demonstrates that the opportunity for effective intervention would appear to be high when there is ambiguity in the initial diagnosis and modifiable risk in the prognosis.

## Model requirements

We examined the available evidence from a range of sources to inform the development of the decision-analytic model. Evidence included information from existing economic evaluations, clinical guidelines and empirical clinical studies, but despite the acknowledgement of false positives in model descriptions, few models considered TIA patients within their scope. Work is ongoing to gain input from experts, and to include the views of service users. Our objective is to identify the relevant clinical events and (non-formalised) service pathways in false positive TIA currently (again by application of disease process and service pathway approaches to conceptual modelling). In addition to this, we want to develop a steering group of interested experts who have experience of treating and managing TIA patients to identify potential service improvements. The overarching objective is to identify the interactions between the disease process, health care resources and doctors-patients on health outcomes and costs.

Literature review of existing economic evaluations and clinical guidelines did not identify a service pathway model which fully considers the trajectory of false-positive patients within the model boundary (Table 1). The NICE guidelines model (which now reflects implemented best practice) acknowledges the relevance of false positive TIA but fails to consider the relevance of the patient sub-group subsequently at any stage in the structural development of the model. This oversight may not be that relevant if TIA mimics did not represent a susceptible group of patients where intervention might benefit patients (considering our thought experiment again). However, evidence across two paradigms (clinic and population-based observational studies in TIA prognosis) indicates that patients with TIA mimic have high morbidity. (Cameron et al, 2011, Bos et al, 2008). The potential for service re-design would seem ripe in relation to documented cardiac risk, given the existing evidence base relating to early intervention in cardiac risk.

The current position is therefore that the implemented (UK) service pathway model (Figure 2) does not consider the efficiency of the service in relation to the total population experiencing TIA symptoms. It therefore seems appropriate to examine the feasibility of a de novo model which augments the existing suspected TIA pathway with some form of cardiac risk assessment.

1. **What is going to be modelled – and how?**

Here we consider the key data considerations and challenges that would be associated with considering cardiac risk in all TNA if we extended the boundary of the modelled system to include it. In this way we begin to ‘draw together’ the disease- and service- pathway models. Table 2 is a method for exploring both the limits of the system. This includes some consideration of the detail in which we interaction between the mechanisms in the health-care system (doctors-patients, resource and disease processes) are represented.

**Table 1: Consideration of TIA mimics in existing economic evaluations (UK)**

(Table work in progress – to include other UK evaluations)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Question** | **Population** | **TIA mimics considered at all stages of model development process?** | | | | | | **Impact of TIA mimics considered within issued guidance?** | |
|  |  |  | **Pre-concept** | **Conceptual schema** | **Model schema** | **Estimate of incidence** | **Estimate of event rate** | **Estimate of intervention effectiveness** | **Cost-effectiveness results** | **Cost-effectiveness discussion** |
| NICE, 2008 | Immediate access clinics, weekly clinics and GO management | TIA (includes some minor stroke) | ✓ | X  No conceptual model is provided. | X  The NICE service pathway model does not account for TIA mimics (NICE pathways). | ✓  Based on the Oxford Vascular Study (Rothwell et al, 2004). | ✓  Not stated explicitly but source data is based on the ‘total’ population presenting to TIA services.  Data source: Johnston et al, 2007). | X  From studies initiating treatment in confirmed TIA only. | X / Unclear  The ICERs appear to relate to confirmed TIA but the event rate and incidence data appears to be drawn from the ‘total’ population presenting to TIA services. | X  TIA mimics are not discussed within recommendation to practice. |

**Table 2: Key data requirements, evidence gaps and proposed methods[[4]](#footnote-4)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Requirement** | **Data identified** | **What would be desirable** | **Proposed methods for closing evidence gap** |
| 1. ***Disease process*** |  |  |  |
| **Identification of differential diagnosis in suspected TIA** | Review of GP diagnostic accuracy revealed that the quality of the diagnostic coding of patients was generally too poor to make inference. Majority of diagnoses non serious. | Empirical quantification in terms of percentages of serious but treatable conditions. | Might not be necessary to close this gap. The diagnostic label appears less important than the prognosis: the majority of diagnostic labels could indicate a benign underlying pathology, which is in contrast to the prognosis of TIA mimics (see below). |
| **Prognosis of TIA mimic** | Kaplan Meier curves have been produced from a Scottish TIA clinic and a Dutch population perspective. Adjusted Hazard ratios are available. | Probability of cardiac events over time (age/sex adjusted). | Currently necessary to read off graphs. |
| 1. ***Service pathway*** |  |  |  |
|  | Decision over who provides the service and where | Consider both neurologist run and geriatrician run clinics (since geriatricians have stronger background in general medicine). It would be desirable to ‘test’ options in the clinical study setting. | Necessary to get a range of expert opinion. |
| 1. **Interaction of disease process and service pathway** |  |  |  |
|  |  |  |  |
|  | Cost drivers | Difference between (likely) increase in costs of assessment and treatment relating to cardiac risk - acute admissions avoided due to cardiac events | To identify guidance in managing cardiac r risk. |
|  | Consequences | Estimates of LYG and QALYG relating to successful early intervention in cardiac risk in the modelled population |  |
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### Five causal relations that are rather complex

As a spin-off from Table 2 and following the approaches of others, we identify a few of the causal relations we have discussed in meetings. We outline reasons for why understanding the hypothesised relation may be desirable but are yet to consider methods for closing the evidence gaps. In some cases, where the evidence gaps can’t be closed, it may be the role of the model to explore these hypothesised relations as structural and parameter uncertainties.

1. What is the effectiveness of assessing cardiac risk sooner in patients with suspected TIA?

* Desirable as: A measure of intervention effectiveness is needed to assess benefit of intervention.

1. Although distinct, are the diagnoses made by specialists linked to patient’s subsequent prognosis?

* Desirable as: Intuition would suggest that some diagnoses would imply a prognosis, this could be tackled by longitudinal follow-up of all patients referred to TIA clinic. If diagnosis is linked to prognosis knowledge of this could influence who is treated and how.

1. Is there a basis for different decision rules in TIA mimics presenting with different symptoms i.e. non-focal vs. mixed (focal and non-focal) symptoms?[[5]](#footnote-5)

* Desirable as: One population based study suggests that mixed symptoms are associated with particularly poor outcomes. (Bos et al,, 2008)

1. Would service re-design have any impact on the proportion of patients incepted into the (new) pathway?

* Desirable as: It is hard to anticipate the effect of a change in service design on the numbers of patients likely to be referred for investigations by GPs. It is possible that GPs currently refer patients to TIA clinics because this ensures they are seen promptly; the high proportion of false-positives may be an artefact of a disease-driven system that ignores patients with suspected TIA.

1. Would primary prevention initiatives (e.g. in hypertension, or else revising referral proformas) potentially negate the need for assessment of cardiac risk?

* Desirable as: Need to consider how service innovations elsewhere in the system might impact on modelled outcomes

## Discussion

Although this is the discussion, it is also a beginning of our modelling journey. We have not yet begun to truly evaluate the implications of alternative service pathway models in transient neurological disturbances. Nevertheless, we have provisionally indicated *what is going to be modelled and how*. We now look to further develop this conceptual model with appropriate input from others, and we hope our paper provides a forum for discussion. To this end, we identify some questions below.

More generally, this paper has exposed a potential problem with guidance based on disease-driven models of care. We suspect there may be other areas of Health Services Research where there could be service innovations if the conceptualisation of the problem was made more explicit.

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| *Possible areas for discussion that we have thought of are :* |
|  |
| 1. *Guidance welcomed on problem structuring methods in potential service pathway models (particularly with respect to involving stakeholders including service users)* |
| 1. *Other disease areas where the ‘real’ population receiving an intervention is not the same as the target population* |
| 1. *Ideas on the analytical methods used (those presented and others possible) to suggest that the alternate service pathway models are a feasible option for model development (see Table 2)* 2. *Idea on next steps – author is engaged in the development of ‘an empirical thought experiment’ to test the feasibility of a model of service provision which considers cardiac risk factors* |

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1. By us we are referring to those engaged in the HTA development process, and we are primarily referring to guidance/guidelines relating to service delivery models (and our unique example of transient neurologic disturbances). [↑](#footnote-ref-1)
2. By structuring the problem, we refer to the identification of the problem (i.e. the statement of the research question according to the ‘PICO’ mnemonic or similar criteria) and the setting of model boundaries (i.e. what the abstractions of the model are such that it a representation of reality, rather than reality itself) (Robinson, 2010). [↑](#footnote-ref-2)
3. [↑](#footnote-ref-3)
4. This table is non-exhaustive. [↑](#footnote-ref-4)
5. Note that a focal transient neurological attack equates to a TIA and the existence of non-focal symptoms usually suggests a differential diagnosis (Cameron et al, 2011). In brief, focal symptoms are those which *tend to be localised to a particular part of the body (e.g. left side of face or arm, as opposed to global symptoms e.g. confusion (Medline plus, 2014).* [↑](#footnote-ref-5)