PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Effectiveness of a nurse educational oral feeding program on feeding outcomes in neonates: protocol for an interrupted time series design.
AUTHORS	Touzet, Sandrine; Beissel, Anne; Denis, Angelique; Pillet, Fabienne; Gauthier Moulinier, Hélène; Hommey, Sophie; Claris, Olivier

VERSION 1 - REVIEW

REVIEWER	Nathalie Maitre Nationwide Children's Hospital Columbus OH USA
REVIEW RETURNED	25-Dec-2015

GENERAL COMMENTS	This manuscript represents an important advance in implementation of a nursing education protocol for feeding of preterm infants. However a few major points detract from the strength of the study design and the validity of the conclusions: this is a quality improvement design, and as such should include essential components: 1- Balancing measures: the design does not address the measures that could be negatively impacted by non-blinding of nursing staff in the context of outcomes such as shorter length of stay and shorter time to feeding tube removal. For example, fatigue, increased apnea, desaturations, possible microaspiration episodes, stress (cortisol levels) , decreased weight gain, etc.. These can easily be addressed and measured to strengthen the results.The rejection signs mentioned in the secondary outcomes are a good start, but should be analyzed a balancing measures, not simply as secondary outcomes. 2- Measures of intervention implementation and treatment fidelity: these are crucial to detect whether the results are due to the intervention in this design r to change in epoch. In addition to convincing reviewers that the results are due to the intervention and not to other changes in the NICU, the treatment fidelity measures would provide an essential component to the statistical analysis modeling proposed by the study investigators. If the intervention is being more or less implemented, the results could vary due to this factor instead of simply to the strength of the intervention. The vague questionnaire mentioned in the methods does not address implementation or fidelity. 3- The intervention design itself is somewhat weakened by not using the most evidence-based components: the choice of using Dr Lessen's PIOMI is not the most optimal: Drs Fucile and Lau have published excellent Oral and Tactile Kinesthetic intervention data and Dr Jadcherla has the feeding program (including nursing interventions) with the highest quality data to support it. Using the

	pilot study by Dr Lessen is interesting but confuses the protocol: Is this about testing a nursing education intervention or is this about implementing her protocol on a larger scale? Overall, my recommendations would be to either separate this into two protocols, one about implementing a feeding program and one about testing a new oromotor stimulation or to ensure that the study is accomplished in several steps, each designed to address a sepaarte outcome.

REVIEWER	Chantal Lau Baylor College of Medicine Houston TX USA
REVIEW RETURNED	02-Jan-2016

GENERAL COMMENTS	The title of this manuscript is “Effectiveness of a nurse educational oral feeding program on feeding outcomes in neonates: an interrupted time series design.” It is very well recognized that changing clinical practice is difficult. The authors are commended for the attention given to many areas of this practice that lack stringencies. But without any data, even preliminary results, one cannot evaluate its effectiveness on neonates’ feeding outcomes which is the research question. What happens if their hypothesis is not confirmed? It does provide a detailed description of the educational nursing program developed by the authors to improve the practice of infant oral feeding in neonatal intensive care units. So before evaluating this program’s ‘effectiveness’ on infant feeding outcomes, should the first step be the evaluation of the nursing staff’s compliance to the program, then the effect of the program on infant feeding outcomes? At present, there are no results presented of any kind. Editorial assistance would be beneficial Minor comment - Line 239: It is unclear whether PMA is used as the gestational age (at birth) or PMA = gestational age + postnatal age in weeks.

REVIEWER	Annie Rohan Stony Brook University, USA
REVIEW RETURNED	19-Jan-2016

GENERAL COMMENTS	This is a very well-developed paper. Your writing is excellent and leads the reader through an organized, detailed journey of your subject. You make a strong case for the interrupted time series design. Some suggestions for improvement follow: Title: It wasn’t clear to me initially that I was not going to see study results in this manuscript. I think that a stronger title might be, “Study protocol for ‘effectiveness of a nurse-educational oral feeding program on feeding outcomes in neonates’ using an interrupted time series design.” Abstract: Clear abstract. Consider changing subtitle “methods and analysis” to

	"methods and design." In addition, the subtitle "strengths and limitations of this study" is again confusing. Consider rephrasing as "strengths and limitations of the proposed study." Introduction/Review of Literature: Please rephrase throughout from "this study" to "the proposed study." Alternatively, can use the future tense to make clear that this is not a manuscript with study results, but rather describing the study design (e.g.: change "the study describes…" to "the study will describe…") Line 78: Background and rationale (check spelling). Intervention, Outcome measures: Well described. Please elaborate on how the questionnaires will be developed (Line 220) in a way that they will be reliable and valid. Study sample design: Line 238: Would rephrase as "Based upon census data, it is anticipate that we will be able to recruit 20-25 new patients into the proposed study each month." Statistical Considerations: Future tense used in this section – good! Time frame, Ethics: Well described. Discussion: Well described. I would recommend that you add a few lines about "implementation support strategies" to describe methods that you will use to facilitate the intervention after staff training. There are several "bookmark not defined" notations in this section. It is not clear what these mean. Figures: No suggestions.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Nathalie Maitre
Institution and Country: Nationwide Children's Hospital, Columbus OH, USA Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

This manuscript represents an important advance in implementation of a nursing education protocol for feeding of preterm infants.
However a few major points detract from the strength of the study design and the validity of the conclusions:
this is a quality improvement design, and as such should include essential components:
1- Balancing measures: the design does not address the measures that could be negatively impacted by non-blinding of nursing staff in the context of outcomes such as shorter length of stay and shorter time to feeding tube removal. For example, fatigue, increased apnea, desaturations, possible microaspiration episodes, stress (cortisol levels) , decreased weight gain, etc.. These can easily be addressed and measured to strengthen the results. The rejection signs mentioned in the secondary outcomes are a good start, but should be analyzed a balancing measures, not simply as secondary outcomes.

Response to the reviewer:
As suggested by Reviewer 1, we separated the outcomes into three distinctive categories: outcome measures, process measures and balancing measures.

The following balancing measures will be analyzed: feeding difficulties (defined in our study as no demonstration of hunger cues, bottle refusal, coughing, choking or vomiting during feedings, hypoxia or unstable heart rate during feeding sessions; feeding intake exceeding 30 minutes, excitement, discomfort or arching of the back during feedings, and gagging or falling asleep during feedings).

However, as pointed out by reviewer 1, a certain number of measures, which could negatively impact the achievement of full oral feeding with premature neonates, are not addressed in our study protocol. These measures, among others, are icterus, weight loss, concomitant medication administration, stress, fatigue, miscroaspiration episodes or decreased .weight gain. Defining the level from which these measures will negatively impact feedings (percentage of weight loss, level of bilirubine) seems questionable to us, which is the reason why we did not integrate them into the balancing measures.

2- Measures of intervention implementation and treatment fidelity: these are crucial to detect whether the results are due to the intervention in this design r to change in epoch. In addition to convincing reviewers that the results are due to the intervention and not to other changes in the NICU, the treatment fidelity measures would provide an essential component to the statistical analysis modeling proposed by the study investigators. If the intervention is being more or less implemented, the results could vary due to this factor instead of simply to the strength of the intervention. The vague questionnaire mentioned in the methods does not address implementation or fidelity.

Response to the reviewer:
1. Change in epoch:
Choosing a time series design allows us to consider the secular trend (change in epoch). Indeed, we will analyze neonates' data during a 6 month period preceding the implementation phase. This pre-intervention period will give us a temporal control that will help us determine whether the particular intervention has a significantly greater effect than the underlying secular trend (change in epoch).

2. Treatment fidelity:
We will determine nurses' protocol compliance throughout the implementation phase: to assess nurses' protocol compliance, a questionnaire will be developed by health providers working at the neonatal unit, and will be revised by questionnaire design experts. The instruments' question and response categories will be phrased in simple terms. The items will be revised and improved upon, following evaluation by questionnaire design experts. Finally, they will be tested for comprehensibility by health providers from the neonatal unit, who are not participating in the study protocol.
Moreover, in terms of process measures:
- Nurses involvement in the training modules will be evaluated through their presence at the training sessions.
- Caregivers' knowledge acquisition and satisfaction scores will be assessed through a questionnaire following each training module.
- The time dedicated to routine practice nurse coaching (also called feeding rounds) in their routine feeding practice and application of feeding protocols will be measured.

3. Other changes:
All events, such as leadership changes, and protocol modifications, that occur during the study period and may interact with the intervention or the study results, will be recorded in a logbook.

We have included these 3 points in our manuscript.

3- The intervention design itself is somewhat weakened by not using the most evidence-based components: the choice of using Dr Lessen's PIOMI is not the most optimal: Drs Fucile and Lau have published excellent Oral and Tactile Kinesthetic intervention data and Dr Jadcherla has the feeding program (including nursing interventions) with the highest quality data to support it. Using the pilot study by Dr Lessen is interesting but confuses the protocol: Is this about testing a nursing education intervention or is this about implementing her protocol on a larger scale?

Response to the reviewer:
We agree that Drs. Fucile and Lau's Oral and Tactile Kinesthesic intervention data is excellent. However, a 12 to 15 minutes intervention, as described by Drs. Fucile, Gisel and Lau could not be applied in our neonatal unit, due to a lack of time.
Dr Lesson's PIOMI may not be the most optimal rating scale because being published in a single pilot study. Our intervention is likely weakened by not using their scale.
However, a second study published by Lessen, in 2015, demonstrates its high interrater reliability, indicating its accuracy for systematically rating the specific intervention behaviors.
Lastly, Dr Jadcherla's proposes an innovative feeding program for neonates presenting with feeding difficulties. However, our study does not address this particular population. Consequently, nursing interventions are not comparable.

Our study is designed to evaluate a nursing education program on feeding patterns in neonates. It is not designed to implement Dr Lesson's PIOMI specifically.

Overall, my recommendations would be to either separate this into two protocols, one about implementing a feeding program and one about testing a new oromotor stimulation or to ensure that the study is accomplished in several steps, each designed to address a sepaarte outcome.

Response to the reviewer:
Our study is designed to evaluate the effectiveness of a nurse educational oral feeding program on feeding outcomes in neonates. The study design does not address the evaluation of a new oral intervention.
In the event of negative results, we will discuss whether the lack of impact is due to the nursing

education program or the components of the feeding protocol proposed.

Reviewer: 2
Reviewer Name: Chantal Lau
Institution and Country: Baylor College of Medicine, Houston TX USA Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

The title of this manuscript is "Effectiveness of a nurse educational oral feeding program on feeding outcomes in neonates: an interrupted time series design."

It is very well recognized that changing clinical practice is difficult. The authors are commended for the attention given to many areas of this practice that lack stringencies. But without any data, even preliminary results, one cannot evaluate its effectiveness on neonates' feeding outcomes which is the research question. What happens if their hypothesis is not confirmed?

Response to the reviewer:
Whatever are our study results, we will discuss the quality of the intervention implementation, the nurses training modalities, and the length of the study periods (in particular the 22-month implementation period). The collected process indicators will help us to discuss these different items. If our hypothesis is not confirmed, we will discuss whether the lack of impact is due to the nursing education program, or to the choice of the different components that are part of the feeding protocol. The statistical power of the study will also be discussed in relation to the initial assumptions used to calculate the required number of subjects.

It does provide a detailed description of the educational nursing program developed by the authors to improve the practice of infant oral feeding in neonatal intensive care units. So before evaluating this program's 'effectiveness' on infant feeding outcomes, should the first step be the evaluation of the nursing staff's compliance to the program, then the effect of the program on infant feeding outcomes?

Response to the reviewer:
See response to Reviewer 1.
Our study is designed to evaluate the effectiveness of a nurse educational oral feeding program on feeding outcomes in neonates. The study design does not address the evaluation of a new oral intervention.
In the event of negative results, we will discuss whether the lack of impact is due to the nursing education program or the components of the feeding protocol proposed.

At present, there are no results presented of any kind.
Editorial assistance would be beneficial Minor comment
- Line 239: It is unclear whether PMA is used as the gestational age (at birth) or PMA = gestational age + postnatal age in weeks.

Response to the reviewer: Line 239:
PMA is used as the gestational age and postnatal age in weeks.
We specify this definition in the manuscript.

Reviewer: 3
Reviewer Name: Annie Rohan
Institution and Country: Stony Brook University, USA Please state any competing interests or state 'None declared': none declared

Please leave your comments for the authors below

Full Title: Effectiveness of a nurse-educational oral feeding program on feeding outcomes in neonates: an interrupted time series design

This is a very well-developed paper. Your writing is excellent and leads the reader through an organized, detailed journey of your subject. You make a strong case for the interrupted time series design. Some suggestions for improvement follow:

Title:

It wasn't clear to me initially that I was not going to see study results in this manuscript. I think that a stronger title might be, "Study protocol for 'effectiveness of a nurse-educational oral feeding program on feeding outcomes in neonates' using an interrupted time series design."

Response to the reviewer:
The title is "Effectiveness of a nurse educational oral feeding program on feeding outcomes in neonates: protocol for an interrupted time series design."

Abstract:
Clear abstract. Consider changing subtitle "methods and analysis" to "methods and design." In addition, the subtitle "strengths and limitations of this study" is again confusing. Consider rephrasing as "strengths and limitations of the proposed study."

Response to the reviewer:
We have followed the Instructions for authors of the BMJ Open (study protocol)
"Abstract: this should be structured with the following sections. Introduction; Methods and analysis; Ethics and dissemination."
"Strengths and limitations of this study" is also required by the BM Open journal.

Introduction/Review of Literature:

Please rephrase throughout from "this study" to "the proposed study." Alternatively, can use the future tense to make clear that this is not a manuscript with study results, but rather describing the study design (e.g.: change "the study describes…" to "the study will describe…")

Response to the reviewer:
Having clarified the fact that it is a study protocol, we chose not to add "the proposed study" each time.
All the verbs were modified to future tense. We removed all dates from the document (subsection "Time frame"), and specified the dates of the study periods phases, in the letter to the editor, as required by the BMJ Open journal.

Line 78: Background and rationale (check spelling).
Response to the reviewer:
We checked and corrected the spelling as required.

Intervention, Outcome measures:

Well described. Please elaborate on how the questionnaires will be developed (Line 220) in a way that they will be reliable and valid.

Response to the reviewer:
The aim of the questionnaire is to assess nurses' protocol compliance at the end of the 22-month implementation phase. The instruments' question and response categories will be phrased in simple terms. The items will be revised and improved upon, following evaluation by questionnaire design experts. Finally, they will be tested for comprehensibility by health providers from the neonatal unit, who are not participating in the study protocol.

Study sample design:

Line 238: Would rephrase as "Based upon census data, it is anticipate that we will be able to recruit 20-25 new patients into the proposed study each month."

Response to the reviewer:
We rephrased he sentence:
"Based upon census data, it is anticipated that we will be able to recruit 20-25 new patients from 24 to 34 weeks PMA into the proposed study each month. Which means that 138 premature infants may be included during the 6 months pre educational program period; 506 during the 22 months training period, and 138 during the 6 months post educational program. A total of 680 premature infants may be included during the 34 month study period."

Statistical Considerations:

Future tense used in this section – good!

Time frame, Ethics:

Well described.

Discussion:

Well described. I would recommend that you add a few lines about "implementation support strategies" to describe methods that you will use to facilitate the intervention after staff training.

Response to the reviewer:
Implementation support strategies will be introduced to facilitate the intervention. These methods consist of 'expert' feeding rounds that will take place on a regular basis, of one round per day for the physiotherapist and one round per week for the speech therapist and the pediatrician. These expert feeding rounds will have multiple aims: (1) reinforce the key messages of the standardized feeding protocol, (2) monitor nurses' and assistant nurses' compliance to the feeding protocol (3) identify the neonates for whom the feeding protocol is not applied correctly, (4) engage provider focused feeding discussions.

There are several "bookmark not defined" notations in this section. It is not clear what these mean.

Response to the reviewer:
We made the corrections.

Figures:

No suggestions.

VERSION 2 – REVIEW

REVIEWER	Dr. Annie Rohan Stony Brook University, New York USA
REVIEW RETURNED	17-Feb-2016

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript following revision. I am satisfied with how you have addressed my concerns and the concerns of the other reviewers. I believed that this manuscript, if published, will be an important contribution to the literature related to oral feeding in neonates.