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Virtual patient simulations for health professional education (Protocol)

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Virtual patient simulations for health professional education

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A B S T R A C T

This is the protocol for a review and there is no abstract. The objectives are as follows:

The objective of this review is to evaluate the effectiveness of virtual patient simulation as an educational intervention versus traditional learning, other types of e-Learning interventions and other forms of virtual patient simulation interventions for delivering pre-registration and post-registration healthcare professional education. We will primarily assess the impact of these interventions on learners' knowledge, skills and attitudes. Our secondary objective is to assess the cost-effectiveness of these interventions.

B A C K G R O U N D

Description of the problem

Health professional education is faced with many challenges worldwide. The push towards shorter hospital stays, specialisation of hospitals, new regulations on working hours and increased focus on patient safety diminishes traditional opportunities for training of health professionals through direct patient contact (Moalem 2009; Ramani 2008). Early education is often dominated by the theoretical and science-oriented presentation of knowledge without adequate connection to clinical practice (Dev 2014). Orienta-

tion towards specific disciplines leads to fragmentation of knowledge, mismatch of competences to needs and a limited view of the patient from a holistic perspective (Frenk 2010). Therefore, researchers have looked for methods that can be used to improve the relevance, increase the reach and accelerate the educational process for health professionals (Crisp 2008). The need to increase numbers and quality among the health workforce is especially visible in low-income countries, where needs for scaling up high-quality health education and the practice of educational innovations are imminent (Frenk 2010). Those already trained have equally important continuing educational needs. The 'knowledge explosion', notably demonstrated by exponential growth in the number of scientific reports in research databases (Lu 2011), leads to the constant need for updates of competence. Of concern is the currently slow incorporation of new knowledge into clinical practice (Davis 2003). Expectations regarding the quality of health services are increasing (Kohn 2000) - a fact that could potentially be addressed by provision of better training, with the help of modern health information technologies (Frenk 2010; Institute of Medicine 2010).

Description of the intervention

Application of information technology to education (e-Learning) has the potential to supplement or replace some of the teacher´ s functions and to create new educational opportunities, providing more time, flexible opportunities for learning and decreased distance barriers, which may help in scaling up health education for greater numbers of users (Ruiz 2006). e-Learning, which has been widely applied in health professional education to address various types of learning needs (Ellaway 2008; George 2014), provides the opportunity for increasingly self directed learners and introduces challenges associated with delivery of training to this audience (Sandars 2012). These challenges lead many to advocate a 'blended learning' approach, which combines use of technology with 'traditional' classroom and group activities and settings (Department of Health 2011). As the line between these approaches is blurred and as division of these approaches has been criticised (Oliver 2005). we will refer to pure e-Learning and blended learning by using the same term - 'e-Learning'. e-Learning technologies currently in use include tools such as virtual learning environments, digital game-based learning, virtual reality environments, e-assessment systems, psychomotor skills training and different types of simulations. We have conducted this review to focus on the simulation modality called 'virtual patients'. Parallel systematic reviews conducted in this Cochrane series will focus on other e-Learning modalities.

Virtual patients are defined as "interactive computer simulations of real-life clinical scenarios for the purpose of medical training, education, or assessment" (Ellaway 2006). This broad definition encompasses a great variety of systems that use different technologies and address various learning needs (Kononowicz 2015). The term 'virtual patients' appeared for the first time in the literature around 1990 to describe a simulation of haemodynamics used to teach physiology (Davis 1990). However, the idea of using computers to model the clinical encounter can be traced back to the 1960s (Bitzer 1966; De Dombal 1969; Harless 1971). The *patient story* is of central importance in virtual patient simulations presenting variations of signs and symptoms that model a medical condition (Posel 2009). The learner is cast into the active role of a healthcare provider who must make decisions about the type and order of clinical information acquired, differential diagnosis and management and follow-up of the patient. These behaviours have led scholars to suggest that virtual patients are primarily addressing learning needs in clinical reasoning (Cook 2009; Posel 2014). However, the influence of virtual patients on other training outcomes (Kraiger 1993) is also expected and has been reported in previous literature (Kononowicz 2015). In addition to presenting the content of simulations to the learner, virtual patient systems often provide tools for authoring cases, controlling access and tracking the progress of learners (Cendan 2012).

Virtual patient simulations have found their way into various medical school curricula. The exact adoption rate worldwide is difficult to estimate, but indications suggest it is substantial, and that interest is growing (Cendan 2012; Huang 2007; Schifferdecker 2012). A survey conducted in 2005 by Huang et al revealed that virtual patient simulations were in use at 26 out of 108 responding medical schools in the United States and Canada (Huang 2007). In 2016, Berman 2016 reported that the MedU collection of virtual patients was in use at 130 medical schools in those countries. A survey conducted in 2011 in North American dental schools showed that 63% of responding schools were using virtual patients for preclinical or clinical exercises (Cederberg 2012). It has been demonstrated that virtual patients can be introduced successfully as part of self study scenarios (Hege 2007), small group activity in problem-based learning (PBL) sessions (Poulton 2009; Poulton 2014) or post-graduate education (Moule 2015; Sperl-Hillen 2014) or can be used as a form of assessment (Forsberg 2011; Round 2009a).

How the intervention might work

Educational use of virtual patients may be understood through experiential learning theory (Kolb 1984; Yardley 2012). In accordance with this theoretical model of action and reflection, virtual patients expose learners to simulated clinical experiences, providing mechanisms for information gathering and clinical decision making in a safe zone (Edelbring 2011). Exposing the learner to many clinical cases can, according to current views on clinical reasoning (Norman 2005), support non-analytical diagnostic processes while acquainting learners with a standardised set of clinical conditions and cases, which may be common in the population but non-accessible in highly specialised teaching hospitals, or may occur rarely (Berman 2009). According to medical education programme accreditation standards in the United States and Canada, "*if a medical student does not encounter patients with a particular clinical condition (e.g., because it is seasonal), the medical student*

should be able to remedy the gap by a simulated experience (e.g., a standardized patient experience, an online or paper case)" (LCME 2011; Tworek 2010). Virtual patients also allow learners to follow a patient case over a long time span - an opportunity that is rarely possible during short clinical placements (Tan 2013). Their use is flexible in terms of time and place, without significant time constraints, as encountered for instance in standardised patient simulation (Stevens 2006). They are believed to bridge the gap between theoretical knowledge and clinical practice (Edelbring 2011). Virtual patients raise few ethical concerns in terms of addressing sensitive topics or dealing with strong emotions that are present in work with actual patients (Hooper 2015). The cost of producing virtual patients is constantly falling, making this a potentially cost-effective solution, and virtual patient cases are easy to author and update (Poulton 2011; Zary 2006). Virtual patient on-line collections open up an additional opportunity for practice-relevant, self directed training of the health workforce when access to traditional continuing medical education is limited (Dewhurst 2009). This applies not only to low-income countries and rural areas with limited numbers of healthcare educators (Bartiet 2015; Kiegaldie 2006), but to all contexts, for example, in cases of rare disease. In addition, this educational innovation is believed to provide opportunities for teacher training, thereby improving the quality of education (Dewhurst 2009; Round 2009b).

Possible risks and disadvantages of the intervention

Use of virtual patients may pose some risks. Virtual patients should be used not to replace but rather to complement contact with real patients (Edelbring 2011). Concerns include that training with virtual patients, especially with text-intensive cases, might result in less empathic learners (Kenny 2004). In addition, technology can still form a significant barrier to the ability to access learning content, even for younger generations of learners (Button 2013; Watson 2011). Virtual patients may be ineffective when technology per se drives the learning instead of addressing actual learning needs (Schifferdecker 2012). Virtual patient activities should be aligned with overall learning objectives and should be well integrated with existing educational activities (Berman 2009; Edelbring 2012); otherwise the new possibilities might be ignored or rejected or might create a learning overload.

Why it is important to do this review

This review will provide evidence relevant to various stakeholders in health professional education: to decision makers in relation to infrastructural investments and curricular changes; to teachers regarding integration of virtual patients into teaching activities; and to students in terms of selection of suitable types of e-Learning resources for self study. This evidence is consistent with UK

Department of Health recommendations stating: "Simulation, e-learning and other technologies have the potential to improve not only the quality of health and social care services but also patient outcomes, safety and experience. The decisions of healthcare, social care and education providers to use technological applications to support learning should be based on a clear understanding of the needs of learners and informed by the best available evidence" (Department of Health 2011, p.32). This review is important and timely in the face of regulations of accreditation bodies (e.g. the Liaison Committee on Medical Education in the United States and Canada), which propose that virtual and real clinical experiences are equal. Collected empirical evidence for this step has not yet entirely convinced clerkship directors (Tworek 2010). Berman 2009 showed that students' satisfaction and their perceptions of improved knowledge and skills whilst using virtual patients depend on reduction and elimination of other forms of learning (e.g. lectures, textbook readings). Yet, specific strategies on how to do this efficiently remain unclear. In fact, many questions remain regarding evidence of learning transfer to the real-life environment, efficient curriculum implementation strategies, self development versus customisation approaches, campus-based versus distance access to virtual patients and optimal types of educational settings and feedback (Botezatu 2010; Cendan 2012; Lang 2013; Tworek 2010). A recently published perspective (Berman 2016) on the role of virtual patients in the future of medical education suggests that "lack of sufficient evidence for the features of VPs that create effective learning remains a significant barrier for those sceptical educators who may have seen educational fads come and go in the past".

This review has been preceded by several narrative reviews (Cendan 2012; Cook 2009; Poulton 2011; Saleh 2010) and two systematic reviews with meta-analyses (Consorti 2012; Cook 2010). A BEME (Best Evidence Medical Education) review (Harden 1999) of virtual patients is in progress, for which no results have yet been published (Khalil 2013).

Our preliminary literature analysis shows that the number of studies including the term 'virtual patient' or 'virtual patients' has more than doubled on PubMed/Medline in comparison with available evidence provided in previous systematic reviews (February 2009 (Cook 2010) and July 2010 (Consorti 2012)). Thus, our review will update the evidence base with many studies not included in previous analyses.

In addition, the outcomes of our review may differ from the outcomes of previous reviews as the result of methodological differences between our study and those previously published. Less than half of the articles included in the review by Cook 2010 were randomised controlled trials. In the most recent review (Consorti 2012) and in the planned review by Khalil 2013, review authors focused only on pre-registration medical education, while not addressing other health professional groups or learners in post-registration training. Our approach is to take a stricter stance in selecting study designs with lesser risk of bias and thus greater cer-

tainty about the effects of interventions. At the same time, we will expand the scope of this review by including health-related disciplines other than medicine, such as nursing and midwifery, dentistry or pharmacy and others, and by including both pre-registration and post-registration courses to gain a modern outlook on health workforce education (Frenk 2010).

Previous meta-analyses were unanimous in showing positive effects of virtual patient interventions in comparison with non-interventions in studies available at the time, but they reported mixed results for comparisons between virtual patients and other types of interventions, or between variants of the same modality (Consorti 2012; Cook 2010). Our review will look more closely into potential reasons for these discrepancies by carrying out subgroup analyses to examine the effectiveness of virtual patient design features described in existing types of virtual patients (Huwendiek 2009; Kononowicz 2015). Furthermore, it does not appear that the impact of virtual patient interaction modalities, case progression mechanisms, forms of feedback and sources of educational content (locally authored or externally purchased cases) has been investigated in depth in the past (Cook 2010). We hypothesise that these factors related to case design, which constitute existing types of virtual patient design (Huwendiek 2009), might influence the outcome of the intervention.

While maintaining awareness and understanding of new approaches to virtual patient simulations, and by viewing them not just as learning artefacts but as more critical parts of situated learning activities (Ellaway 2011; Ellaway 2014), we will consider properties of the educational settings in which the virtual patient simulation was presented by including questions about whether it was a self study activity, a small-group activity (e.g. PBL session) or part of a large audience event. Furthermore, we will consider whether the intervention was part of the curriculum or was an add-on unrelated to any formal educational programme. Other conditions of interest include whether the intervention presented a single virtual patient simulation or a series of related cases. We will also look into financial aspects of the intervention and will include information on whether virtual patients were used in low-, middle- or high-income countries.

OBJECTIVES

The objective of this review is to evaluate the effectiveness of virtual patient simulation as an educational intervention versus traditional learning, other types of e-Learning interventions and other forms of virtual patient simulation interventions for delivering pre-registration and post-registration healthcare professional education. We will primarily assess the impact of these interventions on learners' knowledge, skills and attitudes. Our secondary objective is to assess the cost-effectiveness of these interventions.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) and cluster RCTs (cRCTs). We will exclude cross-over trials because of the high likelihood of carry-over effect.

Types of participants

We will include any study with participants enrolled in a pre-registration or post-registration health-related education or training programme. We will include candidates for and holders of the qualifications listed in the Health Field of Education and Training (091) of the International Standard Classification of Education (ISCEDF) United Nations Educational, Scientific, and Cultural Organization (UNESCO) Institute for Statistics 2013, except students of traditional, alternative and complementary medicine (UNESCO Institute for Statistics 2014). We will therefore include students from the following disciplines: dental studies, medicine, nursing and midwifery, medical diagnostic and treatment technology, therapy and rehabilitation and pharmacy.

We will follow the definition of pre-registration education or basic vocational training as stated in George 2014: "*any type of study leading to a qualification that: (i) is recognised by the relevant governmental or professional bodies of the country where the studies were conducted; and (ii) entitles the qualification-holder to apply for entry level positions in the healthcare workforce*". A post-registration health professional educational programme is defined as any type of study after a qualification that is recognised by relevant governmental or professional bodies that enables the qualification holder entry into or continuation of work in the healthcare workforce in the same or a more independent or senior role. This definition includes continuing medical education (CME) and continuing professional development (CPD) programmes that use virtual patients. By CME, we mean "*all educational activities which serve to maintain, develop, or increase the knowledge, skills, and professional performance and relationships that a physician uses to provide services for patients, the public, or the profession*" (ACCME 2015). CPD is defined as "*a range of learning activities through which health and care professionals maintain and develop throughout their career to ensure that they retain their capacity to practice safely, effectively and legally within their evolving scope of practice*" (HCPC 2015).

Types of interventions

Inclusion criteria

This review focuses on screen-based virtual patient simulations that form a computerised, dynamically unfolding representation of patient cases. A virtual patient simulation is introduced by a case description and might contain answers given by the patient, clinical data (e.g. laboratory results, medical images) and descriptions of patients' signs and symptoms. Of interest are representations of the patient as a whole rather than studies that focus on single parts of the body. In eligible simulations, learners will be cast in the role of healthcare providers (e.g. doctors, nurses, pharmacists) and will interact with the content, which will present the virtual patient and/or influence the way the scenario progresses/unfolds.

Exclusion criteria

We will exclude studies investigating interventions in which the user has a dynamic virtual representation and is able to move within an immersive virtual reality environment, as they will be covered by another review. Additionally, we will exclude studies in which interaction with the virtual patient is human-controlled (e.g. simulated e-mail correspondence or chat-room conversations, situations in which virtual patients are merely graphical representations (avatars) of a real person). We will also consider that simulations representing individual organs or biological systems without presenting the case as part of a clinically relevant scenario are outside the scope of this review. Our review will exclude systems requiring mannequins or other types of non-standard equipment such as haptic devices.

We will include in the review only studies in which virtual patients serve as the core element of the intervention. We will exclude studies in which virtual patients are just a small part of the intervention and those in which the influence of virtual patients is not evaluated separately. We will exclude two-arm RCTs comparing virtual patients with a control group not involved in any type of subject-related learning activity. The rationale for this decision is that previous meta-analyses have already shown a large positive effect when virtual patients were compared with no intervention (Cook 2010). We believe that a new analysis is unlikely to change this outcome.

Types of comparison

We intend to make the following comparisons of the target intervention.
- Virtual patient intervention versus traditional teaching.

- Virtual patient intervention complementary to traditional teaching versus traditional teaching.

- Virtual patient intervention versus other types of simulation intervention (e.g. standardised patients).

- Virtual patient intervention versus other types of e-Learning interventions.

- Virtual patient intervention versus other types of virtual patient intervention.

By traditional teaching, we mean learning activities that do not use information technologies as the main modality for presenting educational content or interacting with students. This includes lectures on campus, classroom-based and teacher-led lessons and hospital rounds. We do not regard mere use of electronic formats (e.g. PowerPoint, PDF) presented in a classroom or lecture hall by a human teacher as e-Learning but categorise these as traditional teaching.

Types of outcome measures

We will adapt the general classification of training evaluation proposed by Kraiger 1993, which divides learning outcomes into three major categories: cognitive (knowledge), skill-based and affective. Cognitive and skills competences will be further divided into competences often addressed in virtual patients in keeping with the virtual patient classification framework proposed by Kononowicz 2015: basic knowledge, clinical reasoning, team training, procedural and basic skills and patient communication. We will exclude from the outcomes psychomotor skills in health professions, as these are the topic of a separate review in the Cochrane series and do not fall within the main scope of virtual patients (Cook 2009). Additionally, we will use the training outcome hierarchy presented by Kirkpatrick 1998 to characterise the level of evaluation as reaction (satisfaction), learning, behaviour or results (patient outcomes).

Primary outcomes

- Knowledge and skills acquired by learners and measured by any validated or non-validated instruments.

- Learners' affective outcomes (attitudinal and motivational) measured by any validated or non-validated instruments or observations.

- Learners' reactions (i.e. satisfaction with the virtual patient intervention) measured by any validated or non-validated instruments.

Secondary outcomes

- Cost and cost-effectiveness (economic, teacher/learner time) of the intervention.

- Patient outcomes, in the case of interventions for postgraduate users (e.g. cholesterol levels in diabetes patients, number of reported medical errors, patient satisfaction).

- Adverse effects (e.g. learners who are less empathic to patients, unnecessary restrictions in access to real patients, technological barriers).

Search methods for identification of studies

Electronic searches

We will search the following databases.
- MEDLINE (via Ovid).
- EMBASE (via Elsevier).
- *The Cochrane Library* (via Wiley).
- PsycINFO (via Ovid).
- Educational Resource Information Centre (ERIC) (via Ovid).
- Cumulative Index to Nursing and Allied Health Literature (CINAHL) (via EBSCO).
- Web of Science Core Collection (via Thomson Reuters).

We will adapt the MEDLINE strategy and keywords presented in Appendix 1 for use with each of the databases above. We will search databases from the year 1990 to the present to highlight recent developments and will apply no language restrictions.

Searching other resources

For all included studies, we will search reference lists and will conduct author and citation searches. We will search lists of references from other identified relevant systematic reviews whilst running our electronic searches.

Data collection and analysis

Selection of studies

We will implement the search strategies described above and will import all identified references to EndNote reference manager software. We will remove duplicate records of the same reports. Two review authors will independently screen titles and abstracts to identify potentially included studies. This screening will be piloted between the review authors to ensure consistency in inclusion of relevant studies. We will retrieve full-text copies of articles deemed potentially relevant, and two review authors will independently assess the full text of retrieved articles for compliance with our inclusion and exclusion criteria. We will resolve disagreements through discussion between the two review authors. If no agreement can be reached, other review authors will act as arbiters. We will list studies that appeared to be relevant but were excluded at the full-text stage in the table *Characteristics of excluded studies*, where we will provide reasons for exclusion. Two review authors will verify the final list of included studies. We will document the study selection process in a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram (Liberati 2009).

Data extraction and management

Two review authors will independently extract and manage data for each of the included studies by using a structured data recording form. Both review authors will pilot data extraction to maximise consistency in the information extracted. We will check the consistency of the two extractions and will call on a third review author to arbitrate should differences in opinion arise. We will use the Cochrane Effective Practice and Organisation of Care (EPOC) data collection checklist (EPOC 2015) as the basis for the data extraction form and will modify it to fit the needs of this review. We will include the additional categories of educational setting (e.g. whether the activity was individual or was performed by a group of students, whether the intervention was part of a formal curriculum or was an extracurricular activity), virtual patient design features (e.g. navigation mode, feedback type (Huwendiek 2009)) and educational content options (e.g. number of virtual patient cases presented, source of virtual patient content).

Assessment of risk of bias in included studies

Two review authors will independently assess the methodological quality of each study by using the 'Risk of bias' tool described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will resolve disagreements by discussion, and if no agreement can be reached, we will consult a third review author. We will pilot the risk of bias assessment between review authors and will contact relevant study authors to request unclear or missing data. We will assess RCTs for risk of bias by using the following domains: random sequence generation, allocation sequence concealment, blinding of participants or personnel, blinding to outcome assessment, completeness of outcome data, selective outcome reporting and other sources of bias (e.g. baseline imbalance, inappropriate administration of an intervention, contamination). For cluster RCTs, we will also assess the risk of these additional biases: recruitment bias, baseline imbalance, loss of clusters, incorrect analysis and comparability with individually randomised trials. We will classify judgements concerning risk of bias for each study by using 'yes', 'no' or 'unclear' to indicate high, low or unclear risk of bias, respectively. We will include outcomes of the risk of bias assessment by preparing risk of bias tables, a graph and a narrative summary. We will summarise the results of this review in a 'Summary of findings' table, which we will use to grade the quality of the evidence.

Measures of treatment effect

For each continuous outcome, we will calculate the mean difference (MD) and 95% confidence interval (CI) for each study. When measurement scales differ across studies, we will normalise these and calculate standardised mean differences. For each dichotomous outcome, we will calculate the risk ratio (RR) and 95% CI for each study. Should outcomes be reported on both

dichotomous and continuous scales, we will pool data by re-expressing RRs as standardised mean differences (SMDs), using the method described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will assess whether significant changes in reported, relevant outcomes were noted in response to the virtual patient simulation intervention.

Unit of analysis issues

For cRCTs, we will extract data on whether the study accounted for unit of analysis error (i.e. incorrectly analysed each participant as an independent individual rather than as the unit to which he or she was randomised) (Higgins 2011). We will attain cluster size, number of clusters and intra-class correlation coefficients (ICCs) (or estimate equivalents) for each study, and we will inflate the variances for clustering accordingly.

Dealing with missing data

When we find that data are missing, we will contact the original investigators to ask for clarification or to request missing information. If we are unable to obtain missing data, we will use available data provided by study authors to assess risk of bias using the criterion 'incomplete outcome data'. We will not impute any missing outcome data. We will discuss in the review all assumptions and subsequent procedures used to deal with missing values.

Assessment of heterogeneity

We will compare the characteristics of included studies to identify content or methodological heterogeneity and to determine the feasibility of performing a meta-analysis. When we encounter substantial content or methodological heterogeneity across studies, we will not report a meta-analysis but instead will use a narrative approach to data synthesis. When meta-analysis is deemed appropriate, we will assess statistical heterogeneity by visually inspecting the scatter of individual study effect estimates via forest plots and through the calculated I^2 statistic (Higgins 2011). This statistic gives the percentage of variability in effect estimates that can be attributed to heterogeneity rather than to chance. We will consider a value greater than 50% to show substantial heterogeneity. If we observe statistical heterogeneity, we will perform subgroup and sensitivity analyses to further explore this.

Assessment of reporting biases

We will assess reporting bias qualitatively on the basis of characteristics of included studies (e.g. we identify for inclusion only small studies that indicate positive findings) and will do so if information that we obtain by contacting experts and authors or from studies suggests the possibility of relevant unpublished studies. If we find at least 10 RCTs with continuous variables expressed by mean differences, we will use the statistical test proposed by Egger 1997 to investigate funnel plot asymmetry. We will not use statistical tests to inspect intervention effects measured by standardised means, as the *Cochrane Handbook for Systematic Reviews of Interventions* recommends no reliable methods (Higgins 2011).

Data synthesis

We will assess participants, interventions and outcomes for comparability across studies, which is necessary for statistical pooling, as described above (assessment of heterogeneity). We will incorporate into our meta-analyses of individual RCTs cluster RCTs that provide a direct estimate of the required effect measure, obtained via analyses correctly accounting for unit of analysis error (e.g. multi-level model, variance components analysis, generalised estimating equations). We will seek statistical advice to determine whether the method used to account for the unit of analysis error is appropriate. We will enter cRCTs that do not account for unit of analysis errors into separate meta-analyses using a summary measurement for each cluster (*Cochrane Handbook for Systematic Reviews of Interventions*, 16.3.3 Methods of analysis for cluster-randomised trials, Higgins 2011).

For pooled data, we will select a meta-analysis model appropriate to the amount of heterogeneity noted between included studies. We will conduct the analysis according to guidance provided by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). When heterogeneity is minimal, we will use a fixed-effect method, and when heterogeneity is moderate, we will use a random-effects model. This provides a more conservative estimate of effect. If meta-analysis of included studies is feasible and appropriate, we will include all RCTs regardless of their sequence generation bias rating. However, In the event that meta-analysis proves infeasible, we will use a narrative approach to data synthesis.

When studies report more than one measure for each outcome, we will include in the meta-analysis the primary measure as defined by primary study authors. When a study reports an outcome at several time points, we will use the earliest one, as it is most likely to be related to the intervention. When no primary measure has been reported, we will calculate and use a mean value of all measures for the outcome.

"Summary of findings" table

We intend to prepare a 'Summary of findings' table to present results of the meta-analysis, in keeping with the methods described in Chapter 11 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011). We will present results of meta-analyses for major comparisons of the review and for each of the major primary outcomes, as well as potential adverse effects, as defined in the "Types of outcome measures" section. We will provide a source and a rationale for each assumed risk cited in the table. Two review authors will use GRADE (Grades of Rec-

ommendation, Assessment, Development and Evaluation Working Group) criteria to rank the quality of the evidence by using GRADEprofiler (GRADEpro) software (Schünemann 2011). If meta-analysis is not feasible, we will present results in a narrative "Summary of findings" table format, such as that used by Chan (Chan 2011; Cochrane 2014).

Subgroup analysis and investigation of heterogeneity

When possible, we will carry out the following subgroup analyses, stratified by:

- discipline (medicine, dental studies, nursing and midwifery, medical diagnostic and treatment technology, therapy and rehabilitation, pharmacy and other health professional disciplines);
- registration stage (pre-registration and post-registration interventions);
- income of the country (low- and middle-income countries vs high-income countries);
- integration into the curriculum (part of the curriculum or alternative teaching);
- collaboration setting (self directed, small group, large group);
- source of educational content provided by virtual patient (self developed, externally sourced (commercial), free repositories);
- number of exposed virtual patient cases (single case, series of cases);
- virtual patient case progression (linear, branched, free navigation, as defined in Cook 2010);
- communication with virtual patient (menu-driven, free-text (written), oral);
- feedback timing (in progress of the virtual patient simulation, post-activity summary);

- multi-media content of virtual patient cases (includes videos, does not include videos);
- place where the virtual patient simulation is accessed (designated room at the campus, distance access from other locations);
- language used in virtual patient (native/foreign to learners);
- target competency (basic knowledge, clinical reasoning, team training, patient communication); and
- level of evidence (reaction, learning, behaviour and results).

Sensitivity analysis

We will consider performing sensitivity analyses to explore the impact of risk of bias dimensions on overall outcomes of the review. We will remove from the analysis studies judged to be at high risk of bias after examination of individual study characteristics, according to the following filters.

- High risk of bias.
- Small number of participants.
- Unpublished results.
- Virtual patients as part of a composite intervention (mixed with other interventions).

ACKNOWLEDGEMENTS

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* *Indicates the major publication for the study*

A P P E N D I C E S

Appendix 1. Appendix 1. MEDLINE (Ovid) search strategy

1. exp education, professional/ not education, veterinary/
2. Education, Predental/
3. Education, Premedical/
4. exp Students, Health Occupations/
5. ((medic* or premedic* or dent* or laborator* or predent* or midwi?e* or nurs* or nutrition* or orthop* or podiat* or pharmac* or psycholog* or psychiatr* or health or healthcare or occupational therap* or physiotherap* or physical therap* or clinical orsurg* or radiolog* or obstetric* or gyn?ecolog* or orthodont* or An?esthesi* or Dermatolog* or Oncolog* or Rheumatolog* orNeurolog* or Patholog* or P?ediatric* or Cardiolog* or Urolog*) adj3 (student* or graduate* or undergraduate* or staff orpersonnel or practitioner* or clerk* or fellow* or internship* or residen* or educat* or train* or novice* or tutor*)).tw,kf.
6. or/1-5
7. Computer-Assisted Instruction/
8. exp Internet/
9. Computer Simulation/
10. Patient Simulation/
11. software/
12. Mobile Applications/
13. User-Computer Interface/
14. Video Games/
15. Web Browser/
16. Education, Distance/
17. Computers/
18. exp Microcomputers/
19. exp Cell Phones/
20. Games, Experimental/
21. exp Models, Anatomic/
22. Audiovisual Aids/
23. Educational Technology/
24. Electronic Mail/
25. exp Telemedicine/
26. Telenursing/

27. Telecommunications/
28. Webcasts/
29. exp Videoconferencing/
30. ((computer* or digital* or hybrid or blended or mixed mode or distance or remote* or electronic or mobile or online* orinteractiv* or multimedia or internet or web* or virtual* or game* or gaming or Videogame* or Videogaming) adj3 (classroom*or course* or educat* or instruct* or learn* or lecture* or simulat* or train* or teach* or tutor* or platform*)).tw,kf.
31. (Simulat* adj3 (course* or educat* or instruct* or learn* or train* or teach* or platform* or high-fidelity)).tw,kf.
32. e-learn*.tw,kf.
33. elearn*.tw,kf.
34. m-learn*.tw,kf.
35. mlearn*.tw,kf.
36. smartphone*.tw,kf.
37. smart-phone*.tw,kf.
38. ((mobile or cell) adj2 phone*).tw,kf.
39. iphone*.tw,kf.
40. android*.tw,kf.
41. ipad*.tw,kf.
42. Personal digital assistant*.tw,kf.
43. handheld computer*.tw,kf.
44. Mobile App?.tw,kf.
45. Mobile Application?.tw,kf.
46. webcast*.tw,kf.
47. webinar*.tw,kf.
48. flipped classroom*.tw,kf.
49. Serious game*.tw,kf.
50. Serious gaming.tw,kf.
51. Patient Simulat*.tw,kf.
52. Virtual patient*.tw,kf.
53. ((educat* or instruct* or learn* or simulat* or train* or teach* or interactiv*) adj2 technolog*).tw,kf.
54. Massive Open Online Course?.tw,kf.
55. Mooc?.tw,kf.
56. (Canvas network or Coursera or Coursesites or edx or Futurelearn or iversity or miriada x or moodle or novoed or openlearning or open2study or plato or spoc or udacity or pingpong).tw,kf.
57. or/7-5658. 6 and 57
59. Education.fs.
60. Education/
61. Teaching/
62. Learning/
63. exp Inservice Training/
64. Curriculum/
65. educat*.tw,kf.
66. learn*.tw,kf.
67. train*.tw,kf.
68. instruct*.tw,kf.
69. teach*.tw,kf.
70. or/59-69
71. Health Personnel/
72. exp Allied Health Personnel/
73. Anatomists/
74. "Coroners and Medical Examiners"/
75. exp Dental Staff/
76. exp Dentists/
77. Health Educators/

78. Infection Control Practitioners/
79. Medical Laboratory Personnel/
80. exp Medical Staff/
81. exp Nurses/
82. exp Nursing Staff/
83. Personnel, Hospital/
84. Pharmacists/
85. exp Physicians/
86. Physician*.tw,kf.
87. Doctor*.tw,kf.
88. Nurs*.tw,kf.
89. Surg*.tw,kf.
90. Health Personnel.tw,kf.
91. healthcare professional*.tw,kf.
92. radiolog*.tw,kf.
93. dentist*.tw,kf.
94. Pharmacist*.tw,kf.
95. Hospital Administrator*.tw,kf.
96. Podiatr*.tw,kf.
97. Psycholog*.tw,kf.
98. Psychiatr*.tw,kf.
99. An?esthesi*.tw,kf.
100. Clinician*.tw,kf.
101. Dermatolog*.tw,kf.
102. General practioner*.tw,kf.
103. Cardiolog*.tw,kf.
104. Oncolog*.tw,kf.
105. Rheumatolog*.tw,kf.
106. Neurolog*.tw,kf.
107. Patholog*.tw,kf.
108. P?ediatric*.tw,kf.
109. Physiotherap*.tw,kf.
110. Physical therap*.tw,kf.
111. Occupational therap*.tw,kf.
112. dieti?ian*.tw,kf.
113. Dietetic*.tw,kf.
114. midwi?e*.tw,kf.
115. nutrition*.tw,kf.
116. orthopti*.tw,kf.
117. obstetric*.tw,kf.
118. gyn?ecolog*.tw,kf.
119. orthodont*.tw,kf.
120. Urolog*.tw,kf.
121. or/71-120
122. Health Occupations/
123. exp Allied Health Occupations/
124. Biomedical Engineering/
125. Chiropractic/
126. exp Dentistry/
127. exp Evidence-Based Practice/
128. exp Medicine/
129. exp Nursing/
130. Dietetics/

131. Optometry/
132. Orthoptics/
133. exp Pharmacology/
134. exp Pharmacy/
135. Podiatry/
136. Psychology, Medical/
137. Serology/
138. Specialization/
139. exp Surgical Procedures, Operative/
140. exp Radiography/
141. or/122-140142. 121 or 141143. 57 and 70 and 142
144. Psychomotor Performance/
145. motor skills/
146. ((psychomotor or procedural or technical) adj3 skill*).tw,kf.
147. (psychomotor adj3 performance).tw,kf.
148. or/144-14
149. 6 and 148
150. 58 or 143 or 149151. limit 150 to yr="1990 -Current"

CONTRIBUTIONS OF AUTHORS

JC conceived the idea for the review. AK wrote the protocol with substantial contribution from LW. LTC provided methodological guidance, drafted some of the methodology related sections and critically revised the protocol. LW, CG, SE, NS, DD, IM, NS, JC, NZ provided comments on the protocol. We wish to acknowledge the help of Jayne Alfredsson , Monika Semwal and Anneliese Lilienthal at early stages of protocol writing.

DECLARATIONS OF INTEREST

Andrzej A. Kononowicz is author of an RCT on the topic of virtual patient simulation (Kononowicz 2012) and will refrain from deciding on its inclusion/exclusion or risk of bias assessment. The review authors have no other conflicts of interest to declare.

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