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Selecting pH cut-offs for the safe verification of nasogastric feeding tube placement: a decision analytical modelling approach

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Selecting pH cut-offs for the safe verification of nasogastric feeding tube placement: a decision analytical modelling approach

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ABSTRACT

Objectives It is unclear which pH cut-off (e.g. 4, 5 or 5.5) is the safest for verifying the location of nasogastric tubes. Feeding incidents are more likely under a higher cut-off whereas feeding delays and unnecessary x-rays are more likely under a lower cut-off. Our aim is to use a decision analytic modelling approach to systematically assess pH cut-offs from 1 to 9.

Materials and Methods We mapped out the care pathway according to the existing safety guideline. Decision outcomes were scored on a 0-100 scale in terms of safety. Sensitivities and specificities of the pH test at each cut-off were extracted from our previous research. Aggregating outcome scores and probabilities resulted in weighted scores which enabled an analysis of the relative safety of the pH test under various cut-offs.

Results The pH test was the safest under cut-off 5 when 30% or more of the nasogastric tubes were misplaced in the lung or oesophagus. Under cut-off 5, respiratory feeding was excluded; oesophageal feeding was kept to a minimum to balance the need to reduce feeding delays caused by unnecessary chest x-rays. Routine chest x-rays was shown to be less safe than the pH test whilst to feed all was the most risky.

Discussion The safety of the current checking procedure depended on the pH cut-offs, the impact of feeding delays, the accuracy of the pH in the oesophagus, as well as the extent of tube misplacements.

Conclusions The pH test with cut-off 5 was the safest overall. It is important to understand the local clinical environment to inform the choice of pH cut-offs.

Keywords: decision analysis, pH monitoring, nasogastric tube, adult feeding

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Using a decision analytic approach, we analysed the safety of the checking procedure under various pH cut-offs. We considered both the impact and the probabilities of various outcomes. Feeding delays due to chest x-rays were formally incorporated, through a safety score less than ideal (85). The entire range of pH cut-offs was analysed, in addition to the commonly used ones. The safety of routine chest x-rays and feeding all patients without checks were similarly analysed using the same framework.
- The largest uncertainty remains in the oesophageal pH especially in the critical range between cut-offs 4 and 5.5. We did not consider costs in this analysis. However, the same framework can be updated when new evidence becomes available and can be extended to incorporate additional factors of importance, e.g. costs.

INTRODUCTION

Every year at least 1 million nasogastric tubes (NG tubes) are being used in the UK and 1.5 billion worldwide. Inadvertent tube placement outside the stomach has been classified as a 'never event' by NHS England[1]. Nevertheless incidents of tube misplacements remained commonplace. Reported rates of misplacement on insertion and tube migration after correct initial placement varied between 1.3% and 50% in adults [1]. Misplacement into the respiratory tract occurs in 1 to 3% of patients [2] and can have catastrophic consequences, including death. Guidelines on nutrition support for adults issued by the National Institute for Health and Care Excellence (NICE) recommend that the position of NG tubes be verified on initial placement and before each use [3]. The English National Patient Safety Agency (NPSA) recommends testing the pH of tube aspirates [4 5]. Feeding can only start if a pH at or below 5.5 has been established; otherwise chest x-rays, the gold-standard, should be used.

Commissioned by NPSA, we investigated evidence behind various bedside tests including pH, aspirate appearance, capnometry/colorimetric, auscultation ('whoosh' test), and magnetic guidance [6]. The pH test has the best bedside usability and accuracy underpinned by a large body of clinical evidence. In addition to respiratory placements, oesophageal placements emerged as a major source of safety concern during our consultations with clinical experts. We therefore recommended lowering the cut-off to 4 in order to increase the sensitivity of the test towards oesophagus. Subsequent safety recommendations continued to uphold 5.5 as the safety threshold [7]. The main disadvantage of lowering the pH cut-off is an increase in the number of chest x-rays. Chest x-rays are not only more expensive but also cause delays in feeding and medication.

A drawback of our previous research was an exclusive focus on the risks from using various bedside tests. However the recommended checking procedure in fact utilises a combination of two tests: the pH test followed by chest x-rays (the gold-standard) should the pH test fail.

[1] https://www.england.nhs.uk/wp-content/uploads/2015/03/never-evnts-list-15-16.pdf

The question of selecting suitable pH cut-offs must be addressed using the same context. The aim of this research is to employ a decision analytic modelling approach [8] which allows us to systematically analyse the safety of pH test under various cut-offs when embedded in the clinical setting [9].

METHODS

Analysis of the National Reporting and Learning System

To provide an overview of the feeding incidents, we carried out a narrative analysis of incident reports submitted to the National Reporting and Learning System (NRLS). We included all cases with evidence of nasogastric tube misplacement at any site outside the stomach between October 2003 and 28th February 2009. Paediatric cases were excluded. Two authors (OHP, SO) independently reviewed the adverse event reports and classified these according to whether or not current safety guidelines were followed (cut-off 5.5). For reports containing sufficient details, the reasons for misfeeding were extracted and analysed.

Safety of pH under various cut-offs

Study design

We mapped out the clinical pathway of the safety guidelines with regard to naso-gastric tube feeding (figure 1). We assumed that the cut-off could take any number between 1 and 9 (the recommended range), as well as 5.5 (the current recommendation). Decision outcomes were scored with points out of 100, with 100 assigned to the outcomes with the best safety and 0 to the outcomes with the worst safety. The sensitivities and specificities of the pH test under various cut-offs were derived from our previous research. Aggregating the outcome scores by their respective probabilities resulted in a set of weighted scores. These weighted scores enabled a comparison of the relative safety of the pH test under various cut-offs.

Outcomes of feeding decisions

Decision outcomes were identified from the clinical pathway (figure 1). There were five outcomes in total. *Feeding into the stomach* by pH took place if the pH was at or below a certain cut-off *and* when the tube had been placed inside the stomach. *Feeding into the lung* or *oesophagus* took place when a low pH (<=cut-off) was combined with tube misplacements. If the pH exceeded a certain cut-off, then chest x-rays were used to establish tube sites. If the tube was in fact placed inside the stomach, the x-ray was *unnecessary* in addition to *feeding delays*. The remaining patients who received chest x-rays would reveal misplaced tubes – these were correctly identified and excluded, thus *no feeding outside the stomach*.

The safest outcomes (i.e. feeding into the stomach by pH, no feeding outside the stomach) were assigned a score of 100 and the least safe outcomes (i.e. feeding into the lung) was assigned a score of 0. For the remaining outcomes, we applied the Analytic Hierarchy Process [10], converting qualitative judgments into quantitative scores. Two clinicians who were experts in gastroenterological diseases were invited to a face-to-face meeting with one of the authors (MN). During the meeting they were briefed about the project and asked to first rank all the outcomes according to safety. They were then asked to make pair-wise comparisons and articulate the strength of their preferences. For instance, feeding into the oesophagus was considered safer than feeding into the lung and the preference was *very strong*.

Consensus was reached through discussions, producing preference judgments ranging from no difference, weak, moderate, strong to extreme. We entered these into the MACBETH [11]component of the decision analysis software HiView. The software first checked that the judgments were consistent with the safety rankings and once satisfied, converted the judgments into numeric ratings. Further consistency checks were performed on the scores. For instance, suppose an outcome X scored 50. This means that the safety of X was considered half-way in between the safest outcome (stomach feeding) and the least safe outcome (lung feeding). This should mirror the pair-wise comparisons, where the preference for stomach feeding over X was equivalent to the preference for X over lung feeding, i.e. *very strong* in both cases.

Outcome probabilities were driven by two independent factors – the initial insertion (prior distribution of tube sites) and the accuracy of the pH test in differentiating various tube sites (i.e. test sensitivity and specificity). Given the wide range of variations in reported tube misplacements and tube migrations (1.3%-50%), we assumed an average risk of insertion errors whereby 70% of the tubes were inside the stomach with an equal number (15%) of misplacements in the lung and oesophagus (see **Appendix 1** for reasoning). The sensitivities and specificities under individual pH cut-offs were extracted from our previous research. They were based on a clinical database with 1035 unique patient records from multiple clinical trials by a single clinician. This database included 754 stomach placements and 281 lung placements (e.g. [12 13]), with pH measured by both pH meter (our basis for analysing pH accuracy) and pH papers. Lack of evidence for oesophageal placements was remedied by reviewing studies on healthy cohorts under observations for reflux [14-16] Distribution of oesophageal pH was estimated based on the proportion of time when pH decreased below the various cut-offs.

Aggregating outcome scores by their respective probabilities resulted in a set of weighted scores. These reflected the relative safety of the recommended checking procedure under different pH cut-offs. In addition to the pH test, we analysed a scenario where patients are fed without safety checks (feed all) and where all patients are sent for chest x-rays before feeding (*routine x-rays*).

Sensitivity analyses

To capture the spectrum of insertion errors we analysed two additional scenarios with low (10%) and high (50%) probability of tube misplacements (see **Appendix 1** for reasoning). Lung and oesophageal intubations were equally likely, i.e. at 5% and 25% respectively.

Tornado diagrams were used to identify variables of importance. All outcome and probabilistic inputs were varied +/-15% within range (0-1 for probabilities and 0-100 for outcomes). Three-way sensitivity analyses were carried out to examine the direction of impact.

We carried out the analyses in Microsoft Excel and TreeAge Pro (2015). Throughout the analysis, we assumed that chest x-rays were 100% accurate without interpretation or reporting errors.

RESULTS

Analysis of feeding incidents reported to NRLS

A total number of 2368 adverse event reports were identified. After excluding cases that were irrelevant or with incomplete information, we reviewed 104 cases with documented feeding tube misplacement. These included 6 counts of death, 15 counts of severe harm and 23 counts of moderate harm. The remaining 60 cases recorded no harm (43 cases) or low harm (17 cases). Further analysis was carried out on 75 out of 104 narratives containing sufficient details. In eleven reports the wrong tube location was discovered prior to feed or medication (either by pH or by chest x-rays). Of the remaining 64 cases, we analysed reasons for misfeeding. The most frequently cited reason was misinterpretation of chest x-rays (25). The pH test (with 5.5 as the cut-off) itself was responsible for 10 feeding incidents. There were also 23 cases where safety guidelines were not followed, including 12 cases where feeding was carried out without safety checks (**Appendix 2** for further details).

Safety of the pH test under various cut-offs

Figure 2 displays the distributions of the feeding outcomes under various pH cut-offs. Within each bar, different colours indicate contributions made by individual outcomes, with an added total of 100%. Given our assumption of 30% tube misplacements, stomach feeding (blue bars) and feeding delays (purple bars) must add up to 70% whereas misfeeding (red and green bars) and no feeding outside the stomach (turquoise bars) must add up to 30%.

At cut-off 5.5 or lower, respiratory feeding was excluded (red bars) since at this range the pH test had perfect specificity in the lung. As the cut-off increased, however, stomach feeding increased alongside misfeeding into the oesophagus and lung (Appendix 3).

This trade-off between feeding incidents and feeding delays (unnecessary x-rays) was illustrated by figure 3. As we lower the pH cut-offs, the number of unnecessary x-rays (i.e. feeding delays, x-axis) increased much faster than the number of feeding incidents (y-axis) decreased. In fact, in the case of cut-off 5 versus 6, the difference was four times, i.e. 9% (=22%-13%) difference in unnecessary x-rays versus 2.1% (=2.9%-0.8%) difference in feeding incidents (primarily in the oesophagus).

Nevertheless, it would be misleading to select pH cut-offs based on the number of feeding delays or feeding incidents alone. This is because outcomes have different impact on patient safety. Feeding into the oesophagus, for instance, had a safety score of 45 compared to delayed feeding (unnecessary x-rays) which had a score of 85. In other words, if we use lung feeding (score 0) as the benchmark, delayed feeding from chest x-rays was nearly twice as safe as oesophageal feeding. Delayed feeding was however less safe than immediate feeding as enabled by the pH (score 100).

We aggregated safety scores by probabilities to assess the relative safety under different pH cut-offs. **Appendix 3** contains the further details. An ideal test has a score of 100, by identifying every tube in the stomach for feeding (part score 70) whilst excluding every tube outside the stomach (part contribution 30). To feed all is the least safe strategy with a weighted score of 76.75, from feeding correctly (though randomly) in 70% of patients with stomach placements (part score 70) but misfeeding in 15% oesophageal placements (part score 6.75) and in 15% lung placements (part score 0). By contrast, routine use of chest x-rays had a weighed score of 89.5 due to causing feeding delays in 70% of the patients (part score 59.5), and correctly identifying all 30% of misplaced tubes (part score 30).

Figure 4 displays the weighted scores at each pH cut-off, along with part-score contributions made from individual outcomes. At lower cut-offs the scores were primarily made up of delayed feeding and no feeding outside the stomach, whereas at higher cut-offs stomach feeding made increasingly significant contribution to the overall safety. No points were attributed to lung feeding with a safety score of 0. Across all cut-offs, cut-off 5 and cut-off 6 had the highest safety score (96.2), and therefore the 'safest' overall.

Sensitivity analysis

The largest impact on the overall safety was attributable to safety of delayed feeding (scores 50-95) and to the pH specificity in the oesophagus (range 0.6-0.99). Decreasing the score assigned to delayed feeding by 5 points (from 85 to 80) would make cut-off 5 the safest option. A 10% increase at 5.5 (from 0.81 to 0.89) whilst keeping the specificities at 5 constant (0.948) would result in cut-off 5.5 becoming the safest overall. Varying the initial tube misplacements also had a large impact, influencing safety across *all* cut-offs. However cut-off 5 remained the 'safest' under 50% tube misplacements.

DISCUSSION

Summary of main findings

The recommended safety procedure prior to feeding by nasogastric tube is comprised of two tests, the pH test and chest x-rays when the pH test fails (>5.5). Our analysis showed that with a score of 96.2 out of 100, the checking procedure was the safest under cut-off 5 given 30% or more of tube misplacements. Respiratory feeding is excluded; misfeeding in the oesophagus was kept to a minimum to balance the need to reduce feeding delays from unnecessary chest x-rays. Routine chest x-rays was less safe than the pH test (score 89.5) and to feed all was the most risky (score 76.76).

Strengths and limitations

Using a decision analytic approach, we analysed the safety of the checking procedure under various pH cut-offs. We considered both the impact and the probabilities of various outcomes. Feeding delays caused by chest x-rays were formally incorporated, by a safety score lower than the ideal 100. The entire range of pH cut-offs was analysed, in addition to the commonly used ones. The safety of routine chest x-rays and feeding all patients without checks was similarly analysed.

The largest uncertainty remains in the oesophageal pH especially in the critical range between cut-offs 4 and 5.5. We did not consider costs in this analysis. However, the same framework can be applied when new evidence becomes available as well as can be extended to incorporate additional factors of importance, e.g. costs.

Comparison with existing literature

As a universal first-line test for ensuring feeding safety, numerous studies investigated the pH test for its accuracy in identifying stomach and lung placements, e.g. [12 13]. However all the studies focused on the accuracy of the pH test per se. By contrast, the checking procedure in fact contains two tests: the pH test followed by chest x-rays when necessary. Thus the safety of the pH test must be evaluated in the context of its use, by considering its downstream implications for clinical decision making. We found that the key issue was actually a balance between reducing feeding incidents and reducing unnecessary chest x-rays. The decision analytic approach provides the normative framework for an analysis with conflicting objectives.

Implications for practice

Although the current recommended pH cut-off is 5.5, the British Society of Gastroenterology guidance for enteral feeding suggests tube aspirate pH measurement needs to be less than 5.0 prior to every use, but advises caution when the patient is on acid suppression [17]. Routine use of x-rays was not advised. Reducing the pH cut-off from 5.5 to 5 would increase the number of chest x-rays being requested. However misinterpretations of chest x-ray led to feeding errors. There is a clear need to develop cost-effective bed-side tests which not only have high accuracy but also the ability to withstand human errors in its applications.

CONCLUSIONS

The pH test with an upper cut-off at 5 was the safest test for the verification of nasogastric tube locations. The choice of pH cut-off depended on the prevalence of tube misplacements, the impact of feeding delays and the specificity of the pH test for oesophageal placements. Routine data collection at the local level should be implemented to optimise safety recommendations.

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Figure 1. Clinical pathway of using pH test to ensure safety in feeding by nasogastric tubes.

Figure 2. Distribution of feeding outcomes under pH cut-offs 1-9.

Figure 3. Trade-off between the number of unnecessary x-rays and feeding incidents.

Figure 4. Safety of the checking procedure under pH cut-offs 1-9, showing separate contributions made by each decision outcome to the overall weighted safety scores.

DECLARATION

Financial support

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Ethics

Ethics approval from London – Chelsea REC, REC Reference: 16/LO/0998.

Availability of data and materials

The dataset(s) supporting the conclusions of this article is (are) included within the article and its appendicitis.

Author contributions

GBH and LDP designed the study; MN, OP and SO conducted research. , OP and SO analysed the NRLS database. MN, OP and SO interpreted the data. MN carried out the decision analysis. MN, JRH and PB drafted the manuscripts. Final manuscript approved by all authors. GBH had final responsibility for the final content.

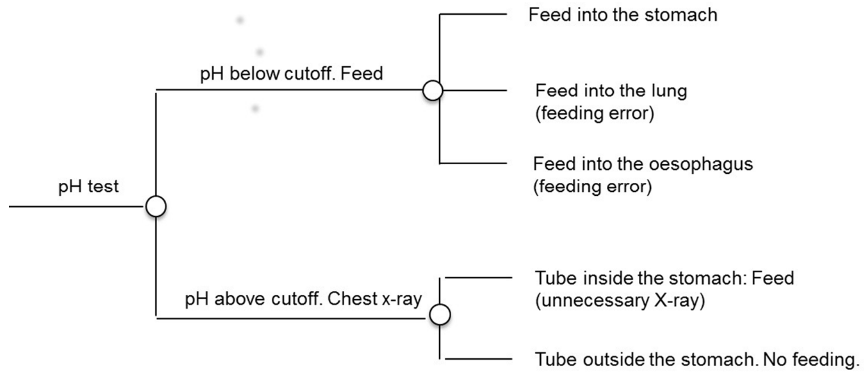

Figure 1. Clinical pathway of using pH test to ensure safety in feeding by nasogastric tubes.

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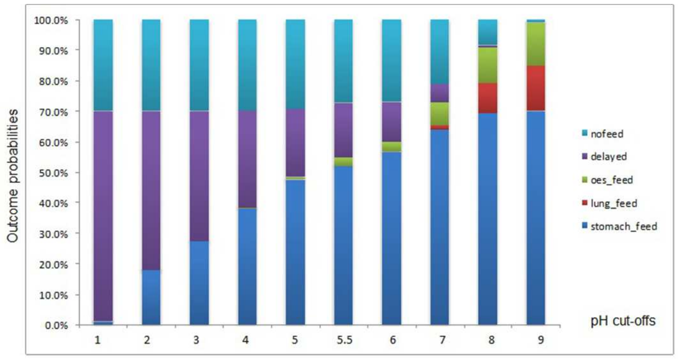

Figure 2. Distribution of feeding outcomes under pH cut-offs 1-9.

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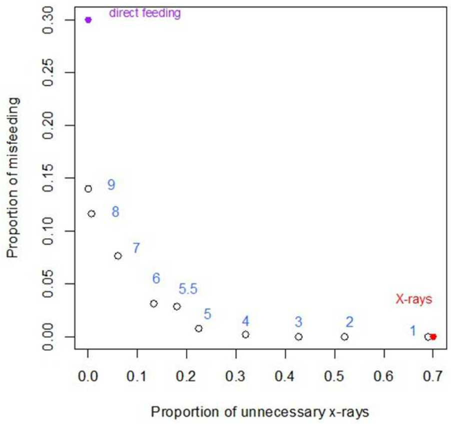

Figure 3. Trade-off between the number of unnecessary x-rays and feeding incidents.

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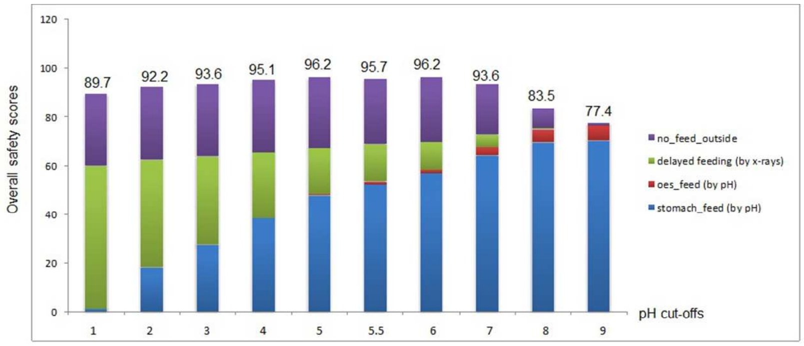


Figure 4. Safety of the checking procedure under pH cut-offs 1-9, showing separate contributions made by each decision outcome to the overall weighted safety scores.

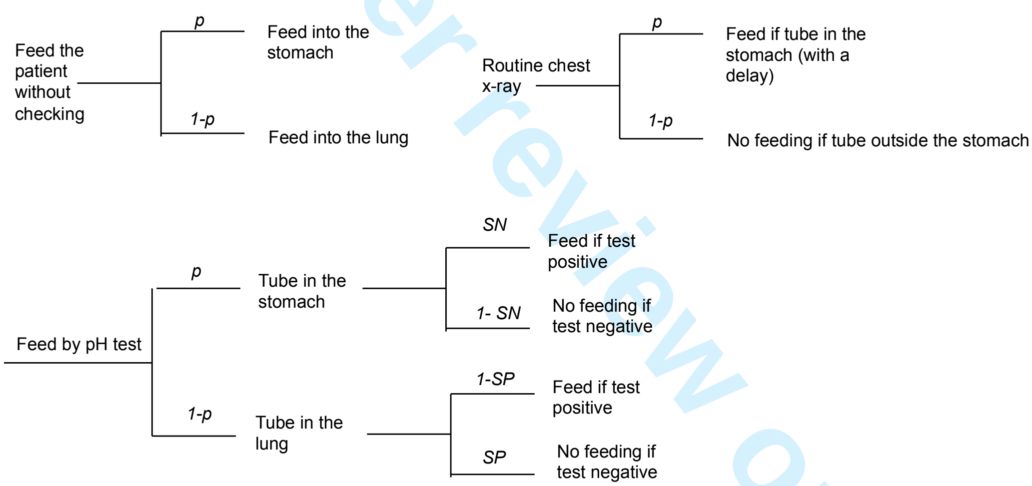
97x60mm (300 x 300 DPI)

Appendix 1. Setting up boundary values in the analysis

Consider three feeding strategies, namely to feed all patients without checking (feed all), send all patients for chest x-rays (routine x-rays) and to test the pH and only feed given a low pH but no feeding when the pH is above the threshold. Note that the last strategy is different from the recommended pH test whereby a high pH would trigger the use of chest x-rays.

There is general agreement that routine x-ray is safer than testing pH which is again safer than to feed all. From this we can make certain deductions in terms of the perceived safety of outcomes and probability distributions.

To illustrate, consider a simplified scenario where the tube is either inserted into the stomach or lung. The three strategies can be represented in decision trees:



We assume, as in the main text, that stomach feeding has the maximum safety score of 100 whereas lung feeding has the minimum safety score of 0. No feeding when the tube is outside the stomach (i.e. lung) is also safe (score 100). However, feeding following chest x-rays incurs a delay and therefore is less than ideal. So is no feeding when the tube is placed inside the stomach. Let

- *p* to denote the probability of stomach placement and *1-p* the probability of lung placement;
- *x* to denote safety of feeding into the stomach with a delay, x<100;
- *y* to denote the safety scores assigned to no feeding given stomach placement and y<100;

- *SN* be the sensitivity of the pH test and
- *SP* be the (lung) specificity of the pH test.

By aggregating safety scores and probabilities (see Appendix 3) we assess the safety of each of the three strategies:

- Safety(Feed_all)=100*prob(stomach)+0*prob(lung)
- Safety(Xray) =x*prob(stomach)+100*prob(lung)
- Safety(pH) =100*prob(stomach)*SN+y* prob(stomach)*(1-SN)+ 0*prob(lung)*(1-SP)+ 100*prob(lung)*SP

Suppose we are primarily interested in pH cutoffs at 5.5 or lower. At this range, the test has a lung specificity at 1. Entering this value into the above equations, and after simplifications, we obtain an assessment of the relative safety of the three strategies in algebra forms:

- Safety(Feed_all)=100*p -Eq.1
- Safety(Xray)=100-(100-x)*p -Eq.2
- Safety(pH)= 100*p*SN+p(1-SN)*y+(1-p)*100 -Eq.3

Since routine x-ray is safer than the pH test which is safer than to feed all, the expected utility theory predicts that the safety scores will exhibit the relationship as in Eq1<Eq.3<Eq.2.

Firstly, given Eq.1<Eq.2, we have 100*p<100-(100-x)*p, or

x>100(2-1/p) -Eq.4

Since *x* represents the safety of feeding with a delay (by chest x-rays), *x* must be less than 100. This means that the probability of stomach placement ***p* > 0.5**. This is why we set the risky scenario in the main text to have a 50% of tube misplacement rate.

Secondly, from Eq.3<Eq.2, we have 100*p*SN+p(1-SN)*y+(1-p)*100<100-(100-x)*p, or

x>100*SN+y*(1-SN) -Eq.5.1

or

y<(x-100*SN)/(1-SN) -Eq.5.2

Since y must be greater than 0, from Eq.5.2 we have ***x>100*SN***. That is, the safety of delayed feeding must be greater than the product of sensitivity of the pH test and 100 (the scaling unit).

To see what this means, consider the sensitivity of the pH test when the cut-off is 5.5. Our previous research (Hanna et al) established that the sensitivity of the pH is around 075 (0.743), thus the safety of feeding with a delay (*x*) must exceed 75 on the 0-100 scale for chest x-ray to be considered safer than the pH test. Based on Eq.5.2, suppose that delayed feeding has a safety score of 90, we can workout that no feeding when the tube is in the stomach will have a maximum score of 60.

In summary, from the simple preference ordering between the three decision strategies, we can set the boundary values as:

For pH cut-offs >=5.5	Range (minimum, maximum)	Corresponding value in paper
Stomach placements (probability *p*)	(0.5-1)	70%
Feeding delayed by x-ray (safety score x)	(100*SN, 100)	85
No feeding given stomach placements (safety score y)	(0, (x-100*SN)/(1-SN))	not applicable

APPENDIX 2 NRLS database analysis results

Methodology

Database search

Inclusion criteria for the search were all cases with evidence of nasogastric tube misplacement at any site outside the stomach entered into the National Reporting and Learning System (NRLS) database from the date of inception in October 2003 to 28th February 2009. Exclusion criteria were all paediatric cases as the safety guideline was applicable only to adults.

Case selection and Analysis

The narratives from the initial NRLS dataset were further examined to identify cases of nasogastric tube misplacement in any site outside the stomach. Two independent reviewers classified the adverse event reports according to whether or not current NPSA safety alert guidelines were followed prior to enteral feed being commenced. This was only possible for those reports that included sufficient information in the narratives. For reports that described tube feed or medication being administered via incorrectly placed nasogastric tubes, the reason for this was identified and classified.

The classification of the failure to correctly identify a misplaced tube originated from process mapping based on the existing and proposed safety guidelines.

Results

The number of incidents found from the NRLS database using the predefined search terms was a total of 2368 adverse event reports. Further examination of these reports yielded a total of 104 cases with documented feeding tube misplacement. The outcomes of tube misplacement in terms of patient harm are summarised in Table A1. In 29 reports there was too little information to support further analysis of the checking procedure employed to identify tube misplacement. Of the 75 narratives which allowed for further analysis, 11 reports described the wrong location of NG tube being discovered prior to feed or medication administration. These 11 cases included 5 incidents of tube misplacement identified by a tube aspirate pH > 5.5 followed by chest radiography and 6 incidents identified by chest radiography alone. For the remaining 64 cases in which the correct test was not used to locate the nasogastric tube or the results were incorrect, analysis of the reasons for failing to identify tube placement prior to tube use was performed and the results detailed in Table A2.

Table A1. Patient harm resulting from feeding tube misplacement – NRLS database

Effect on patient	No. of cases
Death	6
Severe harm	15
Moderate harm	23
Low harm	17
No harm	43

Table A2. Mode of failure to identify tube misplacement

Type of failure	No. of cases
pH test correctly carried out but invalid (pH <5.5 but tube not in stomach)	10
pH test wrongly interpreted (thought OK if pH = 6)	1
Aspiration used as checking procedure; unclear whether pH tested	5
Bubble or Whoosh test used as only checking procedure	2
CXR incorrectly interpreted	25
Correct test indicated tube in stomach but tube moved prior to starting feed	4
No action taken to assess tube placement	12
CXR done but not checked prior to feeding	2
Other (misinterpretation of CXR report) (CT scan misreported)(direct vision and no further checks)	3
Total	**64**

Chest radiographs were misinterpreted by the junior House Officer in 4 cases and the Senior House Officer in 6 cases, while it was not clear what level of doctor misread the radiograph in 14 cases. The chest radiograph from the wrong date was reviewed in 2 cases of tube misplacement.

Appendix 3. Probability distributions, outcome scores and weighted scores

We assessed safety through aggregating outcome scores by their respective probabilities. Table A lists the outcome scores and probability calculation; Table B shows sensitivity and specificity of the pH test under cut-offs 1-9. The weighted scores are thus the sum product of Column 2 and Column 3 of Table A.

Table C and Table D show respectively the probability distributions and outcome score contributions under cut-offs 1-9.

Table A. Probability and safety of decision outcomes of the pH test

Outcome	Probability	Score
Feeding into the stomach by pH	Prior probability of stomach x Sensitivity of pH	100
Feeding into the lung by pH (feeding error)	Prior probability of lung x (1- Specificity in lung)	0
Feeding into the oesophagus by pH (feeding error)	Prior probability of oesophageal x (1- Specificity in oesophagus)	45
Delayed feeding into the stomach by x-rays (unnecessary x-rays)	Prior probability of stomach x (1-Sensitivity of pH)	85
No feeding outside the stomach by pH or by x-rays	Prior probability of lung/oesophagus x Specificity in lung/oesophagus	100

Table B. Accuracy of pH test under cut-offs 1-9

pH cut-offs	Sensitivity (stomach)	Specificity (Lung)	Specificity (oesophagus)
1	0.015	1	1
2	0.257	1	1
3	0.39	1	1
4	0.544	1	0.985
5	0.68	1	0.948
5.5	0.743	1	0.81
6	0.81	0.996	0.792
7	0.914	0.91	0.492
8	0.991	0.337	0.225
9	1	0.004	0.068

Table C. Probability distributions across pH cut-offs (data for Fig 2 and 3)

Cut-offs	stomach_feed	lung_feed	oes_feed	delayed	Nofeed
1	1.1%	0.0%	0.0%	69.0%	30.0%
2	18.0%	0.0%	0.0%	52.0%	30.0%
3	27.3%	0.0%	0.0%	42.7%	30.0%
4	38.1%	0.0%	0.2%	31.9%	29.8%
5	47.6%	0.0%	0.8%	22.4%	29.2%
5.5	52.0%	0.0%	2.9%	18.0%	27.2%
6	56.7%	0.1%	3.1%	13.3%	26.8%
7	64.0%	1.4%	7.6%	6.0%	21.0%
8	69.4%	9.9%	11.6%	0.6%	8.4%
9	70.0%	14.9%	14.0%	0.0%	1.1%

Table D. Weighted scores with part-contributions from individual outcomes (data for Figure 4)

Cut-offs	stomach_feed	lung_feed	oes_feed	delayed	nofeed	Total
1	1.1	0.0	0.0	58.6	30.0	89.7
2	18.0	0.0	0.0	44.2	30.0	92.2
3	27.3	0.0	0.0	36.3	30.0	93.6
4	38.1	0.0	0.1	27.1	29.8	95.1
5	47.6	0.0	0.4	19.0	29.2	96.2
5.5	52.0	0.0	1.3	15.3	27.2	95.7
6	56.7	0.0	1.4	11.3	26.8	96.2
7	64.0	0.0	3.4	5.1	21.0	93.6
8	69.4	0.0	5.2	0.5	8.4	83.6
9	70.0	0.0	6.3	0.0	1.1	77.4

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Selecting pH cut-offs for the safe verification of nasogastric feeding tube placement: a decision analytical modelling approach

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ABSTRACT

Objectives The existing British NPSA safety guideline recommends testing the pH of nasogastric tube aspirates. Feeding is considered safe if a pH of 5.5 or lower has been observed; otherwise chest x-rays are recommended. Our previous research found that at 5.5, the pH test lacks sensitivity towards oesophageal placements, a major risk identified by feeding experts. The aim of this research is to use a decision analytic modelling approach to systematically assess the safety of the pH test under cut-offs 1-9.

Materials and Methods We mapped out the care pathway according to the existing safety guideline. Decision outcomes were scored on a 0-100 scale in terms of safety. Sensitivities and specificities of the pH test at each cut-off were extracted from our previous research. Aggregating outcome scores and probabilities resulted in weighted scores which enabled an analysis of the relative safety of the checking procedure under various pH cut-offs.

Results The pH test was the safest under cut-off 5 when there was 30% or more of NG-tube misplacements. Under cut-off 5, respiratory feeding was excluded; oesophageal feeding was kept to a minimum to balance the need of chest x-rays for patients with a pH higher than 5. Routine chest x-rays was less safe than the pH test whilst to feed all without safety checks was the most risky.

Discussion The safety of the current checking procedure is sensitive to the choice of pH cut-offs, the impact of feeding delays, the accuracy of the pH in the oesophagus, as well as the extent of tube misplacements.

Conclusions The pH test with cut-off 5 was the safest overall. It is important to understand the local clinical environment so that appropriate choice of pH cut-offs can be made to maximise safety and to minimise use of chest x-rays.

Keywords: diagnostics, decision analysis, pH monitoring, nasogastric tube, adult feeding

STRENGTHS AND LIMITATIONS OF THIS STUDY

- A decision analytic approach was used to map out clinical pathways and to achieve synthesis of evidence from clinical studies, published literature and expert judgments.
- The entire range of pH cut-offs was analysed in addition to the most frequently used ones between 4 and 6.
- The decision analytic framework supported analysis of two related but non-pH test strategies: routine chest x-rays and feeding all patients without safety checks.
- We did not consider financial costs in this analysis. The same framework can be expanded to incorporate additional dimension of importance.
- We focused only on the group of patients with successful aspirations. Unsuccessful aspiration does not change the relative safety of various pH cut-offs but is one reason for using chest x-rays.

INTRODUCTION

Every year at least 1 million nasogastric tubes (NG tubes) are being used in the UK [1] and 1.5 billion worldwide[1]. Inadvertent tube placement outside the stomach has been classified as a 'never event' by NHS England[2]. Nevertheless incidents of tube misplacements remained commonplace. Reported rates of misplacement on insertion and tube migration after correct initial placement varied between 1.3% and 50% in adults [2]. Misplacement into the respiratory tract occurs in 1 to 3% of patients [3] and can have catastrophic consequences, including death. Guidelines on nutrition support for adults issued by the National Institute for Health and Care Excellence (NICE) recommend that the position of NG tubes be verified on initial placement and before each use [4]. The British National Patient Safety Agency (NPSA) recommends testing the pH of tube aspirates [5-7]. Feeding can only start if a pH at or below 5.5 has been established; otherwise chest x-rays, the gold-standard, should be used.

Commissioned by NPSA, we investigated evidence behind various bedside tests including pH, aspirate appearance, capnometry/colorimetric, auscultation ('whoosh' test), and magnetic guidance [8]. The pH test has the best bedside usability and accuracy underpinned by a large body of clinical evidence. In addition to respiratory placements, oesophageal placements emerged as a major safety concern during our consultations with feeding experts, e.g. [9]. To address this and to remedy the lack of published studies in oesophageal pH from NG-tubes, we carried out a literature review of pH distributions in patients with reflux. We found that reducing the cut-off from 5.5 to 4 would increase the sensitivity of the pH test to tubes placed in the oesophagus. Subsequent safety recommendations continued to uphold 5.5 as the safety threshold [10]. The main disadvantage of lowering the pH cut-off is that more patients with tubes placed inside the stomach will be sent for chest x-rays which is the second-line test. This is not ideal since chest x-rays are not only more expensive but can

[1] Worldwide usage of 1.5 billion was estimated from NHS usage by assuming demand proportional to population size.
[2] https://www.england.nhs.uk/wp-content/uploads/2015/03/never-evnts-list-15-16.pdf

delay feeding for up to 47 hours[3]. In addition chest x-rays, despite being considered the gold-standard of tube site verifications, are subject to misinterpretation errors [7 11].

A drawback of our previous research was an exclusive focus on the risks from various bedside tests. However the recommended checking procedure in fact utilises a combination of two tests: the pH test followed by chest x-rays should the pH test fail. The question of selecting suitable pH cut-offs must be addressed using the same context. We are primarily interested in understanding the trade-offs in patient safety between maximising feeding in time and minimising feeding incidents. The aim of this research is to employ a decision analytic modelling approach [12] which allows us to systematically analyse the safety of pH test under various cut-offs when embedded in the clinical setting [13] to better inform policy makers and clinicians performing safety checks.

ETHICS

This work is partially supported by an Innovate UK grant for developing a new pH paper test for nasogastric tube placements. We have gained ethics approvals from the Research Ethics Committee which supported a clinical study as well as interview studies related to the use of pH tests in the clinical setting.

[3] Mean delay 17 hours, range 1.5 hours- 47 hours. Unpublished audit data carried out in 2016 at the St Mary's hospital, London, UK from 23 patients.

METHODS

Analysis of the National Reporting and Learning System

To provide an overview of the feeding incidents, we carried out a narrative analysis of incident reports submitted to the National Reporting and Learning System (NRLS). We included all cases with evidence of nasogastric tube misplacement at any site outside the stomach between October 2003 and 28th February 2009. Paediatric cases were excluded. Two authors (OHP, SO) independently reviewed the adverse event reports and classified these according to whether or not current safety guidelines were followed (cut-off 5.5). For reports containing sufficient details to enable an analysis of possible reasons of tube misplacements, we extracted the reported reasons for misfeeding and carried out thematic analyses to generate categories. Disagreements between the two reviewers were solved by discussion till consensus was reached.

Safety of pH under various cut-offs

Study design

We mapped out the clinical pathway of the safety guidelines with regard to naso-gastric tube feeding (figure 1). Since our target was the relative safety between different pH cut-offs, we focused on the subgroup of patients for whom aspirations were successful but analysed implications of unsuccessful aspirations on patient safety in the sensitivity analysis. We assumed that the pH cut-off values could take any number between 1 and 9 (the recommended range), as well as 5.5 (the current recommendation). Decision outcomes were scored with points out of 100, with 100 assigned to the outcomes with the best safety and 0 to the outcomes with the worst safety. The sensitivities and specificities of the pH test under various cut-offs were derived from our previous research. Aggregating the outcome scores by their respective probabilities resulted in a set of weighted scores. These weighted scores enabled a comparison of the relative safety of the pH test under various cut-offs.

Outcomes of feeding decisions

Decision outcomes were identified from the clinical pathway (figure 1) assuming that all patients have successful aspirations. There were five outcomes in total. *Feeding into the stomach* by pH took place if the pH was at or below a certain cut-off *and* when the tube had been placed inside the stomach. *Feeding into the lung* or *oesophagus* took place when a low pH (<=cut-off) was combined with tube misplacements. If the pH exceeded a certain cut-off, then chest x-rays were used to establish tube sites. For those patients with tubes placed inside the stomach, the x-ray was deemed unnecessary since gastric placement could have been determined solely by pH. We distinguish between feeding by pH and feeding by chest x-rays since the latter carries radiation risks and could cause *feeding delays* for up to 47 hours (footnote 3). The remaining patients who received chest x-rays would reveal misplaced tubes – these were correctly identified and excluded, thus *no feeding outside the stomach*.

The safest outcomes (i.e. feeding into the stomach by pH, no feeding outside the stomach) were assigned a score of 100 and the least safe outcomes (i.e. feeding into the lung) was assigned a score of 0. For the remaining outcomes, we applied the Analytic Hierarchy Process [14], converting qualitative judgments into quantitative scores. Two clinicians who were experts in gastroenterological diseases were invited to a face-to-face meeting with one of the authors (MN). During the meeting they were briefed about the project and asked to first rank all the outcomes according to safety. They were then asked to make pair-wise comparisons and articulate the strength of their preferences. For instance, feeding into the oesophagus was considered safer than feeding into the lung and the preference was *very strong*.

Consensus was reached through discussions, producing preference judgments ranging from no difference, weak, moderate, strong to extreme. We entered these into the MACBETH [15] component of the decision analysis software HiView. The software first checked that the judgments were consistent with the safety rankings and once satisfied, converted the judgments into numeric ratings (**Table 1**, last column). Further consistency checks were performed on the scores. For instance, oesophageal feeding received a safety score of 45, which means that its safety was considered nearly half-way in between the safest outcome (stomach feeding) and the least safe outcome (lung feeding). This should mirror the pair-wise comparisons, where the preference for stomach feeding over oesophageal feeding (100 vs 45) was slightly stronger than the preference for oesophageal feeding over lung feeding (45 vs 0).

Table 1. Probability and safety of decision outcomes of the pH test

Outcome	Probability	Score
Feeding into the stomach by pH	Prior probability of stomach x Sensitivity of pH	100
Feeding into the lung by pH (feeding error)	Prior probability of lung x (1- Specificity in lung)	0
Feeding into the oesophagus by pH (feeding error)	Prior probability of oesophageal x (1- Specificity in oesophagus)	45
Delayed feeding into the stomach by x-rays (unnecessary x-rays)	Prior probability of stomach x (1-Sensitivity of pH)	85
No feeding outside the stomach by pH or by x-rays	Prior probability of lung/oesophagus x Specificity in lung/oesophagus	100

Outcome probabilities were driven by two independent factors – the initial insertion (prior distribution of tube sites) and the accuracy of the pH test in differentiating various tube sites (i.e. test sensitivity and specificity, **Table 1** middle column). Given the wide range of variations in reported tube misplacements and tube migrations (1.3%-50%), we assumed an average risk of insertion errors whereby 70% of the tubes were inside the stomach with an equal number (15%) of misplacements in the lung and oesophagus (see **Appendix 1** for reasoning). The sensitivities and specificities under individual pH cut-offs were extracted from our previous research. They were based on a clinical database with 1035 unique patient records from multiple clinical trials by a single clinician. This database included 754 stomach placements and 281 lung placements (e.g. [16 17]), with pH measured by both pH meter (Beckman pH1 10 portable pH meters) and pH paper throughout (1-11 Vivid pH paper). Since pH meter reading and paper reading do not always agree, we used pH meter reading to derive the accuracy data. Lack of evidence for oesophageal placements was remedied by reviewing studies on healthy cohorts under observations for reflux [18-20] Distribution of oesophageal pH was estimated based on the proportion of time when pH decreased below the various cut-offs. Table 2 summarises the accuracy of pH tests.

Table 2. Accuracy of pH test under cut-offs 1-9

pH cut-offs	Sensitivity (stomach)	Specificity (Lung)	Specificity (oesophagus)
1	0.015	1	1
2	0.257	1	1
3	0.39	1	1
4	0.544	1	0.985
5	0.68	1	0.948
5.5	0.743	1	0.81
6	0.81	0.996	0.792
7	0.914	0.91	0.492
8	0.991	0.337	0.225
9	1	0.004	0.068

Aggregating outcome scores by their respective probabilities resulted in a set of weighted scores. These reflected the relative safety of the recommended checking procedure under different pH cut-offs. In addition to the pH test, we analysed a scenario where patients are fed without safety checks (feed all) and where all patients are sent for chest x-rays before feeding (*routine x-rays*).

Sensitivity analyses

To capture the spectrum of insertion errors we analysed two additional scenarios with low (10%) and high (50%) probability of tube misplacements (see **Appendix 1** for reasoning). Lung and oesophageal intubations were equally likely, at 5% and 25% respectively. Tornado diagrams were used to identify variables of importance. All outcome and probabilistic inputs were varied +/-15% within range (0-1 for probabilities and 0-100 for outcomes). Three-way sensitivity analyses were carried out to examine the direction of impact.

We considered the impact of successful aspirations whereby aspirations were successful 90% of the time [21]. For the remaining 10%, chest x-rays are used instead. We considered the impact of chest x-ray misinterpretations by assuming that chest x-ray of tubes located outside the stomach was interpreted as inside 10% of the time which resulted in feeding into the wrong places (equally likely in lung and oesophagus). We then analysed the joint impact of unsuccessful aspirations combined with radiography misinterpretations.

We carried out the analyses in Microsoft Excel and TreeAge Pro (2015). Since chest x-rays were used as the reference standard across pH accuracy studies, chest x-rays were assumed to be 100% accurate in the main body of analysis.

RESULTS

Analysis of feeding incidents reported to NRLS

A total number of 2368 adverse event reports were identified. After excluding cases that were irrelevant or with incomplete information, we reviewed 104 cases with documented feeding tube misplacement. These included 6 counts of death, 15 counts of severe harm and 23 counts of moderate harm. The remaining 60 cases recorded no harm (43 cases) or low harm (17 cases). Further analysis was carried out on 75 out of 104 narratives containing sufficient details. In eleven reports the wrong tube location was discovered prior to feed or medication (either by pH or by chest x-rays). Of the remaining 64 cases, we analysed reasons for misfeeding. The most frequently cited reason was misinterpretation of chest x-rays (25). The pH test (with 5.5 as the cut-off) itself was responsible for 10 feeding incidents. There were also 23 cases where safety guidelines were not followed, including 12 cases where feeding was carried out without safety checks (**Table 3**, **Appendix 2** for further details).

Table 3. Mode of failure to identify tube misplacement

Type of failure	No. of cases
pH test correctly carried out but invalid (pH <5.5 but tube not in stomach)	10
pH test wrongly interpreted (thought OK if pH = 6)	1
Aspiration used as checking procedure; unclear whether pH tested	5
Bubble or Whoosh test used as only checking procedure	2
CXR incorrectly interpreted	25
Correct test indicated tube in stomach but tube moved prior to starting feed	4
No action taken to assess tube placement	12
CXR done but not checked prior to feeding	2
Other (misinterpretation of CXR report) (CT scan misreported)(direct vision and no further checks)	3
Total	**64**

Safety of the pH test under various cut-offs

The higher the cut-off, the more sensitive and the less specific the pH test becomes (**Table 2**). This is evident in **Figure 2** which shows the trade-off between feeding incidents (more numerous under higher cut-offs) and feeding delays (more numerous under lower cut-offs). In addition, as the cut-off reduced, the increase in the number of unnecessary x-rays (feeding delays, x-axis) was faster than the reduction in feeding incidents (y-axis). Consider cut-off 5 versus 6 for instance. The magnitude of difference was four times, i.e. 9% (=22%-13%) increase in unnecessary x-rays versus 2.1% (=2.9%-0.8%) decrease in feeding incidents (primarily in the oesophagus).

Nevertheless, it would be misleading to select pH cut-offs based on the number of feeding delays or feeding incidents alone since different outcomes have different impact on patient safety. Instead, we used the aggregated safety scores to assess the relative safety under different cut-offs. These are shown in **Figure 3**, along with part-score contributions made from individual outcomes. At lower cut-offs the scores were primarily made up of delayed feeding and no feeding outside the stomach, whereas at higher cut-offs stomach feeding made increasingly significant contribution to the overall safety. No points were attributed to lung feeding with a safety score of 0.

Cut-off 5 and cut-off 6 had the highest safety score (96.2), and therefore the 'safest' overall. This is in a context of an ideal (and hypothetical) test which has a score of 100, by identifying every tube in the stomach for feeding whilst excluding every tube outside the stomach. By contrast, to feed all patients without discrimination is the least safe strategy with a weighted score of 76.75, from feeding correctly (though randomly) in 70% of patients with stomach placements (part score 70) but misfeeding in 15% oesophageal placements (part score 6.75) and in 15% lung placements (part score 0). Routine use of chest x-rays had a weighed score of 89.5 from correctly identifying all 30% of misplaced tubes (part score 30) and from feeding correctly in 70% of the patients though with a delay (part score 59.5, mean delay 17 hours, range 1.5 hours- 47 hours, footnote 3; see **Appendix 3** for further details).

Sensitivity analysis

The largest impact on the overall safety was attributable to safety of delayed feeding (scores 50-95) and to the pH specificity in the oesophagus (range 0.6-0.99). Decreasing the score assigned to delayed feeding by 5 points (from 85 to 80) would make cut-off 5 the safest option. A 10% increase at 5.5 (from 0.81 to 0.89) whilst keeping the specificities at 5 constant (0.948) would result in cut-off 5.5 becoming the safest overall. Varying the initial tube misplacements also had a large impact, influencing safety across *all* cut-offs. However cut-off 5 remained the 'safest' under 50% tube misplacements. Similarly, unsuccessful aspirations and/or chest x-ray misinterpretations reduced the safety across all cut-offs and more so for lower cut-offs than for higher cut-offs since chest x-rays were used more often at lower cut-offs. Despite this, pH test under cut-off 5 remained the safest within range 1-5.5.

DISCUSSION

Summary of main findings

The recommended safety procedure prior to feeding by nasogastric tube is comprised of two tests, the pH test and chest x-rays when the pH test fails (>5.5). Our analysis showed that with a score of 96.2 out of 100, the checking procedure was the safest under cut-off 5 given 30% or more of tube misplacements. Respiratory feeding is excluded; misfeeding in the oesophagus was kept to a minimum to balance the need to reduce feeding delays from unnecessary chest x-rays. Routine chest x-rays was less safe than the pH test (score 89.5) and to feed all was the most risky (score 76.76).

Strengths and limitations

Using a decision analytic approach, we analysed the safety of the checking procedure under pH cut-offs 1-9 based on combined evidence from expert judgments, literature and clinical studies. We considered both the impact and the probabilities of various outcomes. Feeding delays caused by chest x-rays were formally incorporated, by a safety score lower than the ideal 100. The entire range of pH cut-offs was analysed, in addition to the commonly used ones. The safety of routine chest x-rays and feeding all patients without checks was similarly analysed.

The key evidence base underlying this analysis comes from Metheny et al over a 12-year period (1989-2001). Though slightly dated, this research, we believe, remains the most impressive body of evidence on aspirate pH measurement and prediction of feeding tube position by using a standard well-designed study protocol from 6 acute care hospitals.

The largest uncertainty remains in the oesophageal pH especially in the critical range between cut-offs 4 and 5.5 due to a lack of direct evidence. We did not consider costs in this analysis. However, the same framework can be applied when new evidence becomes available as well as extended to incorporate additional factors of importance, e.g. costs. A further limitation of our study is that our evidence on gastric and respiratory pH came from pH meter measurement whereas in practice pH papers are widely used. This will not influence our conclusion since pH paper is known to be less sensitive compared to pH meter. Additional, we have focused only on the subgroup of patients with successful aspirations since we are primarily interested in the *relative* safety of pH cut-offs. Our sensitivity analysis explored impact from unsuccessful aspirations as well as chest x-ray misinterpretations. Although safety across all pH cut-offs has been reduced, cut-off 5 remains the safest test to use.

Comparison with existing literature

As a universal first-line test for ensuring feeding safety, numerous studies investigated the pH test for its accuracy in identifying stomach and lung placements, e.g. [16 17]. However all the studies focused on the accuracy of the pH test per se. By contrast, the checking procedure in fact contains two tests: the pH test followed by chest x-rays when necessary. Thus the safety of the pH test must be evaluated in the context of its use, by considering its downstream implications for clinical decision making. We found that the key issue was to achieve a balance between reducing feeding incidents and reducing unnecessary chest x-rays. The decision analytic approach provides the normative framework for dealing with conflicting objectives. One study closer to our remit [22] investigated cost utility of the clinical algorithm (i.e. checking procedures) for nasogastric tube placement confirmation in adult patients. Our study differs from this study in that in our study accuracy of the pH test is not a given but constitutes the key source of uncertainties for achieving safe nasogastric feeding.

Implications for practice

Although the current recommended pH cut-off is 5.5, the British Society of Gastroenterology guidance for enteral feeding suggests tube aspirate pH measurement needs to be less than 5.0 prior to every use, but advises caution when the patient is on acid suppression [23]. Routine use of x-rays was not advised. Our study showed that reducing the pH cut-off from 5.5 to 5 can reduce the number of feeding incidents. Because majority of the patients have stomach placements, and because gastric pH has a mean value around 4 [8], a lower threshold means that more patients will be sent for chest x-rays. Chest x-rays, when misinterpreted, can lead to feeding incidents{, #110}. There is a clear need to develop cost-effective bed-side tests which not only have high accuracy but also the ability to withstand human errors in its applications.

CONCLUSIONS

The pH test with an upper cut-off at 5 was the safest test for the verification of nasogastric tube locations. The choice of pH cut-off depended on the prevalence of tube misplacements, the impact of feeding delays and the specificity of the pH test for oesophageal placements. Routine data collection at the local level should be implemented to optimise safety recommendations.

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Figure 1. Clinical pathway of using pH test to ensure safety in feeding by nasogastric tubes.

Figure 2. Trade-off between the number of unnecessary x-rays and feeding incidents.

Figure 3. Safety of the checking procedure under pH cut-offs 1-9, showing separate contributions made by each decision outcome to the overall weighted safety scores.

DECLARATION

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Ethics

Ethics approval from London – Chelsea REC, REC Reference: 16/LO/0998.

Availability of data and materials

The dataset(s) supporting the conclusions of this article is (are) included within the article and its appendicitis.

Author contributions

GBH and LDP designed the study; MN, OP and SO conducted research. , OP and SO analysed the NRLS database. MN, OP and SO interpreted the data. MN carried out the decision analysis. MN, JRH and PB drafted the manuscripts. Final manuscript approved by all authors. GBH had final responsibility for the final content.

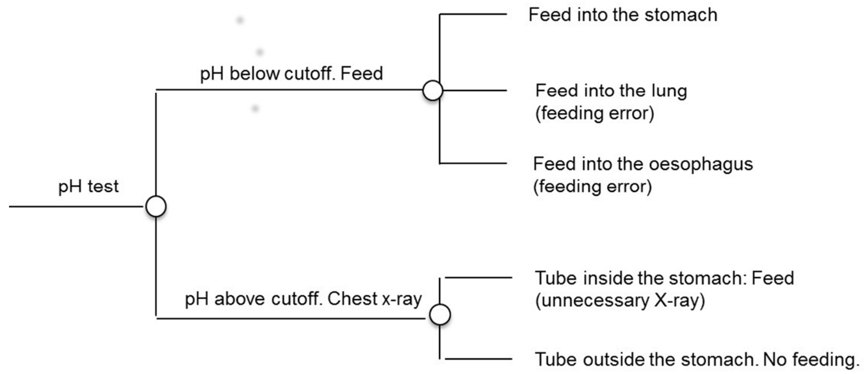

Figure 1. Clinical pathway of using pH test to ensure safety in feeding by nasogastric tubes.

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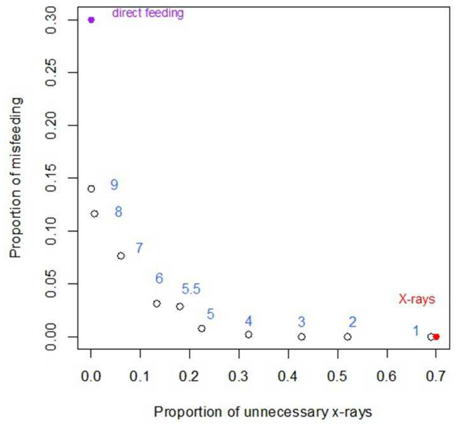


Figure 2. Trade-off between the number of unnecessary x-rays and feeding incidents.

97x60mm (300 x 300 DPI)

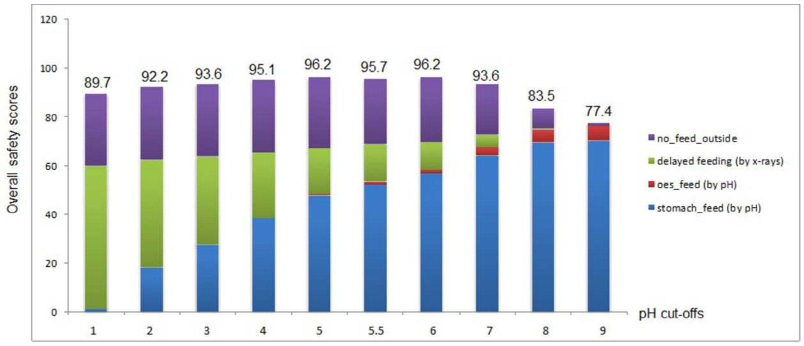


Figure 3. Safety of the checking procedure under pH cut-offs 1-9, showing separate contributions made by each decision outcome to the overall weighted safety scores.

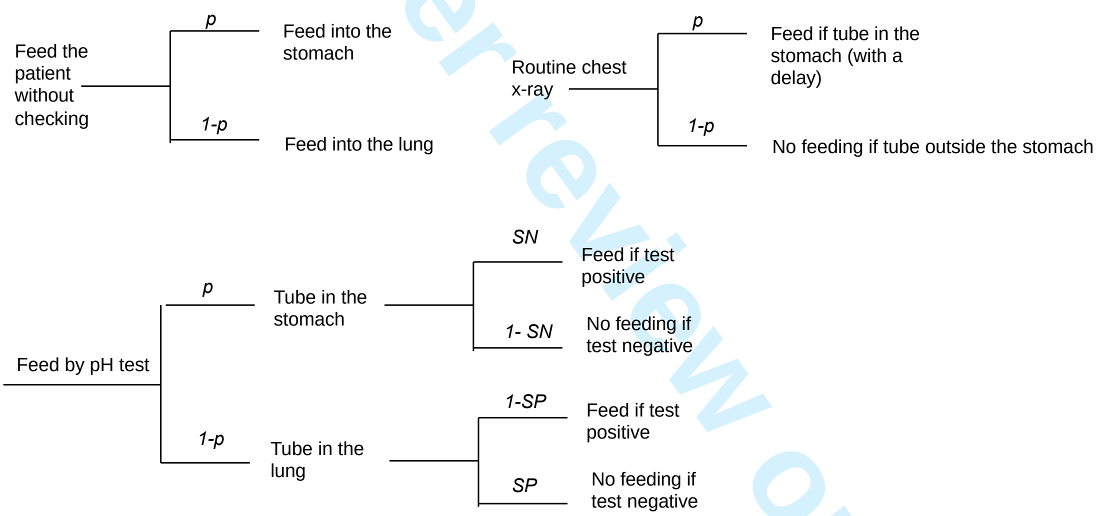
97x60mm (300 x 300 DPI)

Appendix 1. Setting up boundary values in the analysis

Consider three feeding strategies, namely to feed all patients without checking (feed all), send all patients for chest x-rays (routine x-rays) and to test the pH and only feed given a low pH but no feeding when the pH is above the threshold. Note that the last strategy is different from the recommended pH test whereby a high pH would trigger the use of chest x-rays.

There is general agreement that routine x-ray is safer than testing pH which is again safer than to feed all. From this we can make certain deductions in terms of the perceived safety of outcomes and probability distributions.

To illustrate, consider a simplified scenario where the tube is either inserted into the stomach or lung. The three strategies can be represented in decision trees:



We assume, as in the main text, that stomach feeding has the maximum safety score of 100 whereas lung feeding has the minimum safety score of 0. No feeding when the tube is outside the stomach (i.e. lung) is also safe (score 100). However, feeding following chest x-rays incurs a delay and therefore is less than ideal. So is no feeding when the tube is placed inside the stomach. Let

- *p* to denote the probability of stomach placement and *1-p* the probability of lung placement;
- *x* to denote safety of feeding into the stomach with a delay, x<100;
- *y* to denote the safety scores assigned to no feeding given stomach placement and y<100;

- *SN* be the sensitivity of the pH test and
- *SP* be the (lung) specificity of the pH test.

By aggregating safety scores and probabilities (see Appendix 3) we assess the safety of each of the three strategies:

- Safety(Feed_all)=100*prob(stomach)+0*prob(lung)
- Safety(Xray) =x*prob(stomach)+100*prob(lung)
- Safety(pH) =100*prob(stomach)*SN+y* prob(stomach)*(1-SN)+ 0*prob(lung)*(1-SP)+ 100*prob(lung)*SP

Suppose we are primarily interested in pH cutoffs at 5.5 or lower. At this range, the test has a lung specificity at 1. Entering this value into the above equations, and after simplifications, we obtain an assessment of the relative safety of the three strategies in algebra forms:

- Safety(Feed_all)=100*p -Eq.1
- Safety(Xray)=100-(100-x)*p -Eq.2
- Safety(pH)= 100*p*SN+p(1-SN)*y+(1-p)*100 -Eq.3

Since routine x-ray is safer than the pH test which is safer than to feed all, the expected utility theory predicts that the safety scores will exhibit the relationship as in Eq1<Eq.3<Eq.2.

Firstly, given Eq.1<Eq.2, we have 100*p<100-(100-x)*p, or

x>100(2-1/p) -Eq.4

Since *x* represents the safety of feeding with a delay (by chest x-rays), *x* must be less than 100. This means that the probability of stomach placement ***p* > 0.5**. This is why we set the risky scenario in the main text to have a 50% of tube misplacement rate.

Secondly, from Eq.3<Eq.2, we have 100*p*SN+p(1-SN)*y+(1-p)*100<100-(100-x)*p, or

x>100*SN+y*(1-SN) -Eq.5.1

or

y<(x-100*SN)/(1-SN) -Eq.5.2

Since y must be greater than 0, from Eq.5.2 we have ***x>100*SN***. That is, the safety of delayed feeding must be greater than the product of sensitivity of the pH test and 100 (the scaling unit).

To see what this means, consider the sensitivity of the pH test when the cut-off is 5.5. Our previous research (Hanna et al) established that the sensitivity of the pH is around 075 (0.743), thus the safety of feeding with a delay (*x*) must exceed 75 on the 0-100 scale for chest x-ray to be considered safer than the pH test. Based on Eq.5.2, suppose that delayed feeding has a safety score of 90, we can workout that no feeding when the tube is in the stomach will have a maximum score of 60.

In summary, from the simple preference ordering between the three decision strategies, we can set the boundary values as:

For pH cut-offs >=5.5	Range (minimum, maximum)	Corresponding value in paper
Stomach placements (probability *p*)	(0.5-1)	70%
Feeding delayed by x-ray (safety score x)	(100*SN, 100)	85
No feeding given stomach placements (safety score y)	(0, (x-100*SN)/(1-SN))	not applicable

APPENDIX 2 NRLS database analysis results

Methodology

Database search

Inclusion criteria for the search were all cases with evidence of nasogastric tube misplacement at any site outside the stomach entered into the National Reporting and Learning System (NRLS) database from the date of inception in October 2003 to 28th February 2009. Exclusion criteria were all paediatric cases as the safety guideline was applicable only to adults.

Case selection and Analysis

The narratives from the initial NRLS dataset were further examined to identify cases of nasogastric tube misplacement in any site outside the stomach. Two independent reviewers classified the adverse event reports according to whether or not current NPSA safety alert guidelines were followed prior to enteral feed being commenced. This was only possible for those reports that included sufficient information in the narratives. For reports that described tube feed or medication being administered via incorrectly placed nasogastric tubes, the reason for this was identified and classified.

The classification of the failure to correctly identify a misplaced tube originated from process mapping based on the existing and proposed safety guidelines.

Results

The number of incidents found from the NRLS database using the predefined search terms was a total of 2368 adverse event reports. Further examination of these reports yielded a total of 104 cases with documented feeding tube misplacement. The outcomes of tube misplacement in terms of patient harm are summarised in Table A1. In 29 reports there was too little information to support further analysis of the checking procedure employed to identify tube misplacement. Of the 75 narratives which allowed for further analysis, 11 reports described the wrong location of NG tube being discovered prior to feed or medication administration. These 11 cases included 5 incidents of tube misplacement identified by a tube aspirate pH > 5.5 followed by chest radiography and 6 incidents identified by chest radiography alone. For the remaining 64 cases in which the correct test was not used to locate the nasogastric tube or the results were incorrect, analysis of the reasons for failing to identify tube placement prior to tube use was performed and the results detailed in Table A2.

Table A1. Patient harm resulting from feeding tube misplacement – NRLS database

Effect on patient	No. of cases
Death	6
Severe harm	15
Moderate harm	23
Low harm	17
No harm	43

Table A2 (Table 3 in the main text). Mode of failure to identify tube misplacement

Type of failure	No. of cases
pH test correctly carried out but invalid (pH <5.5 but tube not in stomach)	10
pH test wrongly interpreted (thought OK if pH = 6)	1
Aspiration used as checking procedure; unclear whether pH tested	5
Bubble or Whoosh test used as only checking procedure	2
CXR incorrectly interpreted	25
Correct test indicated tube in stomach but tube moved prior to starting feed	4
No action taken to assess tube placement	12
CXR done but not checked prior to feeding	2
Other (misinterpretation of CXR report) (CT scan misreported)(direct vision and no further checks)	3
Total	**64**

Chest radiographs were misinterpreted by the junior House Officer in 4 cases and the Senior House Officer in 6 cases, while it was not clear what level of doctor misread the radiograph in 14 cases. The chest radiograph from the wrong date was reviewed in 2 cases of tube misplacement.

Appendix 3. Probability distributions, outcome scores and weighted scores

We assessed safety through aggregating outcome scores by their respective probabilities. Table A lists the outcome scores and probability calculation; Table B shows sensitivity and specificity of the pH test under cut-offs 1-9. The weighted scores are thus the sum product of Column 2 and Column 3 of Table A.

Table C and Table D show respectively the probability distributions and outcome score contributions under cut-offs 1-9.

Table A (Table 1 main text). Probability and safety of decision outcomes of the pH test

Outcome	Probability	Score
Feeding into the stomach by pH	Prior probability of stomach x Sensitivity of pH	100
Feeding into the lung by pH (feeding error)	Prior probability of lung x (1- Specificity in lung)	0
Feeding into the oesophagus by pH (feeding error)	Prior probability of oesophageal x (1- Specificity in oesophagus)	45
Delayed feeding into the stomach by x-rays (unnecessary x-rays)	Prior probability of stomach x (1-Sensitivity of pH)	85
No feeding outside the stomach by pH or by x-rays	Prior probability of lung/oesophagus x Specificity in lung/oesophagus	100

Table B (Table 2 main text). Accuracy of pH test under cut-offs 1-9

pH cut-offs	Sensitivity (stomach)	Specificity (Lung)	Specificity (oesophagus)
1	0.015	1	1
2	0.257	1	1
3	0.39	1	1
4	0.544	1	0.985
5	0.68	1	0.948
5.5	0.743	1	0.81
6	0.81	0.996	0.792
7	0.914	0.91	0.492
8	0.991	0.337	0.225
9	1	0.004	0.068

Table C. Probability distributions across pH cut-offs (data for Fig 2)

Cut-offs	stomach_feed	lung_feed	oes_feed	delayed	Nofeed
1	1.1%	0.0%	0.0%	69.0%	30.0%
2	18.0%	0.0%	0.0%	52.0%	30.0%
3	27.3%	0.0%	0.0%	42.7%	30.0%
4	38.1%	0.0%	0.2%	31.9%	29.8%
5	47.6%	0.0%	0.8%	22.4%	29.2%
5.5	52.0%	0.0%	2.9%	18.0%	27.2%
6	56.7%	0.1%	3.1%	13.3%	26.8%
7	64.0%	1.4%	7.6%	6.0%	21.0%
8	69.4%	9.9%	11.6%	0.6%	8.4%
9	70.0%	14.9%	14.0%	0.0%	1.1%

Table D. Weighted scores with part-contributions from individual outcomes (data for Figure 3)

Cut-offs	stomach_feed	lung_feed	oes_feed	delayed	nofeed	Total
1	1.1	0.0	0.0	58.6	30.0	89.7
2	18.0	0.0	0.0	44.2	30.0	92.2
3	27.3	0.0	0.0	36.3	30.0	93.6
4	38.1	0.0	0.1	27.1	29.8	95.1
5	47.6	0.0	0.4	19.0	29.2	96.2
5.5	52.0	0.0	1.3	15.3	27.2	95.7
6	56.7	0.0	1.4	11.3	26.8	96.2
7	64.0	0.0	3.4	5.1	21.0	93.6
8	69.4	0.0	5.2	0.5	8.4	83.6
9	70.0	0.0	6.3	0.0	1.1	77.4

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Selecting pH cut-offs for the safe verification of nasogastric feeding tube placement: a decision analytical modelling approach

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ABSTRACT

Objectives The existing British NPSA safety guideline recommends testing the pH of nasogastric tube aspirates. Feeding is considered safe if a pH of 5.5 or lower has been observed; otherwise chest x-rays are recommended. Our previous research found that at 5.5, the pH test lacks sensitivity towards oesophageal placements, a major risk identified by feeding experts. The aim of this research is to use a decision analytic modelling approach to systematically assess the safety of the pH test under cut-offs 1-9.

Materials and Methods We mapped out the care pathway according to the existing safety guideline. Decision outcomes were scored on a 0-100 scale in terms of safety. Sensitivities and specificities of the pH test at each cut-off were extracted from our previous research. Aggregating outcome scores and probabilities resulted in weighted scores which enabled an analysis of the relative safety of the checking procedure under various pH cut-offs.

Results The pH test was the safest under cut-off 5 when there was 30% or more of NG-tube misplacements. Under cut-off 5, respiratory feeding was excluded; oesophageal feeding was kept to a minimum to balance the need of chest x-rays for patients with a pH higher than 5. Routine chest x-rays were less safe than the pH test whilst to feed all without safety checks was the most risky.

Discussion The safety of the current checking procedure is sensitive to the choice of pH cut-offs, the impact of feeding delays, the accuracy of the pH in the oesophagus, as well as the extent of tube misplacements.

Conclusions The pH test with cut-off 5 was the safest overall. It is important to understand the local clinical environment so that appropriate choice of pH cut-offs can be made to maximise safety and to minimise use of chest x-rays.

Keywords: diagnostics, decision analysis, pH monitoring, nasogastric tube, adult feeding

STRENGTHS AND LIMITATIONS OF THIS STUDY

- A decision analytic approach was used to map out clinical pathways and to achieve synthesis of evidence from clinical studies, published literature and expert judgments.
- The entire range of pH cut-offs was analysed in addition to the most frequently used ones between 4 and 6.
- Two non-pH test strategies were analysed using the same framework: routine chest x-rays and feeding all patients without safety checks.
- We did not consider financial costs in this analysis. The same framework can be expanded to incorporate additional dimensions of importance.
- We focused only on the group of patients with successful aspirations. Unsuccessful aspiration does not change the relative safety of various pH cut-offs but is one reason for using chest x-rays. Our analysis assumed that chest x-rays were 100% accurate. However reducing pH cut-offs will not increase misfeeding due to chest x-ray misinterpretations.

INTRODUCTION

Every year at least 1 million nasogastric tubes (NG tubes) are being used in the UK [1] and 1.5 billion worldwide[1]. Inadvertent tube placement outside the stomach has been classified as a 'never event' by NHS England[2]. Nevertheless incidents of tube misplacements remained commonplace. Reported rates of misplacement on insertion and tube migration after correct initial placement varied between 1.3% and 50% in adults [2]. Misplacement into the respiratory tract occurs in 1 to 3% of patients [3] and can have catastrophic consequences, including death. Guidelines on nutrition support for adults issued by the National Institute for Health and Care Excellence (NICE) recommend that the position of NG tubes be verified on initial placement and before each use [4]. The British National Patient Safety Agency (NPSA) recommends testing the pH of tube aspirates [5-7]. Feeding can only start if a pH at or below 5.5 has been established; otherwise chest x-rays, the gold-standard, should be used.

Commissioned by NPSA, we investigated evidence behind various bedside tests including pH, aspirate appearance, capnometry/colorimetric, auscultation ('whoosh' test), and magnetic guidance [8]. The pH test has the best bedside usability and accuracy underpinned by a large body of clinical evidence. In addition to respiratory placements, oesophageal placements emerged as a major safety concern during our consultations with feeding experts, e.g. [9]. To address this and to remedy the lack of published studies in oesophageal pH from NG-tubes, we carried out a literature review of pH distributions in patients with reflux. We found that reducing the cut-off from 5.5 to 4 would increase the sensitivity of the pH test to tubes placed in the oesophagus. Subsequent safety recommendations continued to uphold 5.5 as the safety threshold [10]. The main disadvantage of lowering the pH cut-off is that more patients with tubes placed inside the stomach will be sent for chest x-rays which is the second-line test. This is not ideal since chest x-rays are not only more expensive – on

[1] Worldwide usage of 1.5 billion was estimated from NHS usage by assuming demand proportional to population size.
[2] https://www.england.nhs.uk/wp-content/uploads/2015/03/never-evnts-list-15-16.pdf

average each chest x-ray costs £30 whereas a tube of 100 pH strips costs slightly over £10[3] – but can delay feeding for up to 47 hours[4]. In addition chest x-rays, despite being considered the gold-standard of tube site verifications, are subject to misinterpretation errors [7 11].

A drawback of our previous research was an exclusive focus on the risks from various bedside tests. However the recommended checking procedure in fact utilises a combination of two tests: the pH test followed by chest x-rays should the pH test fail. The question of selecting suitable pH cut-offs must be addressed using the same context. We are primarily interested in understanding the trade-offs in patient safety between maximising feeding in time and minimising feeding incidents. The aim of this research is to employ a decision analytic modelling approach [12] which allows us to systematically analyse the safety of pH test under various cut-offs when embedded in the clinical setting [13] to better inform policy makers and clinicians performing safety checks.

ETHICS

This work is partially supported by an Innovate UK grant for developing a new pH paper test for nasogastric tube placements. We have gained ethics approvals from the Research Ethics Committee which supported a clinical study as well as interview studies related to the use of pH tests in the clinical setting.

[3] Costs of chest x-rays were derived from NHS reference price 2015 and price of pH strips were from NHS supply chain website (https://www.supplychain.nhs.uk/).
[4] Mean delay 17 hours, range 1.5 hours- 47 hours. Unpublished audit data carried out in 2016 at the St Mary's hospital, London, UK from 23 patients.

METHODS

Analysis of the National Reporting and Learning System

To provide an overview of the feeding incidents, we carried out a narrative analysis of incident reports submitted to the National Reporting and Learning System (NRLS). We included all cases with evidence of nasogastric tube misplacement at any site outside the stomach between October 2003 and 28th February 2009. Paediatric cases were excluded. Two authors (OHP, SO) independently reviewed the adverse event reports and classified these according to whether or not current safety guidelines were followed (cut-off 5.5). For reports containing sufficient details to enable an analysis of possible reasons of tube misplacements, we extracted the reported reasons for misfeeding and carried out thematic analyses to generate categories. Disagreements between the two reviewers were solved by discussion till consensus was reached.

Safety of pH under various cut-offs

Study design

We mapped out the clinical pathway of the safety guidelines with regard to naso-gastric tube feeding (figure 1). Since our target was the relative safety between different pH cut-offs, we focused on the subgroup of patients for whom aspirations were successful but analysed implications of unsuccessful aspirations on patient safety in the sensitivity analysis. We assumed that the pH cut-off values could take any number between 1 and 9 (the recommended range), as well as 5.5 (the current recommendation). Decision outcomes were scored with points out of 100, with 100 assigned to the outcomes with the best safety and 0 to the outcomes with the worst safety. The sensitivities and specificities of the pH test under various cut-offs were derived from our previous research. Aggregating the outcome scores by their respective probabilities resulted in a set of weighted scores. These weighted scores enabled a comparison of the relative safety of the pH test under various cut-offs.

Outcomes of feeding decisions

Decision outcomes were identified from the clinical pathway (figure 1) assuming that all patients have successful aspirations. There were five outcomes in total. *Feeding into the stomach* by pH took place if the pH was at or below a certain cut-off *and* when the tube had been placed inside the stomach. *Feeding into the lung* or *oesophagus* took place when a low pH (<=cut-off) was combined with tube misplacements. If the pH exceeded a certain cut-off, then chest x-rays were used to establish tube sites. For those patients with tubes placed inside the stomach, the x-ray was deemed unnecessary since gastric placement could have been determined solely by pH. We distinguish between feeding by pH and feeding by chest x-rays since the latter carries radiation risks and could cause *feeding delays* for up to 47 hours (footnote 3). The remaining patients who received chest x-rays would reveal misplaced tubes – these were correctly identified and excluded, thus *no feeding outside the stomach*.

The safest outcomes (i.e. feeding into the stomach by pH, no feeding outside the stomach) were assigned a score of 100 and the least safe outcomes (i.e. feeding into the lung) was assigned a score of 0. For the remaining outcomes, we applied the Analytic Hierarchy Process [14], converting qualitative judgments into quantitative scores. Two clinicians who were experts in gastroenterological diseases were invited to a face-to-face meeting with one of the authors (MN). During the meeting they were briefed about the project and asked to first rank all the outcomes according to safety. They were then asked to make pair-wise comparisons and articulate the strength of their preferences. For instance, feeding into the oesophagus was considered safer than feeding into the lung and the preference was *very strong*.

Consensus was reached through discussions, producing preference judgments ranging from no difference, weak, moderate, strong to extreme. We entered these into the MACBETH [15] component of the decision analysis software HiView. The software first checked that the judgments were consistent with the safety rankings and once satisfied, converted the judgments into numeric ratings (**Table 1**, last column). Further consistency checks were performed on the scores. For instance, oesophageal feeding received a safety score of 45, which means that its safety was considered nearly half-way in between the safest outcome (stomach feeding) and the least safe outcome (lung feeding). This should mirror the pair-wise comparisons, where the preference for stomach feeding over oesophageal feeding (100 vs 45) was slightly stronger than the preference for oesophageal feeding over lung feeding (45 vs 0).

Table 1. Probability and safety of decision outcomes of the pH test

Outcome	Probability	Score
Feeding into the stomach by pH	Prior probability of stomach x Sensitivity of pH	100
Feeding into the lung by pH (feeding error)	Prior probability of lung x (1- Specificity in lung)	0
Feeding into the oesophagus by pH (feeding error)	Prior probability of oesophageal x (1- Specificity in oesophagus)	45
Delayed feeding into the stomach by x-rays (unnecessary x-rays)	Prior probability of stomach x (1-Sensitivity of pH)	85
No feeding outside the stomach by pH or by x-rays	Prior probability of lung/oesophagus x Specificity in lung/oesophagus	100

Outcome probabilities were driven by two independent factors – the initial insertion (prior distribution of tube sites) and the accuracy of the pH test in differentiating various tube sites (i.e. test sensitivity and specificity, **Table 1** middle column). Given the wide range of variations in reported tube misplacements and tube migrations (1.3%-50%), we assumed an average risk of insertion errors whereby 70% of the tubes were inside the stomach with an equal number (15%) of misplacements in the lung and oesophagus (see **Appendix 1** for reasoning). The sensitivities and specificities under individual pH cut-offs were extracted from our previous research. They were based on a clinical database with 1035 unique patient records from multiple clinical trials by a single clinician. This database included 754 stomach placements and 281 lung placements (e.g. [16 17]), with pH measured by both pH meter (Beckman pH1 10 portable pH meters) and pH paper throughout (1-11 Vivid pH paper). Since pH meter reading and paper reading do not always agree, we used pH meter reading to derive the accuracy data. Lack of evidence for oesophageal placements was remedied by reviewing studies on healthy cohorts under observations for reflux [18-20] Distribution of oesophageal pH was estimated based on the proportion of time when pH decreased below the various cut-offs. Table 2 summarises the accuracy of pH tests.

Table 2. Accuracy of pH test under cut-offs 1-9

pH cut-offs	Sensitivity (stomach)	Specificity (Lung)	Specificity (oesophagus)
1	0.015	1	1
2	0.257	1	1
3	0.39	1	1
4	0.544	1	0.985
5	0.68	1	0.948
5.5	0.743	1	0.81
6	0.81	0.996	0.792
7	0.914	0.91	0.492
8	0.991	0.337	0.225
9	1	0.004	0.068

Aggregating outcome scores by their respective probabilities resulted in a set of weighted scores. These reflected the relative safety of the recommended checking procedure under different pH cut-offs. In addition to the pH test, we analysed a scenario where patients are fed without safety checks (feed all) and where all patients are sent for chest x-rays before feeding (*routine x-rays*).

Sensitivity analyses

To capture the spectrum of insertion errors we analysed two additional scenarios with low (10%) and high (50%) probability of tube misplacements (see **Appendix 1** for reasoning). Lung and oesophageal intubations were equally likely, at 5% and 25% respectively. Tornado diagrams were used to identify variables of importance. All outcome and probabilistic inputs were varied +/-15% within range (0-1 for probabilities and 0-100 for outcomes). Three-way sensitivity analyses were carried out to examine the direction of impact.

We considered the impact of successful aspirations whereby aspirations were successful 90% of the time [21]. For the remaining 10%, chest x-rays are used instead. We considered the impact of chest x-ray misinterpretations by assuming that chest x-ray of tubes located outside the stomach was interpreted as inside 10% of the time which resulted in feeding into the wrong places (equally likely in lung and oesophagus)[5]. We then analysed the joint impact of unsuccessful aspirations combined with radiography misinterpretations.

We carried out the analyses in Microsoft Excel and TreeAge Pro (2015). Since chest x-rays were used as the reference standard across pH accuracy studies, chest x-rays were assumed to be 100% accurate in the main body of analysis.

[5] There is no reported data on the frequency of chest x-ray misinterpretations for verifying NG tube insertions. Reported error rates of diagnostic x-rays for lung cancers ranged between 5.3% and 24%. Since chest x-ray is a second-line test, the greater the likelihood of its misinterpretations, the more a higher rather than lower pH cut-off would be preferred.

RESULTS

Analysis of feeding incidents reported to NRLS

A total number of 2368 adverse event reports were identified. After excluding cases that were irrelevant or with incomplete information, we reviewed 104 cases with documented feeding tube misplacement. These included 6 counts of death, 15 counts of severe harm and 23 counts of moderate harm. The remaining 60 cases recorded no harm (43 cases) or low harm (17 cases). Further analysis was carried out on 75 out of 104 narratives containing sufficient details. In eleven reports the wrong tube location was discovered prior to feed or medication (either by pH or by chest x-rays). Of the remaining 64 cases, we analysed reasons for misfeeding. The most frequently cited reason was misinterpretation of chest x-rays (25). The pH test (with 5.5 as the cut-off) itself was responsible for 10 feeding incidents. There were also 23 cases where safety guidelines were not followed, including 12 cases where feeding was carried out without safety checks (**Table 3**, **Appendix 2** for further details).

Table 3. Mode of failure to identify tube misplacement

Type of failure	No. of cases
pH test correctly carried out but invalid (pH <5.5 but tube not in stomach)	10
pH test wrongly interpreted (thought OK if pH = 6)	1
Aspiration used as checking procedure; unclear whether pH tested	5
Bubble or Whoosh test used as only checking procedure	2
CXR incorrectly interpreted	25
Correct test indicated tube in stomach but tube moved prior to starting feed	4
No action taken to assess tube placement	12
CXR done but not checked prior to feeding	2
Other (misinterpretation of CXR report) (CT scan misreported)(direct vision and no further checks)	3
Total	**64**

Safety of the pH test under various cut-offs

The higher the cut-off, the more sensitive and the less specific the pH test becomes (**Table 2**). However, it is impossible to be free from x-ray related feeding delays and at the same time to be free from feeding incidents due to the lack of accuracy of the pH test. This is captured in **Figure 2** which shows the trade-off between feeding incidents (more numerous under higher cut-offs) and feeding delays (more numerous under lower cut-offs). As the cut-off reduced, the increase in the number of unnecessary x-rays (feeding delays, x-axis) was faster than the reduction in feeding incidents (y-axis). Consider cut-off 5 versus 6 for instance. The magnitude of difference was four times, i.e. 9% (=22%-13%) increase in unnecessary x-rays versus 2.1% (=2.9%-0.8%) decrease in feeding incidents (primarily in the oesophagus).

Nevertheless, it would be misleading to select pH cut-offs based on the number of feeding delays or feeding incidents alone since different outcomes have different impact on patient safety. Instead, we used the aggregated safety scores to assess the relative safety under different cut-offs. These are shown in **Figure 3**, along with part-score contributions made from individual outcomes. At lower cut-offs the scores were primarily made up of delayed feeding and no feeding outside the stomach, whereas at higher cut-offs stomach feeding made increasingly significant contribution to the overall safety. No points were attributed to lung feeding with a safety score of 0.

Cut-off 5 and cut-off 6 had the highest safety score (96.2), and therefore the 'safest' overall. This is in a context of an ideal (and hypothetical) test which has a score of 100, by identifying every tube in the stomach for feeding whilst excluding every tube outside the stomach. By contrast, to feed all patients without discrimination is the least safe strategy with a weighted score of 76.75, from feeding correctly (though randomly) in 70% of patients with stomach placements (part score 70) but misfeeding in 15% oesophageal placements (part score 6.75) and in 15% lung placements (part score 0). Routine use of chest x-rays had a weighed score of 89.5 from correctly identifying all 30% of misplaced tubes (part score 30) and from feeding correctly in 70% of the patients though with a delay (part score 59.5, mean delay 17 hours, range 1.5 hours- 47 hours, footnote 3; see **Appendix 3** for further details).

Sensitivity analysis

The largest impact on the overall safety was attributable to safety of delayed feeding (scores 50-95) and to the pH specificity in the oesophagus (range 0.6-0.99). Decreasing the score assigned to delayed feeding by 5 points (from 85 to 80) would make cut-off 5 the safest option. A 10% increase at 5.5 (from 0.81 to 0.89) whilst keeping the specificities at 5 constant (0.948) would result in cut-off 5.5 becoming the safest overall. Varying the initial tube misplacements also had a large impact, influencing safety across *all* cut-offs. However cut-off 5 remained the 'safest' under 50% tube misplacements. Similarly, unsuccessful aspirations and/or chest x-ray misinterpretations reduced the safety across all cut-offs and more so for lower cut-offs than for higher cut-offs since chest x-rays were used more often at lower cut-offs. Despite this, pH test under cut-off 5 remained the safest within range 1-5.5 (Table 4).

Table 4. Sensitivity analysis of the safety of various pH cut-offs

cutoffs	value (original)	value of delayed feeding = 50	value of delayed feeding = 95	Oesophagus specificity inc. by 10% at 5.5	initial misplace-ment = 10%	initial misplace-ment = 50%	Unsucc-essful Aspirat-ions	CXR mis-interpret-ation
1	89.7	65.5	96.6	89.7	86.7	92.6	86.7	86.6
2	92.2	74.0	97.4	92.2	90.0	94.4	89.2	88.9
3	93.6	78.7	97.9	93.6	91.8	95.4	90.6	90.2
4	95.1	83.9	98.3	95.1	93.8	96.4	92.1	91.5
5	96.2	88.4	98.5	96.2	95.5	96.9	93.3	92.6
5.5	95.7	89.4	97.5	96.4	96.0	95.5	93.0	92.4
6	96.2	91.6	97.6	96.2	96.8	95.6	93.5	92.8
7	93.6	91.4	94.2	93.6	97.0	90.1	91.5	91.0
8	83.6	83.3	83.6	83.6	94.4	72.7	82.7	83.1
9	77.4	77.4	77.4	77.4	92.5	62.3	77.3	78.2

DISCUSSION

Summary of main findings

The recommended safety procedure prior to feeding by nasogastric tube is comprised of two tests, the pH test and chest x-rays when the pH test fails (>5.5). Our analysis showed that with a score of 96.2 out of 100, the checking procedure was the safest under cut-off 5 given 30% or more of tube misplacements. Respiratory feeding is excluded; misfeeding in the oesophagus was kept to a minimum to balance the need to reduce feeding delays from unnecessary chest x-rays. Routine chest x-rays were less safe than the pH test (score 89.5) and to feed all was the most risky (score 76.76).

Strengths and limitations

Using a decision analytic approach, we analysed the safety of the checking procedure under pH cut-offs 1-9 based on combined evidence from expert judgments, literature and clinical studies. We considered both the impact and the probabilities of various outcomes. Feeding delays caused by chest x-rays were formally incorporated, by a safety score lower than the ideal 100. The entire range of pH cut-offs was analysed, in addition to the commonly used ones. The safety of routine chest x-rays and feeding all patients without checks was similarly analysed.

The key evidence base underlying this analysis comes from Metheny et al over a 12-year period (1989-2001). Though slightly dated, this research, we believe, remains the most impressive body of evidence on aspirate pH measurement and prediction of feeding tube position by using a standard well-designed study protocol from 6 acute care hospitals.

The largest uncertainty remains in the oesophageal pH especially in the critical range between cut-offs 4 and 5.5 due to a lack of direct evidence. We did not consider costs in this analysis. However, the same framework can be applied when new evidence becomes available as well as extended to incorporate additional factors of importance, e.g. costs. A further limitation of our study is that our evidence on gastric and respiratory pH came from pH meter measurement whereas in practice pH papers are widely used. This will not influence our conclusion since pH paper is known to be less sensitive when compared to pH meter. Additional, we have focused only on the subgroup of patients with successful aspirations since we are primarily interested in the *relative* safety of pH cut-offs. Our sensitivity analysis explored impact from unsuccessful aspirations as well as chest x-ray misinterpretations. Although safety across all pH cut-offs has been reduced, cut-off 5 remains the safest test to use.

Comparison with existing literature

As a universal first-line test for ensuring feeding safety, numerous studies investigated the pH test for its accuracy in identifying stomach and lung placements, e.g. [16 17]. However all the studies focused on the accuracy of the pH test *per se*. By contrast, the checking procedure in fact contains two tests: the pH test followed by chest x-rays when necessary. Thus the safety of the pH test must be evaluated in the context of its use, by considering its downstream implications for clinical decision making. We found that the key issue was to achieve a balance between reducing feeding incidents and reducing unnecessary chest x-rays. The decision analytic approach provides the normative framework for dealing with conflicting objectives. One study closer to our remit [22] investigated cost utility of the clinical algorithm (i.e. checking procedures) for nasogastric tube placement confirmation in adult patients. Our study differs from this study in that in our study accuracy of the pH test is not a given but constitutes the key source of uncertainties for achieving safe nasogastric feeding.

Implications for practice

Although the current recommended pH cut-off is 5.5, the British Society of Gastroenterology guidance for enteral feeding suggests tube aspirate pH measurement needs to be less than 5.0 prior to every use, but advises caution when the patient is on acid suppression [23]. Routine use of x-rays was not advised. Our study showed that reducing the pH cut-off from 5.5 to 5 can reduce the number of feeding incidents. Because majority of the patients have stomach placements, and because gastric pH has a mean value around 4 [8], a lower threshold means that more patients will be sent for chest x-rays. Chest x-rays, when misinterpreted, can lead to feeding incidents[7]. There is a clear need to develop cost-effective bed-side tests which not only have high accuracy but also the ability to withstand human errors in their applications.

Chest x-rays misinterpretations

Although chest x-ray misinterpretations constituted a major source of feeding errors (e.g. Table 3), our main analysis assumed that chest x-rays were 100% accurate based on a number of considerations. Firstly, we limited our evidence base to a cohort of clinical studies with clear demonstration of administering and interpreting a reference standard (see above). This gave us confidence in the accuracy of chest x-rays in *our* evidence base. Secondly, there is little data on the actual distributions of chest x-ray misinterpretations in relation to NG-tube feedings, obscuring the direction in which the analysis would be influenced by such an assumption. A stomach tube might be misinterpreted as located outside the stomach, resulting in either over-estimation of the specificity of the pH test (when pH >5.5) or under-estimation of test sensitivity (when pH<5.5). Similarly, a non-stomach tube might be misinterpreted as located inside the stomach, with opposite implications for test sensitivity and specificity.

It is also important to note that in practice, reducing pH cut-offs from the existing 5.5 to 5 will *not* increase misfeeding attributable to chest x-ray misinterpretations. This is because the change will affect those patients with a pH between 5 and 5.5. All these patients will receive feeding under the existing cut-off whereas under the new, lower cut-off, only a proportion of them, who have demonstrated stomach intubation from chest x-rays, will be fed. An important lesson here is that the quality of a formal analysis is inevitably constrained by the availability of the evidence, and the quality of it.

CONCLUSIONS

The pH test with an upper cut-off at 5 was the safest test for the verification of nasogastric tube locations. The choice of pH cut-off depended on the prevalence of tube misplacements, the impact of feeding delays and the specificity of the pH test for oesophageal placements. Routine data collection at the local level should be implemented to optimise safety recommendations.

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Figure 1. Clinical pathway of using pH test to ensure safety in feeding by nasogastric tubes.

Figure 2. Trade-off between the number of unnecessary x-rays and feeding incidents.

Figure 3. Safety of the checking procedure under pH cut-offs 1-9, showing separate contributions made by each decision outcome to the overall weighted safety scores.

DECLARATION

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Ethics

Ethics approval from London – Chelsea REC, REC Reference: 16/LO/0998.

Availability of data and materials

The dataset(s) supporting the conclusions of this article is (are) included within the article and its appendicitis.

Author contributions

GBH and LDP designed the study; MN, OP and SO conducted research. , OP and SO analysed the NRLS database. MN, OP and SO interpreted the data. MN carried out the decision analysis. MN, JRH and PB drafted the manuscripts. Final manuscript approved by all authors. GBH had final responsibility for the final content.

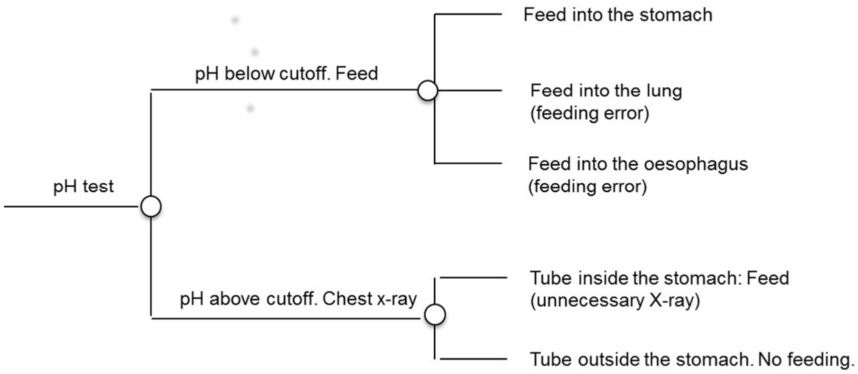

Figure 1. Clinical pathway of using pH test to ensure safety in feeding by nasogastric tubes.

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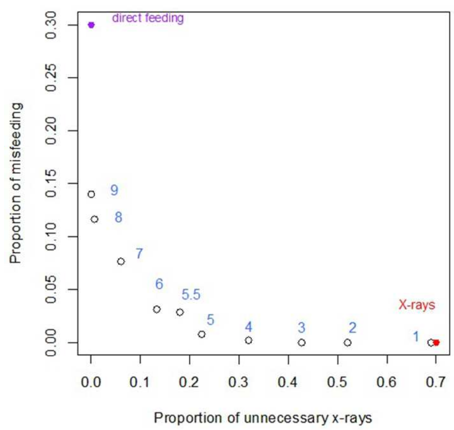

Figure 2. Trade-off between the number of unnecessary x-rays and feeding incidents.

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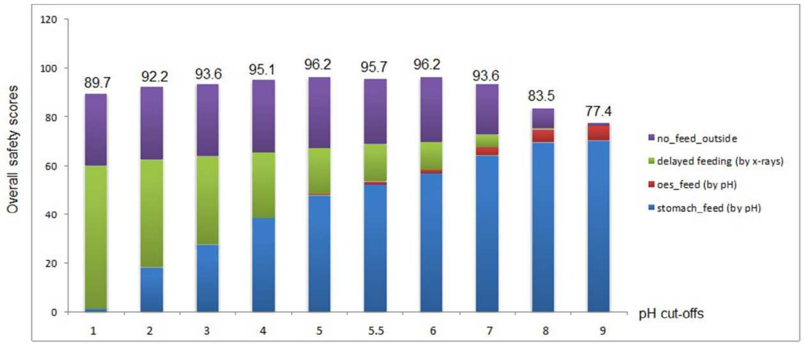


Figure 3. Safety of the checking procedure under pH cut-offs 1-9, showing separate contributions made by each decision outcome to the overall weighted safety scores.

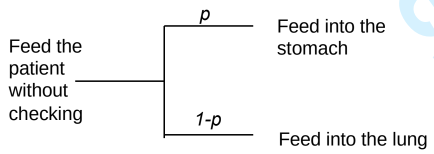
97x60mm (300 x 300 DPI)

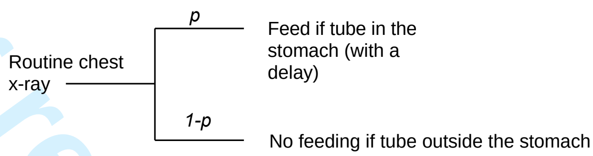
Appendix 1. Setting up boundary values in the analysis

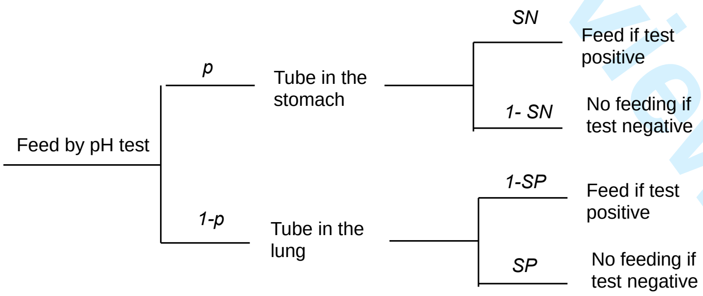
Consider three feeding strategies, namely to feed all patients without checking (feed all), send all patients for chest x-rays (routine x-rays) and to test the pH and only feed given a low pH but no feeding when the pH is above the threshold. Note that the last strategy is different from the recommended pH test whereby a high pH would trigger the use of chest x-rays.

There is general agreement that routine x-ray is safer than testing pH which is again safer than to feed all. From this we can make certain deductions in terms of the perceived safety of outcomes and probability distributions.

To illustrate, consider a simplified scenario where the tube is either inserted into the stomach or lung. The three strategies can be represented in decision trees:







We assume, as in the main text, that stomach feeding has the maximum safety score of 100 whereas lung feeding has the minimum safety score of 0. No feeding when the tube is outside the stomach (i.e. lung) is also safe (score 100). However, feeding following chest x-rays incurs a delay and therefore is less than ideal. So is no feeding when the tube is placed inside the stomach. Let

- *p* to denote the probability of stomach placement and *1-p* the probability of lung placement;
- *x* to denote safety of feeding into the stomach with a delay, $x<100$;
- *y* to denote the safety scores assigned to no feeding given stomach placement and $y<100$;

- *SN* be the sensitivity of the pH test and
- *SP* be the (lung) specificity of the pH test.

By aggregating safety scores and probabilities (see Appendix 3) we assess the safety of each of the three strategies:

- Safety(Feed_all)=100*prob(stomach)+0*prob(lung)
- Safety(Xray) =x*prob(stomach)+100*prob(lung)
- Safety(pH) =100*prob(stomach)*SN+y* prob(stomach)*(1-SN)+ 0*prob(lung)*(1-SP)+ 100*prob(lung)*SP

Suppose we are primarily interested in pH cutoffs at 5.5 or lower. At this range, the test has a lung specificity at 1. Entering this value into the above equations, and after simplifications, we obtain an assessment of the relative safety of the three strategies in algebra forms:

- Safety(Feed_all)=100*p -Eq.1
- Safety(Xray)=100-(100-x)*p -Eq.2
- Safety(pH)= 100*p*SN+p(1-SN)*y+(1-p)*100 -Eq.3

Since routine x-ray is safer than the pH test which is safer than to feed all, the expected utility theory predicts that the safety scores will exhibit the relationship as in Eq1<Eq.3<Eq.2.

Firstly, given Eq.1<Eq.2, we have 100*p<100-(100-x)*p, or

x>100(2-1/p) -Eq.4

Since *x* represents the safety of feeding with a delay (by chest x-rays), *x* must be less than 100. This means that the probability of stomach placement ***p* > 0.5**. This is why we set the risky scenario in the main text to have a 50% of tube misplacement rate.

Secondly, from Eq.3<Eq.2, we have 100*p*SN+p(1-SN)*y+(1-p)*100<100-(100-x)*p, or

x>100*SN+y*(1-SN) -Eq.5.1

or

y<(x-100*SN)/(1-SN) -Eq.5.2

Since y must be greater than 0, from Eq.5.2 we have ***x>100*SN***. That is, the safety of delayed feeding must be greater than the product of sensitivity of the pH test and 100 (the scaling unit).

To see what this means, consider the sensitivity of the pH test when the cut-off is 5.5. Our previous research (Hanna et al) established that the sensitivity of the pH is around 075 (0.743), thus the safety of feeding with a delay (*x*) must exceed 75 on the 0-100 scale for chest x-ray to be considered safer than the pH test. Based on Eq.5.2, suppose that delayed feeding has a safety score of 90, we can workout that no feeding when the tube is in the stomach will have a maximum score of 60.

In summary, from the simple preference ordering between the three decision strategies, we can set the boundary values as:

For pH cut-offs >=5.5	Range (minimum, maximum)	Corresponding value in paper
Stomach placements (probability *p*)	(0.5-1)	70%
Feeding delayed by x-ray (safety score x)	(100*SN, 100)	85
No feeding given stomach placements (safety score y)	(0, (x-100*SN)/(1-SN))	not applicable

APPENDIX 2 NRLS database analysis results

Methodology

Database search

Inclusion criteria for the search were all cases with evidence of nasogastric tube misplacement at any site outside the stomach entered into the National Reporting and Learning System (NRLS) database from the date of inception in October 2003 to 28th February 2009. Exclusion criteria were all paediatric cases as the safety guideline was applicable only to adults.

Case selection and Analysis

The narratives from the initial NRLS dataset were further examined to identify cases of nasogastric tube misplacement in any site outside the stomach. Two independent reviewers classified the adverse event reports according to whether or not current NPSA safety alert guidelines were followed prior to enteral feed being commenced. This was only possible for those reports that included sufficient information in the narratives. For reports that described tube feed or medication being administered via incorrectly placed nasogastric tubes, the reason for this was identified and classified.

The classification of the failure to correctly identify a misplaced tube originated from process mapping based on the existing and proposed safety guidelines.

Results

The number of incidents found from the NRLS database using the predefined search terms was a total of 2368 adverse event reports. Further examination of these reports yielded a total of 104 cases with documented feeding tube misplacement. The outcomes of tube misplacement in terms of patient harm are summarised in Table A1. In 29 reports there was too little information to support further analysis of the checking procedure employed to identify tube misplacement. Of the 75 narratives which allowed for further analysis, 11 reports described the wrong location of NG tube being discovered prior to feed or medication administration. These 11 cases included 5 incidents of tube misplacement identified by a tube aspirate pH > 5.5 followed by chest radiography and 6 incidents identified by chest radiography alone. For the remaining 64 cases in which the correct test was not used to locate the nasogastric tube or the results were incorrect, analysis of the reasons for failing to identify tube placement prior to tube use was performed and the results detailed in Table A2.

Table A1. Patient harm resulting from feeding tube misplacement – NRLS database

Effect on patient	No. of cases
Death	6
Severe harm	15
Moderate harm	23
Low harm	17
No harm	43

Table A2 (Table 3 in the main text). Mode of failure to identify tube misplacement

Type of failure	No. of cases
pH test correctly carried out but invalid (pH <5.5 but tube not in stomach)	10
pH test wrongly interpreted (thought OK if pH = 6)	1
Aspiration used as checking procedure; unclear whether pH tested	5
Bubble or Whoosh test used as only checking procedure	2
CXR incorrectly interpreted	25
Correct test indicated tube in stomach but tube moved prior to starting feed	4
No action taken to assess tube placement	12
CXR done but not checked prior to feeding	2
Other (misinterpretation of CXR report) (CT scan misreported)(direct vision and no further checks)	3
Total	**64**

Chest radiographs were misinterpreted by the junior House Officer in 4 cases and the Senior House Officer in 6 cases, while it was not clear what level of doctor misread the radiograph in 14 cases. The chest radiograph from the wrong date was reviewed in 2 cases of tube misplacement.

Appendix 3. Probability distributions, outcome scores and weighted scores

We assessed safety through aggregating outcome scores by their respective probabilities. Table A lists the outcome scores and probability calculation; Table B shows sensitivity and specificity of the pH test under cut-offs 1-9. The weighted scores are thus the sum product of Column 2 and Column 3 of Table A.

Table C and Table D show respectively the probability distributions and outcome score contributions under cut-offs 1-9.

Table A (Table 1 main text). Probability and safety of decision outcomes of the pH test

Outcome	Probability	Score
Feeding into the stomach by pH	Prior probability of stomach x Sensitivity of pH	100
Feeding into the lung by pH (feeding error)	Prior probability of lung x (1- Specificity in lung)	0
Feeding into the oesophagus by pH (feeding error)	Prior probability of oesophageal x (1- Specificity in oesophagus)	45
Delayed feeding into the stomach by x-rays (unnecessary x-rays)	Prior probability of stomach x (1-Sensitivity of pH)	85
No feeding outside the stomach by pH or by x-rays	Prior probability of lung/oesophagus x Specificity in lung/oesophagus	100

Table B (Table 2 main text). Accuracy of pH test under cut-offs 1-9

pH cut-offs	Sensitivity (stomach)	Specificity (Lung)	Specificity (oesophagus)
1	0.015	1	1
2	0.257	1	1
3	0.39	1	1
4	0.544	1	0.985
5	0.68	1	0.948
5.5	0.743	1	0.81
6	0.81	0.996	0.792
7	0.914	0.91	0.492
8	0.991	0.337	0.225
9	1	0.004	0.068

Table C. Probability distributions across pH cut-offs (data for Fig 2)

Cut-offs	stomach_feed	lung_feed	oes_feed	delayed	Nofeed
1	1.1%	0.0%	0.0%	69.0%	30.0%
2	18.0%	0.0%	0.0%	52.0%	30.0%
3	27.3%	0.0%	0.0%	42.7%	30.0%
4	38.1%	0.0%	0.2%	31.9%	29.8%
5	47.6%	0.0%	0.8%	22.4%	29.2%
5.5	52.0%	0.0%	2.9%	18.0%	27.2%
6	56.7%	0.1%	3.1%	13.3%	26.8%
7	64.0%	1.4%	7.6%	6.0%	21.0%
8	69.4%	9.9%	11.6%	0.6%	8.4%
9	70.0%	14.9%	14.0%	0.0%	1.1%

Table D. Weighted scores with part-contributions from individual outcomes (data for Figure 3)

Cut-offs	stomach_feed	lung_feed	oes_feed	delayed	nofeed	Total
1	1.1	0.0	0.0	58.6	30.0	89.7
2	18.0	0.0	0.0	44.2	30.0	92.2
3	27.3	0.0	0.0	36.3	30.0	93.6
4	38.1	0.0	0.1	27.1	29.8	95.1
5	47.6	0.0	0.4	19.0	29.2	96.2
5.5	52.0	0.0	1.3	15.3	27.2	95.7
6	56.7	0.0	1.4	11.3	26.8	96.2
7	64.0	0.0	3.4	5.1	21.0	93.6
8	69.4	0.0	5.2	0.5	8.4	83.6
9	70.0	0.0	6.3	0.0	1.1	77.4

Correction: *Selecting pH cut-offs for the safe verification of nasogastric feeding tube placement: a decision analytical modelling approach*

Ni MZ, Huddy JR, Priest OH, *et al*. Selecting pH cut-offs for the safe verification of nasogastric feeding tube placement: a decision analytical modelling approach. *BMJ Open* 2017;7:e018128. doi: 10.1136/bmjopen-2017-018128

In the 'Outcomes of feeding decisions' section, the sentence: "For the remaining outcomes, we applied the analytic hierarchy process,[14]…"
should read: "For the remaining outcomes, we applied the Measuring Attractiveness by a Categorical Based Evaluation Technique (MACBETH) approach.[14]…"
Reference 14 should be: Bana e Costa CA, De Corte JM, Vansnick JC. "MACBETH". *International Journal of Information Technology and Decision Making* 2012;11:359–387.
Reference 15 should be: Bana e Costa CA, Chagas MP. A career choice problem: an example of how to use MACBETH to build a quantitative value model based on qualitative value judgments. *Eur J Operational Res* 2004;153:323–331.

BMJ Open 2018;**8**:e018128corr1. doi:10.1136/bmjopen-2017-018128corr1