ROYAL PHARMACEUTICAL SOCIETY

Research Paper

A pilot randomised controlled trial to assess the utility of an e-learning package that trains users in adverse drug reaction causality

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Abstract

Objectives Causality assessment of adverse drug reactions (ADRs) by healthcare professionals is often informal which can lead to inconsistencies in practice. The Liverpool Causality Assessment Tool (LCAT) offers a systematic approach. An interactive, web-based, e-learning package, the Liverpool ADR Causality Assessment e-learning Package (LACAeP), was designed to improve causality assessment using the LCAT. This study aimed to (1) get feedback on usability and usefulness on the LACAeP, identify areas for improvement and development, and generate data on effect size to inform a larger scale study; and (2) test the usability and usefulness of the LCAT.

Methods A pilot, single-blind, parallel-group, randomised controlled trial hosted by the University of Liverpool was undertaken. Participants were paediatric medical trainees at specialty training level 1+ within the Mersey and North-West England Deaneries. Participants were randomised (1 : 1) access to the LACAeP or no training. The primary efficacy outcome was score by correct classification, predefined by a multidisciplinary panel of experts. Following participation, feedback on both the LCAT and the LACAeP was obtained, via a built in survey, from participants.

Key findings Of 57 randomised, 35 completed the study. Feedback was mainly positive although areas for improvement were identified. Seventy-four per cent of participants found the LCAT easy to use and 78% found the LACAeP training useful. Sixty-one per cent would be unlikely to recommend the training. Scores ranged from 4 to 13 out of 20. The LACAeP increased scores by 1.3, but this was not significant.

Conclusions Improving the LACAeP before testing it in an appropriately powered trial, informed by the differences observed, is required. Rigorous evaluation will enable a quality resource that will be of value in healthcare professional training.

Introduction

Causality assessment of adverse drug reactions (ADRs) is formally undertaken by the pharmaceutical industry, regulators and researchers in clinical trials but rarely by clinicians. For example, regulatory authorities use causality assessment to assess spontaneous ADR reports to help with signal detection and inform risk–benefit decisions regarding medicines. Anecdotally, clinicians' assessment of ADR causality is gener-

ally done informally and sometimes subconsciously, which leads to variability in decision making, specifically in terms of when to alter drug therapy and reporting of ADRs.

There are many causality assessment tools available. The Naranjo tool is probably the most widely used worldwide.[1] In two recent large paediatric ADR studies, the Naranjo tool was found to be inadequate for ADR causality assessment and have poor reproducibility.[2,3] For instance, in the assessment of ADRs detected in children acutely admitted to hospi-

tal over a 12 month period,[2] inter-rater reliability using the Naranjo tool was poor. The investigators concluded that some of the questions in the tool were not appropriate, leading to a lack of sensitivity, with the overall score obtained being artificially lowered. This led to underestimation of the likelihood of an ADR. In addition, the weighting for each question within the Naranjo tool was not justified in the original publication. Subsequently, a new causality assessment tool, the Liverpool Causality Assessment Tool (LCAT, see Appendix S1), was developed, formally tested and internally validated.[4] This tool aimed to overcome the issues identified with the Naranjo tool, while (1) making it as easy, or easier, to use than the Naranjo tool and (2) maintaining the basic principles of causality assessment. Given that there is variability in clinical decision making around ADRs, we aimed to develop a means to disseminate this new approach of ADR causality assessment to practitioners. We developed an interactive, web-based e-learning package designed to improve assessment by individual practitioners: The Liverpool ADR Causality Assessment e-learning

Package (LACAeP) (see Box 1 for the attributes of this package). The use of e-learning packages for medical training has been shown to have good uptake and to be effective.[5]

The purpose of this pilot randomised controlled trial was to gain feedback on the usability and usefulness of the LCAT and the LACAeP. Feedback obtained for the latter will be used to identify areas for improvement and development. This trial also aimed to generate data on effect size enabling a larger hypothesis testing study to be conducted.

Methods

This was a pilot, single-blind, parallel group study conducted by the University of Liverpool. This pilot aimed to inform a larger scale study that would formally compare the effect that the LACAeP has on improving the consistency of assigning causality using the LCAT. This trial was supported by the Mersey Deanery and approved by their ethics committee. The

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Box 1   Attributes of the Liverpool ADR Causality Assessment e-learning Package

Content and navigation
- The e-learning package takes approximately 1 hour to complete
- The package contains interactive bespoke learning activities that require the user to interact with the software in order to continue, and will offer instructive feedback. The package includes:
  - An interactive diagram (based on the causality flowchart) that allows the use to zoom/pan/rollover to navigate the tool and to gain more information about items in the diagram
  - Logical question arrangement that underlines the sequential nature of the assessment tool
  - Real-life case studies: use real-life case studies to build a causality assessment by answering each of the questions on the LCAT in turn
  - Expert opinion: The package includes the availability of an 'expert' or panel of expert characters who can provide feedback and hints on decisions made by the user during the case studies exercise
- The interface contains a straightforward navigation system, with a short tutorial available explaining the functionality of all buttons in the interface
- A content menu and glossary are included
- The package has no formal assessment but will require users to complete interactive activities in order to progress

Reporting and user tracking
- The package bookmarks user progress between sessions and retain options chosen in completed activities
- Administrators of the package will be able to access the following information (via the Learning Management System where the package will be hosted):
  - The participant demographic details; the current progress of the participant; which activities they have undertaken; the outcome of each assessment made, i.e. what was the classification, what path did they take on the LCAT to get there and was the classification correct.
- At the end of the package, the user is asked to complete a feedback survey which assesses the usability and usefulness of the package and of the LCAT

Accessibility
- An e-book provides alternative test-based content for the package
- The package has been tested for Sharable Content Object Reference Model (SCORM) compliance with the ADL test suite
- The package complied with World Wide Web Consortium (W3C) web standards wherever possible
- Flash or Javascript-based content is accompanied by alternative html content

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study obtained organisational approval from NHS North of England, and permission was obtained from the Head of Schools at the North West and Mersey Deaneries to include trainees from that region.

Eligibility criteria were defined to ensure that improvements in classifications were attributed to the intervention and so that prior knowledge or experience of the participants could be managed as appropriate. In the UK, trainees in paediatrics progress through specialty training (ST) levels, ST 1 being the first year of training. Eligible participants were specialist trainees in paediatrics (ST level 1 and above) within the Mersey ($n = 165$) and North West Deaneries ($n = 214$). Trainees who had previously received formal training in causality assessment or had obtained a professional qualification in clinical pharmacology or pharmacy were excluded. Recruitment commenced on 15 January 2013 and continued until 18 February 2013. Eligible trainees were recruited through email and by advertising the trial on the Alder Hey Children's Hospital intranet and in workplaces. Invitations to participate were also included in induction packs for new doctors. All participants completed a consent form when they registered to participate and returned an electric or hard copy. Random allocation sequence was generated by computer by an independent statistician and was stratified by speciality training level.

Both the control and intervention arm received access to the LCAT to assist causality assessment. Participants in the intervention arm accessed an interactive training module with self-directed e-learning components that guided users when making causality assessments using the LCAT (LACAeP). Appendix S2 and S3 show illustrative screenshots of the introduction page and a worked example, respectively. Training was provided using five preloaded ADR case studies. Although trainees were aware of the allocated arm, data analysts were kept blinded to the allocation until after the analyses were finalised.

Each trainee was issued a username, password and web link which would allow access to the trial platform according to the randomisation schedule. Following any training, trainees in both arms were required to assess the same 20 ADR cases using the LCAT tool. These cases were randomly ordered to minimise contamination of results. The e-learning package was tested rigorously by the study team for functionality and content before the trial was opened. Several iterations of testing were undertaken until all aspects of the trial and package were suitable for a full pilot study to commence.

Participants were able to access the trial platform from 29th February to 15th March 2013. Email reminders were sent to those who had not completed the assessments during this period to improve completion rates. Trainees who completed the trial were given a training certificate for their training records and entered into a cash prize draw.

ADR case studies used both for post intervention assessment and within the training phase of the e-learning tool were taken from two previous ADR studies.[6,7] Within these studies, causality classification (unlikely, possible, probable or definite) was reached by consensus by a multidisciplinary panel of experts. For the purpose of this trial, these classifications were deemed to be the 'gold standard'. Case studies were selected using quota sampling methods from this cohort of cases to mirror the distribution of possible, probable, definite and unlikely ADRs observed in these studies. The number of correct classifications when compared against the gold standard was defined as the primary efficacy outcome. The maximum possible score for each trainee was 20. As a second efficacy outcome, the route taken on the LCAT flowchart was recorded to ensure that classifications were obtained following a route defined by a multidisciplinary panel of experts. Upon completing the intervention, trainees were encouraged to provide feedback on both LCAT and LACAeP (Appendix S4) by completing an optional survey, built in to the package, made up of a series of open and closed questions.

Statistical considerations

As this was a pilot study, intended to generate data on effect size to enable a larger hypothesis study to be conducted, no formal power analysis was completed prior to the trial. A pragmatic sample of 80 participants of the total 379 trainees at that time was considered a minimum requirement.

Closed items on the feedback questionnaire were analysed quantitatively and reported as count data and percentages. No formal qualitative analysis was conducted on open items which are presented verbatim. To ensure participants remained anonymous, each was given a unique participant number made up of a letter to indicate the intervention arm (A for the intervention arm and B for the control arm) and a sequential number within arm.

Overall series agreement postintervention was summarised for each treatment group, both overall and split by Speciality Training level (groups: 3 and below, 4 and above), using descriptive statistics, means with 95% confidence intervals (CI) or medians with an interquartile range if the scores was non-normally distributed. The effect of the intervention was summarised using descriptive statistics, means with 95% confidence intervals (or medians with an interquartile range if the scores was non-normally distributed).

All statistical analysis was carried out using the statistical software package R (version 2.13.2, R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org/).
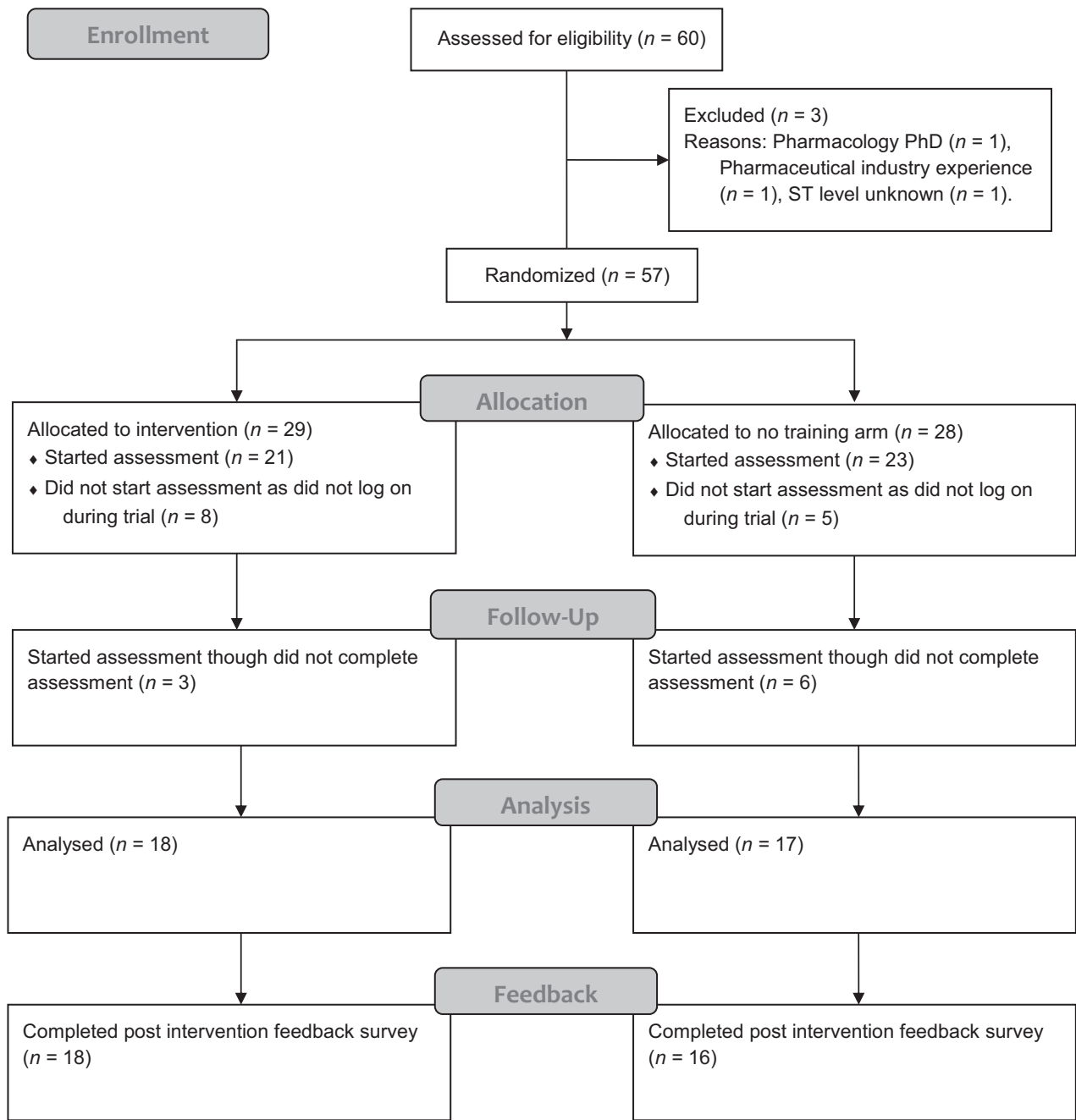
Figure 1 CONSORT 2010 Flow Diagram.

Results

Study population

Figure 1 illustrates the recruitment and retention of participants.

All paediatric trainees within the Mersey ($n = 165$) and North West ($n = 214$) Deanery were approached to

participate. Sixty participants provided consent during the recruitment phase; three were found to be ineligible upon screening; one had a pharmacology PhD, one had pharmaceutical industry experience, and the ST level was unknown for the third. The 57 remaining participants were randomised 1 : 1 to the two intervention arms. Twenty-nine participants were randomised to the intervention (training) arm, 13 were ST level 1–3, and 16 were ST level 4–8. Twenty-one (72%) of

Table 1 Summary statistics of categorical answers to feedback questionnaire

	Question	Answer	*n/N* (%)
LCAT feedback	How easy did you find the Adverse Drug Reaction Liverpool Causality Assessment Tool to use?	Very easy	1/34 (3)
		Easy	25/34 (74)
		Hard	6/34 (18)
		Very hard	2/34 (6)
	Would you use this tool in your role?	Yes	5/34 (15)
		Probably	20/34 (59)
		Probably not	9/34 (26)
		No	0/34 (0)
	How likely is it that you would recommend this tool to others?	Very likely	3/34 (9)
		Likely	20/34 (59)
		Unlikely	11/34 (32)
		Very unlikely	0/34 (0)
LACAeP feedback	How useful did you find the e-learning package?	Very useful	1/18 (6)
		Useful	13/18 (72)
		Useless	4/18 (22)
		Very useless	0/18 (0)
	Do you feel you have learnt anything new?	Yes	13/18 (72)
		No	5/18 (28)
	Do you feel able to put what you have learnt into practice as a result of this learning package?	Yes	12/18 (67)
		No	6/18 (33)
	Was the information in the course clear and easy to understand?	Fully	2/18 (11)
		Mostly	11/18 (61)
		A little	4/18 (22)
		Not at all	1/18 (6)
	How likely is it that you would recommend this e-learning package to others?	Very likely	0/18 (0)
		Likely	7/18 (39)
		Unlikely	11/18 (61)
		Very unlikely	0/18 (0)

those randomised to the intervention arm started the training package and assessment, and of those, 18 (62%) completed the assessment and the feedback questionnaire. Twenty-eight participants were randomised to receive no training, 13 were ST level 1–3 and 15 ST level 4–8. Twenty-three (82%) of those randomised to the control arm started the assessment, 17 (61%) completed the assessment, and 16 (57%) completed the feedback questionnaire.

Feedback on the LCAT and the LACAeP

Thirty-four participants provided feedback on the LCAT, and 18 provided feedback on the LACAeP. Results of the feedback questionnaire is given in Tables 1–4. The unique number system.

Feedback about the LCAT was generally positive. Three-quarters ($n = 26$, 76%, Table 1) of participants found the LCAT easy to use, approximately the same proportion ($n = 25$, 74%, Table 1) said that they would or would probably use the tool in their role, and two-thirds ($n = 23$, 68%, Table 1) stated that they would be likely or very likely to recommend the tool to others.

The majority of participants ($n = 14$, 78%, Table 1) felt that the e-learning package was useful, and many learned something from the package ($n = 13$, 72%, Table 1). Almost all of those that said that they had learnt something from the package felt that they could use what they have learnt in practice ($n = 12$, 92%, Table 1). The majority of participants in the intervention arm (11, 61%, Table 1) said that they would be unlikely to recommend the training to others. Four participants felt that the feedback was inadequate and more explanation was needed (A1, A5, A7 and A17, Table 4). A7 felt that the language was unhelpful and that the package needed work (Table 4), while A10 also thought that the package needed work due to its technical problems (Table 4).

Postintervention scores: by correct classification and correct route

Results of the intervention are given in Table 5. Primary outcome scores ranged from a minimum of 4 to a maximum of 13. The average score by correct classification was 9.22 (95% CI, 7.96 to 10.48) in the intervention arm and 7.88 in the control arm (95% CI, 6.76 to 9.00). The effect of the intervention was to increase the score by 1.34 on average (95% CI, −0.3 to 3.0). Participants in the intervention arm of ST level 1–3 and ST level 4–8 had scores on average of 9.14 (95% CI, 6.45 to 11.84) and 9.27 (95% CI, 7.65 to 10.89), respectively. Similarly, participants in the control arm that were ST level

Table 2 Free text responses to Q4 of the feedback survey: Please write any comments you might have about this tool

Participant	Response
A1	The idea of the tool is great however the area around probability of symptom being due to previous illness unclear particularly post op cases. Several areas needed further clarification. Also at times my instinctive answer was correct but the answer the tool gave me was wrong!
A2	Helpful in making you think through the timings of possible reactions and highlights need to document side effects in notes so that it is easier in retrospect to link cause and effect. Tool is quite 'wordy' and parts slightly confusing.
A3	Easy to use and follow
A4	Found it quite ambiguous at times, many of the cases are possible drug reactions but also possibly due to underlying conditions – I found that my answers were coming out as 'probable' ADR after using the tool, when my gut reaction without using the tool was often 'possible' ADR – the tool seemed to give me a response I didn't intend! Am not entirely sure of the value of this tool in practise.
A5	Fantastic idea but very difficult to use, terminology confusing
A7	I think the tool has its use in considering an approach to adverse drug reactions and I would use it educationally, and if an interest or research. It also allows one to make a standardised qualification of likelihood of causation which could be useful. However it is difficult to see the day to day ward use, as we are encouraged to report any ADR's on the yellow forms which is a quicker process. The tool could help in reflective practice but is quite unwieldy to use in a busy ward round. The way it was presented was very retrospective. Some parts were difficult to understand or qualify such as is there a mechanism for the ADR, and is there previous reported cases seemed to overlap a good deal. Reading BNF and clinical education and high index of suspicion remain best tools. There also remains little quantification for acceptable levels of ADR.
A13	I did not feel that the pre test information explained enough the process of assessing if the ADR was definite, probable or possible well enough. I feel that the learning module is helpful but I did not fully understand the processes behind answering the questions to ascertain how likely the ADR was e.g. if it is still an ADR if it is part of the known pharmacology of the drug, e.g. hypotension and captopril.
A16	Fairly easy to use, some of the questions are a bit ambiguous.
A17	I found the question 'is there any objective evidence supporting the ADR mechanism' difficult to understand and seemed to me to be the same as the question asking whether the adverse effect had been previously recognised with that drug. I think that question re objective evidence was explained once at the beginning of the learning tool but, having returned to the tool a week or so later, it seemed I could not access the material I had already read again
B1	If you process the information yourself to decide whether a SE was due to a drug reaction I expect you could come to the same conclusions therefore I do not understand what it is adding. The problem I found is having the underlying knowledge of how freq. such se are with particular drugs? Is it a normal event with the illness? I think errors regarding judging whether these symptoms are due the ADR lies with learning these things rather than coming to that conclusion. And so it would be better for me to learn these things to improve my ability to assess this rather than use this tool.
B3	The module would benefit from written instruction and an example case to work through prior to completing the module. Very hard modules. To learn from experience the module needs to give feedback.

1–3 and ST level 4–8 had an average score of 7.86 (95% CI, 5.39 to 10.33) and 7.90 (95% CI, 6.53 to 9.27).

The secondary outcome, score based on correct route, ranged from a minimum of 2 to a maximum of 8 out of 20 across both arms. The effect of the training package increased the score by correct route by 1.01 correct classifications (95% CI, −0.3 to 2.3).

Discussion

In our programme of research into ADRs in children, we have developed the LCAT, which has been internally validated.[4] In order to progress this further, we went on to develop an e-learning package (LACAeP), the utility of which was tested in this pilot trial. Before embarking on a larger trial, it is also important to assess the feedback received from the participants on the tools used. Feedback on the LCAT was mostly positive, with trainees indicating they had learnt something about ADR assessment from the tool and would use it in their clinical practice. The user feedback on both the LCAT and LACAeP has highlighted a number of areas that need to be addressed in the educational package such as giving more explanation of some of the terms used and the routes taken to determine causality.

Our data indicate that the LACAeP did not improve causality assessment in trainees, but participants who were given training by the LACAeP in causality assessment obtained a higher score by approximately 1.5 (out of 20) on average for correct classification (mean = 1.34, 95% CI, −0.3 to 3.0).

This was a pilot study to inform a main trial, and data were not available to inform a sample size calculation prior to recruitment. We selected a pragmatic sample size ($n = 80$) based on the eligible population, but we did not reach this recruitment target. However, the inclusion of 35 participants was adequate to fulfil the aims of this pilot study. We consider that a difference of 2 correctly classified ADRs out of 20 between the groups would be the minimum worthwhile clinical difference. Based on the results obtained and this

Table 3 Free text responses to Q7 of the feedback survey: Give an example of what you have learnt

Participant	Response
A1	What to consider when looking at ADR
A2	Highlighted ways to think about side effects of medications. To look carefully at timings of medications and effects when certain medications discontinued. Need to improve my pharmacological knowledge of side effects.
A3	How to interpret causality
A5	Awareness of drug reactions
A7	A framework for quantifying the assessment of ADR
A8	Systemic approach in suspected ADR
A10	Flow chart for causality
A11	More about ADR and way to assess
A13	I learnt what the process is to determine whether there is an adverse drug reaction.
A15	Adverse reactions are Common and should be considered at the bedside with new complications.
A18	To analyse a suspected adverse drug reaction in a systematic way

consideration, a trial with 90 participants (45 per group) is required to have adequate power to detect a true clinically relevant difference of 2.0 at the 5% significance level and 80% power.

There are three main strengths to this study. First, it shows that a novel trial design where participants can take part remotely is feasible and results in a reasonable proportion of participants completing the trial; overall, 61.4% of participants who were randomised completed the trial. Second, this pilot offers a template for easy expansion to a larger trial that will represent the package utility in a larger cohort, not only in size but also in geographical expansion to represent a wider proportion of trainees across the UK. A similar e-learning approach has been used by Gordon *et al.* who conducted an RCT to investigate the effectiveness of an e-learning course on paediatric prescribing[5] in North West England. This research attained a sample size of 206 from a pool of 1150 (17.9%) of which 113 completed the trial (54.9%). This is comparable with our sample size of 57 from a pool of 379 (15.0%) of

Table 4 Free text responses to Q11 of the feedback survey: Please write any comments about the e-learning package

Participant	Response
A1	The e-learning was very brief and just doing the examples with minimal explanation did not help with my decision making. Each area of the tool needed explanation with examples of what would be considered a positive answer and what would be considered a negative.
A2	E learning needs you to be able to repeat examples and repeat questions. Felt examples in assessment were too long and time consuming and need more like 10 questions for participants to be able to really give the time this deserves. As part of an induction process to hospital could be useful to give to doctors. Main drug reactions noted for patients are documented by GPs for antibiotics so need a tool that would be able to be used by them also. Highlights a need to learn more about medication side effects, awareness of importance of timing and documentation of reactions. Food for thought!
A3	More cases to practice with would have been useful before the assessment
A5	Learning package good but all of the practice questions I got incorrect & unsure where I went wrong.
A7	I did not feel the E-learning module was very good. I think there was far too little on the actual Causality pathway itself, not enough explanation or instruction in grey areas etc. I also found the language and affect used in the doctor/nurse part EXTREMELY CONDESCENDING and not very helpful. I am sure that some of the errors made in applying tool would be quite common, i.e. assuming antibiotics cause diarrhoea, or side effects of certain diseases, and it would be more helpful if there was some explanation of error, or why 'expert' choice was right or discussion of certain choices but there was not. While the idea was right I overall felt quite irritated by the tone of the learning module, and did not feel it actually guided me into how to make the decisions using ADRIC, simply stated I had made the wrong one without qualification. If I had paid to use this, or had to use it for CPD I would complain and not feel it was a useful tool. Needs a lot of work.
A10	Many technical problems with this learning platform – lost data, restarted without acknowledging previous questions answered. Content easy to understand and use.
A17	At first I found it confusing as to whether I was in the learning or assessment part of the package as the learning seemed like an assessment. I thought I had completed the package -unsuccessfully – after failing a 5 question assessment then to be taken into a 20 question assessment with no feedback in between re the questions out of the 5 questions that I got wrong. With no further 'teaching' in between the 5 question assessment and the 20 question assessment then there is unlikely to be any further improvement. I found the package showed me the tool but there was inadequate feedback to improve use. Occasionally the tool forced me into a conclusion which I did not agree with e.g. the oral candida had not yet got better in the case where this occurred following antibiotics (nystatin had only just been started so I would not expect it to have improved yet) however stating that it has not improved after stopping the abx leads to the conclusion being that the chance of ADR is only possible, when I feel in that case it is at least probable. NB in one case study the date a medication is discontinued is earlier than the date it was started.

Table 5 Outcome data for 35 participants split by group at trial closure

Outcome measure		Mean (95% CI) [minimum, maximum]		Effect (95% CI)
		Training (n = 18)	No training (n = 17)	
Primary				
Score by correct classification	Overall	9.22 (7.96, 10.48) [4, 13]	7.88 (6.76, 9.00) [4, 12]	1.34 (−0.3, 3.0)
	ST 1–3	9.14 (6.45, 11.84) [4, 13]	7.86 (5.39, 10.33) [5, 12]	
	ST 4–8	9.27 (7.65, 10.89) [6, 12]	7.90 (6.53, 9.27) [4, 10]	
Secondary				
Score by correct route	Overall	5.89 (5.07, 6.70) [2, 8]	4.88 (3.84, 5.92) [2, 8]	1.01 (−0.3, 2.3)
	ST 1–3	5.57 (3.44, 7.70) [2, 8]	5.29 (3.46, 7.11) [2, 8]	
	ST 4–8	6.09 (5.33, 6.85) [4, 8]	4.60 (3.08, 6.11) [2, 8]	

The maximum score is 20. CI, confidence interval; ST, specialty training level.

which 35 completed the assessment phase of the trial (59.5%). Third, the use of trainees as participants means that differences observed are indeed down to the intervention and not prior knowledge or experience.

This study also had limitations. First, only a postintervention assessment was undertaken stratifying by ST level. The inclusion of a preintervention assessment of all participants would have been the optimum approach to determining the impact of the intervention. However, the study relied on the availability of trainees to participate, so the design was adapted to minimise the time commitment required from participants, with the aim of enhancing participation rates. Second, and for the same reason, the study was held remotely hosted on a server such that trainees could participate in their own time, and so, the possibility of participants discussing their responses cannot be eradicated. However, the study management team did not consider this likely as participants consented to not discussing aspects of the trial with their peers. Third, as this trial relied on the participation of volunteers, the generalisability of the results may be questionable.

We have recently shown the importance of ADRs in paediatric medicine,[6–8] and previously in adult medicine.[2,3] The burden overall is very large leading to a great deal of morbidity in patients, occasional mortality, unnecessary investigations, increased length of stay in hospital and a huge cost burden. It is incumbent on all healthcare professionals to rec-

ognise ADRs and act accordingly (stop the drug and/or reduce the dose, and report the ADR to their own hospitals and regulatory authorities).[9] However, because ADRs can affect any bodily system, and can present in a multitude of ways, they are sometimes difficult to recognise, and even when recognised, there may be difficulties in assigning causality.[10] Many causality assessment tools have been developed;[11] more complicated tools may potentially be more accurate but extremely difficult to use in clinical practice. Our aim with the LCAT was to develop a user-friendly and easy-to-complete tool[4] which would improve assessment of ADRs and their reporting in daily clinical practice. The feedback from participants that they would use such a tool in their clinical practice is thus encouraging. Although this trial included medical trainees, the LCAT was developed by a multidisciplinary team[4] and has been used by nurses and pharmacists for the evaluation of causality in a research setting.[6,7] Therefore, we anticipate it being used by both medical and nonmedical professionals in a clinical setting. Nevertheless, the appropriate use of the tool needs an educational package such as the one developed as part of this study.

Conclusions

Feedback on the LCAT and LACAeP was mainly positive although we have identified areas of the LACAeP that need improving before conducting a trial to formally assess the

effectiveness of the tool. This study was not powered to detect a difference between allocation arms though preliminary findings show a non-significant improvement of 1.5 (out of 20) on average in the LACAeP arm. The data collected were sufficient to enable a formal sample size calculation for a main study, and thus, our next step will be to improve the educational tool and then test it again in an appropriately powered trial of 90 participants (*n* = 45 per group).

Declarations

Conflict of interest

All authors are members of the research team on the Adverse Drug Reactions in Children project. Outputs of this project included the Liverpool Causality Assessment Tool and the Liverpool ADR Causality Assessment e-Learning Package.

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Authors' contributions

MPir conceived the idea for the study. EJC, JJK, MPir, MPe, RLS and PW developed the protocol. EJC analysed the results. EJC, JJK, MPir, RLS and PW interpreted the results. EJC drafted the article with substantial support by JJK, JB and MPir. MPe, RLS and PW revised the paper critically. All authors approved the submitted version to be published. All Authors state that they had complete access to the study data that support the publication.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1 The Liverpool Causality Assessment Tool.
Appendix S2 The LACAeP home page.
Appendix S3 A LACAeP worked example.
Appendix S4 LCAT and LACAeP feedback survey.