PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Nurse compliance with a protocol for safe injectable medication administration: comparison of two multicenter observational studies.
AUTHORS	Schutijser, Bernadette; Klopotowska, Joanna; Jongerden, Irene; Spreeuwenberg, Peter; Wagner, Cordula; de Bruijne, Martine

VERSION 1 – REVIEW

REVIEWER	Alvisa Palese Udine University, Italy
REVIEW RETURNED	01-Oct-2017

GENERAL COMMENTS	the manuscript is really relevant in the field. The research process has been well conducted as well as well reported. This manuscript may be important for policy makers and managers, as well as for clinicians around the world. I have the following suggestions: a. in general in the background you have focused on the protocol adopted by you country. No data with regard other countries that have adopted similar strategies have been reported; b. in the study process, you have stated that the observation was performed by informing the nurses without discovering the procedure observed. I think that this is below the ethical standards and more data supporting this decision is required; c. no data with regard the turn over rates, the stability of the nursing workforce as well as the stability in the nurse-to-patient ratio over the years have bene reported and this is the main lack of this study that should be highlighted or addressed. d. with regard to the lack of compliance by the second nurse, I suggest a more consistent discussion. With the changes in the workforces, it is really critical to obtain for each IV a second nurse for the check: increased workloads and models of care delivery functional models) may prevent this standard. This point should be addressed e. I am aware that this is out of the scope of your study; however, you have missed a great opportunity to compare also the MAEs occurred in the periods. I suggest to consider also this point. f. The reference style should be checked again in accordance with the journal rules.

REVIEWER	PMLA van den Bemt Erasmus University Medical Centre Dpt of Hospital Pharmacy Rotterdam, The Netherlands
REVIEW RETURNED	02-Oct-2017

GENERAL COMMENTS	This is a repetition of an earlier study performed by the same group, which holds some merit as its purpose is to show whether the protocol adherence by nurses has increased compared to the previous study period. The paper is well written. I have a few comments that need to be addressed. 1. Line 19 introduction page 4 states that medication administration errors occur most often in insulins, anesthetics and anticoagulants. However, the reference refers to a study on adverse drug events; not on errors. It is logical these narrow therapeutic range drugs cause ADEs more frequently, but there is no reason to assume they are more error-prone than other iv drugs. So, please rephrase. 2. There appears to be more than one primary outcome (line 35 page 7), but no adjustment for multiple testing was included in both the sample size calculation and the choice of the 5% significance limit. 3. line 45 and following page 7: why were nurse-related characteristics such as degree of eduction or years of experience not included? and why were workload-related characteristics such as number of drugs to be dispensed per round per nurse not included? 4. Improvement strategies implemented were studied. It would be interesting to know whether certain improvement strategies are associated with better protocol adherence. Why was this not studied?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Alvisa Palese
Institution and Country: Udine University, Italy Competing Interests: None declared

We would like to thank reviewer #1 for carefully reading our manuscript and for the thoughtful comments and constructive suggestions. Our response follows (the reviewer's comments are in italics).

General Comments:
The manuscript is really relevant in the field. The research process has been well conducted as well as well reported. This manuscript may be important for policy makers and managers, as well as for clinicians around the world.

Reply:
We appreciate the positive feedback from the reviewer.

Major comments:
1. In general in the background you have focused on the protocol adopted by you country. No data with regard other countries that have adopted similar strategies have been reported.

Reply:
Protocols regarding preparing and administering injectable medication are comparable in other countries in the world.[1-3] Moreover, protocol steps such as 'patient identification' and 'hand hygiene', are generally seen as important and included in these protocols. We have included an extra sentence at the end of the second paragraph of the 'Introduction' section, page 4, to address this ("In other countries, comparable protocols have been implemented and protocol steps such as 'patient identification' and 'hand hygiene' are generally seen as important and included in these protocols.").

2. In the study process, you have stated that the observation was performed by informing the nurses without discovering the procedure observed. I think that this is below the ethical standards and more data supporting this decision is required.

Reply:
Based on the comment of the reviewer, we realize that we haven't described our procedure well enough. Before the start of the observations, nurse managers of the participating wards were fully informed about the purpose of the study, i.e. the evaluation of the administration of injectable medication through observations of protocol proceedings. Nurses were informed about the goal of the observations (correct administration of injectable medication) but not about the specific protocol proceedings being observed, in order to prevent bias (Hawthorne effect). We did not violate ethical standards, since these proceedings are publicly accessible in all hospitals (as they are part of a national patient safety program) and nurses should be acting upon them. Furthermore, participation in the study was voluntary and anonymous for the nurses; if a nurse did not want to participate, then he/she was not observed. For clarity, we have added additional information in the 'Participants' paragraph of the 'Method' section, page 6 ("Nurse managers of the participating wards were fully informed about the purpose of the study. Nurses were informed about the goal of the observations (correct administration of injectable medication) but not about the specific protocol proceedings being observed, in order to prevent bias (Hawthorne effect).[4] However, nurses could be aware of the observed proceedings on the observation form, since all proceedings follow the current protocol which is publicly accessible in all hospitals. Participation in the study was voluntary and anonymous for nurses; if a nurse did not want to participate, then he/she was not observed.").

3. No data with regard the turnover rates, the stability of the nursing workforce as well as the stability in the nurse-to-patient ratio over the years have bene reported and this is the main lack of this study that should be highlighted or addressed.

Reply:
Turnover rates, the stability of the nursing workforce, and the stability of the nurse-patient ratio would indeed provide useful information over the influence of context factors on our results. However, these numbers are complex and the way these variables are calculated vary widely among Dutch hospitals and are therefore difficult to compare and collect in a reliable way. Therefore, we decided not to collect these data. In general, mean patient-to-nurse ratio in the Netherlands is 7.0 (range 5.1-8.1).[5] It is suggested that nurses with less patients (a lower patient-to-nurse ratio) judge patient safety more positive, but this is based on perception and not observed in practice.[5] It is not clear to what extent these numbers affect protocol compliance. We have included a limitation about this point in the 'Discussion' section, page 16 ("Thirdly, no data about nurse-related characteristics (degree of education and years of experience) and workload-related characteristics (turnover rates, stability of the nursing workforce, stability of the nurse-to-patient ratio over the years, and number of drugs to be dispensed per round per nurse) have been collected.

This may have resulted in an incomplete overview of factors associated with protocol compliance. The nurse-related characteristics have not been collected because we used the same observation form as in the first evaluation which did not include these characteristics. The workload-related characteristics have not been collected because these data appeared too complex and the way these variables are calculated varied per ward and per hospital.").

4. With regard to the lack of compliance by the second nurse, I suggest a more consistent discussion. With the changes in the workforces, it is really critical to obtain for each IV a second nurse for the check: increased workloads and models of care delivery functional models) may prevent this standard. This point should be addressed.

Reply:
We rewrote the fourth paragraph of the 'Discussion' section, page 14-15, thereby emphasizing the importance of the check by a second nurse and the difference between knowledge and practice of this critical protocol proceeding ("In theory, the check by a second nurse for all IV medications has become a standard and critical proceeding. Alsulami et al. (2012) described that most healthcare professionals prefer the double check, but that staff shortage can prevent for correctly conducting this proceeding.[6] In practice, we observed that increased workload, indeed, may prevent this standard. Therefore, this proceeding must be prioritized in future studies. In order to facilitate the check by a second nurse, intervention strategies such as adjusting the timing of the check by a second nurse (10 hospitals) and having a buddy-system (9 hospitals) have been implemented in the participating hospitals. However, qualitative studies on the check by a second nurse showed that the focus should lie on training and education, automating the proceeding, and seeing the check by a second nurse as a method to share opinions.[7]").

5. I am aware that this is out of the scope of your study; however, you have missed a great opportunity to compare also the MAEs occurred in the periods. I suggest to consider also this point.

Reply:
We agree with the reviewer that the information on MAEs would be of additional value to the study and we have acknowledged this limitation in the 'Strengths and Limitations of this study' section of the manuscript, page 3. However, as the reviewer already pointed out, measuring MAEs was out of the scope of this study. Since MAEs are to a limited extent retrievable from the hospital Electronic Health Record (EHR) system, measuring MAEs would require an additional study with longer time investment and financial resources. In, for example, the study of Westbrook et al. (2011), low protocol compliance was associated with an increased number of MAEs, so we are confident that measuring protocol compliance is a valid alternative to gain insight in safety of the medication administration process.[8]

Minor comments:
6. The reference style should be checked again in accordance with the journal rules.

Reply:
We have checked the reference style again as suggested and adjusted where appropriate according to the journal rules.

Reviewer: 2
Reviewer Name: PMLA van den Bemt
Institution and Country: Erasmus University Medical Centre, Dpt of Hospital Pharmacy, Rotterdam, The Netherlands Competing Interests: None declared.

We would like to thank reviewer #2 for carefully reading our manuscript and for the thoughtful comments and constructive suggestions. Our response follows the reviewer's comments (which are in italics).

General Comments:
This is a repetition of an earlier study performed by the same group, which holds some merit as its purpose is to show whether the protocol adherence by nurses has increased compared to the previous study period. The paper is well written. I have a few comments that need to be addressed.

Reply:
We appreciate the positive feedback from the reviewer.

Major comments:
1. Line 19 introduction page 4 states that medication administration errors occur most often in insulins, anesthetics and anticoagulants. However, the reference refers to a study on adverse drug events; not on errors. It is logical these narrow therapeutic range drugs cause ADEs more frequently, but there is no reason to assume they are more error-prone than other iv drugs. So, please rephrase.

Reply:
We thank the reviewer for pointing out this misinterpretation of reference #8. We have removed the part of the sentence 'MAEs with IV medication occur most often with insulins, anesthetics, and anticoagulants'' on page 4. We agree with the reviewer that there is no reason to assume that this specific groups of medications are prone to MAEs.

2. There appears to be more than one primary outcome (line 35 page 7), but no adjustment for multiple testing was included in both the sample size calculation and the choice of the 5% significance limit.

Reply:
We thank the reviewer for pointing out this issue. Since we have calculated our sample size using protocol compliance as an outcome of interest, complete protocol compliance is our primary outcome. Compliance to the three separate protocol proceedings as well as mean number of proceedings are therefore our secondary outcomes. We have adjusted this accordingly in our 'Protocol compliance' paragraph of the 'Method' section, page 7 ("The primary outcome was the complete protocol compliance with the Dutch injectable medication protocol. Each observed IV medication administration was scored (0-9), and then dichotomized into complete compliance (9 safety proceedings conducted) and incomplete compliance (≤8 safety proceedings conducted).[9] The secondary outcomes were the mean number and percentage of correctly conducted individual proceedings, in particular compliance with: 'patient identification', 'hand hygiene', and 'check by a second nurse'. These three proceedings were the three least conducted protocol proceedings during the first evaluation."). Furthermore, for the primary outcome and the three secondary outcomes (compliance with the proceedings patient identification, hand hygiene, and check by a second nurse), separate multilevel analyses were conducted since these outcomes represent different concepts. The problem of multiple testing typically arises when dozen of tests are conducted, which is not the case in our study.

We have adjusted this in the ‘Data analyses’ paragraph of the ‘Method’ section, page 8 (“To assess the associations over time between potential explanatory variables (i.e. hospital type, ward type, and administration time) and protocol compliance, separate univariate multilevel logistic regression analyses were conducted for four dependent variables: complete protocol compliance (yes/no), patient identification compliance (yes/no), hand hygiene compliance (yes/no), and check by a second nurse compliance (yes/no).”).

3. line 45 and following page 7: why were nurse-related characteristics such as degree of education or years of experience not included? and why were workload-related characteristics such as number of drugs to be dispensed per round per nurse not included?

Reply:
We agree with the reviewer that these characteristics would be very interesting to include. However, since this study was a repeated study, we used the same observation form as in the first evaluation study of 2011/2012. On this form, degree of education, years of experience, and number of drugs to be dispensed per round per nurse were not included. We will remember this suggestion and in a future study, we will add these characteristics on the observation form. We addressed this point as a limitation in the ‘Discussion’ section, page 16.

4. Improvement strategies implemented were studied. It would be interesting to know whether certain improvement strategies are associated with better protocol adherence. Why was this not studied?

Reply:
We agree with the reviewer that it would be interesting to determine whether certain improvement strategies are associated with better protocol compliance. This was, however, not analyzed since the goal was to get a first impression (using the SEIPS model) of current improvement strategies implemented in Dutch hospitals. Furthermore, the information about improvement strategies was collected during two interviews, and therefore based on what was said to be implemented. We did not observe whether the strategies were actually implemented by all professionals. To determine associations between strategies and protocol compliance, we would recommend to conduct a new study to observe if the strategies are conducted as indicated in daily practice. We added a sentence in the ‘Discussion’ section, page 16, about this point (“Finally, since the information about implemented improvement strategies was collected during two interviews, it is uncertain how well these strategies are implemented in daily practice on the wards. Therefore, this information provides only a first impression. To be able to determine associations between strategies and protocol compliance, we would recommend to perform a new study aiming to observe the execution of the mentioned strategies on the wards.”).

References:
1 Kim J, Bates DW. Medication administration errors by nurses: adherence to guidelines. J Clin Nurs 2013;22:590-8.
2 Choo J, Johnston L, Manias E. Nurses' medication administration practices at two Singaporean acute care hospitals. Nurs Health Sci 2013;15:101-8.
3 Alemanni J, Touzin K, Bussieres JF, et al. An assessment of drug administration compliance in a university hospital centre. J Eval Clin Pract 2010;16:920-6.
4 Dean B, Barber N. Validity and reliability of observational methods for studying medication administration errors. Am J Health Syst Pharm 2001;58:54-9.
5 Aiken LH, Sloane DM, Bruyneel L, et al. Nurse staffing and education and hospital mortality in nine European countries: a retrospective observational study. Lancet 2014;383:1824-30.
6 Alsulami Z, Conroy S, Choonara I. Double checking the administration of medicines: what is the evidence? A systematic review. Arch Dis Child 2012;97:833-7.
7 Hewitt T, Chreim S, Forster A. Double checking: a second look. J Eval Clin Pract 2016;22:267-74.

8 Westbrook JI, Rob MI, Woods A, et al. Errors in the administration of intravenous medications in hospital and the role of correct procedures and nurse experience. BMJ Qual Saf 2011;20:1027-34.
9 Schilp J, Boot S, de Blok C, et al. Protocol compliance of administering parenteral medication in Dutch hospitals: an evaluation and cost estimation of the implementation. BMJ Open 2014;4:e005232.

VERSION 2 – REVIEW

REVIEWER	alvisa palese University of Udine, Italy
REVIEW RETURNED	19-Nov-2017

GENERAL COMMENTS	Thank you for having given the opportunity to revise the manuscript which is timely and important. All suggestions have been addressed and all required changes have been performed. Now it is informative, well structured, balanced in the discussion and informative. Thank you for your work

REVIEWER	Patricia van den Bemt Department of Hospital Pharmacy, Erasmus University Medical Centre, Rotterdam, The Netherlands
REVIEW RETURNED	08-Nov-2017

GENERAL COMMENTS	Well revised; no additional comments