PEER REVIEW HISTORY

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This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Delay in patients suspected of transient ischaemic attack: a cross-sectional study
AUTHORS	Dolmans, Louis; Kappelle, Jaap; Bartelink, Marie-Louise EL; Hoes, Arno W; Rutten, Frans

VERSION 1 – REVIEW

REVIEWER	Ashok Handa Nuffield Department of Surgical Sciences John Radcliffe Hospital Headley Way Oxford UK
REVIEW RETURNED	23-Oct-2018

GENERAL COMMENTS	This is an interesting study and aims to replicate the UK study from a TIA clinic published in the British Journal of surgery It would be helpful if the authors could address the following questions: 1. Did the 23 patients who had had a prior TIA behave differently e.g. present earlier or to Secondary care first? 2. Did patients with symptom at the weekend delay presentation longer than those at weekdays? 3. Did Patients presenting to GP's on weekends take longer to get to a TIA clinic 4. Are the TIA clinics available daily including weekends or is the availability restricted in any way during the week. 5. What percentage of the patients presented with Eye symptoms and did this influence when they presented (i.e. early or late?) 6. Did the authors look at the effect of having a partner on timing of presentation/ 7. Did the authors ask the GP's reasons for delaying referral to TIA clinics?

REVIEWER	Noreen Kamal University of Calgary, Canada
REVIEW RETURNED	25-Oct-2018

GENERAL COMMENTS	This paper describes the delay in receiving specialist assessment and treatment for TIA patients in 2 Dutch TIA clinics. This is an important research topic that is important to assessed and published. This small exploratory study provides significant foundation for further quality improvement and systems

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	improvement, and it warrants publication. However, there are some significant changes that should be done prior to publication: * For the abstract, I would prefer that the authors provide the results that show the full delay from onset of stroke symptoms to the TIA clinic. This can then be broken down into the patient delay and system delay. I really don't understand why the 2.8 hour is included here, and it is not fully clear what this time refers to. Time from first contact to GP consultation... What is first contact if it is not the GP consult. * The introduction refers to the ABCD2 score without much critical thought. This score has actually been shown to not be a good predictor of stroke severity. The authors should include this relevant critique of the score in the introduction. Please reference: Hill MD, Weir NU. Is the ABCD score truly useful? Stroke 2006; 37: 1636. Hill MD, Yiannakoulias N, Jeerakathil T, Tu JV, Svenson LW, Schopflocher DP. The high risk of stroke immediately after transient ischemic attack: a population-based study. Neurology. 2004;62:2015– 2020. Perry JJ, Sharma M, Sivilotti ML, Sutherland J, Symington C, Worster A, et al. Prospective validation of the ABCD2 score for patients in the emergency department with transient ischemic attack. CMAJ. 2011;183:1137–1145. Additional references should be included that also reflect the importance of rapid assessment and treatment of TIA patients: Kamal N, Hill MD, Blacquiere DP, Boulanger JM, Boyle K, Buck B, Butcher K, Camden MC, Casaubon LK, Côté R, Demchuk AM. Rapid assessment and treatment of transient ischemic attacks and minor stroke in Canadian emergency departments: time for a paradigm shift. Stroke. 2015 * In the results section, there needs to be greater clarity on the patient delay and what exactly is meant by "first medical contact" and how this differs from the GP visit. It seems that patient delay is also talked about int he "Delay until consultation at the TIA service", as the time from onset to GP consult is shown as 25.5 hours. It is confusing why this time is indicated in this section. As the time delays are among the most important finding that directly relates to this study better explanation of these delays needs to be provided. I am confused about how the total time can end up being 114.5 hours when it seems that it takes 25.5 hours to get the GP consult and then 40.8 hours to the TIA visit. Something doesn't add up here. I figure showing the timeline and average delays from onset to First Medical contact to GP visit to TIA service would really help clarify these critical results. These can then be show or highlighted as those parts that are associated with "the patient" and those that are associated with "the system". * I feel that the discussion can be better and the authors need to put these results into a broader context. - how does the Netherlands compare to other countries? - how do Dutch patients knowledge of TIA compare to other countries (I think that they are actually better than most) - where is the bulk of the delay and what is causing the delay? % patient related and % system related.

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	- is the current Dutch system of TIA management adequate? What are some other models that perhaps may work better? - what recommendation do the authors have for improving both patient and system delays?

REVIEWER	Dr Dawn Coleby Coventry University UK
REVIEW RETURNED	29-Oct-2018

GENERAL COMMENTS	Overall this is a clearly written paper, however I do question the originality of the study. As the authors state, patient delay in reporting TIA symptoms has been previously examined and published in the UK. Abstract - The conclusion could do with re-wording, to make it more succinct and easier to read. In the discussion, the authors describe no clear reduction in patient delay despite large campaigns. The authors mention 'FAST' earlier in the paper, but I am only aware of the 'ACT FAST' campaign which was distributed nationally across the UK. This campaign would have had little impact in the Netherlands. For a UK audience, it would be useful for the authors to include brief details of the campaign(s) they are referring too. The authors state the data was collected by a survey/interview. There are obvious limitations with this type of data collection, namely 'recall' error by the participant. This should be included as a limitation. The authors have also omitted to describe how they dealt with erroneous participant responses (if at all). Where the responses verified medical records, or maybe a relative? The method section is lacking detail. How was the participant survey data collected? Did it involve an audio recorded interview, or did the interviewer manually record responses into a questionnaire? How was interviewer bias avoided? Ethics - The authors state no formal ethics approval was required. In the UK collection of data from participants must not proceed without formal ethics approval and approval from the hospitals involved. Also the authors state no informed consent was required. Again this would not be permitted in the UK, and would be a major concern to a UK audience. The lack of ethics and consent needs clear justification. In the conclusion, the authors state that physician education is required. I'm unclear how the authors have come to this conclusion. The results show that 43.5% of patients were given anti-thrombotics by a GP, but no further exploration was undertaken to explore this finding. Could the lack of prescribing be due other factors besides lack of education? Could some patients just be unsuitable for the treatment (eg because of clotting disorders), or perhaps the GP believed the patient would not be seen in the TIA clinic on the same day and so could not prescribe it? No funding details are provided, though it appears this may be reporting the work of a PhD student.

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REVIEWER	Andrew Wilson University of Leicester, UK
REVIEW RETURNED	31-Oct-2018

GENERAL COMMENTS	The main strength of this paper is that it shows that delays experienced in accessing specialist assessment for TIA as reported in the UK in 2010 and 2014 are broadly replicated in the Netherlands in the present day. Its main weakness is that it is smaller than the other studies (93 participants versus about 1000 and 300) and so it lacks statistical power to undertake the comparisons and subgroup analysis reported in the UK studies. Suggestions for improvement are as follows: Abstract Last sentence of results: would be clearer to say 'of the 62 patients naïve to antibiotic who consulted their GP, 27 (43.5%) received antiplatelet therapy'. Introduction Second para: would be good to reference systematic review evidence: https://jnnp.bmj.com/content/80/8/871 Also that Wilson's paper suggested response to symptoms was not influenced by FAST campaign. Third para; UK guidelines now recommend all TIA suspects should be seen within 24 hours of referral and not to use risk stratification. https://www.strokeaudit.org/SupportFiles/Documents/Guidelines/2016-National-Clinical-Guideline-for-Stroke-5t-(1).aspx Methods More detail needed re data collection: eg was this semi-structured interview? Was there any validation of patient reported delay from the clinical record? If there wasn't, this should be reported as a limitation. Also more detail re referral procedures. For example how does the GP make contact with the clinic to arrange an appointment? What is the role of the receptionist in ensuring that these patients were seen promptly? How did some patients first report their symptoms to an outpatient clinic? Results Can the number of eligible patients who were not included be presented, is there a risk of selection bias? It would be useful to compare delay in those using GP versus emergency services Was the severity scale a validated questionnaire? Discussion There should be a more detailed account of the limitations of the study (eg single centre, numbers too small for detailed analyses, reliant on patient self-report) Conclusion Would it be reasonable to conclude (as other have) that suspected TIA patients should contact emergency services rather than their GP?

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VERSION 1 – AUTHOR RESPONSE

Reviewer 1

Comments:

1. ***Did the 23 patients who had had a prior TIA behave differently e.g. present earlier or to secondary care first?***

   We thank the reviewer for bringing up this issue and we added the delay times for these subgroups.

   - Line 198: 'Patients who had had a prior TIA or stroke (n=23, 24.7%) contacted the GP in 78.3% of cases (during office hours, n=17; GP out of hours service, n=1), and the median delay to first contact was 3.0 (IQR 0.8-40.5) hours, which was lower than in those without prior TIA/stroke; 19.0 (IQR 1.0-67.5) hours, p=0.29.'
   - Line 212: 'Referral delay was 105.0 (IQR 27.3-228.8) hours in the 23 (24.7%) patients who had had a prior TIA or stroke, and 30.0 (IQR 22.5-98.5) in those without prior TIA/stroke (p=0.09.)'

2. ***Did patients with symptom at the weekend delay presentation longer than those at weekdays?***

   Yes, this is a useful comparison indeed. We therefore added the delays for these two groups.

   Line 197: 'In the 31 (33,3%) patients with symptom initiation during the weekend delay was 21.0 (IQR 13.0-65.3) hours, and 8.8 (IQR 0.5-103.5) hours in those with symptoms during weekdays (p=0.29).'

3. ***Did Patients presenting to GP's on weekends take longer to get to a TIA clinic?***

   We also added the delays for these groups.

   Line 210: 'In the patients who consulted their own GP during office hours (n=69), referral delay was 30.5 (IQR 23.2-141.3); in the patients who (first) consulted a GP out of hours service (n=7) this was 58.4 (IQR 13.7-96.4) hours (p=0.62).'

4. ***Are the TIA clinics available daily including weekends or is the availability restricted in any way during the week?***

   We added this information in the methods section of our revised document.

   Line 136: 'Availability of TIA services in the Netherlands is restricted to weekdays.'

5. ***What percentage of the patients presented with eye symptoms and did this influence when they presented (i.e. early or late?)***

   In table 1 we show that 27 (29.0%) patients had visual symptoms.

   In this study we did not aim to analyse determinants of patient delay. If we would then not only visual symptoms but also other symptoms and determinants should be assessed. As for visual symptoms we would even have to further specify the different types of visual symptoms (i.e. blurry vision, diplopia, amaurosis fugax, etc). In this cohort this would result in estimates with very broad confidence intervals and therefore less useful information.

6. ***Did the authors look at the effect of having a partner on timing of presentation?***

   We want to refer to our answer to question 5.

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7. ***Did the authors ask the GP's reasons for delaying referral to TIA clinics?***

   No, although we agree with the reviewer that this is an important question. However, we performed our study at the TIA outpatient clinic where we could interview the patients, but not their GPs.

Reviewer 2

Comments:

1. ***For the abstract, I would prefer that the authors provide the results that show the full delay from onset of stroke symptoms to the TIA clinic. This can then be broken down into the patient delay and system delay. I really don't understand why the 2.8 hour is included here, and it is not fully clear what this time refers to. Time from first contact to GP consultation... What is first contact if it is not the GP consult.***

   We thank the reviewer and we now added the total time from symptom onset to the visit to the TIA clinic in the abstract.

   Line 39: 'The median time from symptom onset to the visit to the TIA service was 114.5 (IQR 44.0-316.6) hours.'

   It took on average 2.8 hours from first contact with the GP (or GP out-of-hours service) to actual GP consultation. We now clarified this in the abstract and results section of the revised paper.

   Line 42: median time from first contact **with the GP practice** to the **actual** GP consultation

   Line 207: from the first contact by the patient **with the GP practice** to the **actual** GP consultation

2. ***The introduction refers to the ABCD2 score without much critical thought. This score has actually been shown to not be a good predictor of stroke severity. The authors should include this relevant critique of the score in the introduction. Please add references (four suggested).***

   We thank the reviewer and now added information on the critical issues on performance of the ABCD2 score and also added the suggested references.

   Line 112: '… since new studies showed that the ABCD2 is an inaccurate predictor of early stroke.'

3. ***In the results section, there needs to be greater clarity on the patient delay and what exactly is meant by "first medical contact" and how this differs from the GP visit. It seems that patient delay is also talked about in the "Delay until consultation at the TIA service", as the time from onset to GP consult is shown as 25.5 hours. It is confusing why this time is indicated in this section. As the time delays are among the most important finding that directly relates to this study better explanation of these delays needs to be provided. I am confused about how the total time can end up being 114.5 hours when it seems that it takes 25.5 hours to get the GP consult and then 40.8 hours to the TIA visit. Something doesn't add up here. I figure showing the timeline and average delays from onset to First Medical contact to GP visit to TIA service would really help clarify these critical results. These can then be show or highlighted as those parts that are associated with "the patient" and those that are associated with "the system".***

   In the methods section we point out the three time intervals we have determined: the interval from onset of symptoms to the patient's first contact with a medical service (in 80% of cases the GP), the interval to the actual visit to the GP, and the interval to the TIA service visit. In the results section we describe which health care providers were first contacted. In response

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to this reviewer's first question we clarified the interval from the contact with the GP practice to the actual GP consultation: 'The (median) GP delay, i.e. the time from the first contact by the patient with the GP practice to the actual GP consultation ' (Line …).

The delays do not exactly add up because we express the intervals as medians. Importantly, however, the 114.5 hours is the median time from symptom onset to visit of the TIA service of the entire population. In the 80% of patients who first contacted a GP/GP-OHS, it took a median 25.5 hours from symptom onset to actual consultation of the GP, and another median 40.8 hours from GP consultation to the TIA visit.

We now more exactly clarify the different time delays in an extra table in the revised manuscript:

Table 2. Delay for the 93 patients suspected of a TIA.

Type of delay time	Median time (IQR), hours
Patient delay Time from symptom onset to first contact with medical service	17.5 (IQR 0.8-66.4)
▪ Onset during weekdays (N=31) Onset during weekend (N=62)	8.8 (IQR 0.5-103.5) 21.0 (IQR 13.0-65.3) p=0.29
▪ Prior TIA or stroke No prior TIA or stroke	3.0 (IQR 0.8-40.5) 19.0 (IQR 1.0-67.5) p=0.29
GP delay Time from contact with GP to actual GP consultation (N=76)	2.8 (0.5-18.5)
▪ GP during office hours (N=69) GP out of hours service (N=7)	3.0 (0.5-9.5) 1.4 (0.4-7.8) p=0.34
Referral delay Time from GP consultation to assessment at TIA service (N=76)	40.8 (IQR 23.1-140.7)
▪ GP during office hours (N=69) GP out of hours service (N=7)	30.5 (IQR 23.2-141.3) 58.4 (IQR 13.7-96.4) p=0.62
▪ History of TIA/ stroke No history of TIA/stroke	105.0 (IQR 27.3-228.8) 30.0 (IQR 22.5-98.5) p=0.08
Total delay Time from symptom onset to assessment at TIA service	114.5 (IQR 44.0-316.6)

IQR, interquartile range; TIA, transient ischaemic attack; GP, general practitioner.

Line 173: Table 2 shows an overview of the different parts of time delay to the assessment at the TIA service.

4. ***I feel that the discussion can be better and the authors need to put these results into a broader context.***
- How does the Netherlands compare to other countries?

In the discussion we compare our results to available studies on patient delay from the UK.

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We now added information on the Dutch health care system, in a comparison with the UK system: 'Both the Dutch and British health care system have a strong primary care system and rapid-access TIA services. In the Netherlands there have been campaigns promoting recognition of stroke symptoms similar to the UK 'ACT FAST' campaign.' (Line 269)
Next to the similarities, we already mentioned in the original version the differences in guidelines on TIA between the UK and the Netherlands.

- How do Dutch patients knowledge of TIA compare to other countries (I think that they are actually better than most)?

We think this is worthwhile to know, but literature on patient's knowledge of TIA is very limited, and standard and validated questionnaires are lacking thus making an adequate international comparison at this moment impossible.

- Where is the bulk of the delay and what is causing the delay? % patient related and % system related?

We also refer to our responses to reviewer 1.

In the discussion we summarize our main findings. We now better clarify these different parts of the total delay in the revised document (Line 261):
'The majority of patients with symptoms suspected of a TIA in this outpatient population delayed seeking medical help, resulting in a delay of more than 24 hours in 38.7% of patients **(median 17.5 (IQR 0.8-66.4))**. Although **the actual GP consultation took place** after a median of only 2.8 (0.5-18.5) hours from the first contact **with the GP practice (GP delay)**, it took another 40.8 (IQR 23.1-140.7) hours before the patient was seen at the TIA clinic **(referral delay)**.'

The table we added also helps clarifying this for the reader.

- Is the current Dutch system of TIA management adequate? What are some other models that perhaps may work better?

We added the following paragraphs on this issue in the discussion (Line 278):

'Given the time from symptom onset to the visit of the rapid-access TIA service it can be concluded that there is room for improvement of the current Dutch system of TIA management. In everyday practice the guidelines' recommendation of an assessment by the neurologist at a rapid-access TIA service the same or next day is not met. The strong gatekeeper's function of the GPs in the Dutch healthcare system has beneficial effects on selection of referral and health budgets, however, it may also cause undesirable delays in those who actually had a TIA.'

… existing paragraph on the start of antiplatelet therapy …

'If all GPs would follow the recommendation on antiplatelet therapy, the delay time to treatment would only be 2.8 (0.5-18.5) hours. We therefore consider enforcing this recommendation more important than the recommendation on assessment by the neurologist within 24 hours. Our results help to convince GPs that more timely action is needed in patients suspected of TIA.

An alternative care system would be the 'French' model with (i) a 24/7 TIA rapid-access service and (ii) public campaigns raising awareness among lay people that every acute neurological deficit should be considered a medical emergency similarly to acute chest pain, also requiring ambulance transportation, certainly if symptoms persist (possibly stroke). However, this would mean a large shift in the organisation of health care in the Netherlands, a large increase in health care costs.'

- What recommendation do the authors have for improving both patient and system delays?

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In the revised discussion we now added the following recommendations (Line 317-322):

(i) Lay people need to be better informed that also mild stroke-like symptoms that quickly disappear have to be reported to a physician as soon as possible.
(ii) GPs should be better educated about the rationale for an early start of antiplatelet therapy and that they can safely install this medication.
(iii) Furthermore, neurologists should advocate the early start of treatment during their contacts with GPs.
(iv) Further research is needed to explore the main determinants of patient delay and the main reasons for the lack of prescribing antiplatelet therapy by GPs.

Reviewer 3

Comments:

1. ***Abstract - The conclusion could do with re-wording, to make it more succinct and easier to read.***

   We thank the reviewer and changed our conclusion as follows: "There is substantial patient and physician delay in the process of getting a confirmed TIA diagnosis, resulting in suboptimal prevention of an early ischemic stroke. " (Line 46)

2. ***In the discussion, the authors describe no clear reduction in patient delay despite large campaigns. The authors mention 'FAST' earlier in the paper, but I am only aware of the 'ACT FAST' campaign which was distributed nationally across the UK. This campaign would have had little impact in the Netherlands. For a UK audience, it would be useful for the authors to include brief details of the campaign(s) they are referring too.***

   We agree with the reviewer and now better clarify that similarly to the UK, also in the Netherlands the neurologists together with the Netherlands Heart Foundation lounged an awareness campaign among lay people called 'ACT FAST'.

   Line 270: 'In the Netherlands there have been campaigns promoting recognition of stroke symptoms similar to the UK 'ACT FAST' campaign.'

3. ***The authors state the data was collected by a survey/interview. There are obvious limitations with this type of data collection, namely 'recall' error by the participant. This should be included as a limitation. The authors have also omitted to describe how they dealt with erroneous participant responses (if at all). Where the responses verified medical records, or maybe a relative?***

   We agree that recall error may be an issue in our survey as in about all studies on delay. Simply because in many cases symptoms quickly disappear, and it is only the patient or a bystander that can recall these symptoms. What is registered in the medical records, are not the 'objective' findings from the GP or neurologist, but the recall of the symptoms of the patient. Therefore, it is impossible to adequately tackle these problems in the study domain of suspected TIA.
   Importantly, however, we interviewed participant *before* they knew the definite diagnosis. Thus, at least knowledge of the diagnosis has not created hindsight bias regarding delay times, as was the case in many previously published studies.

   We added the following in the paragraph on strengths/limitations: 'Moreover, we interviewed …, importantly, before the definite diagnosis was established and without bias caused by this knowledge. **Recall errors still need to be considered**.' (Line 313)

   We did not check our data from the interview in medical records but we do not consider this as an important limitation. From another study we know that information on exact timing of symptoms and delays are in most cases lacking in GP records. Moreover, the information that

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might be available in the records is based on the same information provided by the patient or his/her relative.

4. ***The method section is lacking detail. How was the participant survey data collected? Did it involve an audio recorded interview, or did the interviewer manually record responses into a questionnaire? How was interviewer bias avoided?***

   In the revised manuscript we now provide more details on the recording:
   - Line 143: 'in a standardized questionnaire (included as a supplementary file)'
   - Line 147: 'Responses were written down by the interviewer'

   We performed the interview before the participant or the interviewer knew the definite diagnosis by the neurologist, thus, reducing the risk of bias because the diagnosis is known (TIA or no TIA).
   We added in the methods section: 'Participants were interviewed at the start of their day at the TIA service before knowing the diagnosis by the neurologist.' (Line 141)

5. ***Ethics - The authors state no formal ethics approval was required. In the UK collection of data from participants must not proceed without formal ethics approval and approval from the hospitals involved. Also the authors state no informed consent was required. Again this would not be permitted in the UK, and would be a major concern to a UK audience. The lack of ethics and consent needs clear justification.***

   We apologize for not providing more details. The study was approved by the Medical Ethics Committee of UMC Utrecht. The committee waived the requirement to obtain formal written informed consent from the participants, but of course oral consent of participants was a prerequisite. We now added this in the revised document (Line 359).

   Differently from the UK, in the Netherlands the Medical Ethics Committee assigns studies that have to comply with the Medical Research Involving Human Subjects Act (in Dutch 'WMO'), i.e. studies with an intervention that imply burden to patients. Studies who use a short questionnaire such as ours are considered to create no or minimal burden to participants and are free of patient risk. In this case also, we submitted the protocol of the study and the Medical Ethics Committee of UMC Utrecht approved the study and provided a waiver for formal ethics approval.

6. ***In the conclusion, the authors state that physician education is required. I'm unclear how the authors have come to this conclusion. The results show that 43.5% of patients were given anti-thrombotics by a GP, but no further exploration was undertaken to explore this finding. Could the lack of prescribing be due other factors besides lack of education? Could some patients just be unsuitable for the treatment (eg because of clotting disorders), or perhaps the GP believed the patient would not be seen in the TIA clinic on the same day and so could not prescribe it?***

   We agree that our conclusion was bluntly because we did not investigate the reasons for not prescribing antithrombotics. In our revised document we now clearly mention this (Line 321).

   We also do mention that in the Netherlands GP guidelines recommend to start antithrombotics in suspected TIA the same day, irrespective of the timing of brain imaging and the definite neurologist's diagnosis. Exceptions are (i) clotting disorders (only in a few cases), (ii) persistent or even progression of symptoms in which case bleeding in the brain could be the underlying cause, and finally (iii) patients who already take antithrombotics because of (a history of) ischaemic cardiovascular disease or atrial fibrillation.
   In the light of the aforementioned, we think there is still room for improvement regarding initiation of antithrombotics.

7. ***No funding details are provided, though it appears this may be reporting the work of a PhD student.***

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We did not clearly mention the funding that was provided by the Dutch GP trainees cooperation ('Stichting Beroepsopleiding Huisartsen' (SBOH)). This was an unrestricted grant to stimulate GPs to combine GP training with a PhD track. The ultimate goal is to bring evidence-based primary care to 'the next level.' We now added this information in the revised manuscript.

Line 349: 'The primary researcher (drs. L.S. Dolmans) performed this study as a general practitioner in training, and combined his training with a PhD track. 'Stichting Beroepsopleiding Huisartsen (SBOH)', employee of Dutch GP trainees (financially) supported the PhD track.'

Reviewer 4

Comments:
Abstract
Last sentence of results: would be clearer to say 'of the 62 patients naïve to antithrombotics who consulted their GP, 27 (43.5%) received antiplatelet therapy'.

We thank the reviewer and reworded this sentence accordingly (Line 43).

Introduction
Second para: would be good to reference systematic review evidence: https://jnnp.bmj.com/content/80/8/871 Also that Wilson's paper suggested response to symptoms was not influenced by ACT FAST campaign.

We added the systematic review by Sprigg et al. as a reference.
We initially referenced three original studies because this review from 2009 included just one study with only TIA patients. The other studies included both patients with stroke and (a minority of) TIA patients recruited in acute settings.

In addition, we now added in the introduction the findings of the recent study by Wolters et al. on medical attention seeking in TIA/minor stroke patients before and after the ACT FAST campaign.

Line 99: 'A before and after evaluation of the 'ACT FAST' showed an improvement of patient delay in stroke patients, but in patients with a TIA or minor stroke there was no improvement in use of emergency medical services or time to first seeking medical attention within 24 hours [7].'

Third para; UK guidelines now recommend all TIA suspects should be seen within 24 hours of referral and not to use risk stratification. https://www.strokeaudit.org/SupportFiles/Documents/Guidelines/2016-National-Clinical-Guideline-for-Stroke-5t-(1).aspx

We thank the reviewer, and added this information (and reference):

Line 107: 'The UK GP guidelines emphasise an immediate start of medication by the GP in any suspected TIA patient, and have recommended the use of the prognostic ABCD2 score (Age, Blood pressure, Clinical features, Duration, Diabetes) to define high-risk patients that have to be examined by the neurologist within 24 hours.[10] However, in the latest update of the UK national clinical guideline for stroke in 2016 the use of the ABCD2 score was abandoned, since new studies showed that the ABCD2 is an inaccurate predictor of early stroke.[11, 12, 13] This guideline now also recommends to refer all suspected TIA patients to a TIA service within 24 hours.'

Methods
More detail needed re data collection: eg was this semi-structured interview? Was there any validation of patient reported delay from the clinical record? If there wasn't, this should be

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reported as a limitation.
Also more detail re referral procedures. For example how does the GP make contact with the clinic to arrange an appointment? What is the role of the receptionist in ensuring that these patients were seen promptly? How did some patients first report their symptoms to an outpatient clinic?

We indeed applied a semi-structured interview with a standardized questionnaire, which we now attach as a supplementary file of the revised document.

We addressed the issue of recall errors and validation in patient records in our response to the third reviewer (third comment).

Regarding referrals; GPs call the neurologist in case they suspect a TIA and the neurologist decides when the patient is seen at the TIA outpatient clinic.

A few patients first reported their symptoms directly to a specialist at an outpatient clinic (for example a cardiologist or internist), or called an outpatient clinic where they are a known patient (for example opthalmology). We added to clarify (Line 194): '… first reported their symptoms to a medical specialist **(other than a neurologist)** via an outpatient clinic.'

Results
- Can the number of eligible patients who were not included be presented, is there a risk of selection bias?

We did not register all eligible patients, but we can say that the willingness to participate was high. The risk of selection and selection bias is therefore low in our study.

- It would be useful to compare delay in those using GP versus emergency services

The number of patients that called the GP OHS was small; only 7 (7.5%) patients (median delay from symptom onset to first contact only 0.5 hours). Only two patients directly contacted the hospital emergency services (median delay to first contact 0.4 hours). Given these low numbers, a comparison between those using GP during office hours and emergency services is not useful.

- Was the severity scale a validated questionnaire?

No, to the best of our knowledge such a questionnaire for delay does not exist. See also our answer to the editor's fourth question.

Discussion; There should be a more detailed account of the limitations of the study (eg single centre, numbers too small for detailed analyses, reliant on patient self-report)

We recruited participants at two TIA services. Indeed our study was smaller than some previous UK studies, but the number of patients was large enough to provide adequate estimations of delay times. In addition we could provide novel data on perception and interpretation of symptoms by patients. We did not aim for detailed analyses of determinants of delay. Finally, this is the first study on patient delay from the Netherlands, thus enriching existing knowledge in the field. Importantly, delay is dependent on health care system organization.
Regarding patient self-report, we pointed out earlier (reviewer 3, comment 3) that we do not consider the use of (only) patient interviews as a limitation in this study.

Conclusion
Would it be reasonable to conclude (as other have) that suspected TIA patients should contact emergency services rather than their GP?

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We do not think this can be concluded from our study. Also, we do not fully agree with the conclusion, at least not for our Dutch system. We also refer to our response to reviewer 2, comment 4.

We consider starting with antiplatelets as early as possible as the most important goal in patients with TIA. There are two strategies that could be considered depending on the health system organisation; a direct start of antiplatelets, also out of hospital and thus in all suspected cases. After neurologic assessment, this therapy can be stopped in those who show not to have had a TIA. The other strategy would be every suspected TIA patient contacting emergency services. This would of course substantially increase their workload in this domain, and without adaptation of the work-up strategy and more personnel working at the TIA service this would result in more delay before the assessment is completed and antiplatelets initiated. The net result might even be that patients receive preventive treatment later than those in the first strategy. Furthermore, the last strategy is much more costly. To get an adequate answer these two strategies should be compared for their cost-effectiveness.

VERSION 2 – REVIEW

REVIEWER	Ashok Handa Nuffield Department of Surgical Sciences, Oxford University United Kingdom
REVIEW RETURNED	21-Jan-2019

GENERAL COMMENTS	This is a good study looking at delays in presentation after suspected TIA and outline the findings and make good recommendations. The references are up to date and this addresses an important clinical and public health issue

REVIEWER	Noreen Kamala Dalhousie University, Canada
REVIEW RETURNED	02-Jan-2019

GENERAL COMMENTS	Thank you. All of my concerns have been addressed.

REVIEWER	Dr Dawn Coleby Coventry University, UK.
REVIEW RETURNED	08-Jan-2019

GENERAL COMMENTS	All reviewer comments appear to be adequately addressed.

REVIEWER	Andrew Wilson University of Leicester, UK
REVIEW RETURNED	11-Jan-2019

GENERAL COMMENTS	I consider the authors have responded adequately to my and other reviewers comments

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