THE POTENTIAL VALUE OF THE INTERACTION BETWEEN LEARNER AND LEARNING MATERIAL IN A WEB-BASED SETTING TOWARDS THE ACQUISITION OF MEDICAL KNOWLEDGE

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To Professor Amélia Ferreira, for believing and inviting me to take this journey.

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To Isabel, my dear wife, for her kindness, love and support during all the hardships.

To this journey, for showing me who I am.

Foreword

I have always been a self-directed learner. As a child my favorite hobby - aside from playing video games with my brother - was building remote controlled Lego robots. At that time I learned elementary mechanics on my own to build evermore-complex systems. I also loved computers and the ability to manipulate them. When the Internet appeared, it provided me with uncountable tutorials on how to use computers to design media and print, record and synthesize music, develop realistic 3D models, among others, which I uncontrollably devoured every day.

Later, in medical school, I was able to put all these less orthodox competences at work to organize the III *Young European Scientist Meeting* and collaborate in research projects in the Biochemistry Department at the Medical School. These new challenges, in addition to the hardship of learning pharmacology, led me to explore software development.

It was an awakening. I was awed by the power to manipulate computers at will, and eagerly developed a system to study pharmacology. This later introduced me to Jorge Guimarães and his company - *ALERT Life Sciences Computing* - which started a project called *ALERT Student* just at the time I was taking my first steps in software development. I joined the ALERT Student project in 2010, in 2011 became the Head of the project, and together with Areo Saffarzadeh, at that time a medical student from University California Irvine, we started studying instructional design, cognitive load theory, spaced repetition, and test enhanced learning, hoping to apply these theories in medical education, through the development of a new version of the system.

That was when it all started. Two medical students trying to solve issues they faced in their own medical education. To me it was a journey of self-discovery, in many fields: medicine, education, psychology, computer science, software development, statistics, and later, machine learning and mathematics. As *a bonus* to this quest, I found the love of my life.

This journey defined who I am and who I want to become - an unorthodox bridge builder - bringing together disciplines that while interdependent, seem to expand in orthogonal directions within a multidimensional space that is hard but incredibly fascinating to map.

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Papers

Below follows the list of papers that were submitted to publication or that were published as part of this work.

Paper 1

A systematic review on computer based learning interventions in medical education - what are we looking for?

Tiago Taveira-Gomes, Patricia Ferreira, Isabel Taveira-Gomes, Milton Severo, Maria Amélia Ferreira

Journal of Medical Internet Research, under review, 2015

Paper 2

A novel collaborative e-learning platform for medical students - ALERT STUDENT

Tiago Taveira-Gomes, Areo Saffazadeh, Milton Severo, Jorge Guimarães, Maria Amélia Ferreira

BMC Medical Education, 2014 14:143 DOI: 10.1186/1472-6920-14-143

Paper 3

Characterization of medical students recall of factual knowledge using learning objects and repeated testing in a novel e-learning system

Tiago Taveira-Gomes, Rui Prado-Costa, Milton Severo, Maria Amélia Ferreira

BMC Medical Education, 2015 15:4 DOI: 10.1186/s12909-014-0275-0

Paper 4

The interaction between learner, learning material and objective assessment

Tiago Taveira-Gomes, Milton Severo, Maria Amélia Ferreira

The International Journal of Higher Education Research, under review, 2016

Resumo

A educação médica é uma área científica em constante atualização. A aprendizagem através de computador tem importante papel na educação médica; no entanto, existe um grande potencial para melhorar competências como a gestão da informação, e auto aprendizagem. Construímos uma plataforma centrada no estudante para desenvolvimento do conhecimento factual tendo em consideração os resultados de uma ampla revisão da literatura nesta área. Esta foi implementada sob a forma de uma aplicação *online* e permite estudar e avaliar o conhecimento através da segmentação do material de aprendizagem em pedaços curtos denominados *Flashcards*, construídos com base nos princípios de desenho instrucional, teoria da carga cognitiva, aprendizagem complementada por testes, julgamentos sobre aprendizagem e teoria dos objetos de aprendizagem. A plataforma foi bem classificada pelos estudantes. A ferramenta de *quiz* permitiu a medição de um julgamento de aprendizagem que, mais tarde, denominamos *recall accuracy*.

A plataforma foi utilizada para desenvolver um estudo controlado e randomizado com 96 estudantes de Medicina da Faculdade de Medicina da Universidade do Porto para validar o efeito de estudar *online* sobre o *recall accuracy*. Demonstrou que o *recall accuracy* aumenta ao longo das sessões de estudo e que o peso das fontes de variância difere em função de estudar ou não estudar. Essa informação pode ser utilizada para caraterizar a dificuldade do material de aprendizagem. Realizou-se um estudo para avaliar a interação entre o estudante e o material de aprendizagem utilizando o braço experimental do estudo anterior. Demonstrou-se a existência de relações importantes entre a duração de estudo, *recall accuracy* e padrões de sublinhado que permitiam prever resultados da avaliação objetiva utilizando questões de escolha múltipla em ambiente experimental.

Finalmente, refletimos sobre esses resultados, delineando estratégias para a implementação de sistemas aplicados a situações reais, sugerindo que este tipo de dados capturados em tempo real podem informar estudantes, professores e sistemas de inteligência artificial para adaptar as estratégias de aprendizagem aos objetivos de aprendizagem e dificuldades específicas de cada estudante, que poderão constituir assim um passo para a melhoria da gestão da informação e da auto-aprendizagem em medicina.

Abstract

Medical education is a scientific field in constant update. Computer based learning currently takes an important role in medical education. However, the potential for improving competencies such as information management and self-directed learning through this approach can be greatly enriched.

A student-centered system for the acquisition of factual knowledge was built taking into consideration the results of a thorough review of the literature in this field. It was implemented as an online platform allowing study and quizzing by splitting the learning material in small chunks that we named *Flashcards*, which took into consideration principles from instructional design, cognitive load theory, spaced-repetition, test enhanced learning, judgments of learning and learning object theory. The platform was well rated by students. The quiz feature allowed the assessment of a judgment of learning that was later named *recall accuracy*.

The platform was used to conduct a randomized controlled study with 96 medical students from the Faculty of Medicine of the University of Porto to validate the ability to study online and its effect on *recall accuracy*. It demonstrated that *recall accuracy* increases along study sessions and that the weight of its sources of variance differs according to the setting. This information can be used to characterize the difficulty of the learning material.

Afterwards, the interaction between learner and learning material was assessed using the experimental arm of the prior study. It was shown that there are important relationships between study duration, *recall accuracy* and text highlight patterns that predict the outcomes in objective assessment using multiple choice questions in a laboratory setting.

Finally, we reflected upon these findings, delineating an approach for implementation of similar systems in a real world scenario, suggesting that this kind of data collected in real-time can inform learners, teachers and intelligent instructional systems to adapt learning strategies to the desired learning outcomes and specific learner difficulties. Such leap would constitute an important step towards better medical information management and self-directed learning.

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General Introduction

Medical education is a scientific field in constant change. The advances that it has achieved in terms of educational approaches, instructional software and revision in knowledge are vast. Computer based learning (CBL) has been one of the enablers of this transition, namely due to the possibility of information sharing and asynchronous collaboration, that have spawned a new set of learning environments and experiences.

This transition accounts for one the competences to be held by the XXI century physician named information management [1,2], which regards the ability to search, identify and integrate relevant information that can be further used for critical reasoning in clinical practice [3] and is currently one of the most compelling challenges facing medical doctors. This competence can be attained in part through self-directed learning - the ability of continuously improve one's own knowledge deliberately and on it's own [4,5]. This is a fundamental skill for future physicians to cope with the changing landscape of medical knowledge that has not been lessened by the technological advances in education. Rather, with the increase in medical knowledge, these tools have been used to compactly distribute information, in compressed and more demanding courses, much of which is readily forgotten [6]. The progress in medical knowledge is mainly confined to factual knowledge, which is the foundation for the development of clinical reasoning and competence [7].

The advances made in terms of cognitive psychology that yielded insightful recommendations on how to design instructional interventions [8] to effectively deal with cognitive load [9] and boost learning, among other research lines in psychology, hold promise to be put into practice in online learning platforms to aid in this quest. Since the major advances in software platforms are usually carried in niche areas [10–17], little has been done in terms of creating a learner-centered computer supported collaborative learning system (CSCL), able to empower learners with tools to improve study management, track performance and boost learning, despite the aforementioned evidence from cognitive psychology [18–22]. Some studies have been carried in spacing study sessions to boost learning - spaced repetition [23] - and in using questions to boost learning [7,24].

Another important problem yet to be addressed refers to the redundancy in medical information as the learner progresses in the curriculum, which is indirectly acknowledged in literature regarding curriculum planning in medical education [25–27]. The learner will revisit the same concepts many times, but usually on a new media substrate. While revisiting is desired since it reinforces knowledge schemata, it would be enriching that recorded information about the interaction between the learner and learning content is made available when revisiting in the future and in a different learning setting [19]. That information could not only inform the learner, but also the teacher, in a way that may allow a better understanding of the needs of each student, and tailor synchronous and asynchronous activities in order to address these needs.

Developing such a system and recording such metrics, during undergraduate, post-graduate and continuous medical education, would consist of an important step towards the improvement of self-directed learning in the sense that learners would become empowered to make judgments about their own learning and manage their study in ways that would not be feasible without CBL.

Main Objectives

This work aims to understand the general picture of how medical education has evolved in terms of computer based learning (CBL), and build a study instrument that embodies the principles that have been put forth to empower learners in the medical setting. It focuses on the development of a learner-centered software platform dealing with the problem of acquiring factual knowledge, and the study of the interaction between learner and learning material in a controlled setting, from which metrics to inform the tailoring of learning activities may be determined.

Thus, we intend to derive knowledge to build intelligent systems using learner and learning content interaction data to aid the learner in the task of information management, by meeting the following objectives:

a) To provide a general overview of research being done in CBL in medical education;
b) To develop a platform that implements relevant instructional design and cognitive load principles enabling online study, measurement of judgments of learning and rich interaction with the learning material;
c) To characterize the effect of online study in a judgment of learning named *recall accuracy* and assess its reliability and construct validity;
d) To characterize the interaction between student and learning content with respect to study duration, *recall accuracy* and text highlighting.

Each objective corresponded to a task, namely:

Task 1 - A systematic review of the literature regarding CBL in medical education

This task intended to inform the authors about the state of the art in CBL in medical education, and inform of flaws and recommendations for further study that should be embodied in the design of the software platform and intervention.

Task 2 - Specification, design and implementation of a computer supported collaborative learning system

This task intended to create a study instrument according to the results of the prior review regarding principles of instructional design, cognitive lead theory, learning object theory and judgments of learning. This was the base instrument upon which became possible to collect data about the behavior of a judgment of learning (initially referred to as *perception of knowledge* and later named *recall accuracy),* and measure the interaction between the students and the learning materials. This platform was also built with the intention to deliver objective assessment to the students using multiple-choice questions.

Task 3 - Randomized controlled study conducted to characterize student *recall accuracy* along study sessions using the platform

This study aimed at assessing the reliability and construct validity of *recall accuracy* namely by considering how it evolves along sessions and how online study affects it.

Task 4 - Characterization of the interaction between learner and learning content

This study intended to explore the interplay among, study duration, *recall accuracy*, text highlighting and how these factors affected the outcome of objective assessment using multiple-choice questions. This was the final step from which the strongest evidence could be derived with respect to the usefulness of measuring *recall accuracy* to affect knowledge acquisition.

Finally, we discussed further steps to take in order to empower medical students through advanced web-based instruction to enhance self-directed learning and the specific difficulties that we anticipated while trying to do so.

Results - PAPERS

This section presents the papers written in connection to each of the four tasks. The papers were re-formatted according to the style of this document and the references of each paper were re-indexed and presented in the *References* chapter - *p.113*.

PAPER 1

A systematic review on computer based learning interventions in medical education - what are we looking for? *

Introduction

Medical education is a field that reflects the constant revision of medical knowledge, educational technology and teaching strategies. For over a century a shift from the traditional instructor-centered model into a learner-centered model has been taking place in education in general [28] and medical education in particular,[29–31] a shift in which the learner has greater control over the learning methodology and the teacher becomes a facilitator of the learning process.[32] This transition was required, since advances in medical knowledge and changes in how healthcare is delivered have weighted on the teaching responsibilities of medical schools.[33] The need to review and incorporate emerging fields in the curricula required medical schools to look for means to deliver education with less reliance on instructor availability.[33] The broadening of the setting in which healthcare is delivered - from hospital to community setting - prompted adaptation of these venues to ensure education could be delivered remotely.[34] Digital technology enabled the development of computer-based learning (CBL), and later web-based learning (WBL) methodologies, which enabled medical schools to cope with the pressing changes in the medical education landscape.[31]

The increasing interest and pervasiveness of CBL and WBL in the field was accompanied by research on how such methods compared to traditional instruction on a wide spectrum of different educational endpoints, leading Friedman in 1994 to reflect on *the research we should be doing* regarding CBL.[35] In 2000, Adler *et al.* quantified medical literature on CBL, concluding that researchers should focus on which settings are CBL methods most adequate, rather than comparing them with the classroom setting.[36] According to Adler and Friedman, provided that CBL offers tools that cannot be replicated by other means, the

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* Journal of Medical Internet Research, under review, 2015

typical classroom setting cannot be considered a sound comparison group, as it undermines study internal validity.[36,37]

The apparent lack of accommodation of this recommendation in subsequent studies, that kept growing in variety of setting and design, led Cook *et al.* in 2005 to establish an agenda for research in medical education, suggesting once again that CBL research should look at relative benefits between different CBL methods.[38] In 2008, a broad meta-analysis regarding the effects of CBL in health sciences education was conducted, showing that CBL interventions are generally better than no intervention, and marginally superior to traditional instruction.[39] Studies using multimedia learning content and student-feedback reported the best results.[39]

While the issue around CBL arose nearly 22 years ago, and over 8 years have passed since Cook *et al.* meta-analysis, comparative research between CBL methods is still a contemporary problem.[40] It is relevant to study what features of educational software are researchers reporting, how interventions are being conducted, what endpoints are being measured, and whether prior recommendations are informing current research. To our knowledge, since 2008 this issue has not been looked again in broad and systematic way, and is yet to be carried specifically in medical education, as opposed to heath sciences education in general.

Thus, this work aims to identify reports of CBL software and CBL interventions, specifically in medical education, and systematically describe features of educational software, instructional design considerations, as well as the design, setting and endpoints of CBL interventions. Finally, we intend to summarize these findings through the determination of subgroups of similar papers regarding educational software features and intervention endpoints, and understand the extent to which prior work is being taken into consideration through the analysis of the reference and citation network of these publications.

Methods

Study eligibility

We included medical education studies written in English regarding the development of educational software, interventions using educational software, or both. We considered interventions during training or clinical practice that reported effects on learner attitudes, knowledge and skills, as well as records of online activity. We included pretest-posttest studies, randomized and non-randomized studies, parallel group and crossover studies, and studies in which a software-based intervention was added to other instructional methods.[39]

We did not include studies that exclusively surveyed perceptions and attitudes of students or professionals towards CBL in general, or studies that solely described course structure or reported how CBL strategies were implemented in medical schools.

Study identification

We designed a strategy to search PubMed, Scopus, Web of Science and EBSCO databases. Search terms included *Medical education*, *Medical students*, *E-learning*, *Blended learning*, *Information technology*, *Instructional design*, *Software*, *Web-based platform*, among other terms. The exact queries are available in Appendix 1. We established an 11-year period from 1st Jan 2003 to 31st Dec 2013. Final database search was performed on the 5th January 2015.

Study selection

Working independently and in duplicate, reviewers (PF, ITG) screened all paper titles and abstracts, and in full text all potentially eligible abstracts, abstracts with disagreement, or with insufficient information. Independently and in duplicate the reviewers considered the eligibility of studies in full text with adequate chance adjusted inter rater agreement (.92 by intra-class correlation using *psych* package [41] for the *R* programming language).

Study analysis

Data extraction

The data extraction and reporting were conducted in accordance to the PRISM guidelines for systematic review.[42,43] Reviewers abstracted data from each eligible study using a standardized data abstraction spreadsheet. The spreadsheet was developed, tested and revised based on the review results of the first 30 assessed papers. Conflicts were resolved by consensus with a third reviewer (TTG). We abstracted information on publication year and country, study design, software used, instruction delivery method, CBL interactive features, CBL sharing features, instructional design principles, participant number and training level, study duration, type of comparison between groups, instruments used for assessment of knowledge, attitudes and skills, correlations between study endpoints, and records of student online activity. For all categories, information was based on explicit report of the variables of interest, except for instructional design principles, which the researchers inferred from descriptions and figures using standardized criteria, whenever there were no explicit references.[8] In addition, papers that reported interventions were graded using the MERSQI scale for paper reporting quality in medical education.[44,45]

Data analysis

Data manipulation and preparation for statistical analysis was performed using *Numpy* [46] and *Pandas* [47] libraries for the *Python* language. Latent class analysis (LCA) was used to uncover distinct homogeneous groups of articles from the study population, considering that the performance of each paper in a set of papers is explained by a categorical latent variable with *k* classes, commonly called *latent classes*.[48] Interpretation of the model was based on paper profiles for each category, obtained from the probability of observing each variable on each class. The number of latent classes was defined according to the *Bayesian Information Criterion* (BIC), which is a measurement of model fit that penalizes models with many parameters, preventing model overfit.[48] Starting from a model with one class and increasing one class at a time, the best model was chosen as the one with best interpretability and lowest BIC.[48] We created two latent class models, one taking into consideration educational software variables, and another one taking into consideration intervention endpoint variables. Variables reported in less than 2% of the studies were not used to compute the classes. Statistical analysis was conducted using the *R* programming language. Class models were fitted using the *poLCA* package.[49] Summary panels were created using the *ggplot2* package.[50]

Reference and citation analysis

Data extraction

References of the included papers were obtained from Scopus using *Digital Object Identifiers* (DOIs). Citations of the included papers were obtained from Google Scholar by searching for each of the articles by title and abstracting the papers on the *cited by* link. This procedure was carried using a script built with the *webdriver* library [51] for the

JavaScript programming language. In order to uniquely identify every reference and citation, a duplicate match and removal procedure was performed by looking for similar matches of the title and authors names using the *fuzzywuzzy* library [52] for the *Python* programming language. Two references or citations were considered to be the same when the matching probability was grater than 85%. Matching probability was computed using *Levenshtein* string distance.[53]

Data analysis

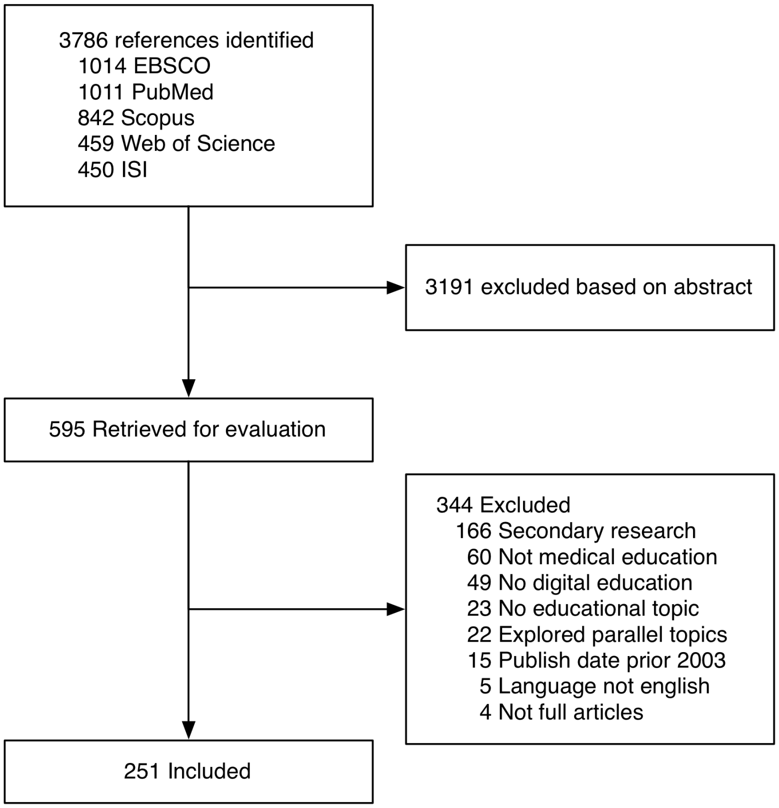
We analyzed the distribution of the total number of references and citations for each paper, and grouped papers based on whether they had one or more references or citations in common. We looked for relationship between the number of citations and interventions comparing traditional instruction to CBL methods, or CBL *versus* CBL. In addition, we assessed whether the number of related papers was associated with *Educational software* latent classes, *Intervention endpoint* latent classes and with specific references to Cook *et al.* reviews on CBL.[38,39,54] Linear models adjusted for article publication year were used for this purpose. Statistical analysis was performed using the *R* language. Article network plots were constructed using the *graph-tool* library for the *Python* programming language.[55] Distribution plots were created using the *ggplot2* package [50] the *R* programming language.

Results

Study eligibility, identification and selection

The search strategy yielded 3786 citations, from which 595 potentially eligible articles were identified based on the abstract. From these, 344 articles were excluded based on a full-text review. In total 251 articles were included and analyzed. Overall mean ICC was .98. Specific ICC values are reported for variables that were not always explicitly present and relied on reviewer judgment, or when lower than .95. Details regarding the trial flow are available in Figure 1.

Figure 1 - Trial flow



Study analysis

The number of publications has been rising along the years, from 13 publications in 2003 - 2004 (5%), to 82 in 2012 - 2013 (33%). Medical schools in Germany, UK and USA have contributed with more than 30 papers each between 2003 and 2013. Medical Schools from Australia, Canada and Spain have contributed with more than 10 papers each. Contributions per medical school nationality are presented in **Error! Reference source not found.**.

A total of 38 different software platforms were reported, which were listed in Appendix 2. From these, 13 plaftorms were general educational platforms (34%), the most frequently used being Moodle [10,56–62] and Blackboard [63–71] mentioned in 8 papers and WebCT [16,72–76] mentioned in 6 papers. The online virtual world Second Life [77,78] has been mentioned in 2 papers. 9 additional platforms are mentioned once.

25 out of the 38 platforms were developed specifically for medical education (66%). From these platforms, 4 were virtual patient simulators that were mentioned in 3 papers each - *CASUS*,[79–82] *HINTS*,[83–85] *INMEDEA* [86–88] and finally *Web-SP.*[12,60,89] One learning management system named *MEFANET* was mentioned in 2 papers.[90,91]

Figure 2 - Articles published per country of medical school

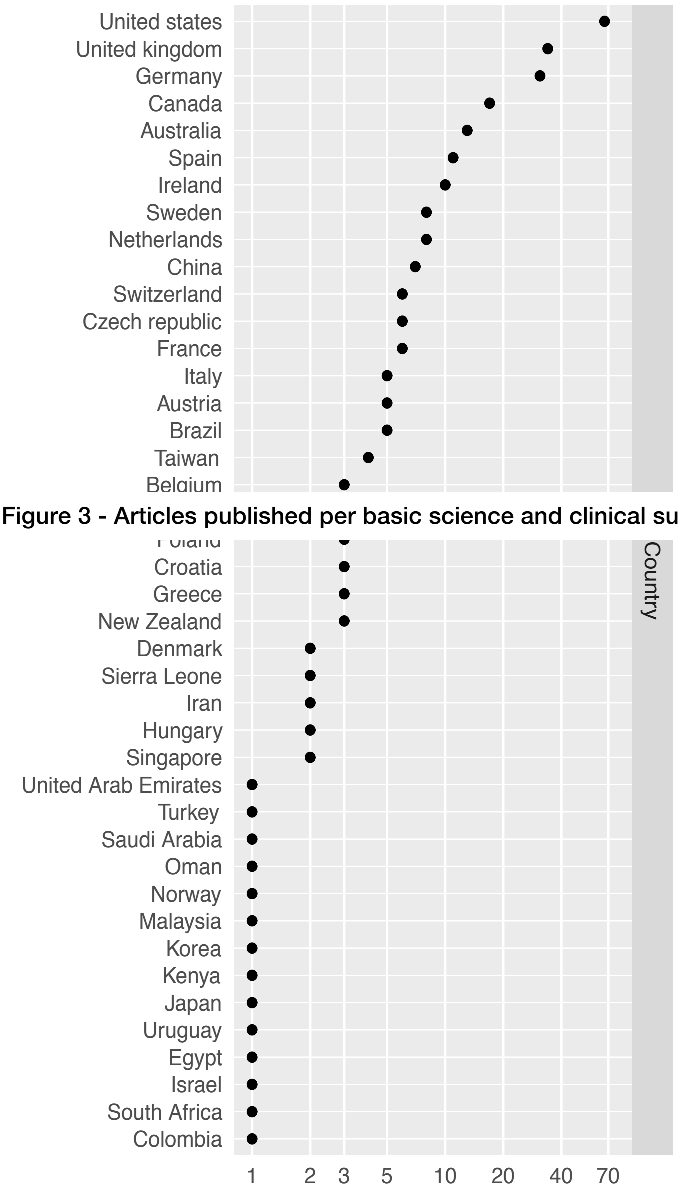


Figure 3 - Articles published per basic science and clinical subject

The article count axis is presented in logarithmic scale for better data representation.

Finally there were 20 other platforms mentioned once. These platforms were either learning management systems or virtual patient simulators. From these, 4 systems were specialized in medical fields namely, a serious 3D game named *EMSAVE*,[92] a system for learning electrocardiography named *EKGtolkning*,[93] a platform entitled *Radiology Teacher*[94] and a virtual microscope named *MyMiCROscope*.[95] 146 studies took into consideration clinical specialties (58,1%), 70 studies regarded basic sciences (28%) and 36 studies were conducted on surgical specialties (14%). Radiology was the clinical specialty with most studies - 23 articles (9%) - followed by pediatrics with 13 (5%). The basic science subjects with most publications were anatomy with 18 articles (7%) and physiology with 9 articles (4%). The most studied surgical specialties were urology with 12 studies (5%) and general surgery with 10 (4%). There is at least a paper in most basic sciences and medical specialties, as depicted in Error! Reference source not found..

Web based learning software

From the 251 studies assessed, 113 of those studies reported settings in which blended learning was used (45%, ICC=.98) while the remaining 138 reported e-learning environments (55%, ICC=.99). Results for this section are summarized in Figure 4, which depicts the percentage of studies and relative contribution of each of the learning software variables to the software latent classes described below.

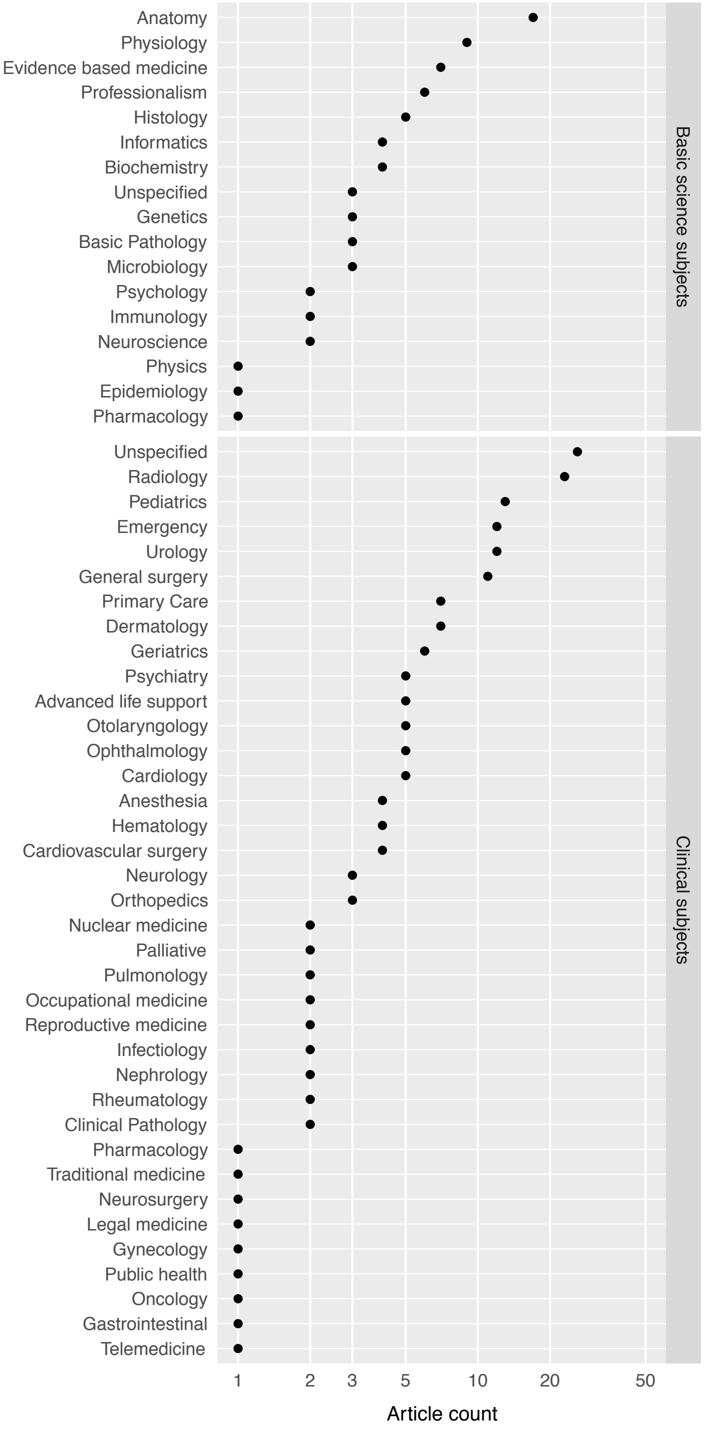
Platform type

217 studies employed websites (86.5%), 16 used videoconference (6%) and 16 other studies used email (6%). 9 used podcasts (4%) or portfolios (4%). Wikis were reported in 8 studies (3%, ICC=.90), as well as CDs (3%, ICC=.83), and blogs were reported in 6 studies (2%). E-books were reported in 4 studies (2%), and audience response systems in 3 papers (1%).

Media support

174 studies provided content in text format (69.3%), and 138 studies used images (55.0%). Video was reported in 99 studies (39%), and diagrams in

Figure 3 - Articles published per basic science and clinical subject



The article count axis is presented in logarithmic scale for better data representation.

94 studies (37%). Audio files were used in 85 papers (34%), and animations were reported in 28 articles (11%).

Interacting with content

138 studies reported unspecified interactive features (55.0%). The software provided feedback to the learner on 103 studies (41.0%). 103 papers reported quizzes (41.0%), 66 reported clinical cases (26%), 54 described simulations (22%) and 45 tracked learner performance (18%). Features allowing collaboration between learners and instructors were reported in 38 studies (15%). Virtual patients were reported in 18 studies (7%) and games were described in 10 studies (4%).

Sharing content

47 studies reported communication and content sharing through discussion forums (19%), 27 studies reported the ability store documents (11%), and 7 studies used instant messaging communication systems (3%). Calendars were reported in 7 studies (3%).

Instructional design principles

The media principle was apparent in 74 studies (29%, ICC=.94), followed by the segmenting principle in 34 studies (15%, ICC=.98) and the contiguity principle in 23 studies (9%, ICC=1.00). The pre-training principle was identified in 16 studies (6%, ICC=.98), and the signaling principle in 13 studies (5%, ICC=.97). The coherence principle was identified in 10 studies (4%, ICC=.97), and the modality principle in 9 studies (4%, ICC=1.00). Finally, the personalization and voice principles were identified in 5 studies each (2%, ICC=1.00).

Latent classes

We considered 4 distinct classes for educational software, according to the model statistics reported in Table i. Class 1 was composed by 115 studies (46%), mostly about website-based interactive systems presenting content using text, images, audio and video. Student feedback features were frequently described, namely quizzes and clinical cases. Aside from the Multimedia principle, instructional design considerations were rarely present. Class 1 was thus labeled *Multimedia*.

Class 2 was composed by 64 studies (26%) using websites, and to a smaller extent e-mail, to deliver instructional content mostly in the form of text. Interactive features were less frequent than in Class 1 and instructional design considerations were scarce. Class 2 was thus labeled *Text*.

Class 3 was composed by 64 studies (22%) making use of websites and videoconference platforms to provide video and audio content. Interactivity and instructional design principles were nearly inexistent. Class 3 was thus labeled *Web-conference*.

Class 4 contained 18 studies (7%) mostly regarding web-based interactive multimedia applications in which the use of multiple instructional principles was frequent. Class 4 was thus labeled *Instructional*. The four right columns on Figure 4 depict the composition of each class and the relative weight of each variable on class assignment.

Table i - Latent class analysis per number of latent classes for educational software

Class number	Log Likelihood	Parameter number	BIC
1 class	-2340	21	4797
2 classes	-2017	43	4273
3 classes	-1923	65	4207
4 classes	**-1866**	**87**	**4214**
5 classes	-1854	109	4230

Bold typeface indicates the number of classes selected for the educational software model. Decision was based on picking the model with the best interpretability and lowest BIC.

Interventions

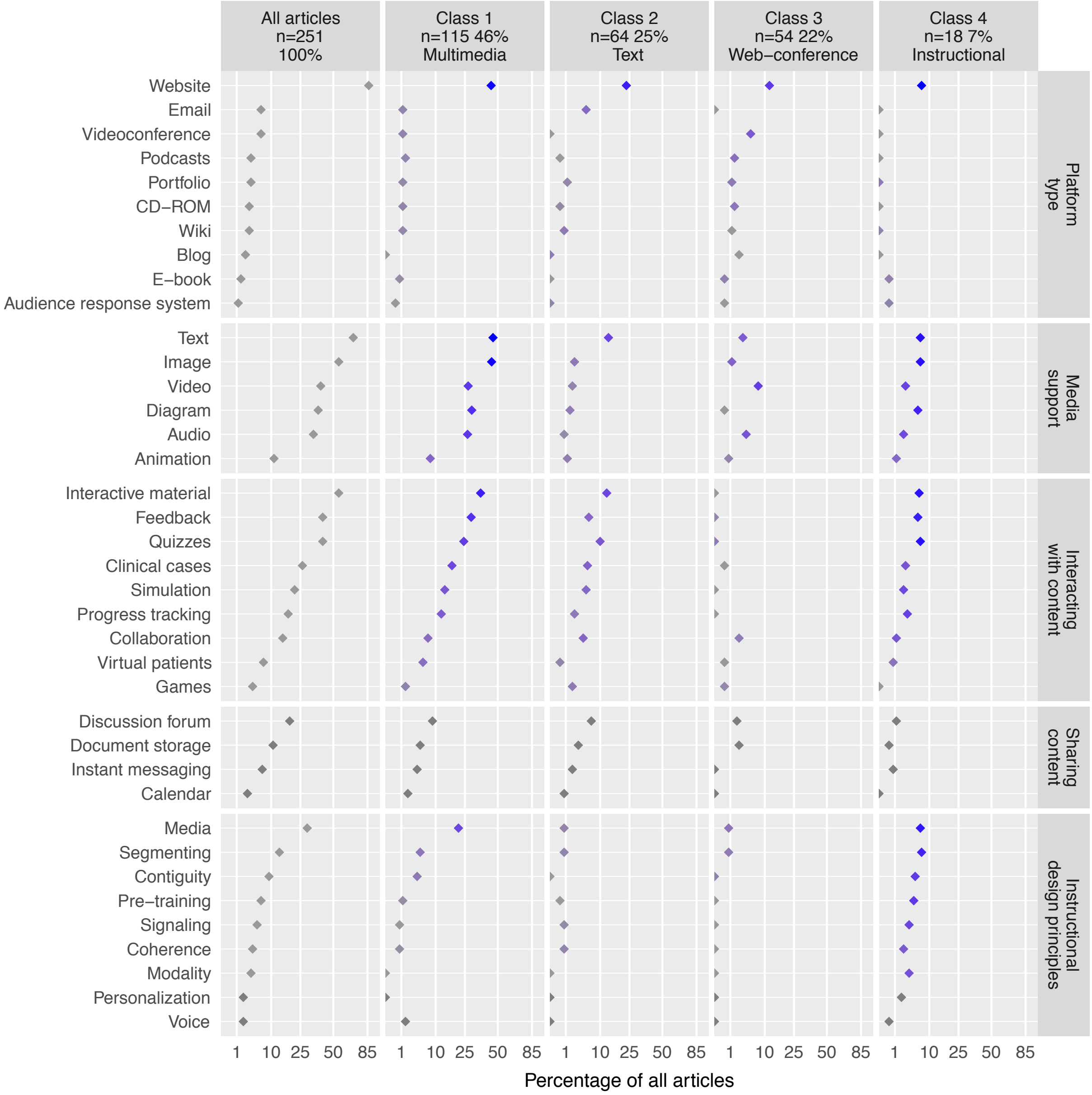
From the 251 papers included in this study we identified 212 conducting interventions on the endpoints of interest (84.5%). Results for this section are summarized in Figure 5, which depicts the percentage of studies for each intervention characteristic, and the relative contribution of intervention endpoint variables to the *Intervention endpoint* latent class described below.

Study design and study sample

81 studies out of 212 were conducted using medical students from pre-clinical years (38%) and 56 studies employed students during clinical rotations (26%). 32 studies were conducted on specialist medical doctors (15%), and 31 studies were conducted on medical residents (15%).

55 interventions were carried with less than 50 subjects (26%), 97 studies had a sample size ranging between 50 - 200 subjects (46%), and 59 studies were conducted with more than 200 students (28%).

Figure 4 - Prevalence of articles per educational software feature and software latent class



Horizontal axis ranges between 0 and 100 on a squared root scale. Point color specifies the probability of assigning a paper to each class based on the presence of each variable. From the listed variables, those present in more than 2% of all articles were used to determine the educational software latent classes.

54 studies were conducted during less than one week (24%), 90 papers reported interventions lasting between one week and 3 months (42%) and 50 studies were conducted for more than 3 months (24%).

84 studies repeatedly tested subjects in a pre-post approach (40%), and 93 made use of control groups (44%). 61 studies were randomized (29%) and 37 studies employed subjects from more than one institution (17%). 40 studies compared different CBL approaches (19%), while 53 studies compared CBL with traditional methods (25%).

Mean MERSQI score for the assessed studies was 9.54 (SD=1.84).

Conducted comparisons between groups

28 studies out of 212 regarded controlled interventions between blended learning approaches and traditional lectures (13%), while 11 studies compared e-learning approaches with traditional lectures (5%). 8 studies compared spaced repetition *versus* bolus learning (4%), and 7 studies compared e-learning *versus* no intervention (3%). 5 studies compared the usage of 3D models *versus* 2D images (2%). A multitude of other comparisons were performed, namely exploratory *versus* blocked learning approaches,[96–98] complex *versus* simple user interfaces,[96,99,100] immediate *versus* delayed completing of lectures in CBL systems,[14] multimedia *versus* text on CBL media,[96,101–103] among others. Appendix 3 lists the different comparison groups identified for each of the 212 papers reporting interventions.

Knowledge endpoint

Knowledge outcomes were assessed in 120 out of 212 papers (56.6%). Objective knowledge assessment was carried using multiple-choice questions (MCQs) on 98 out of 120 studies (82%). 9 papers used free text fields (7%) and 8 papers used open-ended questions (OEQs) (7%, ICC=.89). 5 studies used True/False questions (4%). Judgments of knowledge were collected using Likert scales in 27 papers (23%). Researchers directly assessed knowledge in 9 studies (8%). 31 studies were conducted in a laboratory setting (26%). Knowledge assessment was part of a final exam in 39 papers (33%), and in 9 studies assessment was part of a formative assessment (8%). 90 papers reported that interventions improved knowledge acquisition (75%) while 27 studies failed to find significant effects (22%). 3 multicenter randomized-controlled trials reported that interventions did not positively affect knowledge acquisition (3%).[12,104,105]

Attitude endpoint

172 out of 212 studies assessed student attitudes (81.1%). 163 of the 172 studies employed Likert scales (94.7%), and 34 used free-text fields (20%). In 8 papers researchers assessed subject attitudes directly (5%). 29 studies were conducted in a laboratory setting (17%) and 16 studies made use of focus groups (10%). 161 papers found positive attitudes towards interventions (75.9%), 8 papers found neutral attitudes (5%), while 3 reported negative attitudes (2%).[106–108]

Skill endpoint

31 papers assessed subject skills (15%). In 26 of these studies skills were assessed directly by researchers (84%) and in 16 studies assessment was conducted in a laboratory setting (55%). 24 papers found positive effects on skills acquisition (77%). 5 papers reported that the interventions had no effect on assessed skills (16%) and 2 papers reported that the intervention had negative effects (6%).[104,108]

Online activity endpoint

Online activity was measured in 76 out of 212 studies (30%). 46 of these studies measured total logins to the system (60%), 39 measured time spent in the system (51%), 18 measured the number of times students used specific learning tools (24%). 16 studies measured the number of student posts (21%), and 12 measured the number of times students viewed the learning materials (16%). 41 papers found no relationship between activity patterns and learning outcomes (54%). 34 studies reported increased activity to have positive effects on learning outcomes (45%) while 1 paper found a negative effect (1%).[12]

Intervention endpoint latent classes

We considered 3 distinct classes to group the 212 studies taking into consideration intervention endpoint variables. Class 1 contained 175 papers assessing knowledge and attitudes (82.5%). Class 1 was labeled *Knowledge & Attitude*. Class 2 represented 25 intervention studies (12%). In addition to assessing knowledge and attitudes, papers in this class also assessed skills. Class 2 was labeled *Knowledge, Attitude & Skill*. Class 3 represented 12 studies that assessed online activity, specifically through number of posts and number of reads (7%). Attitudes were always assessed but knowledge and skill assessment were nearly absent. Class 3 was labeled *Online activity*.

Table ii reports model statistics for the *Intervention endpoint* latent classes, and Figure 5 depicts the prevalence of articles per intervention feature and intervention endpoint latent class.

Table ii - Latent class analysis per number of latent classes for intervention endpoints

Class number	Log Likelihood	Parameter number	BIC
1 class	-1631	22	3382
2 classes	-1510	45	3265
3 classes	**-1451**	**68**	**3270**
4 classes	-1424	91	3268

Bold typeface indicates the number of classes for the intervention endpoint model. Decision was based on picking the model with the best interpretability and the lowest BIC.

Reported correlations between assessment outcomes

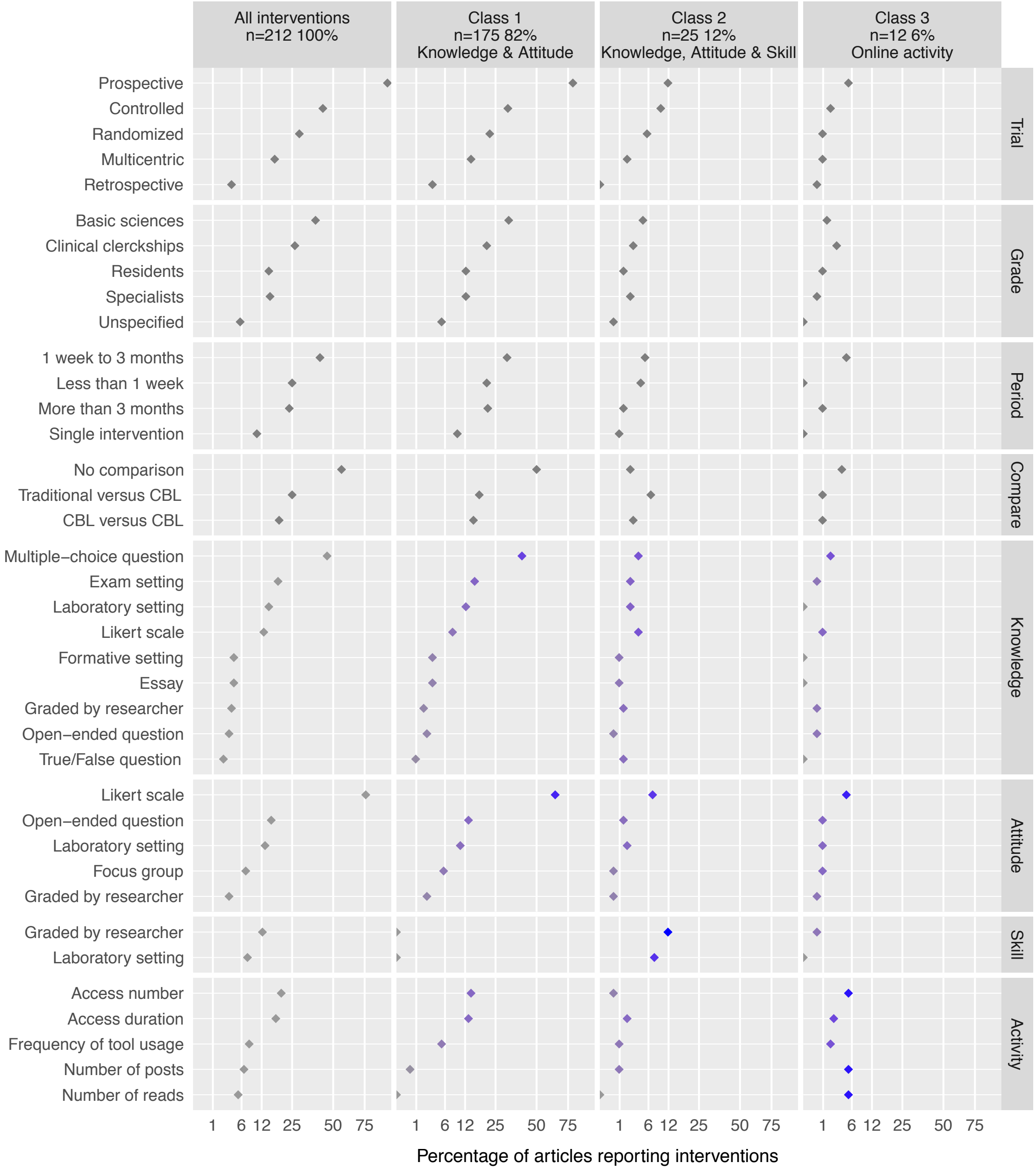
25 out of 212 studies correlated different variables with knowledge outcomes (12%). One study correlated system interactivity with knowledge scores and concluded that lower levels of interactivity benefit knowledge acquisition.[96] Correlations between knowledge gains and time using online platforms were also sought. These were found to be positive in four papers,[74,109–111] and neutral in one paper.[99] One paper described a modest positive correlation between increased knowledge scores on the learning system and an increase in exam scores.[112] Increased learning platform usage has been correlated positively with knowledge acquisition in 5 papers,[112–116] while 4 papers found no association.[71,117–119] Other papers found positive relationships between knowledge and the number of posts in online forums,[120,121] and comprehensiveness of student study materials.[122] Regarding attitudes, 2 papers found a mild positive correlation between judgments of knowledge and knowledge score.[15,123] Other correlations were assessed, namely confidence and skill,[124] study duration and skill,[125] and study duration and learning style,[126] but failed to reach statistical significance.

Reference and citation network analysis

Reference and citations analysis

References and citations were obtained for 227 out of the 251 papers included in this review (90.4%). Mean number of references was 26.12 (SD=17.41). In total, the abstracted papers held 4010 references to other papers. The most referenced articles were from Ruiz *et al.*[31] Cook *et al.,*[39] Chumley *et al.,*[127] Greenhalgh *et al.,*[128] Ward *et al.,*[129] Muller *et al.*[130] and Ellaway *et al.*.[131] Mean number of paper citations was 14.43 (SD=12.12). More than half of the references were common to various abstracted papers, while a smaller percentage of studies held independent sets of references.

Figure 5 - Prevalence of articles per intervention feature and intervention endpoint latent class



Horizontal axis ranges between 0 and 100 on a squared root scale. Point color specifies the probability of assigning a paper to each class based on the presence of each variable. Only variables regarding assessment of knowledge, attitudes, skills and online activity (the four last panels) were used to determine intervention endpoint latent classes. CBL- Computer-based learning.

Related article analysis

169 out of 227 papers had at least one reference or citation in common with other abstracted papers (74.4%), and were thus said to be related, as depicted in Figure 6. 58 articles were not related to any other studies since they did not share references or citations (26%). The mean number of related studies for each paper was 4.74 (SD=5.42).

Citation differences between intervention group type

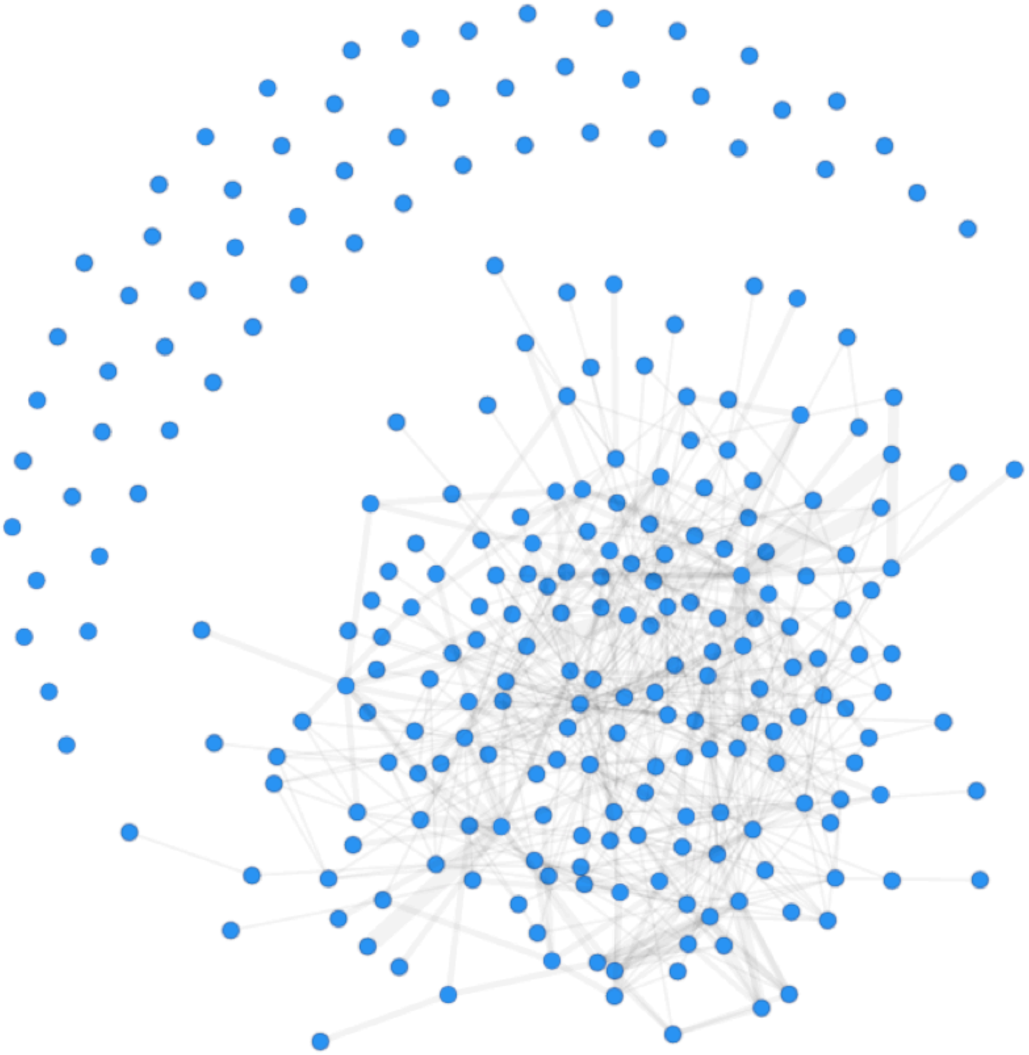
Studies comparing traditional to CBL methods were cited a mean of 11.92 times (CI=[9.31, 14.6]). Studies comparing different CBL methods were cited a mean of 16.71 times, which was statistically significant (CI=[13.95, 20.17], *P*=.02). This result is depicted in Figure 7.

Associations to latent classes and Cook *et al.* review

Regarding educational software latent classes, papers in the *Multimedia* class had a mean of 3.95 related studies (CI=[2.99, 4.91]), while the *Text* class had a mean of 4.98 (CI=[3.69, 6.26], *P*=.19). Papers from the *Web-conference* class had a mean of 5.02 relationships to other studies (CI=[3.64, 6.45], *P*=.22) and papers in the *Instructional* class had a statistically significant mean of 6.78 studies (CI=[4.37, 9.20], *P*=.03). Regarding the *Intervention endpoint* latent classes, papers in the *Knowledge & Attitude* class had a mean of 2.63 related studies (CI=[1.46, 3.80]) and the *Knowledge, Attitude & Skill* class had a mean of 2.88 studies, reaching statistically significance *versus* the former class (CI=[.71, 5.04], *P*=.04). Papers from the *Online activity* class had a mean of 6.78 related studies (CI=[3.60, 9.96], *P*=.03), also reaching a significant value when compared to the *Knowledge & Attitude* class.

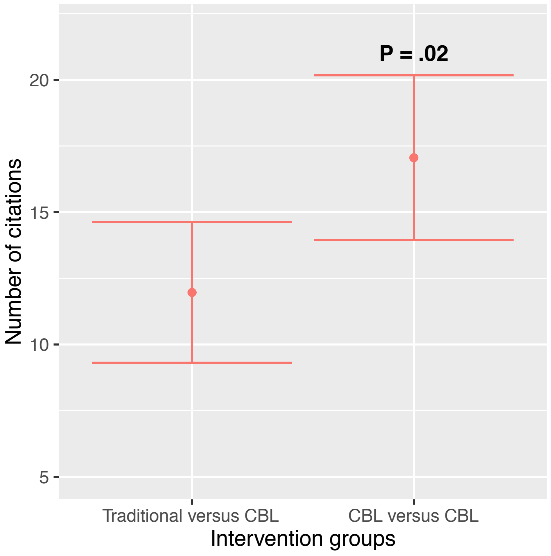
Finally, articles not citing Cook *et al.* work had a mean related article count of 4.42 (CI=[3.74, 5.11]), while articles citing Cook *et al.* had a mean count of 6.64 (CI=[4.61, 8.68], *P*=.04), which was significantly different. Complete results for this section are plotted in Figure 8.

Figure 6 - Relationships between articles included in this review



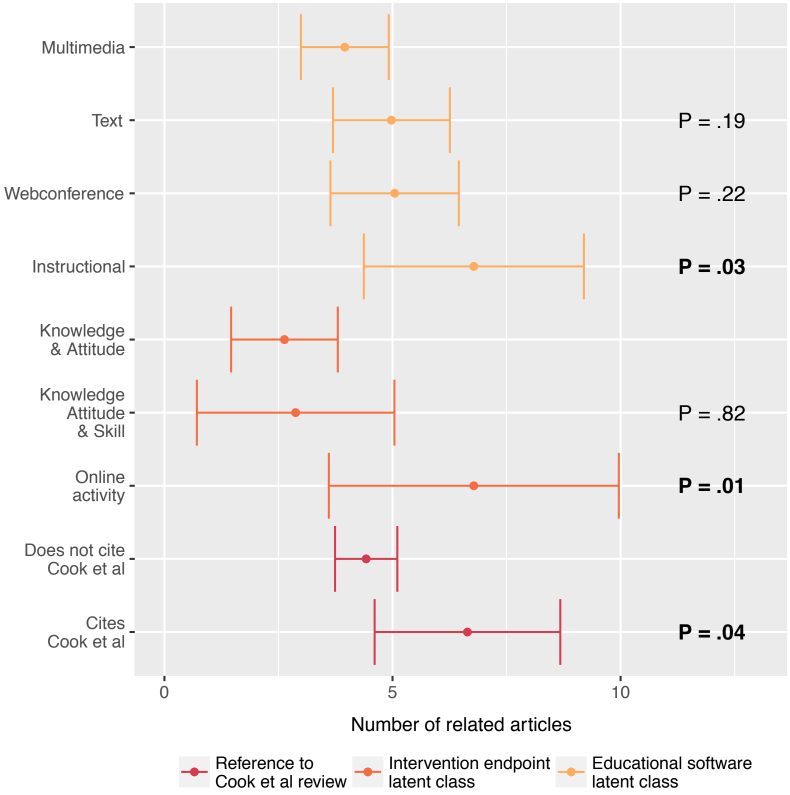
Nodes indicate papers included in this study. Links between nodes indicate that studies hold common references and citations between themselves. The width of the link indicates the number of common studies, which ranged from 1 to 5. Nearly over a quarter of the studies had no common references or citations. Only 227 out of the 251 the studies were included on this analysis due to missing information (90.4%).

Figure 7 - Mean citation number between different intervention group types



Mean citation number differences between traditional versus computer-based learning (CBL) and CBL versus CBL adjusted for publication date. Only 227 out of the 251 the studies were included on this analysis due to missing information (90.4%). Error bars represent confidence intervals.

Figure 8 - Mean number of related articles per latent class and reference to Cook *et al.* review



Number of related articles was adjusted for publication date. P values indicate pair-wise differences to the top-most element of each color-coded class. Significant relationships were marked with bold typeface. Only 227 out of the 251 the studies were included on this analysis due to missing information (90.4%). Error bars represent confidence intervals.

Discussion

CBL publications in medical education have been rising, with reports of over 38 different software systems, 25 of which were specifically developed for medical education (66%). From the 251 studies most employed interactive websites making use of text and image (46%) and to a smaller extent websites delivering text-based materials (25%). A similar amount of reports delivered instruction using web-conferencing systems (22%) and a smaller group of studies reported highly interactive websites with multimedia learning content built according to instructional design principles (7%). From the 212 interventions, most did not employ comparison groups and lasted between 1 week and 3 months. CBL *versus* CBL studies were less numerous than traditional *versus* CBL studies. Nearly all studies assessed student attitudes, from which a large fraction also assessed knowledge (82%), and a smaller one assessed knowledge and skills (12%). A smaller set of studies looked specifically for patterns of online activity, namely the number of reads and posts (6%). Finally, nearly 75% of papers held common references and citations, while a fraction of 25% of the analyzed articles did not hold common references. Papers comparing different CBL methods were more cited than traditional *versus* CBL methods independently of publication date. Papers reporting instructional design principles, papers measuring online activity, and papers citing Cook *et al.* CBL reviews have significantly more references and citations in common than other papers.

Comparison with previous reviews

The last systematic review and meta-analysis performed about this topic encompassed data from 1990 to 2006 and have highlighted the problems of intervention variability and lack of evidence regarding comparative effects of CBL methods.[39,40,54] Recent reviews have also demonstrated that practice exercises, interactivity, feedback and repetition can favorably influence learning outcomes.[40,74] Other reviews have offered summaries of technologies and methods used [132,133], and have addressed specific topics such as the role of blogs,[134] wikis,[135] portfolios,[136] simulations in general,[137] in particular for surgery,[138] gastroenterology,[139] catheterization[140] and airway management.[141] Other authors focused on specific aspects of web-based learning on problem-based learning,[142] the implications of the recent web capabilities namely the *web 2.0* [143,144] and *web 3.0* [145] to medical education. The present study complements previous reviews by encompassing recent work concerning these fields over a large base of abstracted papers.

Despite the considerable time overlap with similar reviews, assessments such as latent class analysis and citation network analysis were yet to be conducted during the considered time period.[40]

Limitations and strengths

This study has limitations. We scrutinized databases where medical education articles are frequently indexed. Although EMBASE was not queried, Scopus covers most literature indexed in EMBASE and thus provided a reasonable proxy. However, we did not abstract papers from grey literature or references from other papers, and thus paper search cannot be considered exhaustive.

We narrowed the study participants to medical education only. This can be considered a limitation insofar these findings cannot be generalized to other health professions. Other reviews have performed similar searches including work in health professions in general.[39] The article abstraction step was performed manually. While the independent reviewing method and ICC reports indicate a low probability of coding error, we cannot completely exclude it. Variables regarding instructional design and assessment outcomes were often not explicitly declared and relied on reviewer judgment. References and citations could not be retrieved for 27 out of the 251 of the papers (11%), and unique reference and citation matching relied on probabilistic algorithms that considered a small but non-negligible error margin.

This study also has strengths. We performed a broad analysis of the literature and accounted for aspects that to our knowledge were not previously referenced, such as specific platforms and its features, correlations assessed between learning endpoints and types of comparisons. We systematically summarized data using latent class analysis, which to our knowledge was for the first time performed in this setting. We described the article citation network and explored relationships between these and the paper latent classes and CBL considerations, which to our knowledge were also for the first time performed in the field. Finally, these results were made available through an interactive visualization that allows researchers to deeply explore papers.

Implications

CBL research should include evidence from more medical schools

Our findings show that while there is significant variation in CBL in medical education, most published articles are from medical schools of a few countries. Medical education has geographical specificities, which makes contributions from different geographies particular enriching and should incite more schools to conduct research in this field.

Platform development should avoid reinventing the wheel

Over 25 platforms and software projects were built specifically for medical education despite having significant overlap in goal and features. While a few provide means to interact with learning materials - such as microscopy images [95] - in ways not before possible, it would be worthwhile for researchers to put efforts on the development of open and generalizable systems addressing specific learning contexts that can be reused by researchers from other medical schools. Initiatives to design pluggable modules for mainstream learning management systems and reusable learning materials - such as Learning Objects [146] - aimed at specific medical contexts, should be preferred over building closed systems from scratch.

Instructional design considerations should be reported

The diversity of methods encompassed by CBL on delivery medium, context, learner and purpose without reports of instructional design considerations obfuscates the effect of different intervention aspects, for which instructional design - or the lack of it - is partly accountable.[35,36,40,142] The value of interactive tools such as quizzes with feedback would also increase. Determining which principles best apply to different medical settings and medical knowledge is also an issue of interest.[35]

Interventions should focus on assessing unexplored outcomes

Studies generally report positive outcomes on knowledge, attitudes and skills. Interestingly, studies that failed to find positive effects in any of the learning outcomes were often randomized controlled trials [12,105–108] some of them running on multiple institutions.[147,148] Studies with little or no description of the learning and teaching methodology had neutral findings.[104,149] Once again, the lack of comparable arms, namely CBL *versus* traditional instructions, or difficulties to objectively assess learning outcomes, make it difficult to interpret these results.

Demonstration that objective knowledge and skills increases, while important, can be used in deeper ways. Real-time collection of student activity together with objective performance assessment through MCQs may hold of predictive value. Judgments of knowledge together with other student activity metrics may provide data for a next generation of intelligent *tutoring* systems able to track, manage and predict student performance.[150] An increase in studies reporting online activity measurements and correlations with other learning outcomes using reproducible tools as described before would contribute a great amount to generate useful evidence on the effectiveness of CBL methods to enhance learning.[151] Metrics could include, for example, student communication style and sentiment [152,153] or time spent on materials of different consistency.[154]

CBL research seems to be progressing to the right track

Even though 25% of the articles seemed not to be based on common CBL literature, our findings suggest that research is moving towards favoring studies comparing CBL based methods rather than comparison with traditional methods. Indeed, we have shown that articles comparing different CBL methods are more cited than papers comparing CBL to traditional settings, which we take as a sign that recommendations put forward by previous authors are being taken into consideration.[35,36,38] Papers on the *Instructional* and *Online activity* latent classes as well as those citing Cook *et al.* meta-analysis [39] have more references and citations in common with other papers, demonstrating greater awareness of research in this field and possibly indicating paths of future research direction.

A further push into a student-centered models is key

The shift to student-centered models needs to continue. However, only few reports put students as the center of the education process, focusing usually on aspects related to teaching.[155] Part of the success of CBL features comes from the empowerment of the student to conduct study at his own pace, richer interactions with learning materials and ease of communication, that were not otherwise feasible. Promoting student self-directedness through social media and rewards may lead to increased engagement and improved learning outcomes.[156] Active learning through engagement in collaborative usergenerated content, facilitation of communication and feedback in which instructors act as moderators may further promote this change.[157] Engaging students in the creation of content can be a good way to help faculty cope with increasing learning material demand.[158] Social media tools such as Wikis have been used in the medical context for various purposes,[159] but in medical education still present limitations in their format, management, and collaborative features.[160] Other approaches using 3D virtual worlds may offer great potential to learners through immersive exploratory worlds and rich feedback environment that may be used to engage learners and simulate real-world medical scenarios.[160]

Conclusions

We have come a long way in CBL in medical education. While the field is filled with high variability and a part of studies seem to be unaware of advances in the field, recommendations on comparing different CBL methods seem to be taken into consideration. Incorporating instructional design principles in the design of learning materials and developing further educational software in ways that can be shared between researchers are paths for further improvement. A focus on measuring online activity and correlating it with outcomes may provide insights into ways that keep promoting student-centered approaches tailored to specific learning settings.

PAPER 2

A novel collaborative e-learning platform for medical students - ALERT STUDENT[*]

Background

Medical education is an area of increasing complexity, considering the education goals of health professionals for the XXI century.[1,2] Successful medical learning requires a considerable time investment not only in the development of core and specific competencies, but also in the ability to transfer basic cognitive competencies to the clinical setting through the integration of personal experience and vast information sources.[1,161] Information management regards the ability to search, identify and integrate relevant information that can be further used for critical reasoning in clinical practice,[3] and is currently one of the most compelling challenges facing medical students.

Approaches to enhance learning

In many settings, information is not effectively managed during learning. The demanding learning process frequently drives students to retain knowledge to meet course goals instead of strengthening competence development.[162] According to the Adaptive Character of Thought (ACT-R) theory “time on task” is the most important factor for developing lifetime competence.[163] As the amount of knowledge to learn increases, how well time is managed in the learning processes becomes key.[163] Cognitive load theory postulates three types of cognitive load: (a) intrinsic load is the net result of task complexity and the learner expertise; (b) extraneous load is caused by superfluous processes that do not directly contribute to learning; (c) germane load is accounted by learning processes handling intrinsic cognitive load.[164] Studies have been carried to identify design guidelines and benefits of this theory in health sciences education.[109,163,165–169] Spaced-repetition, a learning approach that focuses on reviewing content multiple times over optimized time intervals is one of the most effective ways to improve long-term retention.[6,14,40,170,171] While evidence-

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based principles for instructional design are abundant, they are infrequently incorporated into the educational setting in a consistent and deliberate manner.[172]

Learning objects

The way in which content can be organized in order to optimize learning has also been extensively studied.[3,131,146,167,169,173] Learning objects, groupings of instructional materials structured to meet specific educational objectives,[146] define a set of guidelines to make content portable, interactive and reusable,[146,174–177] therefore enhancing and tailoring learning.[176] They may facilitate adaptive learning by offering the chunks of content that the learner needs in order to achieve an accepted level of competence. Other authors have identified the need to simplify the learning object authoring process to gain wider acceptance and use.[109] Additionally, the design of appropriate and effective technologies must take into account individual differences in learning, through systems that adapt based on individual progress and performance or through explicit choices made by the learner.[178] Students need tools to help retain knowledge for longer periods and easily identify materials with lesser retention rates.[6] This goal may be achieved by providing learners with personal insight on their learning effectiveness, using personal and peer progress data based on self-assessment results.[176]

Computer Supported Collaborative Learning

Currently, web applications can be a valuable tool to reach information management goals. The application of new learning technologies that has emerged as a main stream in medical education [179] is known to simplify document management, communication, student evaluation and grading.[180] However, these tools focus mainly on maximizing efficiency of administrative teaching and have little in consideration the learning tasks directed at students. Additionally, over recent years there has been a shift in medical education where traditional instructor-centered teaching is yielding to a learner-centered model.[29,31] With the advent of social media tools that allow for collaboration and community building it is becoming more common for students to create and share materials on-line. [30,175] However, these materials are often not validated or reviewed by teachers [157,181] and may decrease learning effectiveness as the student will need to browse, filter and validate relevant information from numerous and often conflicting information sources.[182]

CSCL can add an instructor role to the learner-centered model. It can place learners in control of their own learning and transforms the role of a teacher from the sole-provider of information to a facilitator of knowledge acquisition [31,181] promoting greater learning satisfaction.[32,40] This type of approach usually takes place in asynchronous collaboration settings where students and teachers can collaborate at different times.[32,183,184] Despite this potential, little evidence of effectiveness on using such tools in the health professions has been gathered.[40,185]

Effective information management during the learning process may be achieved through adoption of computer supported collaborative learning (CSCL) systems that provide validated content in the form of learning objects, allow student self-assessment and display tailored feedback that can be used to support study management. This data should direct further exploratory or limited learning approaches, so that knowledge acquisition may be benefited at the same time information management competences are developed.

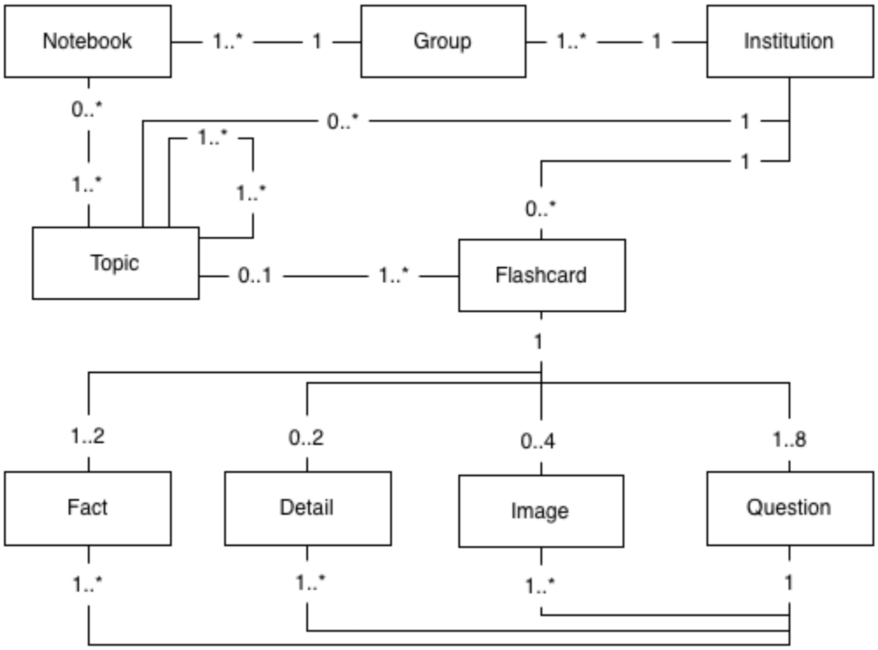
The present study aims to develop and assess the usability of an adaptive CSCL system that helps making decisions regarding personal learning process. So far, existing studies regarding such systems were built and applied in specific medical knowledge fields.[93,109,186–188] To our knowledge no system has been built to be of application to medical curricula in general.[189]

Implementation

Technologies

The present application was built in accordance to current web standards. The user interface was built using *Hyper Text Markup Language* (HTML), *Standard Vector Graphics* (SVG) and *JavaScript*. The application layer of the system was built using *Java* technology over the *Play!Framework* version 1.2. The database layer was built using ORACLE systems. The data model is described using a simplified UML diagram in Figure 9. A simpler version of the application was developed for the iPhone but will not be discussed in this paper.

Figure 9 - Simplified Entity relationship UML diagram



UML diagram that specifies relationships between the main application objects. Multiple *Notebooks* belong to a *Group*, and multiple *Groups* belong to an institution. An institution has multiple topics and *Flashcards*. A *Notebook* may hold multiple topics that are associated to multiple *Flashcards*. Multiple topics can also belong to a broader topic. A *Flashcard* can be composed of one or two facts, up to two description items, up to four images and one to eight questions. Multiple questions can be associated to a Fact, Description or Image.

Content structure

Content was required to be stored as reusable blocks that would allow building of higher order learning blocks as well as assessing knowledge. Knowledge assessment was carried out using open-ended questions. The smallest learning block was named *Flashcard*, and was composed of information on one side and open-ended questions on the other. Each *Flashcard* contained up to 8 knowledge pieces named *Fact*, *Description* and *Image*. Questions can be associated to each of these pieces individually. Each piece would therefore serve as the answer to one or more questions. Since content re-usability was paramount, a *Flashcards* categorization system was implemented using Medical Subject Headings (MeSH) from the United States National Library of Medicine.

Aggregation of *Flashcards* in higher order structures was required to achieve meaningful learning goals. That would require creating custom aggregations of *Flashcards* of different MeSH topics. Topic and *Flashcard* order should be arranged according to the learning goal. We named these custom aggregations *Notebooks*.

In order for students and teachers to create and share content, *Groups* were created. *Groups* reside within institutions. Therefore, users from a given institution could access its *Groups*. A universal institution was created in order to allow all users to create and share content globally.

Learning tools

Table iii - Variables measured by the system

Name	Meaning	Measurement and presentation
Study session count	The number of times a *Notebook* has been studied	The Study Mode provides a button that when clicked increments the study session count for the *Notebook*.
Time spent studying	Time spent studying a *Flashcard* for a study session	Each *Flashcard* provides a button to mark it as studied. Each time that button is pressed, the time lapse since a previous click in any other *Flashcard* is added to the clicked *Flashcard* time for the current study session. Time spent studying is presented as the cumulative time for all sessions per *Flashcard* in a chart. It is represented as the proportion of the *Flashcard* time to the global *Notebook* time on the sunburst chart.
Perception of knowledge	The student self-perception of knowledge regarding a *Flashcard* question.	The student is presented an open-ended question that requires recalling the knowledge to answer it. After recalling the question the student can see the answer and assess the quality of his recall using a 4-point likert scale. Perception of knowledge is presented as the average for a given *Notebook* or per Topic. It is represented as a percentage of the best possible Perception of knowledge for a *Notebook*.

User information regarding study metrics needed to be collected for study management. *Time spent studying* and *Perception of knowledge* were the two identified metrics required to meet this goal (Table iii). *Perception of knowledge* refers to student self perception of how well knowledge could be recalled when an open-ended question is presented.

This data allowed computation of *Flashcard* study priority levels. These features were collected and presented in different sections: one devoted to study - Study Mode; another devoted to self-assessment - Quiz Mode; and a section devoted to analysis of performance metrics per *Notebook* - *Notebook* Dashboard.

System usability and adoption surveys

System usability and feature usefulness of the Study Mode, Quiz Mode and *Notebook* Dashboard was assessed using a group of 48 students from the Faculty of Medicine of the University of Porto (FMUP) and two on-line self-report questionnaires. Students from the 4th and 5th years of the medical course were randomly selected and contacted by email to participate in the study. The study consisted of 2 classroom sessions (S1, S2) in consecutive weeks, with duration of 1 hour. Each student was provided a computer.

The students were instructed to use the Study Mode, Quiz Mode and *Notebook* Dashboard to study and assess their knowledge on a *Notebook* about the *Golgi Complex*. The *Notebook* was created using pedagogical materials provided by the Department of Cellular and Molecular Biology of FMUP. During S1 students had 10 minutes to register in the platform. A 2-minute explanation of how the Study Mode, Quiz Mode and *Notebook* Dashboard worked was given to students before they used the application.

All doubts were clarified. The students then spent 20 minutes on Study Mode, 15 minutes on Quiz Mode and 5 minutes on the *Notebook* Dashboard. After that time the students completed an on-line survey regarding system usability and tool usefulness. Students left the room only after all students completed all tasks. During S2 students spent equal amounts of time on the Study Mode, Quiz Mode and *Notebook* Dashboard.

At the end of the session, the system usability and tool usefulness survey was filled again and an additional survey regarding willingness to adopt the system as a reference tool was also completed. The 3 surveys consisted of a set of objective statements regarding personal experience. Student agreement to each of the items was assessed using a 4-point likert scale: 1 - full disagreement; 2 - partial disagreement; 3 - partial agreement; 4 - full agreement. Paired sample t-test was used to compare differences in the system usability and tool usefulness survey answers between the two sessions.

Significance level was fixed at .05. This study was approved by the Faculty of Medicine University of Porto / *São João* Hospital Ethics Committee in compliance with the Helsinki Declaration.

Results & Discussion

The platform was implemented as a free web application named ALERT STUDENT. Table iv provides an outline of how learning objects principles were implemented in the system and Table v provides detail on how several instructional design features were implemented.

Table iv - Implementation of learning object principles

Principle	**Description**	**Implementation**
Stand alone	Learners can use a single learning object to achieve a specified learning outcome.	Each *Flashcard* encloses a small learning outcome. Combination of *Flashcards* into *Notebooks* allow achievement of broader learning outcome.
Reusability	Learning objects can be used by diverse groups of learners in a variety of educational situations.	*Flashcards* created for a given *Notebook* can be reused to create other *Notebooks* for different learning situations (eg.: within different *Groups*).
Interactivity	Each learning object requires an interactive response from the learner.	*Flashcards* and *Notebooks* require learners to highlight, take notes and self assess their knowledge using features of the Study Mode and Quiz Mode.
Aggregation	Learning objects can be linked into larger collections to form lessons, modules, or courses.	*Flashcards* can be liked into larger collections called *Notebooks*. *Notebooks* can be linked into larger collections by using *Groups*.
Interoperability	A learning object can be used with appropriate “plug-ins” by multiple software applications and on a variety of computers and e-learning platforms.	*Flashcards* and *Notebooks* can be accessed on-line in any computer or using the mobile application for the iPhone. The application interface that allows communication with the iPhone also al- lows integration with external applications.
Accessibility	A learning object must be tagged with standardized indexing information (metadata) that allows it to be easily found by course designers, educators, learners, and evaluators.	*Flashcards* are cataloged using MeSH terms and can be searched within the application by using these terms.

Descriptions are adapted from Ruiz *et al.*

Groups

The application has a section devoted to *Groups* (Figure 10). This section consists of a page listing all *Groups* and specific *Group* pages. The list page allows browsing *Groups* using search by name, tags and filtering by belonging institution. The *Group* page was divided into 4 sections: (a) *Group* wall for posting and commenting; (b) member's page where *Group* administrators can manage members; (c) *Notebook* page that holds *Notebooks* and allows creation or editing; (d) *Group* profile section where non-members can see the *Group* summary.

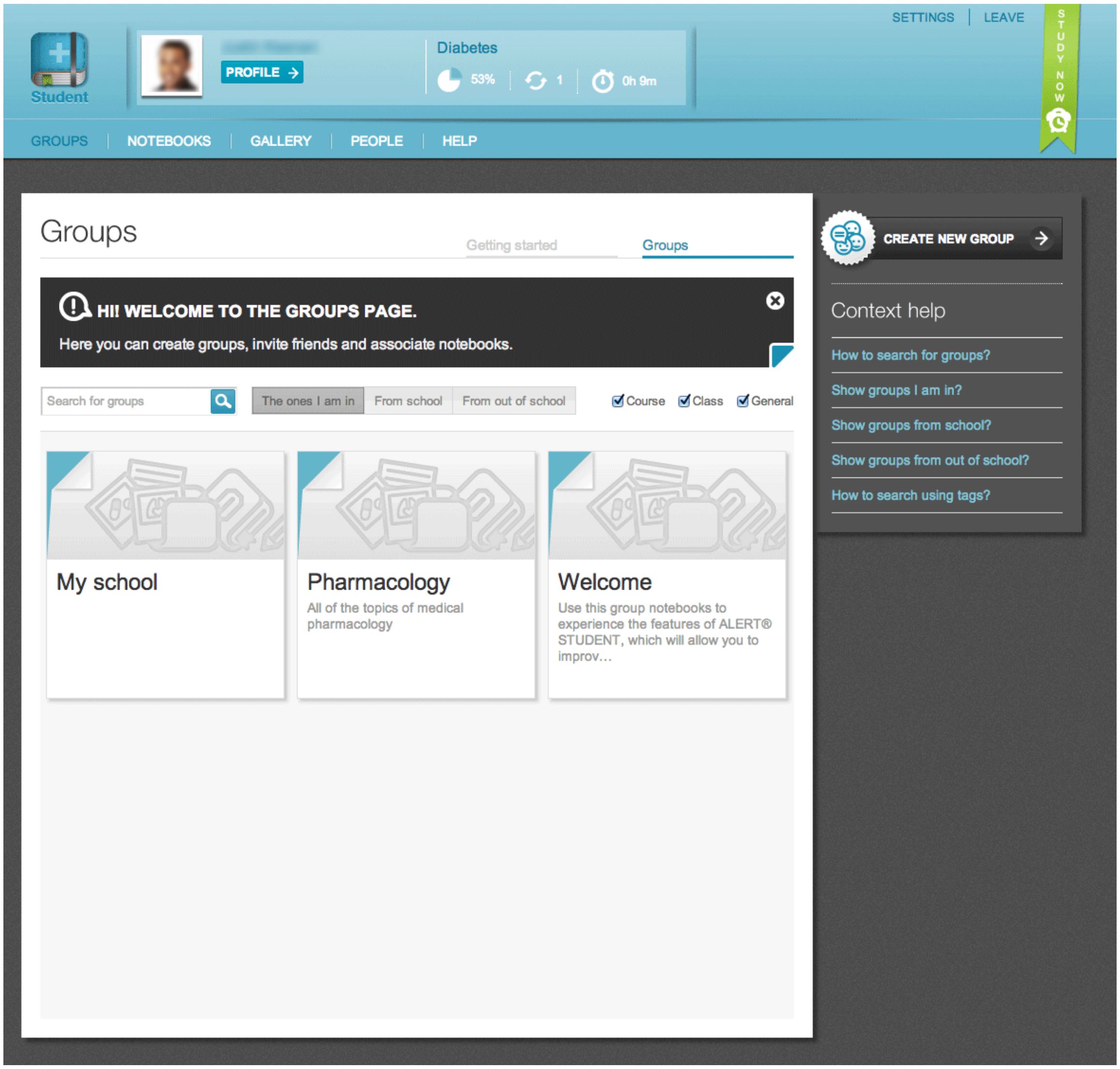
Table v - Implementation of instructional design principles

Principle	Implementation
Coherence principle - Eliminate extraneous material	Splitting of content into facts and description components. Ability to hide tools in Study Mode. Ability to resume from where last study session was left.
Signaling principle - Highlight essential material	Bold typeface for facts. Text marker feature. *Flashcard* color-coded study prioritization based on learner *Perception of knowledge*.
Pre-training principle - Provide pre-training in names and characteristics of key concepts	*Notebooks* with key *Flashcards* can be provided before more advanced *Notebooks* are studied. Introductory *Flashcards* can be added to more advanced *Notebooks*.
Segmenting principle - Break lessons into learner-controlled segments	*Flashcards* breaks *Notebook* content into learner controlled segments
Multimedia principle - Present words and pictures rather than words alone	*Flashcards* support both text and images

Principles enumerated from Mayer *et al*.

Groups allow a closed environment approach where students can interact with a defined set of users and content for a given learning goal. This is similar to the wiki or blog scenario where administrators limit registration and editing privileges to selected users.[175] Allowing *Flashcards* within a *Group* to be available to other *Groups* of the same institution facilitates content sharing within the institution. This helps to reduce content redundancy, allows faster content creation and allows new *Notebooks* to be created using previously studied *Flashcards*. This may lessen intrinsic cognitive load by reducing the exploratory component involved in learning new redundant materials, hence increasing learning performance.[180]

Figure 10 - User *Groups* screen



HI! WELCOME TO THE GROUPS PAGE.

Here you can create groups, invite friends and associate notebooks.

My school

Pharmacology

All of the topics of medical pharmacology

Welcome

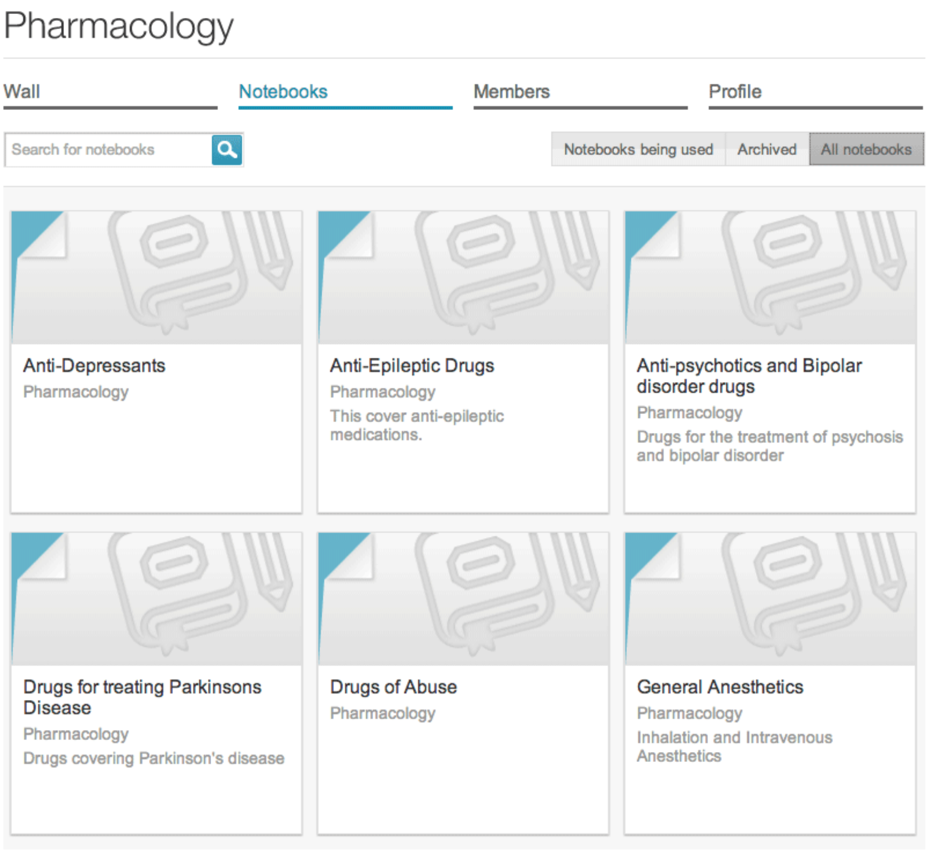
Use this group notebooks to experience the features of ALERT® STUDENT, which will allow you to improv…

A list of *Groups* for a given user is displayed.

Notebooks

Notebooks can be accessed through *Group* pages or through a global *Notebook* page. Both pages provide search and filter features. (Figure 11) The *Notebook* Dashboard shows overall information and study statistics regarding personal study performance. Users can analyze *Flashcard* size and *Time spent studying* using a sunburst chart (Figure 12). A toggle button resizes each *Flashcard* representation to match either its character count or time taken. A bar chart plots *Perception of knowledge* per topic in two series. One series plots user *Perception of knowledge* while another plots mean peer *Perception of knowledge*. A line chart plots *Perception of knowledge* per quiz session in two series as well. One series plots user *Perception of knowledge* while another plots mean peer *Perception of knowledge* (Figure 12).

Figure 11 - User *Notebooks*



Pharmacology

Anti-Depressants
Pharmacology

Anti-Epileptic Drugs
Pharmacology
This cover anti-epileptic medications.

Anti-psychotics and Bipolar disorder drugs
Pharmacology
Drugs for the treatment of psychosis and bipolar disorder

Drugs for treating Parkinsons Disease
Pharmacology
Drugs covering Parkinson's disease

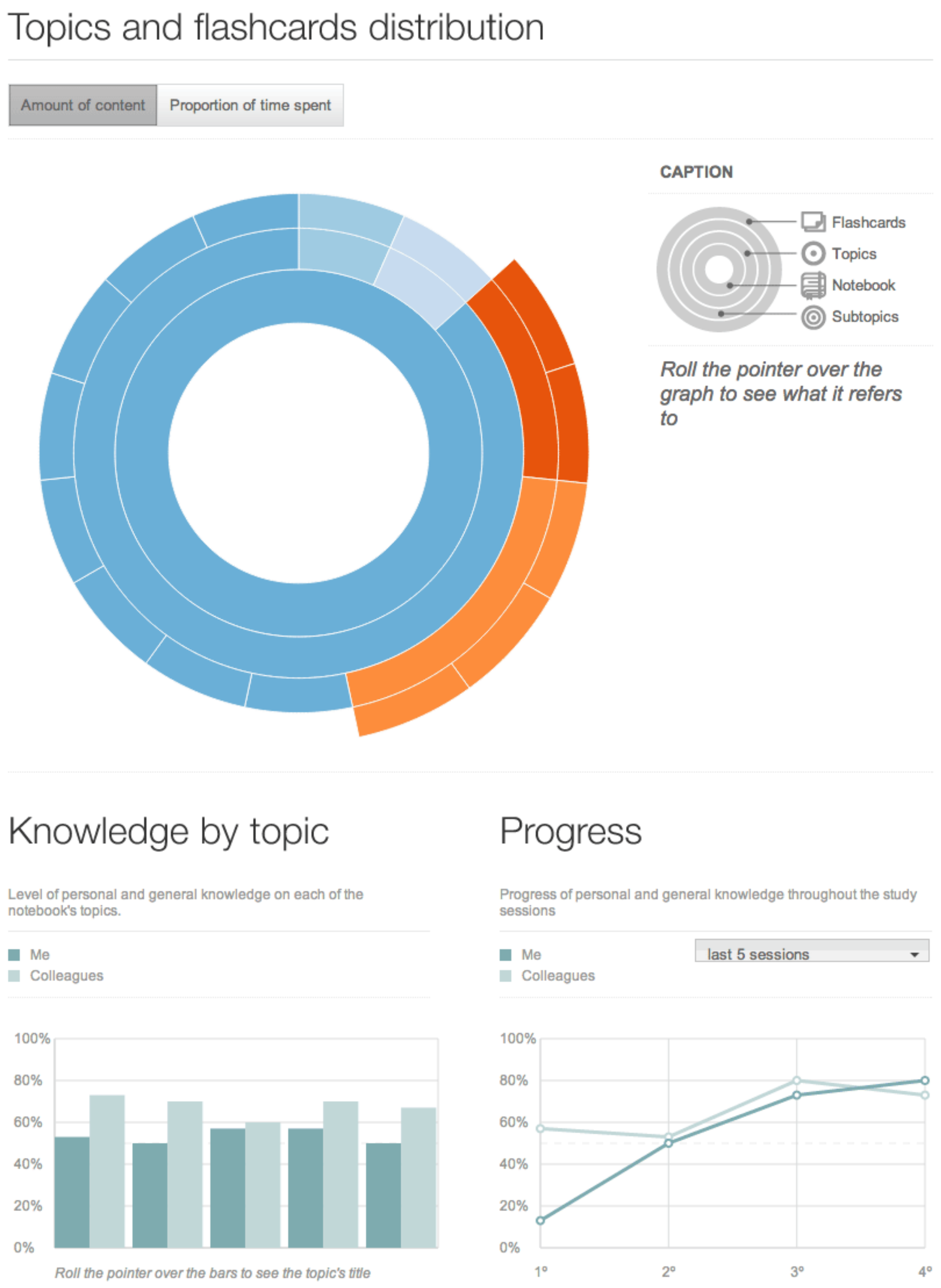
Drugs of Abuse
Pharmacology

General Anesthetics
Pharmacology
Inhalation and Intravenous Anesthetics

A list of the *Notebooks* for a given user is displayed.

The *Notebook* editor allows simultaneous creation of *Notebooks* by searching and selection topics and *Flashcards* available to be part of a *Notebook*. New topics and *Flashcards* can be created as well. A graph of MeSH topic relationships is also displayed and can be used to browse topics (Figure 13).

Figure 12 - *Notebook* Dashboard



Roll the pointer over the graph to see what it refers to

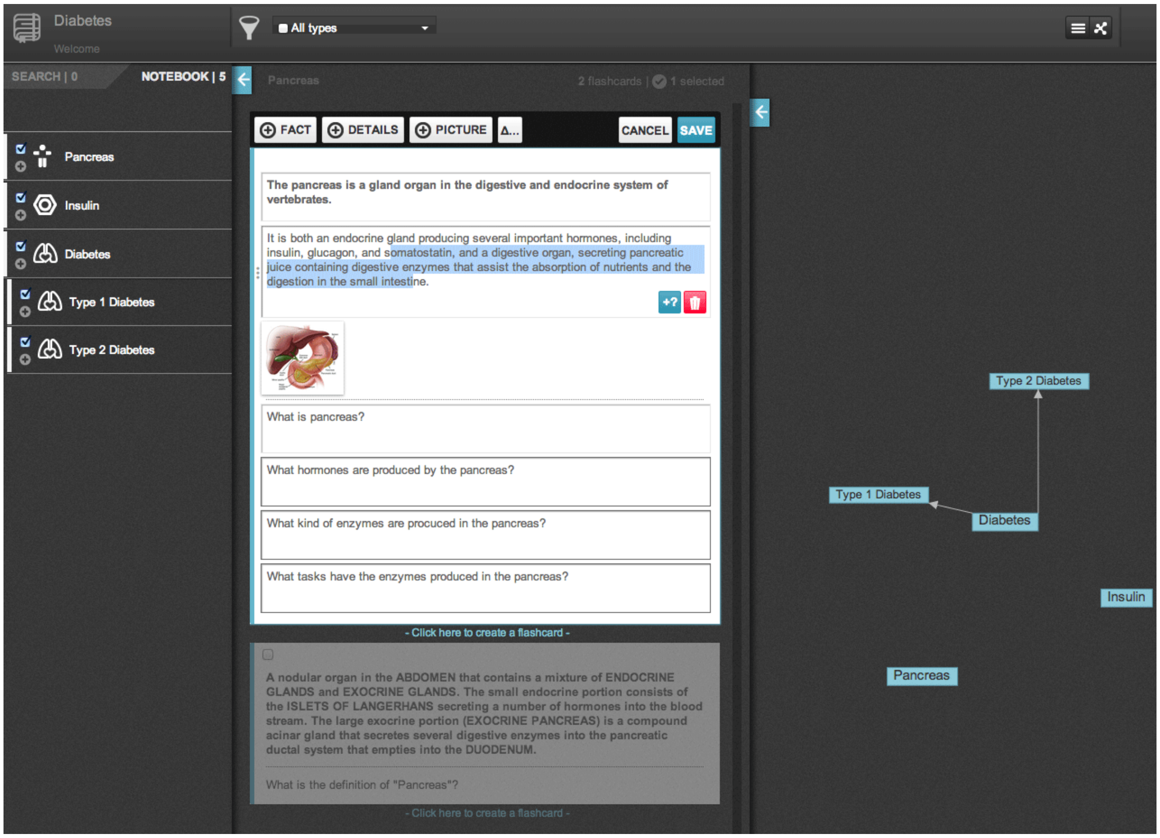
Level of personal and general knowledge on each of the notebook's topics.

Roll the pointer over the bars to see the topic's title

Progress of personal and general knowledge throughout the study sessions

The sunburst chart represents the topic and *Flashcard* distribution. The toggle button switches the configuration between *Flashcard* size (given by the number of characters) and *Time spent studying* on a *Notebook*. The bar chart on the left depicts *Perception of knowledge* per topic, for the user and its peers. The line chart on the right is represents *Perception of knowledge* per quiz session for the user and its peers.

Figure 13 - *Notebook* editor



The pancreas is a gland organ in the digestive and endocrine system of vertebrates.

It is both an endocrine gland producing several important hormones, including insulin, glucagon, and somatostatin, and a digestive organ, secreting pancreatic juice containing digestive enzymes that assist the absorption of nutrients and the digestion in the small intestine.

What is pancreas?

What hormones are produced by the pancreas?

What kind of enzymes are procuced in the pancreas?

What tasks have the enzymes produced in the pancreas?

☐

A nodular organ in the ABDOMEN that contains a mixture of ENDOCRINE GLANDS and EXOCRINE GLANDS. The small endocrine portion consists of the ISLETS OF LANGERHANS secreting a number of hormones into the blood stream. The large exocrine portion (EXOCRINE PANCREAS) is a compound acinar gland that secretes several digestive enzymes into the pancreatic ductal system that empties into the DUODENUM.

What is the definition of "Pancreas"?

Topics can be browsed on the left column on the search tab. Checked topics become part of the *Notebook* and become available on the *Notebook* tab. The center column displays *Flashcards* for the selected topic. Checked *Flashcards* become part of the *Notebook*. New *Flashcards* can be created on any topic. On the right MeSH relationships between topics are represented using a graph that can be used to navigate topics.

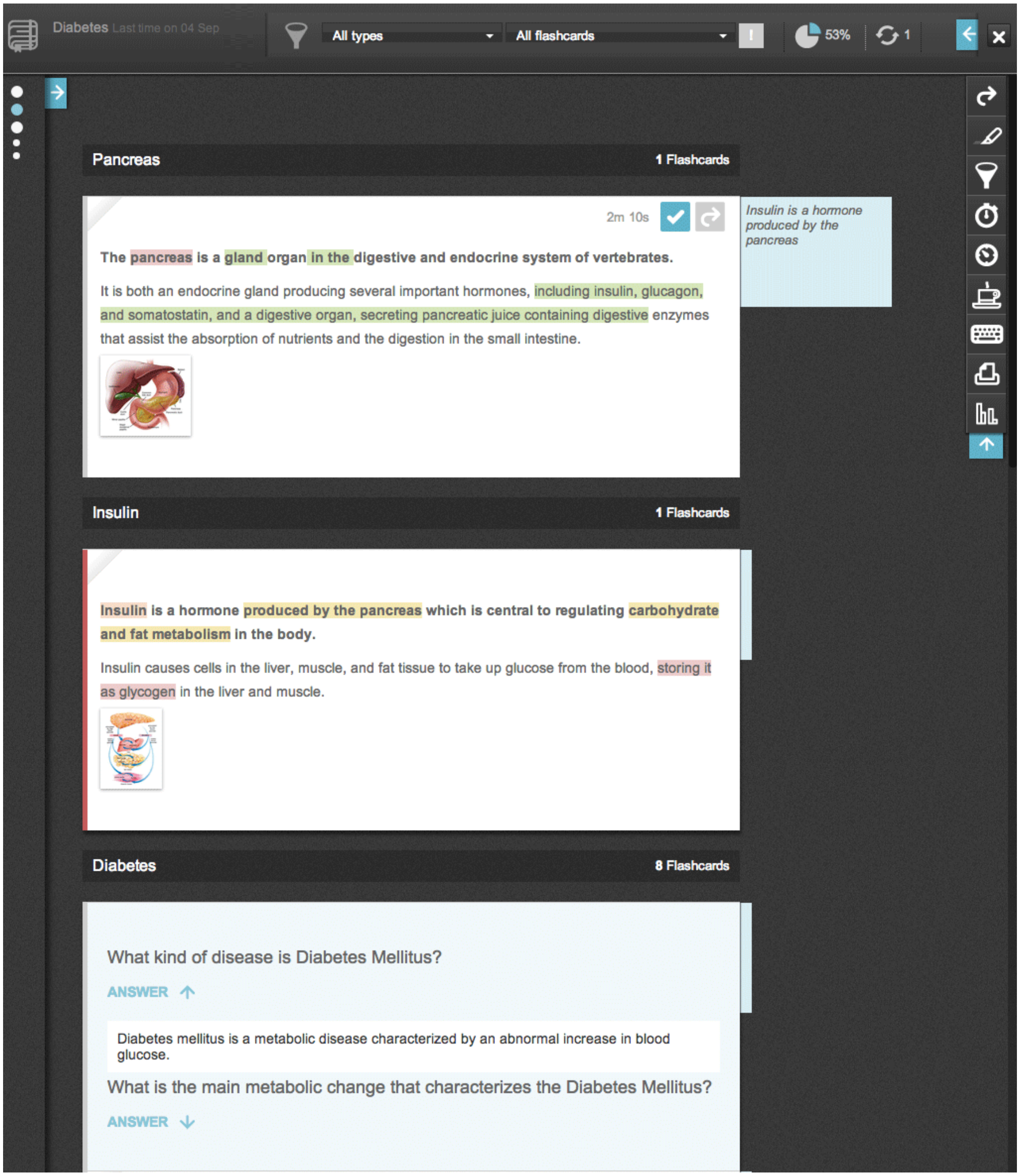
Flashcards allow content to be created in ways that match specific learning goals and can be reused with little effort to match other learning requirements. Though they are in accordance to the learning objects principles of stand-alone, reusability, interactivity and aggregation [146] (Table iv), the amount of context to build these type of learning objects must be balanced in a way that allows isolated usage in different settings as well as chaining with additional *Flashcards* in meaningful ways.[176] Enclosing little context in each *Flashcard* may lead to less articulated *Notebooks*. *Flashcards* are supported by the cognitive load theory. Small chunks of self-enclosed knowledge decrease intrinsic cognitive load. Additionally, since *Notebooks* are combinations of *Flashcards*, they can orient learning in a simple-to-complex strategy that further decreases intrinsic cognitive load.[8,163,165] Furthermore, this process can be extended by refactoring multiple *Notebooks* into smaller summary *Notebooks* containing the most relevant *Flashcards* that leverage the same cognitive load principles further.[8] Performance data for overlapping *Flashcards* can be used to optimize study sessions in a new *Notebook* setting, which also applies to the principles of learning object re-usability, interactivity and aggregation [8] (Table iv).

The charts allow the student to take action on their study sessions based on *Time spent studying* and personal and peer *Perception of knowledge*. Previous works have shown that feedback play a key role in determining learning success,[176] hence, insight into performance metrics may help build motivation to learn further.

Study Mode

The Study Mode allows *Notebook* study in an adequate digital environment, which minimizes sources of distraction (Figure 14). The dark colors used on the interface contrast with the white *Flashcards*, creating focus on the area of interest. The center displays the *Flashcards* stacked as a continuous piece of text. On the side, the index of topics is displayed. It also provides study progress metrics such as percentage of *Flashcards* studied, number of study sessions, time taken per session, total *Time spent studying* and *Time spent studying* on the previous session. *Flashcards* can be flipped one at a time or altogether to reveal the questions. *Flashcards* have a button to increment *Time spent studying* and can be removed from the Quiz Mode assessment by folding the top left corner with a simple click. Additionally, *Flashcards* have a colored bar on the side that expresses *Perception of knowledge*. All tool menus are collapsible to prevent distractions. Available tools include filters for *Flashcard* priority and category, a timer, a stopwatch, notes and text highlighters. Other tools present the keyboard shortcut guide and allow exporting the *Notebook* in .pdf format.

Figure 14 - Study Mode



The pancreas is a gland organ in the digestive and endocrine system of vertebrates.

It is both an endocrine gland producing several important hormones, including insulin, glucagon, and somatostatin, and a digestive organ, secreting pancreatic juice containing digestive enzymes that assist the absorption of nutrients and the digestion in the small intestine.

Insulin is a hormone produced by the pancreas

Insulin is a hormone produced by the pancreas which is central to regulating carbohydrate and fat metabolism in the body.

Insulin causes cells in the liver, muscle, and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle.

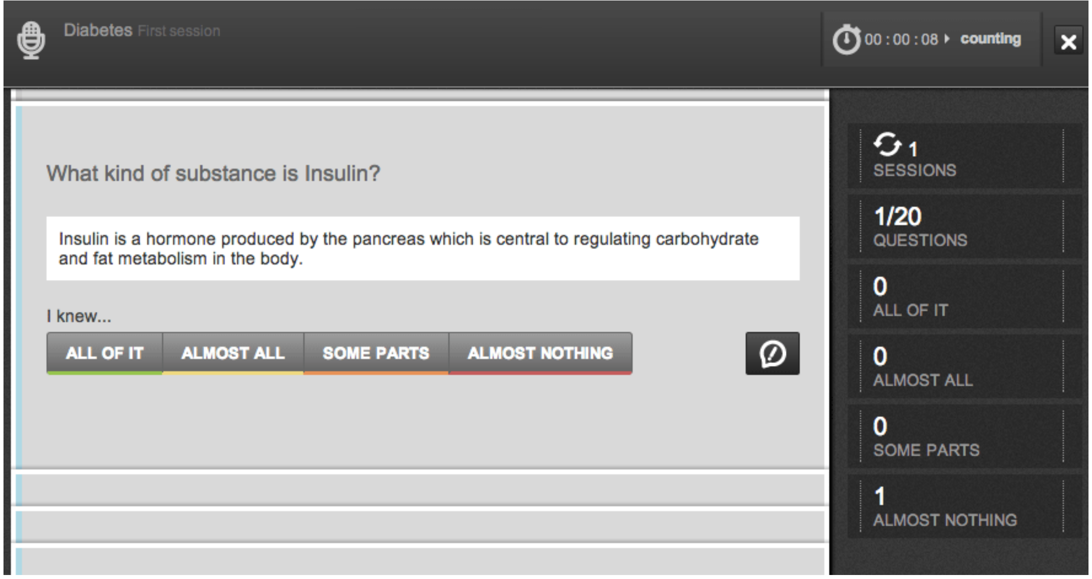
What kind of disease is Diabetes Mellitus?

Diabetes mellitus is a metabolic disease characterized by an abnormal increase in blood glucose.

What is the main metabolic change that characterizes the Diabetes Mellitus?

The left column with circles represent the *Notebook* topic index. The blue circle represents the topic currently displayed. The top bar houses the content filters and progress status. Timers are also available but not shown. The bar in the right side is the actions bar, that houses *Flashcard* flipping, text marker, filter and timer toggle, pause mode, keyboard shortcuts list, print view and shortcut to statistics buttons. The third *Flashcard* displayed is flipped, showing questions and an answer.

Figure 15 - Quiz Mode



What kind of substance is Insulin?

Insulin is a hormone produced by the pancreas which is central to regulating carbohydrate and fat metabolism in the body.

A question card is represented along with the answer. *Perception of knowledge* is graded using the set of four buttons shown. The rightmost button reporting of errors to the *Notebook* owner. The column on the right tracks student progress.

In order to increase reading speed, comprehension, and reduce fatigue from screen reading, spaced lines with a mean of 70 characters in length and large window height were used as mentioned in previous studies.[166,190] The ability to hide tools and the keyboard shortcuts further improves focus. *Flashcard* category and priority filters allow learning sessions to be tailored to personal goals effectively. These features may help reduce extraneous cognitive load related to content navigation tasks and interface visual noise.[8] Flipping the *Flashcard* column provides a tailored "content-and-question" oriented study environment. The ability to resume study sessions from the point that they were last left, further reduces extraneous cognitive load by decreasing distance to the required point of focus.[8]

Quiz Mode

The Quiz Mode is the section devoted to self-assessment (Figure 15). It takes the *Flashcards* of a *Notebook*, and selects a set of *Flashcard* questions that are presented one at a time. For each question the user should recall the required knowledge. Afterwards the user reveals the *Flashcard* section that answers the question and grades *Perception of knowledge*, the quality of the user recall, using a 4-point likert scale. After grading *Perception of knowledge*, the system shows another question. The student also has the option of reporting the *Flashcard* to the *Group* administrators when inaccuracies are found.

After the evaluation step, another card is shown. The system displays student progress and the number of questions rated per grade. When the user finishes the Quiz, statistics about the *Time spent studying* on each session are presented. The student can also review the *Flashcards* for the questions with the lowest *Perception of knowledge*. Questions are chosen so that all Flashcard elements are assessed. If more than one question is available for a given content piece, then the system will chose either the hardest question if there are previous ratings, or will pick a question at random. Global *Perception of knowledge* for each *Flashcard* is computed by calculating a weighted average of the last three sessions *Flashcard Perception of knowledge*. The session *Perception of knowledge* for a *Flashcard* is calculated by averaging the results for every question answered for the *Flashcard* in that session.

The Quiz Mode is essential for the system to compute *Perception of knowledge*. Because each *Flashcard* may have multiple questions regarding the same content piece, the Quiz Mode is able to use the questions with lowest *Perception of knowledge*. This provides a means to assess knowledge using questions that are most difficult thereby tailoring memory retention needs. This is also in accordance to the intrinsic cognitive load strategy of low-to-high fidelity tasks because as the student progress, questions representing harder tasks will be preferentially selected.[8] Spaced repetition promotes development strengthening of long-term memory schemata acquired during previous contacts with the *Flashcards*. This will reduce the amount of elements that will be dealt with using working memory, thus reducing cognitive load and allowing additional focus on the recall process.[8] The way the user grades *Perception of knowledge* is, however, subject to affective factors. Users may feel inclined to overrate their *Perception of knowledge* thus decreasing the beneficial effect of the system.[191] Although self-assessment questions are demonstrated to positively affect learning outcomes,[171,172,191–194] it remains unknown whether self-reported evaluations correlate with exam grades. This question system has as primary goal to allow self-assessment of simple recall questions. Integrated reasoning questions that require integration of multiple pieces of knowledge are a second and more important step that the authors intend to develop in the future.

This system implements other features, such as a content repository for FMUP students, the ability to present the *Notebooks* using full screen *Flashcards* and, a picture gallery, however these are not presented as their purposes are distinct from the goals of this work.

System usability and adoption surveys

Table vi - System usability and tool usefulness survey

		S1		S2		
n	**Item**	**Mean**	**SD**	**Mean**	**SD**	***P***
1	It was easy to study using the computer	3.21	.69	3.38	.61	.04
2	The Study Mode was easy to use and understand	3.68	.52	3.81	.40	.06
3	The division of content using topics and *Flashcards* was easy to understand	3.64	.52	3.68	.47	.60
4	The division of *Flashcards* into Facts, Details, Images and Questions was easy to understand	3.60	.58	3.77	.43	.04
5	The division of *Flashcards* into Facts, Details, Images and Questions helped to understand the key information to memorize	3.43	.58	3.45	.72	.84
6	The information on the *Flashcards* was simple and clear	3.62	.49	3.60	.54	.80
7	The *Flashcards* were presented in a logical sequence that facilitates learning	3.34	.67	3.43	.65	.29
8	It was easy to find the *Flashcards* I wish to study using the *Flashcard* filters	3.38	.61	3.38	.61	1.00
9	The highlighter and the notes are useful features	3.66	.64	3.72	.54	.41
10	The Questions on the *Flashcards* were easy to understand	3.34	.73	3.45	.65	.37
11	The Questions were helpful to help me assess my knowledge about each subject	3.62	.61	3.62	.53	1.00
12	I could easily find the matching Answer to the Question in the *Flashcard* Component box	3.53	.58	3.55	.48	.20
13	The order in which the Questions were presented did not affect my focus on answering	3.34	.90	3.32	.69	.86
14	Without these tools I would not be able to obtain a similar acquired knowledge result	3.30	.81	3.00	.83	.02

SD - Standard deviation. S1 and S2 refer to session 1 and session 2. The tasks performed were the same on both sessions. Student agreement to each of the items was assessed using a 4-point likert scale: 1 - full disagreement; 2 - partial disagreement; 3 - partial agreement; 4 - full agreement. p values denote differences differences between each session mean.

The student participation rate was 100% as all of the 48 students randomized to take part in this work accepted to participate. All students completed the two sessions. The score for all items on the survey regarding system usability and tool usefulness (Table vi, Table vii) approached 3.5 (partial to full agreement) in both sessions and overall there were no significant differences between sessions. Both surveys have shown that students generally agreed that the tools provided were useful and simple and were willing to use them as a privileged element for their medical education.

Table vii - Willingness to adopt the system as a reference tool survey

n	Item	Mean	SD
15	I think this system could be used in other basic science subjects	3.77	.43
16	I think this system could be used in clinical science subjects	3.32	.75
17	I see an advantage in using this system as a tool in my daily study	3.26	.71
18	I think this system would allow me to obtain results similar or better than my average results while investing less time studying	2.96	.83
19	I wish this system would encompass the content in the way I am taught at school	3.51	.62
20	I would like to create content to take advantage of it using this system	3.40	.71
21	I would like to collaborate in real time with my colleagues to build useful content fast	2.94	.63
22	I would like to be able to print the *Notebook*s from the system	3.74	.57
23	I would rather use this system instead of my regular *Notebooks* provided all the required content is available	3.11	.84
24	I would rather use this system instead of lecture materials provided all the required content is available	3.19	.80
25	I would rather use this system instead of the recommended bibliography provided all the required content is available	3.11	.89
26	I would recommend this system to my colleagues	3.66	.52

SD - Standard deviation. Student agreement to each of the items was assessed using a 4-point likert scale: 1 - full disagreement; 2 - partial disagreement; 3 - partial agreement; 4 - full agreement.

Conclusions

Overall the application brings a new set of tools that may be helpful to organize knowledge in meaningful ways as well as to manage study sessions, based on personal performance metrics. The system takes into consideration learning object design, instructional design guidelines and principles from cognitive learning theories. Specifically the system allows students to: (1) create personal and reusable learning materials in a collaborative on-line environment (2) self-assess their knowledge through spaced repetition of open ended questions (3) view detailed feedback on their performance and progress (4) easily use the feedback for deliberate practice and to tailor future learning experiences.

Assessment of student performance on content presented through this system and direct comparison of learning outcomes against other learning tools and methods are the aims of future work. The development of these features is an important step towards bringing information management tools to support study decisions and improving learning outcomes.

PAPER 3

Characterization of medical students recall of factual knowledge using learning objects and repeated testing in a novel e-learning system*

Background

Medical education is a complex field where updates in medical knowledge, educational technology and teaching strategies intertwine in a progressive fashion.[1,2,161,195,196] Over the past decade there has been a shift in this field, where traditional instructor-centered teaching is yielding to a learner-centered model,[29,30,109,175] in which the learner has greater control over the learning methodology and the role of a teacher becomes that of a facilitator of knowledge acquisition, replacing the role of an information provider.[32,40,109,181]

Since the information learned by medical students is easily forgotten, it is important to design methodologies that enable longer periods of retention.[6] There is vast literature regarding the application of educational strategies,[73,109,197–200] instructional design,[40,73,134,164,201,202] and cognitive learning science [165,166,169,171,203] to the field of medical education in order to improve learning outcomes. Two promising approaches that emerge from that literature are *spaced repetition* and *test-enhanced learning*.

Spaced repetition

The term *spaced education* describes educational interventions that are built in order to make use of the *spacing effect*.[6] This effect refers to the finding that educational interventions that are distributed and repeated over time result in more efficient learning and retention compared to massed educational interventions.[204–207] Even though most of the evidence regarding the *spacing effect* has been gathered in settings where interventions ranged from hours to days, there is some evidence suggesting that it can also generate significant improvements in longer-term retention.[6]

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Studies carried in the medical setting show that the application of such spaced interventions increase retention of learning materials. The interventions yielding these results have been designed as spaced-education games,[170] delivery of content by email in spaced periods,[6] blended approaches composed of face-to-face sessions and spaced contacts with on-line material,[14] among others.[171] Cook *et al.* performed a meta analysis that regarded the application of spaced repetition and other methodologies on internet-based learning, and concluded that spaced repetition improves, at least, student satisfaction.[40] That work suggests that educators should consider incorporating repetition when designing internet-based learning interventions, even though the strength of such recommendations still needs reinforcement by further research.[40]

Test-enhanced learning

Even though tests are mainly used as a way to assess students, there is strong evidence that they stimulate learning by increasing retention of the information.[7,208] That has led Larsen *et al.* to define the term *test-enhanced learning* to refer to interventions where tests are explicitly used to stimulate learning.[209,210] This approach is rooted in the observation that after an initial contact with the learning material, being tested on the material increases information retention more than reviewing that material again.[210–212] This effect increases with the number of tests [213] and the spacing of tests.[214] Moreover, tests composed of open ended questions (OEQs) have been shown to be superior to multiple choice questions (MCQs) for that purpose.[172,215] Providing the correct answer as feedback also increases the retention effect.[216] While most evidence indicates that immediate feedback is generally the most effective timing to maximize retention,[217] there is recent evidence indicating that delayed feedback may have a stronger effect in some situations.[218]

The test-enhancement effect is mostly explained by the recall effort required to answer the question, leading to superior retention.[213] In addition, there is also the indirect benefit of exercising judgments of learning (JOLs) that guide further study sessions.[219] JOLs, or meta-memory judgments, are made when knowledge is acquired or revisited.[220] Theories of self-regulated study claim that active learners use JOLs to decide whether to allocate further cognitive resources toward study of a given item or to move on to other items,[221,222] thus supporting the indirect test-enhancement effect.

In the medical education setting, it has been shown that solving concrete clinical problems requires a strong grasp of the underlying factual knowledge that is inherent to the problem. Test-enhanced learning frameworks work particularly well for the retention of the factual knowledge required for higher order clinical reasoning.[210,223] It remains unclear, as in the case of spaced repetition, whether the test-enhancement effect can be maintained in the long term, as most of the evidence regards intervals ranging from weeks to months.[213,218]

Self-assessment and the ALERT STUDENT Platform

The creation of e-learning systems that enable systematic application of retention enhancement methodologies constitutes an important contribution to the information management axis of the core-competences for medical education [3] and may improve students ability to learn and retain the factual knowledge network required for effective clinical reasoning.[203]

Based on the fact that there are few reports of systems implementing these principles in such a fashion,[150] we have developed the platform ALERT STUDENT, a system that empowers medical students with a set of tools to systematically employ spaced repetition and test-enhanced methodologies to study learning materials designed in the form of Leaning Objects (LOs).[150] This platform and the theoretical background supporting each of the features has been described in detail on a previous paper.[150] LOs are groupings of instructional materials structured to meet specific educational objectives [146] which are created using a set of guidelines to make content portable, interactive and reusable,[146,174–177] and have been shown to enhance learning.[176]

The platform implements test-enhanced learning in the form of quizzes. These are composed of sets of OEQs about each of the LOs. The questions are meant to stimulate students to recall learned information, and therefore enable the measurement of JOLs. Typically, JOLs can be estimated as the prediction of the learner about how well it would recall an item after being presented the item.[224] Numerous methods exist to assess JOLs for different purposes.[225] The cue-only JOL, a method where the student must determine the recall of an item (in our case a LO) when only the cue (the OEQ) is presented at the time of judgment,[225] is of particular interest to us. We extend this type of JOL to define a measurement named *recall accuracy*. The *recall accuracy* is similar to the cue-only JOL because after being presented the cue and trying to retrieve the target, the student is presented the LO that contains the target. The student then grades the similarity between the retrieved target and the actual target. The process of measuring *recall accuracy* corresponds to the immediate feedback stage employed on test-enhanced learning approaches. This approach maximizes the potential of LOs and the OEQ to serve as learning material, recall cue and recall feedback.

To sum up, educators can use the platform to publish LOs, and students can apply the spaced repetition and test-enhanced methodologies on those LOs to hopefully improve their learning retention and direct study sessions effectively.

Evaluation of education programs

Even though most educators value the importance of monitoring the impact of their educational interventions, systematic evaluation is not common practice, and is frequently based on inference measures such as extent of participation and satisfaction.[226] Additionally, most program evaluations reflect student cognitive, emotional and developmental experiences at a rather superficial level.[226,227]

This issue also affects medical education.[228] Evaluation should drive both learning and curriculum development and demands serious attention at the earliest stages of change.

To make accurate evaluations of learning programs, it is essential to develop longitudinal databases that allow long term follow up of outcomes of interest.[229] In this line of thought we believe that *recall accuracy* information collected through the ALERT STUDENT platform in real-time may provide an additional resource to be included in student-oriented [228] and program-oriented [228] evaluation approaches, through the estimation of longitudinal student performance, and the determination of instruction and content fitness to student cohorts, respectively.

Aims to this study

Since *recall accuracy* plays a key role in the learning method implemented by the ALERT STUDENT platform, this work aims, firstly, to characterize how *recall accuracy* evolves with usage of the spaced-repetition and test-enhanced learning tools in a controlled setting, and secondly, to characterize the extent to which students, LOs and intervention sessions contribute to the variation in *recall accuracy*. We hypothesize that *recall accuracy* improves along sessions, but we do not know how the contact with the system modulates it.

In addition we hypothesize that *recall accuracy* may constitute a relevant source of information to determine the learning difficulty of a LO for a given student cohort, and believe this information may contribute to the evaluation of the fitness of educational interventions. To elucidate this topic, we performed a G-Study to assess the agreement over the contribution of the LOs to *recall accuracy* scores, and performed a D-Study to characterize the conditions in which the number of students and repetitions of grading *recall accuracy* yield strong agreement on the difficulty of the LOs for the examined student cohort.

Methods

The Faculty of Medicine of the University of Porto (FMUP) implements a 6-year graduate program. Applicants are mainly high school graduates. The first three years focus on basic sciences while the last three focus on clinical specialties. For the purpose of this work, content about the Golgi Complex was designed using lectures from the Cellular and Molecular Biology class, taught in the second semester of the first grade.

ALERT STUDENT platform

The ALERT STUDENT the platform allows the creation and distribution of LOs named *Flashcards*. These are self-contained information chunks with related OEQs. A *Flashcard* is composed of a small number of information pieces and OEQs that correspond to one of the information pieces. Educators can put together ordered sequences of *Flashcards* that describe broader learning objectives, thus forming high-order LOs denominated *Notebooks*.

Notebooks are the units in which the spaced-repetition sessions and the test-enhanced learning tasks can be performed. Spaced-repetition tools are made available through a Study Mode feature that presents in order the complete set of *Flashcards* belonging to a *Notebook* in a study-friendly environment enriched with note taking, text highlighting, and a *Flashcard* study priority cue based on personal *recall accuracy* from corresponding OEQs. The *Flashcard* information and OEQs can be studied in this mode. Test-enhanced learning is achieved through the Quiz Mode, a complementary environment where retention of *Flashcard* information can be self-assessed through *recall accuracy* using the OEQs as cues. Active recall is graded for each question using a 4-point likert scale (0 - no recall, 1 - scarce recall, 2 - good recall, 3 - full recall). On every quiz session, the system picks one OEQ for every piece of information on every *Flashcard*. OEQs are displayed one at a time. In case there is more than one OEQ for an information piece, the system picks one OEQ that has not yet been graded. When all the OEQs have been graded for a given information piece, the system picks the OEQ with the lowest *recall accuracy*. At the end of a Quiz Mode session, the student is presented the set of *Flashcards* and OEQs for which *recall accuracy* was 0.

Pilot study

A pilot study was performed to design a *Notebook* that could be studied in 20 minutes. 5th grade students (n=6) were assigned to a read a *Notebook* with 30 *Flashcards* created using lecture material about the Golgi Complex. The final *Notebook* was created using the *Flashcards* that the students were able to study within the time limit. That *Notebook* consisted of the first 27 *Flashcards*, totaling 37 information pieces and 63 OEQs. Each *Flashcard* contained one or two pieces of information, sometimes accompanied by an image - there were 5 images in total. Each piece of information in a *Flashcard* corresponded to a set of 1 to 4 OEQs. This *Notebook* is available in Appendix 5.

Furthermore, in order to estimate the sample size, 2nd grade students (n=2), 4th grade (n=2), and 5th grade (n=2) medical students were asked to grade their *recall accuracy* for the 63 OEQs. The 4th and 5th year students' knowledge was assumed to correspond to low *recall accuracy* about the Golgi, and was expected to represent the mean *recall accuracy* of a similar student sample before the research intervention. 2nd grade medical students knowledge was assumed to correspond to high *recall accuracy* about the Golgi, and was expected to represent the mean the *recall accuracy* of a student sample after the research intervention.

The average percentage difference in *recall accuracy* between the two student groups was 41%. Finding a similar difference in mean *recall accuracy* before and after an intervention using the study and quiz tools was assumed to be a reasonable expectation. Thus, the sample size required to discriminate statistical significance under such circumstances was n=48, assuming a power of 80% and a significance level of .05. The sample size was incremented to n=96 to take advantage of the laboratory capacity.

Intervention design

Ninety-six (n=96) students from the 4th and 5th grades of our school were randomly picked from the universe of enrolled students (approx. 500), and were contacted via email to participate one month prior to this study. Two students promptly declined to participate and two more students were randomly picked. Students were assigned into *study-quiz* group or *quiz* group using simple randomization.

The intervention employed a study task and a quiz task. The study task consisted in studying the Golgi *Notebook* during 20 minutes using the study mode. The students were able to take notes and highlight the text. The quiz task consisted in using the quiz mode to answer the OEQs about the Golgi and grade *recall accuracy*, within 15 minutes. Before each task students were instructed on the purpose of each task and the researcher exemplified each of the tasks in the system. Students performed each task alone. Doubts raised by the students concerning platform usage were cleared by the researcher.

Table viii - Study design - Representation of the study intervention

Session	Quiz group n=49	Study-Quiz group n=49
0	Quiz - 15 min	Quiz - 15 min
1 week interval		
1	Quiz - 15 min	Study - 20 min Quiz - 15 min
1 week interval		
2	Quiz - 15 min	Study - 20 min Quiz - 15 min

Participants (n=96) were split into quiz and study-quiz groups by simple randomization. During S0 both groups performed the quiz task during 15 minutes. On S1 and S2 the quiz group performed the quiz task again for 15 minutes. The study-quiz group performed a 20-minute study task, immediately followed by the 15-minute quiz task. Sessions were separated by one-week intervals.

Three laboratory sessions (S0, S1 and S2) of 1-hour duration were carried with one-week intervals. On S0, both groups performed the quiz task. On S1 and S2, the quiz group performed the quiz task alone, and the study-quiz group performed the study task immediately followed by the quiz task. Since the platform implements a study workflow centered on performing the study task followed by the quiz task, the study-quiz group was created to indirectly measure changes in *recall accuracy* attributable to the study task. The quiz group describes the changes in *recall accuracy* that are attributable to the quiz task. This procedure is detailed in Table viii.

Sample characterization

In session S0 both groups filled a survey to characterize the student sample. Measured factors were gender, course year, preferred study resource for Cellular Biology, computer usage habits, Cellular Biology grade, mean course grade, and average study session duration during the semester and during the exam season. The Cellular Biology grade was assumed to be the grade that best estimated prior knowledge about the Golgi. These factors were added to characterize the study sample and assess eventual dissimilarities in the sampling of the two groups.

Statistical Analysis

For each session and group, *Flashcard recall accuracy* was computed as the mean *recall accuracy* of the OEQs belonging to a *Flashcard*.

In order to characterize the changes in *recall accuracy* across sessions, we used univariate repeated-measures analysis of variance (ANOVA). Groups were used as between-subjects factor. Session and *Flashcard* were used as within subject factor. Repeated contrast (S0 vs. S1 and S1 vs. S2) was used to evaluate the sessions and the session interaction effect.

In order to estimate the variance components for the *recall accuracy* for both groups, a random effects model was used and the *Flashcard*, the session and the student were used as random variables. The estimation was performed using the Restricted Maximum Likelihood method. In order to estimate the agreement on the *Flashcard* component its specific G-coefficient was calculated. A D-Study was performed to characterize the agreement on the *Flashcard* component for different student and session counts. Guidelines for interpreting G-coefficients suggest that values for relative variance between 81 - 100% indicate almost perfect agreement, 61 - 80% substantial agreement, 41 - 60%

moderate agreement, 21 - 40% fair agreement, and values less than 21% depict poor or slight agreement.[230]

The statistical analysis was performed using *R* software. The package *lme* was used to compute the random effects model.

This study was approved by the Faculty of Medicine University of Porto / *São João* Hospital Ethics Committee in compliance with the Helsinki Declaration. Collected data was analyzed in an anonymous fashion. It was not possible for the researchers to identify the students during any phase of the data analysis.

Results

Study sample characterization

94 participants completed the session S0. 1 participant in the study-quiz group and 1 participant in the quiz group did not complete session S1 and were excluded from the study. By the end of the study there were 47 participants in each group. 59 participants were female and 35 participants were male. 44 participants were enrolled in the 4th grade and 53 were enrolled on the 5th grade.

The preferred study resources for Cellular Biology were Professor texts (n=36), followed by Lecture notes (n=24), Lecture slides (n=23) and finally the Textbook (n=11). Most participants reported using computers every day (n=78). Average course grade was 68%, and the average Cellular Biology grade was 64% - equivalent results for the student population were 65% and 62% respectively, representing a fair score.

Participants reported daily study sessions during the semester to last on average 3.0 hours and daily exam preparation study sessions to last on average 9.5 hours. No significant differences between the study-quiz and quiz groups were found for any of the sample characterization factors.

These results are described in further detail in Table ix.

Recall accuracy characterization

Mean *recall accuracy* increased from 25% in S0, to 53% in S1, to 62% in S2. In the quiz group, mean *recall accuracy* increased from 24% in S0 to 33% in S1 (*P*<.001) to 42% in S2 (*P*<.001). In the study-quiz group, *recall accuracy* increased from 27% at S0 to 73% at S1 (*P*<.001) to 82% at S2 (*P*<.001).

Table ix - Study sample characterization

	Total		Control		Experiment		
Gender	**n**	**%**	**n**	**%**	**n**	**%**	***P***
Female	59	62.8	28	59.6	31	65.9	.67
Male	35	37.2	19	40.4	16	34.1	
Course year	**n**	**%**	**n**	**%**	**n**	**%**	***P***
4th year	44	46.8	23	48.9	21	44.7	.84
5th year	50	53.2	24	51.1	26	55.3	
Preferred resource	**n**	**%**	**n**	**%**	**n**	**%**	***P***
Professor texts	36	28.2	17	36.2	19	40.4	.90
Lecture notes	24	25.5	12	25.5	12	25.5	
Lecture slides	23	24.5	13	27.7	10	21.3	
Textbook	11	11.7	5	11.6	6	12.8	
Computer usage	**n**	**%**	**n**	**%**	**n**	**%**	***P***
Everyday	73	77.7	37	78.2	36	76.6	.19
Not everyday	21	22.3	10	21.2	11	23.4	
Grades	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	***P***
Cellular Biology	64	6.0	65	8.0	64	8.0	.10
Course average	68	5.5	69	5.5	68	5.5	.43
Daily study hours	**Median**	**IR**	**Median**	**IR**	**Median**	**IR**	***P***
During semester	3.0	2.5	3.0	2.0	3.0	2.0	.63
During exam season	9.5	2.0	10.0	2.0	8.0	2.0	.31

Cellular Biology Grade and Course Average are displayed in a 0-100% grading scale.
SD - Standard Deviation; IR - Interquartile range.

At session S0, there were no differences in *recall accuracy* between groups. During S1 and S2, *recall accuracy* differences between groups were statistically significant (*P*<.001). The study-quiz group achieved a sharper increase in *recall accuracy* than the quiz group. The increase in *recall accuracy* was greater between S0 and S1 for both groups. In respect to the study-quiz group, *recall accuracy* had a relative increase of 63% from S0 to S1.

Between S1 and S2 there was a relative increase of 12% in *recall accuracy* for that group. The quiz group had a relative increase of 27% between S0 and S1, and a relative increase of 21% from S1 to S2.

These results are described in further detail in Table x.

Table x - Recall accuracy per session and group

	Total (%)		Control (%)		Experiment (%)		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	P^1
S0	25.3	18.7	24.0	16.7	27.0	17.7	.924
S1	53.0	22.3	33.0	18.0	72.7	18.3	< .001
S2	62.3	21.7	42.0	20.7	82.3	15.0	< .001
p^2		< .001		< .001		< .001	$< .001^3$

SD - Standard Deviation; 1 Differences in *recall accuracy* between study-quiz and quiz group; 2 Differences in *recall accuracy* between pairwise sessions; 3 Interaction effect between session and group.

Regarding the ANOVA, the session and group Dfs equaled 1, Sum square/Mean square difference values were 56.5 for the session, and 23.5 for the group. F-values were 292.2 for the session and 121.2 for the group. Eta-squared values were .32 for the session and .27 for the group.

Table xi - Components of variance of *recall accuracy* for the quiz group

Component	n	Variance	SD	%^{1}
Participant	47	.17	.41	15.1
Flashcard	27	.38	.61	34.7
Sessions	3	.09	.30	8.2
Residual	3440	.46	.68	41.2

SD - Standard Deviation; 1 - Percentage of total variance.

Regarding the components of variance for *recall accuracy* in the quiz group, the largest one was the *Flashcard* (34.7%). The participant and session components explained a small proportion of variance (15.1% and 8.2%, respectively) reflecting small systematic differences among participants and sessions. The residual component accounted for 41.2% of the total variance. These results are described in further detail in Table xi.

In respect to the components of variance for *recall accuracy* in the study-quiz group, the most prominent factor was the session (49.6%). The participant and *Flashcard* components explained a small proportion of variance (5.1% and 15.3%, respectively). The residual component accounted for 30.0% of the variance. These results are described in further detail in Table xii.

Table xii - Components of variance of *recall accuracy* for the study-quiz group

Component	n	Variance	SD	%^{1}
Participant	47	.08	.29	5.1%
Flashcard	27	.25	.50	15.3%
Sessions	3	.81	.90	49.6%
Residual	3422	.49	.70	30.0%

SD - Standard Deviation; 1 - Percentage of total variance.

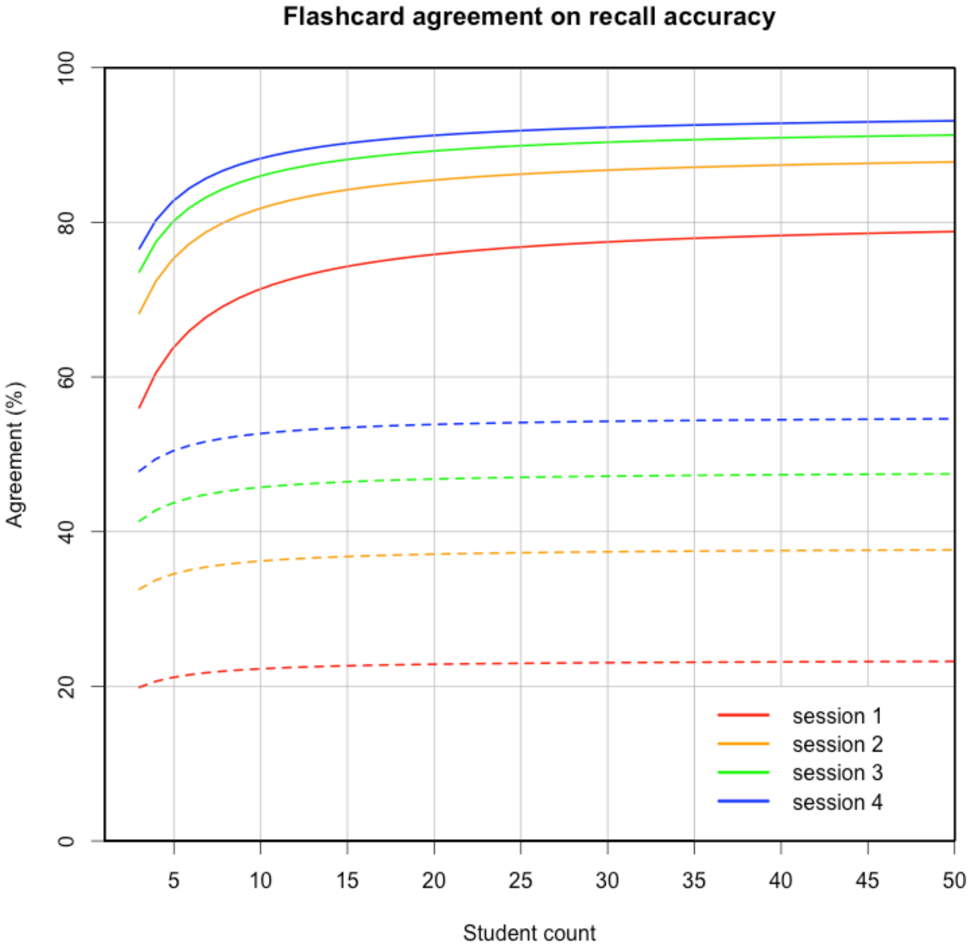
For both groups two-way and three-way interactions were computed and explained a very small fraction of total variance. G-coefficient for the *Flashcard* variance component was 91% in the quiz group, indicating almost perfect agreement. Regarding the study-quiz group, the coefficient value was 47%, indicating moderate agreement.

The D-Study performed for the *Flashcard* variance component showed that almost perfect agreement (>80%) can be achieved by having 10 students perform the quiz task on 2 spaced sessions. Circumstances to obtain such levels of *Flashcard* agreement for the study and quiz task would require unfeasible numbers of students and sessions. Figure 16 plots the D-Study agreement curves for the *Flashcard* variance component in both study-quiz task and quiz task alone, for different student and session counts.

Discussion

It was unclear what difference to expect in terms of *recall accuracy* between groups and between sessions. We selected a basic science topic and 4th and 5th grade medical students, in order to maximize the odds of a low degree of prior knowledge. We chose the Golgi Complex because the majority of the curriculum does not build directly on this concept, and thus it was likely a forgotten topic. This was important because the lowest the a prior knowledge before our intervention, the smaller student sample would be required to discriminate significant differences in *recall accuracy* during the study sessions, thus rendering this study feasible.

Figure 16 - D-Study for agreement on *Flashcard* variance component of *recall accuracy*



G-coefficient for the *Flashcard* component of *recall accuracy* using different combinations of number of students (x axis) and sessions (colored curve sets). The stroked curve set represents quiz group agreement, and the dashed curve set represents study-quiz group agreement. It can be seen that with a small number of students and sessions of using the study and quiz modes (dotted curve set) or quiz mode alone (stroked curve set), substantial (>60%) and strong (>80%) *Flashcard* agreements on *recall accuracy* are obtained, respectively.

Evolution of *recall accuracy* across sessions

There is an effect on *recall accuracy* reported by students along sessions. It was expected that the study-quiz group would out-perform the quiz group in terms of *recall accuracy*, at least on S1. Since the quiz task provides the learning materials as the correct answers to the OEQs and additional feedback at the end of the task, it has high learning value. Because we used a 4-point scale to grade *recall accuracy*, it was reasonable to consider the hypothesis that the quiz task provides enough learning value to master the content and thus expect both groups to report similar *recall accuracy* results.

The *recall accuracy* increase was stronger in session S1 for the study-quiz group. It was expected to see an increase in this session since the content was tailored to be fully covered within the 20-minute time limit. The strong gain indicates that this session was the one that accounted for the greatest increase in *recall accuracy*.

Findings by Karpicke *et al.* suggest that the testing effect plays an essential role in memory retention, and that after an initial contact with the learning material it is more beneficial to test rather than re-study the material.[213] In addition, since using open-ended assessment questions as a means to learn improves knowledge retention,[210,212,219] it was unclear how strong would that increase be in the quiz group. However that increase was only a modest one. That finding might be explained, at least in part, by minimization of the cueing effect - the ability to answer questions correctly because of the presence of certain questions elements [231,232] - through the usage of different questions for each information piece. OEQs are known to minimize cueing [232,233] and in addition, the different questions, although having the same content as answer, minimized that effect. This shows that pairing OEQs with LOs increases the value of the learning material.

In our study we found that *recall accuracy* increased more in the study-quiz than in the quiz group. If we assume that *recall accuracy* represents knowledge, then the most likely explanation for higher the increase in recall for the study-quiz group is the additional time-on-task. We were concerned that, because the metric is a subjective one, repeated contact with the content would cause the *recall accuracy* value to overshoot to nearly 100% after the first contact, regardless of prior knowledge or the time-on-task. However, *recall accuracy* evolved along sessions according to the underlying variables: *recall accuracy* at S0 was low because the student cohort did not have any formal contact with the Golgi over 2 years; the study-quiz group - with longer time-on-task - had higher results than the quiz group; *recall accuracy* improved along the sessions for both groups in part because of the effect of previous sessions.

Thus *recall accuracy* evolved in accordance to the factors influencing learning.

Adequacy of *recall accuracy* as a measurement of knowledge

The consistent differences in *recall accuracy* between groups give and indication that this measurement, although being of subjective nature, seems to be positively related with knowledge acquisition.

Karpicke *et al.* has shown that in a controlled setting, students cannot reliably predict how well they will perform on a test based on their JOL.[213] Other studies conducted in ecological settings also have shown that the relationship of knowledge self-assessment with motivation and satisfaction are stronger than with cognitive learning.[192,234,235] Additional research found that in a blocked practice situation learners tend to be overconfident and JOLs are often unreliable.[236]

Our study design differed from the classical designs for studying the effects of spaced repetition, knowledge retention and JOLs [204] because it was intended to describe *recall accuracy* evolution in a use-case similar to the real-world use of the system. Therefore, available evidence may not be completely applicable to this study. However, based on our results, we cannot completely refute the hypothesis that *recall accuracy* is independent of knowledge acquisition and dependent on affective factors. It is possible, though unlikely, that affective factors introduce a systematic error in *recall accuracy* grading. The colorful nature and intensity of such factors would most likely lead to a random error rather than systematic variation. This finds support in our results regarding *recall accuracy* variance components, since the *Flashcard* component contributed substantially more than the participant component to the total variance. In addition, it is well known that higher time-on-task is one of the most important determinants of learning.[163] Because *recall accuracy* was higher on the study-quiz group - with greater time-on-task - this is likely mainly explained by the learning effect.

Furthermore, other studies have measured JOLs differently than in this study. While other approaches typically measure JOL by requiring the subject to predict how well would they perform when tested in the future,[205,213,236] our approach focuses on requiring subjects to compare their answer with the *Flashcard* containing the correct information. Because our approach does not require a future projection and is additionally performed in the presence of both the recalled and correct answers, it is unlikely to vary independently of the learning effect.

Thus, we hypothesize that measuring *recall accuracy* immediately after the recall effort and in the presence of the correct answer may help students make sound JOLs. However further work is needed to compare *recall accuracy* with an objective measurement of knowledge, such as a MCQ test, in order to prove that hypothesis. Assuming a relationship between both variables is found, it would also be relevant to understand how different degrees of *recall accuracy* map to different degrees of knowledge.

Recall accuracy components of variance

Regarding the quiz group, the recall variance was mainly affected by the differences in *Flashcard* and by the differences in participants. This indicates, firstly, that systematic differences in the *Flashcards* were mainly responsible for the variation in recall scores, and secondly, to a smaller extent, differences between participants, possibly regarding affective and knowledge factors also played a role. The effect of the multiple sessions accounted little for the increase in *recall accuracy* over the sessions. The high G-coefficient for the *Flashcard* variance component indicates the *Flashcards* are very well characterized in terms of *recall accuracy* under these circumstances. Thus, factors intrinsic to the content, such as its size, complexity, or presentation, are very likely responsible for differences in *recall accuracy* between *Flashcards*.

Assuming the *recall accuracy* is related to knowledge acquisition, systematic differences in *recall accuracy* between *Flashcards* can indicate which materials are harder to learn and which materials are easy. Using this information to conduct revisions of the learning material may be useful to find content that would benefit from redesign, adaptation, or introductory information.

With respect to the study-quiz group, the contact with the content over multiple sessions was the main driver of *recall accuracy* improvement. Participant features had little effect in the increase *recall accuracy* over sessions and the *Flashcard* features also accounted for less effect than in the quiz group. This suggests that the students in the study-quiz group increased their knowledge about the content and their prior knowledge had little effect in the learning process when using the study tools. This effect is most likely explained by the additional time-on-task of the study-quiz group. In addition, some of the effect may also be explained by findings in other studies that show that there is benefit in using repeated testing with study session in order to enhance learning.[210,212,219]

Potential implications to educators

The way in which content can be organized to optimize learning has been extensively studied.[3,131,146,167,169,173] This study demonstrates how LOs can be of value for both study and self-assessment when combined with OEQs. The detailed insight on *recall accuracy* can be used by educators to classify LO difficulty and estimate the effort of a course. By providing a diagnostic test on the beginning a course in the form of the quiz task, educators can get a detailed snapshot of the material difficulty for the class. This data can be useful to evaluate educational interventions at a deeper level.[229]

Because the platform can be used by the students to guide learning on their own, educators can access real-time information of *recall accuracy* and use it to tailor the structure of the class to better meet the course goals. Furthermore, research has identified the delivery of tailored learning experiences as one of the aims that blended education approaches have yet fully reached.[38]

In a hypothetical scenario where students repeatedly study and quiz, it is expected that the main component of *recall accuracy* variance is the session count. Deviation from such a pattern could suggest flaws in content design, excessive course difficulty or other inefficacies in teaching and learning methodologies. Sustained increases in *recall accuracy* mainly explained by the session would inform the educator of a continuous and successful commitment of the students. If educators take constructive action from such observations then a positive feedback cycle between student engagement and the success of the learning activity would be established. Because students know educators can take real-time action based on their progress, they engage more strongly in the learning activities. Stronger engagement will lead to better learning outcomes, that will lead to further tailored action by the teacher. Indeed, student engagement is the main driver of learning outcomes.[237] Providing tools that can foster such engagement is key to achieve successful learning.[238,239]

Potential implications to learners

Students need tools to help retain knowledge for longer periods and easily identify materials that are more difficult to learn.[6] This goal may be achieved by providing learners with personal insight on their learning effectiveness, using personal and peer progress data based on self-assessment results.[176]

The past *recall accuracy* can be used as an explicit cue to guide the learning process and help managing study time. Since JOL measurements are implicitly used by learner to guide the learning task,[205,214] an explicit *recall accuracy* cue displayed for each *Flashcard* in the form of a color code can improve the value of the JOL.[150] The feedback that is thus formed between the quiz and the study task further promotes the spaced repetition of study and self-assessment sessions and can improve student engagement, the main driver of successful learning. This is even more important at a time where students need to define tangible goals that allow them cope with course demands.[240]

Each *Flashcard* holds the *recall accuracy* for each student for each assessment. Increasing spaced repetitions of study and quiz increase the available *recall accuracy* data. Since *Notebooks* can be constructed using any available *Flashcard*, it is possible to create *Notebooks* that include *Flashcards* for which *recall accuracy* is already available. Therefore, advanced *Notebooks* requiring background knowledge can include an introductory section composed of the most relevant *Flashcards* about the background topics. This implies that without previous contact with the advanced *Notebooks*, an estimate of how well the student recalls the background topics is already available. This increases the value of learning materials by fostering reutilization and distribution of LOs between different courses, educators and students [146,150,176] and promoting educator and student engagement.[238]

Proposal for curricular integration

In recent years multiple educational interventions have described the benefits of implementing blended learning methodologies in medical education, namely in radiology,[241] physiology,[73] anatomy [200] and others.[242,243] However, the design of these interventions varies widely in configuration, instructional method and presentation.[38] Cook *et al.* asserted that little has been done regarding Friedman's proposal [35] of comparing computer based approaches rather than comparing against traditional approaches.[176]

The platform ALERT STUDENT intends to add value to the blended learning approach, through the collection of *recall accuracy* data, and prescription of a method that can be systematically applied in most areas of medical knowledge. Over this platform, interventions with different configuration, instructional method or presentation can be developed, and thus allow sound comparison between computer assisted interventions and comparison between different fields of medical knowledge. The platform does not intend, however, demote the usage of other tools, rather it intends to potentiate their usage. As an example, the platform could be used to deliver the learning materials and provide the study and quiz features, that would act in concert with MCQ progress tests during class. Educators could use information about *recall accuracy* and number of study and quiz repetitions to gain insight on the relationship between test results and student effort. That information would be relevant to help educators mentor students more effectively. Again, the information brought by *recall accuracy* could be helpful to tailor other instructional methods and thus drive student satisfaction and motivation.

Limitations and further work

This work has several limitations. Recall accuracy cannot be granted to correspond to knowledge retention. As previously mentioned, additional research is required to investigate the relationship between the two. In the light of our findings, it also becomes relevant to characterize *recall accuracy* in ecological scenarios and multiple areas of medical curriculum, under larger learning workloads.

We have indirectly characterized the effect of the study task on the *recall accuracy*. We expect however that an equivalent time on the quiz task alone would yield higher effects in *recall accuracy*, in consonance with the findings by Larsen *et al.*[209,210] That is also a matter that justifies further investigation. The system works around factual knowledge, therefore it is only useful in settings that require acquisition of such knowledge. Complex competences such as multi level reasoning and transfer cannot be translated in terms of *recall accuracy*. Ways in which the system could be empowered to measure such skills would constitute important improvements of the platform.

Conclusions

The present study focus on measuring *recall accuracy* of LOs using OEQs in a laboratory setting through the ALERT STUDENT platform. We found that the quiz task alone led to a modest increase on *recall accuracy*, and that the study-quiz task had high impact in *recall accuracy*. The session effect was the main determinant of *recall accuracy* on the study-quiz group, and the *Flashcard* and participant effects determined most of the increase in *recall accuracy* in the quiz group. We concluded that *recall accuracy* seems to be linked with knowledge retention and proposed further investigation to ascertain the nature of this relationship. Recall accuracy is an easily collectible measurement that increases the educational value of LOs and OEQs. In addition, we have discussed the educational implications of providing real-time *recall accuracy* information to students and educators, and proposed scenarios in which such information could be useful to deliver tailored learning experiences, assess the effectiveness of instruction, and facilitate research comparing blended learning interventions.

The present findings will be explored in more detail in future work, as they may help future physicians and medical schools meet the challenge of information management [3] and instilling a culture of continuous learning, underpinning the core competencies outlined for XXI century physicians.[1,2]

PAPER 4

The interaction between learner, learning material and objective assessment *

Introduction

Self-directed learning is a process through which learners are responsible and in control of their own learning process.[244] It has been shown that learners that took medical courses designed to promote self-directed learning manage their continuing medical education better than learners from traditional courses.[4,245] To this respect, computer supported collaborative learning systems (CSCL) have played a significant role [5] not only through the increased ability to access information,[246] but also by enabling teachers and students to interact asynchronously.[31,150] Notwithstanding these remarkable achievements, data resulting from the interaction between the students and the learning materials is generally not being recorded or studied. This is reflected by the fact that a sizeable fraction of CSCL research in medical education has been focused on comparing the effectiveness new approaches to traditional ones, instead of focusing on which CSCL approaches are most adequate for each scenario.[39]

In our view, data such as text highlighting, study duration, and learners own judgment of learning (JOLs) may potentially be translated into feedback to steer the learning process. JOLs, in particular, can play an important role. It has been shown that JOLs requiring a target to be recalled based on a cue shortly after having studied cue-target pairs strongly correlate with future performance on objective assessment.[247,248] JOLs and study strategies are not epiphenomenal and are known to affect self-directed learning,[18,19] except in a few circumstances.[22,249]

We have previously developed and characterized a JOL named *recall accuracy.*[151] Recall accuracy is a cued JOL that measures the similarity between a segment of learning material - henceforth denominated *Flashcard* - and the recalled response to an open-ended question (OEQ) that can be answered with information from that *Flashcard*. Recall accuracy

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represents the learner retention of factual knowledge, which is the foundation of clinical reasoning. It is a simple measurement that requires splitting the learning material into *Flashcards* according to Mayer's [8] segmentation principle, and the creation of matching OEQs.

We believe that the assessment outcomes of self-directed learning activities can be predicted from JOLs and *learner-to-learning material* interaction data. Thus, the aim of this study is to assess the interplay between text highlighting, study duration and *recall accuracy* using a set of *Flashcards*, in order to predict the outcome of a multiple-choice examination.

Methods

Study Sample

Our medical school implements a 6-year curriculum, in which the first three focus on basic science topics and the last three on clinical clerkships. We selected n=46 medical students from the 4th and 5th grade of our medical school which had been randomly sampled into the experiment group of a simultaneous study regarding *recall accuracy*.[151]

Learning content

The content used for this study was a small lecture on the Golgi Complex that was broken into *Flashcards* according to the segmentation principle.[8] *Flashcards* were validated in terms of size and ability to discriminate *recall accuracy* scores, as described elsewhere.[151] In addition, an MCQ was created for each *Flashcard*. In total, there were 27 *Flashcards*, 63 OEQs and=27 MCQs. 5 *Flashcards* contained images. *Flashcards* had on average 229 characters (SD=118).

Study procedure

The procedure is documented in full detail elsewhere (15). In short, the study was conducted in weekly 1-hour laboratory sessions (S0, S1, S2), using the ALERT STUDENT online platform, which allows note taking, text highlighting, and measurement of study duration and *recall accuracy*.[150] This information is displayed during the study sessions for each *Flashcard*. The students were required to complete a 15-minute study task followed by 10-minute *recall accuracy* task. During the *recall accuracy* task students were presented one OEQ at a time for each *Flashcard* and measured their *recall accuracy* using a 4-point *likert* scale.

On S0 students performed the *recall accuracy* task. On S1 and S2 the students completed the study task, followed by the *recall accuracy*. Finally, specifically for this study, immediately after completing the *recall accuracy* task on S2, students were given 10 minutes to complete a multiple-choice test consisting of the 27 MCQs, which were presented in random order for each student.

Variables

We recorded number of text highlights, study duration and *recall accuracy* for each participant and *Flashcard* during each session. Study duration was expressed in seconds. Recall accuracy was expressed as values between 0 and 1. Incorrect and correct answers to the MCQs were coded as either 0 or 1, respectively.

Statistical analysis

We performed path analysis [250] to assess the effects between highlight count, study duration and *recall accuracy* within each sessions, as well as the effects between these variables across sessions. These variables were used to predict the probability of correctly answering the MCQ for each *Flashcard*. The analysis was performed using a structural equation modeling framework available for the *R* language statistical software [251] and the package SEM.[252] We built two different models. The outcome variables for *model 1* were *recall accuracy* at S1 and S2, study duration at S1 and S2 and the probability answering MCQs correctly. The predictor variable was *recall accuracy* at S0. The outcome variables for *model 2* were text highlight and study duration at S2 and the probability of correctly answering each MCQ. The predictor variables were text highlight count and study duration at S1. Predictors of both models were adjusted for the *Flashcard* character count. The Root Mean Square Error of Approximation (RMSEA) Index and the Confirmatory Fit Index (CFI) were used to assess model fit. RMSEA values less than .05 and CFI values greater the .95 indicate good model fit.[253]

The Ethic Committee at *São João* Hospital approved this study, and the students gave written consent to participate. Collected data was treated anonymously.

Results

All 46 students completed the study. Text highlight count, study duration, *recall accuracy*, and MCQ answers were successfully recorded for the 27 *Flashcards*.

Summary results

Mean *recall accuracy* for session S0 was .16 (SD=.17). On session S1 each *Flashcard* had an average of 1.18 text highlights (SD=.34), and was studied for and average of 38 seconds (SD=18.7). Mean *recall accuracy* at the end of the session was .55 (SD=.30). On session S2 each *Flashcard* was highlighted on average 1.23 times (SD=.40), and studied for 30 seconds (SD=15.5). At the end of session S2 mean *recall accuracy* was .60 (SD=.32). The mean probability of correctly answering each MCQ was .71 (SD=.09). These results are depicted in Table xiii.

Table xiii - Study sample characterization

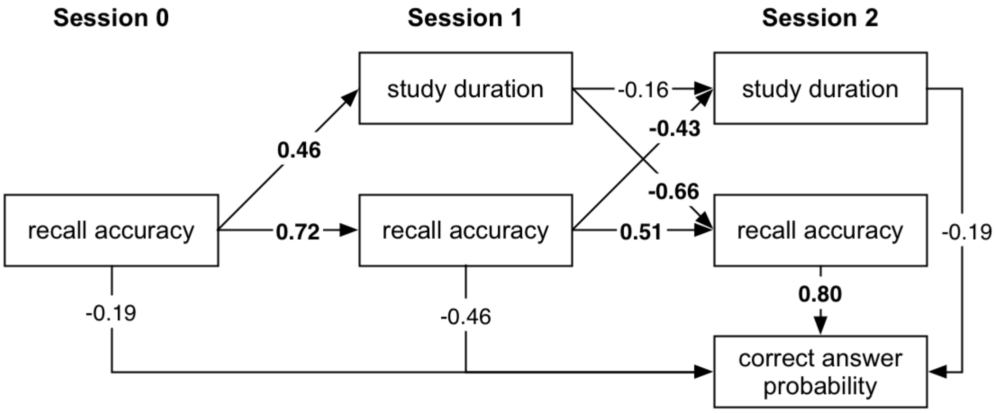
			Mean	**SD**
Outcome	S0	Recall accuracy	.16	.17
	S1	Highlight count	1.18	.66
		Study duration	37.70	18.70
		Recall accuracy	.55	.30
	S2	Highlight count	1.23	.78
		Study duration	30.20	15.50
		Recall accuracy	.60	.32
		Correct answer probability	.73	.09

Study duration expressed in seconds. Recall accuracy ranged from 0 to 1. SD - Standard deviation.

Parameter estimates for model 1

Model structure is depicted in Figure 17. Standard ß coefficients indicate the proportion of change in standard deviations of the outcome variable when the predictor variable increases by 1 SD. A .17 increase in *recall accuracy* in session S0 accounted for an increase of 8.6 seconds in study time in session S1 (ß=.46, *P*<.001). It also accounted for an increase of .22 in *recall accuracy* in session S1 (ß=.72, *P*<.001) and an increase of .17 in *recall accuracy* in session S2 (ß=.53, *P*=.002). Finally, this increase accounted for a not significant decrease of .02 in the probability of correctly answering each MCQ (ß=-.19, *P*=.456).

Figure 17 - Schematic representation of variables included in model 1



Df = 2; CFI = 0.98; RMSEA = 0.03

Relationships between *recall accuracy*, study duration and correct answer probability for the 27 *Flashcard*s studied by 46 students along 3 weekly study sessions. Arrows indicate standard ß estimates between variables. Statistically significant results are presented in bold typeface. The model was adjusted for the number of characters of each *Flashcard*.

A .30 increase in *recall accuracy* in session S1 accounted for a decrease of 6.7s on session S2 study duration (ß=-.43, *P*=.032), but increased *recall accuracy* by .16 for that session (ß=.51, *P*<.001). It also caused a decrease of .04 in the correct answer probability, but was not significant (ß=-.46, *P*=.241).

An increase of 18.7s in study duration on session S1 accounted for a not significant decrease of -2.5s during session S2 (ß=-.16, *P*=.432) as well as a decrease of -.21 in *recall accuracy* in S2 (ß=-.66, *P*<.001).

Regarding session S2, an increase of .32 in *recall accuracy* caused an increase of .07 in the probability of correctly answering the MCQ (ß=.80, *P*=.004). An increase in study duration of 15.5s caused a decrease of .02 in the correct answer probability (ß=-.19, *P*=.301), but it was not significant. Table xiv depicts the standard ß estimates and the *P* values for the described variables.

Table xiv - Path analysis of *recall accuracy*, study duration and correct answer probability

Predictor		**Outcome**		**ß**	***P***
S0	Recall accuracy	S1	Study duration	.46	**< .001**
			Recall accuracy	.72	**< .001**
		S2	Recall accuracy	.53	**.002**
			Correct answer probability	-.19	.456
S1	Study duration	S2	Study duration	-.16	.432
			Recall accuracy	-.66	**< .001**
	Recall accuracy	S2	Study duration	-.43	**.032**
			Recall accuracy	.51	**< .001**
			Correct answer probability	-.46	.241
S2	Study duration	S2	Correct answer probability	-.19	.301
	Recall accuracy	S2	Correct answer probability	.80	**.004**

Standard ß coefficients indicate the proportion of change in standard deviations of the outcome variable when the predictor variable increases by 1 standard deviation. ß estimates were adjusted for the *Flashcard* character count. S0 - Session 0; S1 - Session 1; S2 - Session 2.

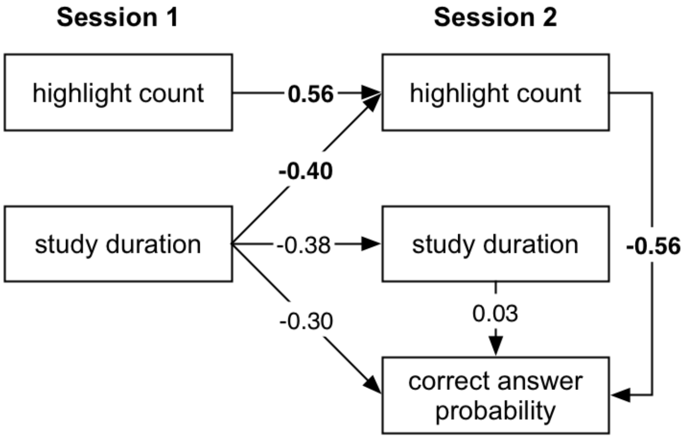
Parameter estimates for model 2

Model structure is depicted in Figure 18. An increase of text highlights of .66 during session S1 caused an increase of .44 text highlights in session S2 (ß=.56, *P*<.001), and a decrease of 6.5s in study duration in S2 (ß=-.42, *P*=.052), which was not significant. It caused a .04 increase in the correct answer probability (ß=.47, *P*=.076), also not significant.

An increase in 18.7s in session S1 caused a decrease of .31 text highlights in session S2 (ß=-.40, *P*=.011), and a decrease in study duration in session S2 of 5.9s (ß=-.38, *P*=.067), which was not significant. Correct answer probability in the exam also decreased by -.03 (ß=-.30, *P*=.122), but was not significant.

Regarding session S2, an increase in text highlight of .78 led to a decrease of -.05 on the correct answer probability (ß=-.56, *P*=.034), and an increase of 15.5s of study duration caused approximately no change in the correct answer probability (ß=.03, *P*=.858). Table xv depicts the standard ß estimates and the *P* values for the described variables.

Figure 18 - Schematic representation of variables included in model 2



Df = 2; CFI = 0.99; RMSEA = 0.02

Relationships between highlight count, study duration and correct answer probability for the 27 *Flashcards* studied by 46 students along 3 weekly study sessions. Arrows indicate standard ß estimates between variables. Statistically significant results are presented in bold typeface. The model was adjusted for the number of characters of each *Flashcard*.

Table xv - Path analysis of highlight count, study duration and correct answer probability

Predictor		Outcome		ß	P
S1	Highlight count	S2	Highlight count	.56	**< .001**
			Study duration	-.42	.052
			Correct answer probability	.47	.076
S1	Study duration	S2	Highlight count	-.40	**.011**
			Study duration	-.38	.067
			Correct answer probability	-.30	.122
S2	Highlight	S2	Study duration	.12	.617
			Correct answer probability	-.56	**.034**
	Study	S2	Correct answer probability	.03	.858

Standard ß coefficients indicate the proportion of change in standard deviations of the outcome variable when the predictor variable increases by 1 standard deviation. ß estimates were adjusted for the *Flashcard* character count. S1 - Session 1; S2 - Session 2.

Confounder effect of *Flashcard* character count

Regarding the *recall accuracy* model, *recall accuracy* was not significantly affected by *Flashcard* character count on session S0 (ß=-.02, P=.930), session S1 (ß=-.13, P=.732), or session S2 (ß=.42, P=.073). Study duration was significantly affected by character count on session S1 (ß=.60, P<.001) and session S2 (ß=.42, P=.006). Considering the highlight model, text highlight count was significantly affected by character count on session S1 (ß=.48 P=.005) and on session S2 (ß=.42, P=.014), indicating that, for every increase in 100 characters, highlight count increased approximately .27 in both sessions. Table xvi depicts these values.

Table xvi - Effects of character count on *recall accuracy*, study duration and highlight count

	Outcome		ß	*P*
Model 1	S0	Recall accuracy	-.02	.930
	S1	Study duration	.60	**< .001**
		Recall accuracy	-.13	.732
	S2	Study duration	.51	**.006**
		Recall accuracy	.42	.073
Model 2	S1	Highlight count	.48	**.005**
		Study duration	.59	**< .001**
	S2	Highlight count	.42	**.014**
		Study duration	.83	**< .001**

Corrected variables considered on both models. Standard ß coefficients indicate the proportion of change in standard deviations of the second variable when the first variable increases by 1 standard deviation.
S0 - Session 0; S1 - Session 1; S2 - Session 2.

Discussion

Effects observed on session S1

Higher *recall accuracy* in S0 predicted an increase in study duration in S1. Because the *Flashcards* were ordered, participants spent most time in the first *Flashcards*, which were also probably easier, thus creating an apparent relationship between *recall accuracy* in S0 and study duration in S1. Indeed a meta-analysis showed that under time pressure individuals tend to study the easier items first.[20] In addition, *recall accuracy* in S0 also predicted a substantial increase in *recall accuracy* in S1, which was expected since the students had spent time studying prior to *recall accuracy* assessment in session S1.[151]

Effects observed on session S2

On session 2 *recall accuracy* was strongly and positively correlated with previous *recall accuracy* values and negatively correlated to study duration at S1. While the increase in recall from session S1 to S2 was concordant with the transition between S0 an S1, study duration in session S1 negatively affected *recall accuracy* in S2, indicating that students reported decreased *recall accuracy* in the *Flashcards* they studied longer in S1. Furthermore, *recall accuracy* in S1 also negatively affected study duration in S2, indicating that during S2 students spent more time studying the materials for which they reported lower *recall accuracy*. Together, these two observations seem to indicate a change in the students study strategy, that transitioned from a top-down sequential approach in session S1 to a planned approach in S2 that took into consideration their past difficulty perceptions, strategically allocating more time to difficult items. Moreover, since total study duration was approximately the same in S1 and S2, the hypothesis that in S2 students allocated more time to the *Flashcards* where they had previously spent less time is further strengthened. On S2, students already knew both the *Flashcards* and the time limit, thus strategically allocated time to the difficult *Flashcards*, which, according to results from other authors, is equivalent to what would happen in a study scenario without a time limit.[20]

Regarding text highlighting, we have seen that it increased in session S2 conditional on whether *Flashcards* were previously highlighted and spent little time on. This is also inline with the results from *recall accuracy* model, since it indicates that students selectively interacted with materials they spent less time with. Study duration in session S2 was rather unaffected by prior highlight or study time.

Effects observed on the probability of correctly answering the MCQs

Recall accuracy at S2 significantly predicted higher probabilities of correctly answering the MCQs. This means students reporting higher *recall accuracy* scores have higher change of correctly answering related MQCs - 1 standard deviation increase over mean *recall accuracy* increased the probability of correctly answering the question by approximately 10% - which is in accordance with findings from other studies.[18,19,254] If the examination was performed with a smaller delay, a stronger effect might be seen, as suggested by other authors.[247] Regarding *recall accuracy* at S0 and S1, the opposite effect was found, which predicted lower chances of answering correctly, but it was not significant. This indicates that the students were able to learn, and correctly answer the items that were considered more difficult at the beginning, benefiting from the intervention. Study duration also failed to exert significant effects on the probability of correctly answering an MCQ. Interestingly, increases in highlight count in S2 negatively affected this probability. This information may imply the materials that students highlighted the most were materials that they found more difficult and that will require further studying in order to being successfully learned. In other words, at an instance in time, the higher the text highlight count, the lower the *recall accuracy*. In addition, because the exam was performed immediately after the study session, it was not possible for the students to assimilate the material so well. We would thus assume that after a few study iterations if the student completely learns the materials, the text highlight stops increasing between sessions. In case it increases, it will probably be in materials that in the meantime were partially forgotten. This may indicate that deciding what to highlight requires a cognitive effort that leads to better knowledge acquisition, as reported by other authors regarding note taking,[21,255] and that content highlighted more frequently has a higher germane cognitive load, which makes the learning material more difficult and requiring additional learning efforts.[9]

Effects of *Flashcard* confounders

Flashcard character count was positively correlated with study time, which was expected since lengthier *Flashcards* will take more time to read. A similar relationship was found considering highlight count, which is also a direct consequence from the fact that a longer text has increased probability of having more text highlight fragments than a smaller text.

Limitations and strengths

This study has limitations. Recall accuracy has only been studied for factual knowledge and it cannot be extrapolated that *recall accuracy* predicts performance on higher order learning tasks such as problem solving and transfer. The platform used for this study prescribed a method using online study tools that may not fit all learners. However there is no feasible way to measure or to make use of this information using paper based media. We have not controlled the models for the fact that 5 *Flashcards* had images, due the low frequency of occurrence.

This study also has strengths. The sample was randomly selected, which increases the generalization potential of our findings. Measurements were performed considering student-*Flashcards* segments and data was aggregated by *Flashcard*. This decision was informed by a prior study on *recall accuracy* showing that the main source of variance for *recall accuracy* in this setting is the *Flashcard*, not the student.[151] This observation enabled the construction of models that capture the greatest sources of variance and thus provides the strongest estimates. In addition, effects were adjusted for potential confounders, which improved the accuracy of results. However, the small aggregated sample sizes (27 *Flashcards* and 46 students) increased the change of type II errors, because of inability to find statistically significant estimates for some parameters.

Implications and further work

Our findings are in line with prior findings from cognitive psychology, extending them to complex content and medical education. Recall accuracy was measured on learning materials from our medical school regarding a ubiquitous topic in medical education and therefore seems reasonable to consider this metric adequate for use in the medical education setting, at least in the basic science subjects.

This study shows that *recall accuracy* and student interaction with content, namely text highlight count, can predict objective assessment outcomes. Thus it becomes worthwhile to assess the impact on learning achievement in real world scenarios of measuring highlight count, study duration and *recall accuracy* impact on small content fragments, as well as considering other metrics that may take into account interactions with richer multimedia content. While there are no widely available tools to conduct these measurements on daily practice, we believe that the evidence presented in this paper can be used to guide the development of new CSCL systems that implement ways of measuring these metrics. Indeed, with the increased pervasiveness of mobile technology such as mobile phones, tablets and laptops, the study habits for younger student generations incorporate, along with paper or exclusively, digital technology.

It is therefore worthwhile to enhance existing systems with tools able to track these metrics on a day-to-day basis. For teachers, such data about their students can be used to dynamically tailor teaching strategies in synchronous or asynchronous learning environments. For learners, this information can be used as feedback by automated systems to facilitate study management and promote self-directed learning. Learner to learning content interaction data may therefore play an important role to improve continuing medical education for the benefit of future generations of medical doctors.

General Discussion and Conclusions

CBL research in medical education is gradually focusing on the problem of determining which computer-based interventions work best in different learning settings, and leaving the comparisons between CBL interventions and traditional methods. In addition, the variation in software tools, instructional methods and study designs make it difficult to derive general recommendations regarding CBL in medical education as a whole. It seems the research community is beginning to consider CBL more than CBL vs. CBL, which is in agreement to the recommendations put forth by other authors in the past.[36,39] Furthermore, only a small fraction of research work is actually being informed by instructional design and cognitive load theory to design systems and interventions that may benefit the students from a learning theory perspective. Nonetheless, this review informed the development of the learning study platform, on which instructional design, learning object theory, cognitive load and judgments of learning (JOL) were taken into consideration. Later in this work, we coined the term *Recall Accuracy* to refer to the JOL implemented by the system.

It has been shown that *recall accuracy* increases with the number of learning sessions and that it is related with the time-on-task. In addition, this metric can be used to estimate the difficulty of learning a content segment and suggested that such information could be used by educators to understand how the learning content matches different learners, and decide the best ways into which adapt the teaching process to compensate for the specific learner difficulties.

Because *recall accuracy* information is bound to each content segment, it that can be reused in many courses and inform in different contexts the knowledge and the effort required to master new content. Recall accuracy effectively measures the knowledge of the students and can be used to characterize the difficulty of content segments.

Finally, *recall accuracy* has a strong correlation with objective assessment using multiple-choice questions, and thus may be used as a predictor of student performance for factual knowledge acquisition. Furthermore, highlighting text has learning value that is independent of the time studying the material. There is also a change is study strategy between the first and second study sessions, from an exploratory approach, to a strategic approach based on the materials that are most difficult. Highlighting text in later sessions likely pinpoints to learner difficulties that predict decreased performance when the subject is tested on the affected content segments.

Another important aspect that has to be taken into consideration, and that was still not explored in this work, is to design strategies that allow the adoption and the effective management of large amounts of information through the system, for both learners and educators. Recommendations have been put forth with this regard but do not directly address this point.[256] Even in the presence of important gains in *recall accuracy* in terms of its practical consequences, the use of these tools must be easy to manage, so that they are populated with the learning content and updated frequently. This may be possible through natural language processing algorithms [257] that extract text and images automatically from documents, slide presentations and websites. Such tools are developed as part of information retrieval systems, that have been used in medical applications,[258] but to our knowledge still have not been used in the educational setting. This type of approach could be used to extract, segment and organize learning materials for validation and adaptation by educators, which could readily adapt them to meet instructional design and cognitive load guidelines, and then made available to learners. This would lessen the initial barrier of entry to use such systems, since the available resources could be easily imported.

Regarding the measurement of *recall accuracy*, it is unfeasible to test more than a few dozens of open-ended questions daily. Thus, the number and the question selection should be independently carried by an artificial intelligence (AI) algorithm by taking into consideration the learner needs and goals. Such algorithm could also be employed to determine the optimal duration of study sessions and its composition. Recall accuracy, study time and highlight count could be used as inputs by the algorithm to perform such tasks, since we have shown that these variables correlate with objective assessment and thus with knowledge acquisition, at least in the short term. Work carried regarding spaced education and test enhanced learning has shown benefits in terms of knowledge acquisition while using static compositions of learning material,[6,15,23,24,259] thus it is feasible to expect that tailored scheduling and compositions based on AI would result in better knowledge outcomes. Indeed AI can play a very important role in medical education, a fact that is pinpointed be the creation in 2013 of a new scientific named *International Journal of Artificial Intelligence in Education*.

AI informed by learner-content interaction data may become an important asset to aid in self-directed learning, as it would enable the learner to focus specifically on the learning process and offload management aspects to the system. When the learning process takes place within the scope of a course, the educator can also be made aware of this information to guide in adapting lectures and assignments according to specific learner needs. This would also free the teacher from managing large numbers of students.

Such challenges become the next steps for enabling the use of segmented content and learner-content interaction data as tenets of future physician concerning factual knowledge acquisition. Effective management of these aspects should allow students to take maximum benefit from the tools developed in this work in the real world setting and thus become empowered to learn on their own. This type of systems should also accompany the medical student and future doctor alongside his/her career as a personal manager for instruction.

Thus, by creating intelligent systems that are aware of learner-content interaction, and that use such information to manage and compose learning activities for the learner, we may become closer to one of the main pillars of the physician for the 21st century, namely, that of information management.

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Appendix

1. Review search queries

PubMed

```
(
    medical education OR
    education, medical[MeSH] OR
    medical students OR
    students, medical[MeSH]
) AND (
    evidence-based learning OR
    student-centered learning OR
    blended learning OR
    spaced learning OR
    e-learning
) AND (
    information technology OR
    e-learning software OR
    software[MeSH] OR
    software tool OR
    web-based platform OR
    blogging[MeSH] OR
    e-portfolio OR
    audience response system OR
    instant messaging OR
    streaming video OR
    computer simulation OR
    computer simulation[MeSH] OR
    computer games OR
    video games[MeSH] OR
    telecasts OR
    podcasts
) AND ("2003/01/01"[PDAT] : "2013/12/31"[PDAT])
```

Scopus

```
(
    ALL("medical education") OR
    ALL("medical students")
) AND (
ALL("evidence-based learning") OR
    ALL("student-centered learning") OR
    ALL("blended learning") OR
    ALL("spaced learning") OR
    ALL("e-learning")
) AND (
    ALL("information technology") OR
    ALL("e-learning software") OR
    ALL("software tool") OR
    ALL("web-based platform") OR
    ALL("e-portfolio") OR
    ALL("audience response system") OR
    ALL("instant messaging") OR
    ALL("streaming video") OR
    ALL("computer simulation") OR
    ALL("computer games") OR
    ALL("telecasts") OR
    ALL("podcasts")
)
AND PUBYEAR > 2002
AND PUBYEAR < 2014
AND LANGUAGE(english)
AND DOCTYPE(ar)
```

EBSCO Host

```
"medical education" OR "medical students"
AND
    "evidence-based learning" OR
    "student-centered learning" OR
    "blended learning" OR
    "spaced learning" OR
    "e-learning"
AND
    "information technology" OR
    "e-learning software" OR
    "software tool" OR
    "web-based platform" OR
    "e-portfolio" OR
    "audience response system" OR
    "instant messaging" OR
    "streaming video" OR
    "computer simulation" OR
    "computer games" OR
    "telecasts" OR
    "podcasts"
```

Source TX All Text

Limit to: scholarly (peer reviewed) journals

Source types: Academic journals

Date: 2003 - 2013

Science Direct / Web of Knowledge

```
(
   "medical education" OR
   "medical students"
)
AND
(
   "evidence-based learning" OR
   "student-centered learning" OR
   "blended learning" OR
   "spaced learning" OR
   "e-learning"
)
AND
(
   "information technology" OR
   "e-learning software" OR
   "software tool" OR
   "web-based platform" OR
   "e-portfolio" OR
   "audience response system" OR
   "instant messaging" OR
   "streaming video" OR
   "computer simulation" OR
   "computer games" OR
   "telecasts" OR
   "podcasts"
)
```

Date: 2003 - 2013

2. Educational software

General educational software used in the studies

Software	Articles	Description
Blackboard [1-9]	8	Learning management system
Moodle [10-17]	8	Learning management system
WebCT [18-23]	6	Learning management system
Second Life [24,25]	2	Online virtual world
Adobe Connect [26]	1	Web-conference software
Angel LMS [27]	1	Learning management system
Blender [28]	1	Open-source 3D software
CLIX [29]	1	Learning management system
Desire2Learn [30]	1	Learning management system
Discourse LLC [31]	1	Virtual patient simulator
Confluence [32]	1	Team collaboration software
MediaWiki [33]	1	Wiki platform
Microsoft Virtual Meeting [34]	1	Web-conference software
Sakai [35]	1	Learning management system

Medical education software used in the studies

Software	Articles	Description
CASUS [36-39]	3	Virtual patient simulator
HINTS [40-42]	3	Virtual patient simulator
INMEDEA [43-45]	3	Virtual patient simulator
Web-SP [14,46,47]	3	Virtual patient simulator
MEFANET [48,49]	2	Learning management system
EleUM [2]	1	Learning management system
ICFAS [50]	1	Web conferencing and LMS
GeriaSims [51]	1	Virtual patient simulator
FACS [52]	1	Virtual patient simulator
EMSAVE [53]	1	Serious 3D game
Xerte [54]	1	Learning management system
EKGtolkning [55]	1	Electrocardiography learning

Software	Articles	Description
INDIAM [56]	1	Mammogram learning
CaseTrain [57]	1	Virtual patient simulator
EEMeC [58]	1	Learning management system
ISP [59]	1	Virtual patient simulator
NLE [60]	1	Learning management system
Surgent [61]	1	Virtual patient simulator
SIMmersion [62]	1	Virtual patient simulator
Schoolbook [63]	1	Learning management system
Radiology Teacher [64]	1	Radiology cases learning system
IVIMEDS [65]	1	Virtual patient simulator
MyMiCROscope [66]	1	Virtual microscope software
MyCourses [67]	1	Learning management system
LRSMed [68]	1	Learning management system

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3. Reference of reviewed papers

Teaching method	
B	Blended Learning
E	E-learning
Platform support	
A	Audio Response System
B	Blog
C	CD/DVD ROM
E	EBook
We	Website
M	Email
Po	Podcast
Pt	Portfolio
T	Video Conference
Wi	Wiki
Media features	
An	Animation
Au	Audio
D	Diagram
I	Image
T	Text
V	Video
Interactive features	
C	Clinical case
Cb	Collaboration
Cl	Calculator
F	Feedback
G	Game
I	Interactive
P	Progress
Q	Quiz
S	Simulation
V	Virtual Patient

Accessibility features	
Ca	Calendar
D	Study documents published on-line
F	Forum
H	Help section
I	Instant Messaging
Instructional design principles	
Ch	Coherence - Eliminate extraneous material
Cn	Contiguity - Place printed words near corresponding graphics
Me	Multimedia - Present words and pictures rather than words alone
Mo	Modality - Present words in spoken form
Pe	Personalization - Present words in conversational or polite style
Pr	Pre-training - Provide pre-training in names and characteristics of key concepts
Se	Segmenting - Break lessons into learner-controlled segments
Si	Signaling - Highlight essential material
V	Voice - Use a human voice rather than a machine voice
Intervention study type	
C	Compares groups
Mt	Multi-centric
Pp	Pre-post design
Pr	Prospective
R	Randomized
Rt	Retrospective
Study duration	
<1Wk	Less than 1 week
<3Mo	Less than 3 months
>3Mo	More than 3 months
Participant education	
B	Medical students in basic sciences grades
C	Medical students in clinical clerkships grades
R	Residents in training
S	Medical Doctors

Knowledge assessment	
E	Assessment performed using summative examination
F	Assessment performed using formative examination
Lb	Measurement performed in a laboratory setting
Li	Judgment of knowledge using likert scale questionnaire
M	Multiple choice question
O	Open ended questions
P	Assessment performed by peers
Tf	True/false questions
Tx	Free text field
Attitude assessment	
Fo	Survey conducted in focus groups
Lb	Measurement performed in a laboratory setting
Li	Survey using likert scale questionnaire
P	Survey conducted by an interviewer
Tx	Survey using free text field
Skill assessment	
A	Measured skill through automated system
Lb	Measurement performed in a laboratory setting
P	Measured skill using and examiner
Platform usage assessment	
A	Measured access
Po	Measured posts
R	Measured views
Ti	Measured time
T	Measured specific tool usage

Study outcomes	
A+	Attitudes improved
A	Attitudes effect inconclusive
A-	Attitudes did not improve
K+	Knowledge improved
K	Knowledge effect inconclusive
K-	Knowledge did not improve
U+	Usage improved
U	Usage effect inconclusive
U-	Usage did not improve
S+	Skills improved
S	Skills effect inconclusive
S-	Skills did not improve

Description of platform features

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
1.	2011	evidence based medicine	B	B A	n/a	n/a	n/a	n/a
2.	2012	reproductive medicine	E	We E	T I D An	Q I F P	I F	Pr Se Me
3.	2013	general	B	We	T I D	S V Q I F	n/a	Cn Se Mo Me
4.	2012	general	B	We	T	Cb S	F	n/a
5.	2009	anatomy	B	A	T I	I F	n/a	n/a
6.	2011	oncology	E	We	T I D	C Q I F P	n/a	n/a
7.	2010	dermatology	E	Po	V Au	n/a	n/a	n/a
8.	2012	geriatrics	E	We	n/a	I	n/a	n/a
9.	2012	cardiology	E	We	n/a	n/a	n/a	n/a
10.	2012	professionalism	E	n/a	V	Q F P	n/a	Se
11.	2010	anatomy genetics histology	B	T	V	n/a	n/a	n/a
12.	2012	emergency	E	We M	T I	I	F	n/a
13.	2008	pulmonology	E	We Wi	T V Au I D	Q I F	F	Me
14.	2008	dermatology	E	We	T I D	S I F	H	n/a
15.	2010	ophthalmology	E	We	T I D	Q I	n/a	n/a
16.	2009	general surgery	E	We Po	T I	n/a	n/a	n/a
17.	2013	general	B	E	n/a	n/a	n/a	n/a
18.	2010	cardiology hematology	E	We	T I D	S V C I F P	n/a	n/a
19.	2007	general	E	We	n/a	Cb S G I F	I F	n/a

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
20.	2012	immunology	B	We	An	n/a	n/a	n/a
21.	2011	general	E	We	T D	n/a	n/a	n/a
22.	2009	general	B	n/a	V	n/a	n/a	n/a
22.	2009	general	B	T	n/a	n/a	n/a	n/a
23.	2013	cardiology	E	We	V	Q I F	n/a	n/a
24.	2004	pathology	E	We	T	C Q I	F Ca	n/a
25.	2013	emergency	E	We	n/a	S G I F	n/a	n/a
26.	2008	professionalism	B	We	T V Au I D	Cb I F	I F D	Me
27.	2004	general	E	Pt	n/a	n/a	n/a	n/a
28.	2012	general	E	T	n/a	n/a	n/a	n/a
29.	2011	radiology	E	T	V Au	n/a	n/a	n/a
30.	2003	primary	E	We	T I D	C I F P	n/a	Se
31.	2012	psychiatry	E	T	V	n/a	n/a	n/a
32.	2009	general	B	We	T I D	C I P	n/a	n/a
33.	2009	general	E	We	T Au I D	S V C I F P	n/a	n/a
34.	2012	radiology	n/a	We	n/a	I F	n/a	n/a
35.	2008	professionalism	B	B	T	n/a	n/a	n/a
36.	2009	orthopedics	B	We	T V I D	n/a	n/a	Me
37.	2009	public health	B	B Wi	T	Cb	F	n/a
38.	2012	ophthalmology	B	We	n/a	n/a	n/a	n/a
39.	2011	anatomy	E	We	T	I	n/a	n/a

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
40.	2012	immunology	E	We B	T	n/a	n/a	n/a
41.	2012	general surgery	E	We	T	Cb I	n/a	n/a
42.	2008	general surgery	B	We	T I	C I F	n/a	Me
43.	2008	general surgery	B	We	n/a	S	n/a	n/a
44.	2012	emergency	E	We	n/a	Cb G I F	n/a	n/a
45.	2009	anesthesia	B	We	T V Au I D	S C Q I F P	n/a	Me
46.	2012	cardiovascular surgery	E	We	T V Au I	Q I F P	n/a	n/a
47.	2013	geriatrics	B	We	T V Au I D	Q I F	n/a	Me
48.	2011	physiology	B	We	T V Au I D An	S C Q I F P	n/a	Ch Pr Se Mo Me Pe
49.	2011	anatomy	B	We	T V I D	Cb Q I F P	D	Me
50.	2012	general	B	We	n/a	n/a	F D	n/a
51.	2007	evidence based medicine	E	We C	T V Au	n/a	n/a	Me
52.	2012	emergency	B	We	V Au	n/a	n/a	n/a
53.	2012	biochemistry	B	We	T V Au I	Cb	F	n/a
54.	2006	general	B	We	T V Au I	n/a	F	n/a
55.	2007	general	E	We	V	n/a	n/a	n/a
56.	2012	anatomy	E	We	n/a	S I	n/a	Ch
57.	2011	nephrology	E	We	T V Au I D	Q I	F	n/a
58.	2009	radiology	E	We	T I D	n/a	n/a	Ch Si Cn Pr Se Mo Me
59.	2010	nuclear medicine	E B	We	T V I D	C Q I F	n/a	Me

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
60.	2005	radiology	E	We	T I D An	S I F	n/a	Cn Me
61.	2012	geriatrics	B	We T Pt	T V Au	G	n/a	n/a
62.	2008	anatomy	B	We	T I D	Cb	F	n/a
63.	2008	palliative	E	We	T	Q	n/a	n/a
64.	2003	n/a	B	We Pt	T I D	Cb Q I F P	F Ca	Se Me
65.	2005	dermatology	E	We	T I D	C Q I F P	n/a	Si Cn Pr Se Me
66.	2013	pediatrics	B	We	T I D	C Q I F	n/a	Si Pr Se
67.	2012	infectious diseases	B	We T Po	n/a	n/a	D	n/a
68.	2009	psychiatry	E	We	T V Au I	S I F	n/a	n/a
69.	2013	radiology	E	We	n/a	n/a	n/a	n/a
70.	2005	cardiovascular surgery	E	We	T V Au I D An	S I	n/a	Cn V
71.	2006	cardiovascular surgery	E	We	T V Au I D An	S I	n/a	Cn
72.	2012	general surgery	B	We	T V I	Cb S C Q I F P	n/a	Me
73.	2006	primary	B	We Pt	T	n/a	n/a	n/a
74.	2013	general	B	We T	n/a	Cb	n/a	n/a
75.	2003	general	E	We	T Au I D	C	D	n/a
76.	2010	pediatrics	E	We Po	T V Au I D	Cb C Q I F	n/a	Me
77.	2012	histology	E	B	n/a	C	n/a	n/a
78.	2013	otolaryngology	B	Pt	T V Au I	Q I F P	D	n/a
79.	2011	pediatrics	E	We	V An	n/a	n/a	n/a
80.	2011	primary	E	We	T V Au I	V C I	n/a	n/a

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
81.	2006	radiology	B	We	T V I D	Cb Q I F	F D	Si Cn Pr Se Me
82.	2008	anatomy	E	n/a	n/a	n/a	n/a	n/a
83.	2012	otolaryngology	E	We	T I	C Q	n/a	n/a
84.	2010	general	B	We	n/a	Cb	F	n/a
85.	2010	palliative	B	We	T V I	C I	n/a	Me
86.	2007	genetics	E	We	T An	I	D	Se
87.	2013	epidemiology	B	We	T V Au I	n/a	F	n/a
88.	2009	radiology	E	We	T I D	S Q I F	n/a	Me
89.	2012	emergency	B	We	n/a	V	n/a	n/a
90.	2013	general surgery	E	We M	T	C Q I	n/a	n/a
91.	2010	evidence based medicine	E	We	n/a	n/a	D	n/a
92.	2011	physics	E	We	T I D	Cb S V Q I F	n/a	n/a
93.	2011	general	E	We	T V Au I D	Q I	n/a	Cn Se Mo Me
94.	2012	advanced life support	E	We	n/a	n/a	D	n/a
95.	2010	pulmonology	B	We	T	Q F	F	n/a
96.	2008	informatics	E	Wi	n/a	Cb	D	n/a
97.	2013	psychiatry	E	We	T V Au I	V I	n/a	n/a
98.	2013	reproductive medicine	E	We	n/a	Q	n/a	n/a
99.	2008	psychology	B	We C Pt	T V Au I	C Q I F	n/a	Me V
100.	2012	professionalism	B	We	V	Q	n/a	n/a
101.	2009	neurology	B	We	T V Au	Q	n/a	Me

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
102.	2012	professionalism	E	We	T V Au I	Q F	n/a	n/a
103.	2010	neuroscience	B	We	T I D	Q I F	n/a	Cn Me
104.	2013	pharmacology	E	C Po	n/a	n/a	n/a	n/a
105.	2006	radiology	E	We	T V Au I D An	Q F	n/a	n/a
106.	2009	physiology	E	We	D	S Q I F	H	Ch Si Cn Pr Se Mo Me Pe
107.	2009	urology	B	We	T I	S C Q I F	n/a	Me
108.	2011	urology	E	We	T I D	S C I F P	n/a	Se
109.	2006	radiology	E	We	T I	n/a	n/a	Cn
110.	2010	otolaryngology	E	We	T	S I	n/a	n/a
111.	2013	general	B	We	n/a	V I F P	n/a	n/a
112.	2009	general	B	We Pt	T	Cb C Q P	n/a	n/a
113.	2011	ophthalmology	B	We	n/a	n/a	n/a	n/a
114.	2012	anatomy	B	We	V Au	n/a	n/a	n/a
115.	2012	gynecology	E	T	T V Au I	n/a	n/a	n/a
116.	2009	dermatology	B	We	T V Au I D An	G Q I F P	D	n/a
117.	2009	otolaryngology	E	We	T I	C Q I	n/a	n/a
118.	2008	urology	E	We	T Au I D	Q I F	n/a	Pr Se Me
119.	2009	urology	E	M	T	Q	n/a	n/a
120.	2012	urology	E	We M	T	G Q I F P	n/a	n/a
121.	2007	urology	E	M	n/a	Q	n/a	n/a

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
122.	2009	urology	E	We M	T I D	Q F	n/a	Se Me
123.	2007	urology	B	We M	T Au	C Q I	n/a	n/a
124.	2010	pathology	E	We M	T I D	Q F	n/a	Se Me
125.	2011	physiology	E	We	T V Au I D	Cb S Q I F P	F	Pr Me V
126.	2013	anatomy	E	We	n/a	S I	n/a	n/a
127.	2010	general	E	We	T V Au I D	S C Q I F	n/a	Me
128.	2008	general	B	We	n/a	Cb S F P	I	Me
129.	2011	physiology	E	We	T V Au I D An	S I F	n/a	n/a
130.	2006	occupational medicine	E	We	T V Au I D	Q I F P	n/a	Me
131.	2012	general	E	We	T V Au I D	Cb	n/a	n/a
132.	2012	advanced life support	B	We	T V I	S V Q I F	n/a	Ch Si Cn Se Me
133.	2005	hematology	B	We	T I	C Q F P	n/a	Cn Pr Se Me
134.	2010	biochemistry	B	We	T Au I D An	Cb S Q I F	n/a	n/a
135.	2008	anatomy genetics histology	B	We	T I D	G Q I F	I	Me
135.	2008	physiology	B	We Wi	n/a	Cb I	I F	n/a
136.	2008	evidence based medicine	E	We C	T Au I	I	D	Me
137.	2013	emergency	B	We Po	T V Au I D	Q	n/a	Se
138.	2010	pediatrics	B	We	T V Au I D	S V I	n/a	Me
139.	2013	pediatrics	B	We	T V Au I D	S Q I F	n/a	Cn Se Mo Me Pe
140.	2012	radiology	E	We	T I	Q I	n/a	Me

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
141.	2011	anesthesia	B	We	T I D	S V C Q I F P	n/a	Se
142.	2009	primary	B	We	T V Au I D An	C Q I	F	n/a
143.	2006	cardiovascular surgery	B	n/a	n/a	S I	n/a	n/a
144.	2005	microbiology	E	We	T I D	G F P	n/a	Me
145.	2006	informatics	E	We	n/a	n/a	F	n/a
146.	2011	psychiatry	B	We M Wi	T	C	F D	n/a
147.	2010	telemedicine	B	T	n/a	Cb	n/a	n/a
148.	2009	radiology	B	We Po	T V Au I D	I F	n/a	n/a
149.	2010	anatomy	E	We	n/a	S I	n/a	n/a
150.	2013	pediatrics	B	We	T V Au I D	Cb S V C Q I F	n/a	Se Me
151.	2008	evidence based medicine	B	We	T	I	n/a	n/a
152.	2011	urology	E	We	T V Au I D An	F	n/a	n/a
153.	2011	radiology	E	We	T I	C Q I F P	n/a	Cn Se Mo Me Pe
154.	2005	microbiology	B	We M	T I An	n/a	I F D	n/a
155.	2009	urology	E	M	T	n/a	n/a	n/a
156.	2013	dermatology	E	We	T I	Q	n/a	n/a
157.	2010	infectious diseases	B	We	n/a	C I	n/a	n/a
158.	2012	neurology	E	We	T I	Q I	n/a	Cn Me
159.	2009	geriatrics	E	We	T	n/a	n/a	n/a
160.	2011	pharmacology	B	We	T V Au I D	Q I	I F	Me

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
161.	2010	pediatrics	B	We Wi	T V I	C I	I	Me
162.	2010	biochemistry	E	We	T V I	G I F P	n/a	Me
163.	2012	hematology	E	We	T V Au I D	C Q I F P	n/a	Ch Si Cn Pr Se Mo Me V
164.	2010	informatics	B	We M	T	Q	D Ca	n/a
165.	2012	general	B	Po	n/a	n/a	n/a	n/a
166.	2009	dermatology	B	We T	V Au	n/a	n/a	Me
167.	2012	anatomy	B	We	T V Au I D	n/a	n/a	n/a
168.	2008	cardiology	B	We	T I D An	S C Q I F	n/a	n/a
169.	2011	emergency	E	We C	n/a	S C I	n/a	n/a
170.	2010	pediatrics	E	We	n/a	n/a	n/a	n/a
171.	2013	anesthesia	E	We	n/a	S	n/a	n/a
172.	2010	radiology	E	T	n/a	n/a	n/a	n/a
173.	2005	cardiology	E	We	T V Au I D	I F	n/a	n/a
174.	2003	general	E	We E	T Au I	C Q I F	I F D	n/a
175.	2008	geriatrics	E	We	T V Au I	S C I F P	D	Me
176.	2011	microbiology	B	We	T	Q I F	n/a	n/a
177.	2004	radiology	E	We	T I D	Cb S Q I F	n/a	n/a
178.	2013	nuclear medicine	E	We T	T V Au I D	V Q I F	I F	n/a
179.	2012	urology	E	C	T I	n/a	n/a	n/a
180.	2012	general surgery	E	We Po	T V Au I	n/a	n/a	n/a

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
181.	2007	anatomy	B	We M	n/a	Q I	F D	n/a
182.	2010	advanced life support	E	C	T V Au I D	S I	n/a	Me
183.	2012	advanced life support	B	We	V Au	Q F	n/a	n/a
184.	2011	neuroscience	B	We	n/a	Q	F	n/a
185.	2006	occupational medicine	B	We	T V Au I D	C Q I F	n/a	Me
186.	2013	primary	E	We	T I	Q	n/a	n/a
187.	2010	physiology	B	We	T I	C Q I F	F	n/a
188.	2012	anatomy	B	We	T I D	Q I F P	n/a	Ch Si Cn Se Mo Me Pe
189.	2007	general surgery	E	We	T Au I D	n/a	n/a	Me V
190.	2012	evidence based medicine	E	We	T	C I	F	n/a
191.	2003	general	B	We	T V Au I D	Cb Q I F P	F D Ca	Se Me
192.	2006	emergency	E	We	T I D An	S I F P	n/a	n/a
193.	2012	radiology	E	We	D	n/a	n/a	n/a
194.	2007	geriatrics	B	We	T V Au I	S Q F	n/a	Pr Me
195.	2013	general surgery	E	We	T V Au I D An	Cb S Q I F P	n/a	Ch Si
196.	2012	histology	B	We	T I D	I F	F	n/a
197.	2008	anatomy	B	C	V	n/a	n/a	n/a
198.	2006	informatics	B	We	T	Cb P	F	n/a
199.	2012	radiology	E	We	T V Au I D	C	n/a	Ch Se
200.	2011	legal medicine	B	We	T Au I D	S C I F P	n/a	n/a

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
201.	2011	histology	E	We	T I	S I	n/a	Me
202.	2013	emergency	B	We	T V Au I D An	S Q I F P	n/a	n/a
203.	2011	physiology	B	We	T V Au I D	Q Cl I	I F D Ca	n/a
204.	2013	radiology	E	We T	V Au	n/a	D	Se
205.	2010	pediatrics	E	We	V	n/a	n/a	n/a
206.	2004	anatomy	B	We	T I D	Cb C Q I	n/a	Cn Pr Se Me
207.	2007	emergency	B	We	n/a	C	n/a	n/a
208.	2011	primary	B	We M	T	C Q F	n/a	n/a
209.	2004	general	E	We T	T V Au I	Cb C I F P	F	Me
210.	2008	radiology	E	We	n/a	n/a	n/a	Se
211.	2011	dermatology	B	We	T V Au I	Q I F	F	Me
212.	2009	pathology	E	We M	T V Au I D An	Q I F	I F D Ca	n/a
213.	2013	urology	B	We	V	n/a	n/a	n/a
214.	2007	emergency	E	We	T I D	S I	n/a	Si Cn Me
215.	2007	pediatrics radiology	E	We	T V I D	C Q I	n/a	Me
216.	2010	neurosurgery	B	We	n/a	S	n/a	n/a
217.	2012	rheumatology	B	We Pt	V	Q I F	D	Si Pr
218.	2012	ophthalmology	E	We	V Au	n/a	n/a	n/a
219.	2009	pathology	E	We	T I D	Cb C Q I F	F D Ca	n/a
220.	2012	pediatrics	B	We	T V Au I	n/a	n/a	Me
221.	2013	ophthalmology	B	We	T V Au I	V C I	n/a	n/a

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
222.	2008	anatomy	B	We	T V Au I D	C Q I F	n/a	Me
223.	2008	pediatrics	E	We	T An	Cb G Q	n/a	n/a
224.	2004	radiology	E	E	T I	n/a	n/a	Cn Se Me
225.	2009	radiology	E	We	T I D	C Q I F	n/a	n/a
226.	2012	otolaryngology	E	We	T I D An	V I	n/a	n/a
227.	2004	physiology	B	We A	T V Au I D An	Cb S Q Cl I F P	I F	Si Pr Se Me
228.	2006	pathology	E	We	n/a	C Q I	n/a	n/a
229.	2008	gastrointestinal	E	We	T V Au I D An	C Q I F P	n/a	Se Me
230.	2011	ALS, pediatrics	B	We	n/a	n/a	n/a	n/a
231.	2011	evidence based medicine	E	We T	T V Au	Q I F	I	n/a
232.	2011	emergency	B	n/a	n/a	n/a	n/a	n/a
233.	2010	professionalism	B	We B Wi	T	Cb	F	n/a
234.	2012	biochemistry	B	We	n/a	C Q F	F D	n/a
235.	2010	psychiatry	B	n/a	n/a	C I	D	n/a
236.	2013	nephrology	E	We	T D	I	n/a	Ch Si
237.	2012	general surgery	E	Pt	n/a	n/a	n/a	n/a
238.	2007	neurology	E	We M	n/a	Cb Q I	I F	n/a
239.	2006	primary	E	We	T	C I	F	n/a
240.	2003	psychology	E	We	T V	I F P	F	Me
241.	2011	physiology	E	n/a	T D	S I	n/a	Me
242.	2006	rheumatology	B	We	T I	S C Q I F	n/a	Me

Ref	Year	Subject	Teaching method	Platform support	Media features	Interactive features	Accessibility features	Instructional design principles
243.	2010	general	B	We Wi	T V Au I	Cb S Q I F P	n/a	Pr Me
244.	2009	traditional medicine	E	We	n/a	C	F	n/a
245.	2013	general	B	We	T V Au I D An	Cb C	I F	n/a
246.	2006	orthopedics	E	We	T Au I An	C Q I F	n/a	Cn
247.	2010	orthopedics	E	We	T V Au I D An	S V C I F P	n/a	n/a
248.	2006	radiology	E	We	V I	n/a	n/a	n/a
249.	2012	general surgery	B	We	T V Au I	V I P	n/a	n/a
250.	2009	anesthesia	E	We	T I D	C Q I F	n/a	Me
251.	2006	radiology	B	We	T V Au I D An	C	n/a	Cn Me

Experiment variables

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
1.	2011	Pr	190	B	<3Mo	n/a	Fo Lb	n/a	n/a	n/a	A+
2.	2012	Pr Pp C	277	C	<3Mo	M Li F E	Li	n/a	n/a	11	K+ A+
3.	2013	Pr	522	C	<3Mo	n/a	Li	A	Ti	6	A+ U˜S+
4.	2012	Pr	130	B	<3Mo	n/a	Li	n/a	Po R A	8	A+ U+
5.	2009	Pr	150	B	<3Mo	M	Li	n/a	n/a	10	K+ A+
6.	2011	Pr R Mt Pp C	37	R	<3Mo	M Li	Li	n/a	A Ti	11	K+ A+ U+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
8.	2012	Pr Pp	40	S	<1Wk	n/a	Li	A P	n/a	10	A+ S+
9.	2012	Pr R C	60	B	<1Wk	M Li	Li	n/a	n/a	10	K˜A+
10.	2012	Pr R Pp C	204	B	<1Wk	n/a	Li Lb	n/a	n/a	11	A-
11.	2010	Rt	200	B	>3Mo	M E	Li	n/a	A Ti	7	K˜A+ U+
12.	2012	Pr	101	S	>3Mo	n/a	Li Tx	n/a	A	9	A+ U˜
14.	2008	Pr Pp	166	n/a	<1Wk	Tx P Lb	Li Lb	n/a	Ti	11	K+ A+ U+
15.	2010	Pr Pp	137	S	<3Mo	M	Li	n/a	n/a	8	K+ A+
16.	2009	Pr R Pp C	148	B	<1Wk	M	Li	n/a	n/a	12.5	K+ A+
17.	2013	Pr Pp C	158	B	<3Mo	n/a	Li	n/a	n/a	10	A+
18.	2010	Pr R Pp C	49	C	>3Mo	n/a	n/a	A	n/a	11	S+
18.	2010	Pr R Mt Pp C	216	C	>3Mo	E	n/a	A P	n/a	11	S+
20.	2012	Pr	125	B	>3Mo	M E	Li	n/a	Ti	11	K+ A+ U+
21.	2011	Pr Mt	963	B	>3Mo	n/a	Tx	n/a	T A	9	A+ U˜
22.	2009	Rt	1736	B	>3Mo	E	n/a	n/a	n/a	11.5	K+
22.	2009	Pr	1736	B	can't tell	E	Li	n/a	n/a	10	K+ A+
23.	2013	Pr R Pp C	55	B	<3Mo	M	n/a	n/a	n/a	11	K+
24.	2004	Pr R Pp C	11	C	<3Mo	n/a	Li P Fo Lb	n/a	Ti	8	A+ U˜
25.	2013	Pr Pp	40	R	<1Wk	M	Li	n/a	n/a	9	K+ A+
26.	2008	Pr C	49	n/a	<3Mo	Li P	Li	A P Lb	Po	11	K+ U˜S˜

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
28.	2012	Pr Mt	10261	S	>3Mo	n/a	Li	n/a	n/a	9	A+
29.	2011	Pr Mt	7405	R	>3Mo	n/a	Li	n/a	n/a	7	A+
30.	2003	Pr R Mt Pp C	3067	S	<1Wk	M	n/a	n/a	n/a	9	K+
31.	2012	Pr Pp C	167	C	<1Wk	M Lb	n/a	n/a	n/a	10	K˜
32.	2009	Pr	50	C	can’t tell	n/a	Li	n/a	n/a	9	A+
33.	2009	Pr R C	80	C	<1Wk	M	Li	n/a	n/a	11	A+
34.	2012	Pr	30	C	can’t tell	n/a	Li	n/a	n/a	9	A+
35.	2008	Pr	90	C	<3Mo	n/a	Li Tx	n/a	Po R A	9	A+ U˜
36.	2009	Pr	309	n/a	<3Mo	n/a	Li	n/a	A	7.5	A+ U+
37.	2009	Pr	10	B	<3Mo	n/a	n/a	n/a	n/a	7	A+
38.	2012	Pr C	150	S	>3Mo	n/a	n/a	n/a	n/a	9	K+
39.	2011	Pr C	12	B	<1Wk	M	Li	n/a	n/a	10	K˜A+
40.	2012	Pr Mt	50	B	<3Mo	n/a	P	n/a	Po A	n/a	A+ U˜
41.	2012	Pr Mt	60	C	<3Mo	n/a	Li Fo Lb	n/a	Po A	8.5	A+ U+
42.	2008	Pr C	117	C	>3Mo	E	Li	n/a	A	10.5	K+ A+ U˜
43.	2008	Pr	118	C	>3Mo	n/a	Li Tx	A P	Po Ti	7	A+ U˜S+
44.	2012	Pr Pp C	30	B	>3Mo	tf Lb	n/a	A P Lb	n/a	10	K+ S+
45.	2009	Pr	149	C	<3Mo	M Tx E Lb	Tx	n/a	T A Ti	10.5	A+ U+
46.	2012	Pr	43	S	>3Mo	n/a	Li	n/a	n/a	7	A+ U+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
47.	2013	Pr Mt C	562	C	<3Mo	M tf E Lb	Li	n/a	n/a	9	K+ A+
48.	2011	Pr	70	S	<1Wk	n/a	Li Lb	n/a	n/a	10	A+
49.	2011	Pr Pp	300	n/a	>3Mo	Li	Li	n/a	n/a	10.5	K+ A+
50.	2012	Pr	387	B C	>3Mo	n/a	Li Fo	n/a	A	9	A+ U˜
51.	2007	Pr R Mt Pp C	229	R	<1Wk	M O P Lb	Li Lb	n/a	n/a	12.5	K˜A+
52.	2012	Pr C	128	S	<1Wk	n/a	n/a	A P Lb	n/a	12	S+
53.	2012	Pr	106	B	>3Mo	n/a	Li	n/a	n/a	6	A+
54.	2006	Pr	355	B	<3Mo	n/a	Li	n/a	n/a	6	A+
55.	2007	Pr	21	B	>3Mo	n/a	Fo	n/a	n/a	6	A+
57.	2011	Pr Pp	20	R	>3Mo	n/a	n/a	n/a	Po R	8	K˜U˜
59.	2010	Pr	246	B	<3Mo	Li	Li	n/a	n/a	10	K+ A+
61.	2012	Pr Pp	137	B	<3Mo	M Lb	Li	n/a	n/a	6	K+ A+
63.	2008	Rt Mt C	612	R	>3Mo	M	n/a	n/a	n/a	6	K+
64.	2003	Pr	can’t tell	B	can’t tell	n/a	n/a	n/a	T A	10.5	A+ U+
65.	2005	Pr	13	C	<1Wk	n/a	Li Tx Lb	n/a	n/a	8	A+
66.	2013	Pr Pp	21	B R	<3Mo	M Li	Li	n/a	n/a	8	K+ A+
68.	2009	Pr R Pp C	102	B	<3Mo	n/a	n/a	A P Lb	n/a	11	S+
69.	2013	Pr Mt Pp	185	R	<1Wk	M Li	n/a	n/a	A Ti	11	K+ U˜
70.	2005	Pr Pp	30	B C R	<3Mo	M E	Li Tx	n/a	n/a	8	K+ A+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
71.	2006	Pr R Pp C	126	B C	<1Wk	M Lb	Li Tx	A P Lb	Ti	9	K˜A+ U+ S+
72.	2012	Pr	116	C	<3Mo	M F	Li	n/a	n/a	7	K+ A+
73.	2006	Pr	6	C	<3Mo	n/a	Li Fo	n/a	Po R A Ti	6	A+ U˜
74.	2013	Pr	26	B	>3Mo	n/a	Li	n/a	n/a	9	A+
77.	2012	Rt C	36	B	<3Mo	E	Li	n/a	n/a	10	K+ A+
78.	2013	Pr	112	C	<3Mo	n/a	Li	n/a	n/a	8	A+
79.	2011	Pr Pp C	223	R	<3Mo	M	Li	n/a	n/a	11	K+ A+
80.	2011	Pr	260	C	<3Mo	n/a	Li	n/a	n/a	10	A+
81.	2006	Pr	276	B	<3Mo	M	Li Tx	n/a	T Po R A Ti	10.5	K+ A+ U˜
82.	2008	Pr Mt	62	B S	<1Wk	n/a	Li	n/a	n/a	8	A+
83.	2012	Pr Pp	245	C	<1Wk	M	Li	n/a	Ti	11	K+ A+ U˜
84.	2010	Pr Pp C	88	C	<3Mo	n/a	Li	A P	Po R A Ti	10	A+ U˜S˜
85.	2010	Pr R Pp C	133	B	<3Mo	M Li tf Tx Lb	Li Lb	A P Lb	n/a	12.5	K+ A+ S+
86.	2007	Pr	93	n/a	can't tell	n/a	Li	n/a	A	6	A+ U˜
87.	2013	Pr Mt	54	R	<1Wk	Li	Li	n/a	Ti	10	A+ U+
89.	2012	Pr R C	155	B	<1Wk	M E	n/a	n/a	Po Ti	11	K- U-
90.	2013	Pr R C	97	R	<3Mo	M	Li	n/a	n/a	12	K+ A+
91.	2010	Pr R Mt Pp C	237	B	<3Mo	M E	n/a	n/a	n/a	12	K˜
92.	2011	Pr	304	B	<3Mo	n/a	Li	n/a	n/a	7	A˜

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
94.	2012	Pr R Pp C	58	R	<1Wk	n/a	n/a	A P	n/a	11	S˜
95.	2010	Pr	10	R	<3Mo	n/a	Li	n/a	Ti	9	A+ U˜
96.	2008	Pr	82	B	>3Mo	n/a	Li Tx	n/a	n/a	6	A˜
97.	2013	Pr R Mt C	120	S	<1Wk	M	n/a	n/a	Ti	11	K˜U˜
98.	2013	Pr	341	B	<3Mo	n/a	Li	n/a	n/a	9	A+
99.	2008	Pr	302	C	<3Mo	Tx P Lb	Li Tx Fo Lb	n/a	n/a	10.5	K+ A+
100.	2012	Pr R Pp C	166	B	<3Mo	n/a	n/a	A P	n/a	13	S+
101.	2009	Pr C	92	C	<3Mo	M E	n/a	A P Lb	n/a	10.5	K˜S+
103.	2010	Rt	can’t tell	n/a	can’t tell	E	n/a	n/a	n/a	9	K+ A+
104.	2013	Pr	62	n/a	<3Mo	n/a	Li	n/a	n/a	7	A+
106.	2009	Pr R Pp C	92	B	<1Wk	M	n/a	n/a	n/a	11	K+
107.	2009	Pr	83	C	can’t tell	n/a	Li Tx P Fo Lb	n/a	n/a	8	A+
110.	2010	Pr R C	100	B C	<1Wk	M Lb	Li Lb	n/a	n/a	11	K˜A+
111.	2013	Pr C	116	C	>3Mo	n/a	Fo	n/a	n/a	11	A+
112.	2009	Pr	can’t tell	n/a	can’t tell	n/a	n/a	n/a	A	n/a	U+
113.	2011	Pr R Pp C	16	R	>3Mo	M	Li	n/a	n/a	11	K˜A+
114.	2012	Pr	91	B	>3Mo	n/a	Li	n/a	A Ti	7	A+ U˜
115.	2012	Pr	84	B	<3Mo	n/a	Li	n/a	n/a	9	A˜
116.	2009	Pr	42	B	<3Mo	M	Li	n/a	n/a	9	K˜A+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
117.	2009	Pr R Pp C	133	B	<1Wk	M	Li	n/a	Ti	11	K+ A+ U+
118.	2008	Pr R C	237	B	<3Mo	M E Lb	Tx	n/a	n/a	12.5	K˜A+
119.	2009	Pr R Mt C	537	R	>3Mo	M	n/a	n/a	n/a	12	K+
120.	2012	Pr R Mt C	1470	R	>3Mo	M	Li	n/a	n/a	11	K+ A+
121.	2007	Pr R Mt Pp C	537	R	>3Mo	M	n/a	n/a	Ti	10	K+ U˜
122.	2009	Pr R Mt Pp C	330	B	>3Mo	M Li Tx E Lb	Li	n/a	n/a	12	K+
123.	2007	Pr R Pp C	133	B	>3Mo	M Lb	Li Tx	n/a	n/a	12	K+
124.	2010	Pr R Mt Pp C	724	R	>3Mo	M	n/a	n/a	n/a	12.5	K+ A+
125.	2011	Pr	164	B	<3Mo	n/a	Li Tx Lb	n/a	Ti	7.5	A+
126.	2013	Pr R C	60	B	<1Wk	M Lb	n/a	n/a	n/a	11	K-
127.	2010	Pr Mt	153	S	can’t tell	n/a	Li	n/a	T	9	A+ U˜
130.	2006	Pr Mt	212	B	<3Mo	n/a	Li	n/a	n/a	9	A+
132.	2012	Pr R Pp C	226	B	<3Mo	tf F Lb	Li	A P Lb	T A Ti	12	K+ A+ U+ S+
133.	2005	Pr	150	B C	<3Mo	M E	Li	n/a	T	7	K+ A+ U+
134.	2010	Pr R C	295	B	<1Wk	M O Tx F	Li	n/a	n/a	10	K+ A+
135.	2008	Pr Mt Pp	68	B	<1Wk	n/a	Li	n/a	T A	11.5	K+ A+ U˜
135.	2008	Pr Mt Pp	68	S	can’t tell	n/a	Li	n/a	n/a	8	K+ A+
136.	2008	Pr Mt Pp	112	S	<1Wk	M	n/a	n/a	n/a	6	K+ A+
137.	2013	Rt Pp	121	C	<3Mo	M	Li	n/a	n/a	8	K+ A+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
138.	2010	Pr	30	C	can’t tell	n/a	Li Tx	n/a	n/a	8	A+
139.	2013	Pr	310	C	<3Mo	Li	Li Tx	A	n/a	8	K+ A+ S+
140.	2012	Pr Pp C	127	C	<3Mo	Lb	Li Lb	n/a	A	11	K+ A+ U+
141.	2011	Pr	140	C	>3Mo	n/a	Li	n/a	A	6	A+ U˜
142.	2009	Pr C	41	B	<3Mo	M E	Li	n/a	Ti	9	K˜A+ U+
143.	2006	Pr	209	B	<1Wk	n/a	Li	n/a	n/a	6	A+
144.	2005	Pr	134	B	<1Wk	n/a	Li	n/a	n/a	8	A+
145.	2006	Pr	1232	B	<1Wk	n/a	Li Lb	n/a	n/a	8	A˜
146.	2011	Pr Pp	272	S	<3Mo	M	Tx	n/a	n/a	8	K+ A+
147.	2010	Pr R Mt C	42	S	<1Wk	M Lb	Li	n/a	Ti	9	K˜A˜U˜
148.	2009	Pr	102	S	<1Wk	n/a	Li	n/a	n/a	9	A+
149.	2010	Pr	22	C	can’t tell	n/a	Li	n/a	n/a	9	A+
150.	2013	Pr R C	207	C	<3Mo	M F E Lb	n/a	n/a	T A	9	K˜U+
151.	2008	Pr	141	B	>3Mo	n/a	Li Tx	n/a	n/a	7.5	A+
152.	2011	Pr Pp	20	C R	<1Wk	M	n/a	n/a	n/a	9	K+
153.	2011	Pr Pp	177	R	<3Mo	M	n/a	n/a	n/a	10	K+
154.	2005	Pr Pp	50	B	<3Mo	n/a	Li	n/a	n/a	9	A˜
155.	2009	Pr R C	55	R	>3Mo	n/a	Li	n/a	n/a	11	n/a
156.	2013	Pr Pp	82	R	<1Wk	M	Li	n/a	n/a	10	K+ A+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
157.	2010	Pr	can’t tell	n/a	<1Wk	n/a	n/a	n/a	R A Ti	n/a	U˜
158.	2012	Pr	52	C S	can’t tell	n/a	Li	n/a	n/a	8	A+
159.	2009	Pr R Pp C	72	R	<3Mo	M	Li	A	R A	12	K+ A+ U˜S+
161.	2010	Pr R Pp C	237	n/a	<3Mo	M Li Lb	Li P Fo	n/a	n/a	12.5	K+
162.	2010	Pr R C	143	n/a	<1Wk	n/a	Li Lb	n/a	n/a	10	A+
163.	2012	Pr R Pp C	520	C	<3Mo	M Lb	Li Tx Lb	n/a	Ti	11.5	K+ A+ U+
164.	2010	Pr Pp	38	B	>3Mo	M E Lb	Li Lb	n/a	n/a	10.5	K+ A+
165.	2012	Pr R Mt C	70	C	<3Mo	n/a	Li	n/a	n/a	10	A+
166.	2009	Pr	325	n/a	>3Mo	n/a	Li	n/a	n/a	8	A+
167.	2012	Pr	804	B	>3Mo	n/a	n/a	n/a	A Ti	9	U+
168.	2008	Pr C	62	B	>3Mo	M E	Li	n/a	A	8	K+ A+ U˜
169.	2011	Pr Pp	93	S	<3Mo	M Li	Li	n/a	n/a	12	K+ A+
170.	2010	Pr Pp	28	B	<3Mo	M Li Lb	Tx	A P Lb	n/a	11	K+ A+ S+
171.	2013	Pr R C	20	B	<1Wk	n/a	n/a	A	n/a	11	S+
172.	2010	Pr	18	R	>3Mo	n/a	Li Tx	n/a	n/a	10	A+
175.	2008	Pr Mt	287	C	can’t tell	n/a	Li	n/a	Ti	8	U˜
176.	2011	Pr Pp	307	B	<3Mo	M	Li	n/a	n/a	10	K+ A+
177.	2004	Pr	17	R	can’t tell	n/a	Li Lb	n/a	n/a	6	A+
179.	2012	Pr Pp	10	S	<1Wk	M Li	Li	n/a	n/a	8	K+ A+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
180.	2012	Pr R Pp C	154	C	<1Wk	M Li	Li	n/a	n/a	11	K˜A-
181.	2007	Pr C	134	B	>3Mo	M E	Li	n/a	A	8	K+ A+ U+
182.	2010	Pr R Mt Pp C	657	S	can’t tell	M E	Li	A P Lb	n/a	13.5	K˜A+ S˜
183.	2012	Pr R Mt Pp C	3732	S	<1Wk	M E	n/a	A P	n/a	12	K- S-
184.	2011	Pr Pp	73	B	<1Wk	M O E Lb	Li	n/a	n/a	11	K+ A+
185.	2006	Pr Mt	557	C	>3Mo	M	Li	n/a	T Ti	8	K+ A+ U˜
186.	2013	Pr	280	S	can’t tell	Li	n/a	n/a	n/a	8	K+
187.	2010	Pr R C	183	C	<3Mo	M Li	n/a	n/a	n/a	11	K+
188.	2012	Pr Pp	129	B	>3Mo	M O Tx E Lb	Li Tx	n/a	A	7	K˜A+ U˜
189.	2007	Pr C	88	C	<3Mo	M E Lb	Li	n/a	A	10	K+ A+ U˜
190.	2012	Pr	61	R	<1Wk	n/a	Li Fo	n/a	n/a	8	A+
192.	2006	Pr Pp C	29	S	<1Wk	M F E	n/a	n/a	n/a	8	K+ U+
193.	2012	Pr Mt C	80	B S	<1Wk	n/a	Li Lb	A P Lb	Ti	10	A+ U˜S+
194.	2007	Pr Pp C	140	B	can’t tell	M Li	Li P Fo Lb	A P Lb	n/a	10.5	K+ A+ S+
195.	2013	Pr	10	S	<1Wk	n/a	Li Tx	n/a	n/a	10	A+
196.	2012	Pr Pp	89	B	>3Mo	n/a	Li	n/a	A	7	A+ U+
197.	2008	Pr	282	B	<3Mo	M E	Li	n/a	A	11	K˜A+ U˜
198.	2006	Pr R Pp C	238	B	<3Mo	Li O Tx F E P	Li	A P Lb	n/a	12.5	K+ A+ S+
200.	2011	Pr Pp	36	B	<3Mo	n/a	Li	n/a	n/a	8.5	A+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
201.	2011	Pr	447	B	<3Mo	n/a	Li	n/a	A	8	A+ U+
203.	2011	Rt C	104	B	>3Mo	M E	Li	n/a	T Po R A Ti	10	K+ A+ U+
204.	2013	Pr C	191	B	<1Wk	P	Li	A P	n/a	10	K+ A+ S+
205.	2010	Pr	100	C	can’t tell	n/a	n/a	n/a	A	9	A+
206.	2004	Pr	508	B	>3Mo	n/a	Li Tx	n/a	n/a	8.5	A+
207.	2007	Pr	210	C	<3Mo	n/a	Li	n/a	n/a	n/a	A+
208.	2011	Pr R C	300	S	>3Mo	n/a	Li	n/a	n/a	14	A+
210.	2008	Pr	62	B	<3Mo	n/a	Li	n/a	n/a	6	A+
211.	2011	Pr R Pp C	44	B	<3Mo	M	Li	n/a	n/a	12.5	K+
212.	2009	Pr	38	C	<3Mo	n/a	Li	n/a	Po R A	9	A+ U+
213.	2013	Pr Pp	7	R	<1Wk	Li	n/a	A P	n/a	7	K+ S+
214.	2007	Pr Pp	41	C	<1Wk	M Lb	Tx Lb	n/a	Ti	10.5	K+ A+ U+
215.	2007	Pr	can’t tell	n/a	can’t tell	n/a	n/a	n/a	Po A Ti	n/a	U˜
216.	2010	Pr R C	65	C R	<1Wk	n/a	Li Lb	A P Lb	n/a	11	A- S-
217.	2012	Rt C	18	C	<3Mo	M E	Li Fo	n/a	A	9	K˜A+ U+
218.	2012	Pr R C	25	B	<1Wk	M	Li	n/a	Ti	11	K+ A+ U+
219.	2009	Pr	14	S	<3Mo	n/a	Li Tx Fo Lb	n/a	n/a	7	A+
220.	2012	Pr R C	81	C	<3Mo	n/a	Li	A P Lb	n/a	12.5	A+ S+
221.	2013	Pr R Mt Pp C	188	C	<3Mo	M	Li	n/a	n/a	11	K+ A+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
222.	2008	Pr	205	B	<3Mo	M E Lb	Li Lb	n/a	n/a	10.5	K˜A˜
223.	2008	Pr R Pp C	108	B	<3Mo	M	Li Tx	n/a	n/a	11	K˜
226.	2012	Pr R C	40	R	<1Wk	M Lb	Li	n/a	n/a	12	K˜A+
227.	2004	Pr C	121	B	<3Mo	Lb	Li Lb	n/a	T	11.5	K+ A+ U+
228.	2006	Pr	can't tell	n/a	can't tell	n/a	n/a	n/a	n/a	n/a	A+
229.	2008	Pr	200	B	<3Mo	n/a	n/a	n/a	n/a	9	A+
230.	2011	Pr Pp	21	B C	can't tell	M Li	Li Tx	n/a	n/a	10.5	K+ A+
231.	2011	Pr	176	S	>3Mo	M F E	n/a	n/a	A	9	K+ U˜
232.	2011	Pr R Pp C	19	C	<3Mo	O E P Lb	Li Tx	n/a	n/a	12.5	K+ A+
233.	2010	Pr	32	B	<3Mo	n/a	Li P Fo Lb	n/a	n/a	8	A+
234.	2012	Pr	60	B	>3Mo	F E	Li Tx	n/a	A	11	K˜A+
235.	2010	Pr R Pp C	389	S	<3Mo	M	Li	n/a	T	11	K˜A+ U+
236.	2013	Pr Pp	35	C	<3Mo	M Li	Li	A P	T	8	K+ A+ S+
237.	2012	Pr	40	R	>3Mo	n/a	Li Fo	n/a	n/a	10	A+
238.	2007	Pr Pp C	41	S	>3Mo	M E	Li	n/a	Ti	8	K+ A+ U˜
239.	2006	Pr R Pp C	159	B	>3Mo	M Tx	Li	n/a	Ti	9	K+ A˜U˜
240.	2003	Pr Mt Pp	10	C	<3Mo	Li O P	Li P Lb	n/a	T Po R A	13.5	K+ A+ U+
241.	2011	Pr	310	n/a	can't tell	n/a	n/a	n/a	T	n/a	U˜
242.	2006	Pr	84	B R	can't tell	M O P	Li Tx	n/a	n/a	n/a	K+ A+

Ref	Year	Study type	Subject N	Educ.	Duration	Knowledge	Attitudes	Skills	Usage	MERSQI	Findings
243.	2010	Pr Pp C	185	B	<3Mo	M E	Li Tx P Lb	n/a	T A	10.5	A+ U+
244.	2009	Pr R C	1267	S	<3Mo	M Li	n/a	n/a	T Po R A Ti	12	K+ U+
245.	2013	Pr R Pp C	120	B C	<1Wk	M tf	Li	n/a	n/a	11	K+ A+
246.	2006	Pr	18	n/a	can’t tell	n/a	Li	n/a	n/a	6	A+
247.	2010	Pr Pp	160	C	<1Wk	M	Li Tx	n/a	A Ti	8	K+ A+ U˜
249.	2012	Pr C	99	B	<3Mo	Li	Li	A P Lb	n/a	10	A+ S˜
250.	2009	Pr Mt Pp	454	S	can’t tell	n/a	n/a	n/a	n/a	9	n/a

Experimental groups for controlled trials

Ref	Year	Controls
2.	2012	B-learning vs. Lecture
6.	2011	B-learning vs. Lecture
9.	2012	Exploratory practice vs. Blocked practice
10.	2012	Virtual Patient vs. OSCE vs. Role-play
16.	2009	E-learning vs. Lecture
17.	2013	B-learning vs. Lecture
18.	2010	Simulation vs. Lecture
18.	2010	Virtual patient + lecture vs. Virtual patient vs. Lecture
23.	2013	Multimedia content vs. Text content
24.	2004	Complex user interface vs. Simple user interface
26.	2008	B-learning vs. Lecture
30.	2003	B-learning vs. No intervention
31.	2012	E-learning vs. Lecture
33.	2009	Adaptive system vs. Non-adaptive system
38.	2012	E-learning vs. Lecture
39.	2011	Simulation vs. Dissection + Simulation vs. No intervention
42.	2008	B-learning vs. Lecture
44.	2012	Immediate feedback vs. Delayed feedback
47.	2013	B-learning vs. Lecture
51.	2007	E-learning vs. Lecture
52.	2012	E-learning vs. No intervention
63.	2008	B-learning vs. Lecture
68.	2009	Simulation vs. No Intervention
71.	2006	Digital multimedia content vs. Printed content
77.	2012	B-learning vs. Lecture
79.	2011	E-learning vs. No intervention
84.	2010	E-learning vs. Lecture
85.	2010	E-learning vs. Lecture
89.	2012	Timed virtual patient vs. Untimed virtual patient
90.	2013	Spaced education vs. No intervention
91.	2010	E-learning vs. Lecture
94.	2012	Lecture notes vs. Lecture + Group discussion
97.	2013	Interactive virtual patient vs. Audio virtual patient vs. No intervention

Ref	Year	Controls
100.	2012	Immediate feedback vs. Delayed feedback
101.	2009	B-learning vs. Lecture
106.	2009	Simulation + Explanation vs. Simulation vs. Multimedia content
110.	2010	3d content vs. 2d content
111.	2013	Different sequences of Lecture, Discussion and Virtual patient activities
113.	2011	E-learning vs. No intervention
117.	2009	Clinical cases vs. Research articles
118.	2008	Spaced education vs. Bolus education
119.	2009	Spaced education vs. Bolus education
120.	2012	Two-week spaced education vs. Four-week spaced education
121.	2007	Spaced education vs. Bolus education
122.	2009	Spaced education vs. Bolus education
123.	2007	Spaced education vs. No intervention
124.	2010	Spaced education vs. Bolus education
126.	2013	3d content vs. 2d content vs. Physical model
132.	2012	B-learning vs. Lecture
134.	2010	Simulation vs. Laboratory vs. No intervention
140.	2012	In-person e-learning session vs. Distant e-learning session
142.	2009	B-learning vs. Lecture
147.	2010	In-person e-learning session vs. Distant e-learning session
150.	2013	Spaced education vs. Bolus education
153.	2011	E-learning vs. No intervention
155.	2009	Spaced education vs. No intervention
159.	2009	B-learning vs. Lecture
161.	2010	Wiki vs. Instant messaging vs. Links to external resources
162.	2010	B-learning vs. Lecture
163.	2012	Integrated web-application vs. Online resources
165.	2012	E-learning vs. No intervention
168.	2008	B-learning vs. Lecture
171.	2013	E-learning vs. No intervention
180.	2012	E-learning vs. Lecture
181.	2007	B-learning vs. Lecture
182.	2010	B-learning vs. Lecture
183.	2012	B-learning vs. Lecture

Ref	Year	Controls
187.	2010	B-learning vs. Lecture
189.	2007	Multimedia content vs. Text content
192.	2006	Adaptive system vs. Non-adaptive system
193.	2012	3d content vs. 2d content
194.	2007	B-learning vs. Lecture
198.	2006	B-learning vs. Lecture
203.	2011	B-learning vs. Lecture
204.	2013	E-learning vs. Lecture
208.	2011	Immediate feedback vs. Delayed feedback
211.	2011	E-learning vs. Lecture
216.	2010	3d content vs. 2d content vs. Physical model
217.	2012	B-learning vs. Lecture
218.	2012	Multimedia content vs. Text content
220.	2012	B-learning vs. Lecture
221.	2013	B-learning vs. Lecture
223.	2008	Exploratory practice vs. Blocked practice
226.	2012	3d content vs. 2d content
227.	2004	B-learning vs. Lecture
232.	2011	Spaced education vs. Bolus education
235.	2010	B-learning vs. Lecture
238.	2007	E-learning vs. No intervention
239.	2006	E-learning vs. Lecture
243.	2010	B-learning vs. Lecture
244.	2009	Many hyperlinks vs. Few hyperlinks, Spaced education vs. Bolus education
245.	2013	Complex user interface vs. Simple user interface
249.	2012	Virtual patient vs. No intervention

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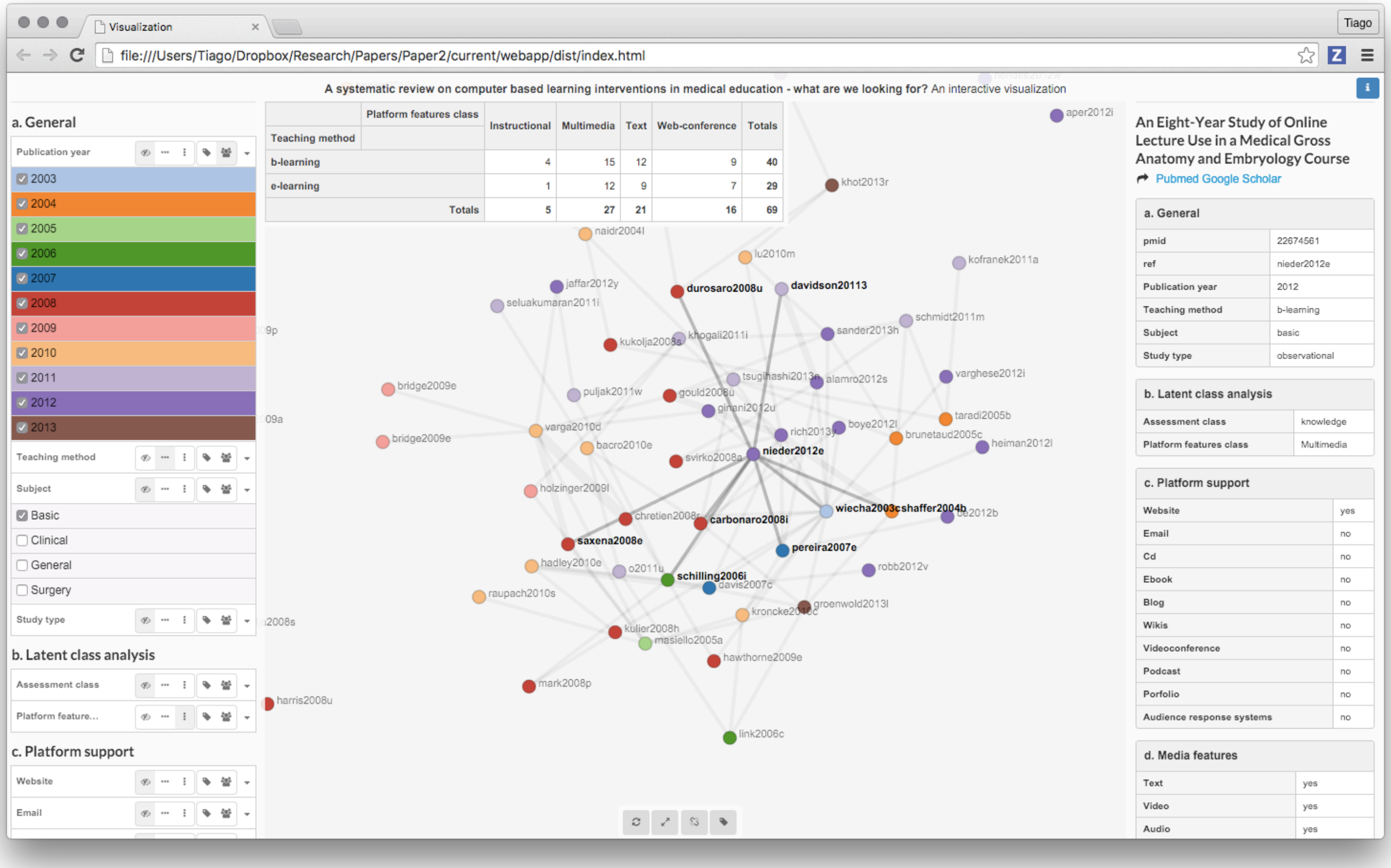
4. Interactive web application for the reviewed papers



A systematic review on computer based learning interventions in medical education - what are we looking for? An interactive visualization

	Platform features class	Instructional	Multimedia	Text	Web-conference	Totals
Teaching method						
b-learning		4	15	12	9	40
e-learning		1	12	9	7	29
Totals		5	27	21	16	69

An Eight-Year Study of Online Lecture Use in a Medical Gross Anatomy and Embryology Course

Pubmed Google Scholar

a. General

pmid	22674561
ref	nieder2012e
Publication year	2012
Teaching method	b-learning
Subject	basic
Study type	observational

b. Latent class analysis

Assessment class	knowledge
Platform features class	Multimedia

c. Platform support

Website	yes
Email	no
Cd	no
Ebook	no
Blog	no
Wikis	no
Videoconference	no
Podcast	no
Porfolio	no
Audience response systems	no

d. Media features

Text	yes
Video	yes
Audio	yes

Screenshot of the accompanying web application used to explore the results of the paper review.

5. Notebook script used in the study

Topic	1	The Golgi network
Flashcard	**1**	
Piece	1	The Golgi network is involved in protein processing, trafficking and the synthesis of glycolipids and polysaccharides.
Question	1	In what processes is the Golgi complex involved?
Piece	2	The proteins are transported from the endoplasmic reticulum (ER) to the cis-Golgi network and complete the process of maturation in the trans-Golgi network, where the proteins are packed into vesicles to be transported to the lysosomes (via endosomes), the plasmatic membrane or to the cell exterior.
Question	2	Where are the proteins from the ER transported to?
Question	3	Where do the proteins from the ER come from?
Question	4	Where do the proteins complete their maturation process?
Question	5	Where are the proteins that pass through the ER sent to?
Flashcard	**2**	
Piece	3	The designation "Golgi Apparatus" is used to refer all the Golgi networks in the same cell.
Question	6	What does the designation “Golgi Apparatus” refer to?
Flashcard	**3**	
Piece	4	Protein maturation by n-glycosylation occurs during the transport along the Golgi network.
Question	7	Through which process does the maturation in the Golgi network occur?
Question	8	When does the protein n-glycosylation takes place?
Flashcard	**4**	
Piece	5	The Golgi network synthesizes glycolipids, sphingomyelin and complex polysaccharides that make part of the plant cell wall.
Question	9	What are the substances synthesized in the Golgi network?
Flashcard	**5**	
Piece	6	The Golgi network is composed by a group of cisterns (dictyosomes) and vesicles.
Question	10	What is the Golgi network composed of?

Topic	**1.1**	**Golgi network compartments**
Flashcard	**6**	
Piece	7	There are three types of functionally distinct compartments in the Golgi network: cis-Golgi face cisterns (subdivided into cis, medial and trans) trans-Golgi face
Question	11	Which compartment types make up Golgi network?
Piece	8	The vesicles from the ER fuse, forming an intermediate compartment between the RE and the Golgi, the ERGIC, that transports proteins to the cis-Golgi network.
Question	12	What is the name of the intermediate compartment between the ER and the Golgi network?
Question	13	Where are the proteins from the EREGIC transported to?
Image	1	The Golgi network compartments
Flashcard	**7**	
Piece	9	The cis, medial and trans cisterns are the sites where the majority of the processing reactions occur.
Question	14	Which are the cisterns where the majority of the processing reactions occur?
Piece	10	The trans-Golgi network works as a center for triage and distribution of the proteins to the endosomes, the lysosomes, the plasmatic membrane or the exterior of the cell.
Question	15	What is the specific of the trans-Golgi network?
Flashcard	**8**	
Piece	11	Proteins from the ER enter through the cis face, also known as formation face. This face is convex and oriented towards the cell nucleus.
Question	16	Where is the point of entrance on the Golgi network for proteins coming from the ER?
Question	17	What are the characteristics of the cis-Golgi face?
Piece	12	The proteins that are transported along the Golgi network, exit through the concave trans-Golgi face, also designated maturation face. These proteins are sent to endosomes, lysosomes, the plasmatic membrane and the exterior of the cell, as illustrated in the picture.
Question	18	From which point do carried proteins leave the Golgi network?
Question	19	What are the characteristics of the trans-Golgi face?
Question	20	What are the destination locations of the proteins that leave the Golgi network?
Image	2	Electron microscopy of the Golgi network

Topic	1.2	Transport from the endoplasmic reticulum to the Golgi complex
Flashcard	**9**	
Piece	13	The proteins that belong to the ER are named resident proteins. These proteins are transported in a non-specific manner from the ER to the Golgi, and are recovered via retrograde transport to the ER.
Question	21	How are resident proteins from the ER recovered from the Golgi network?
Piece	14	Resident proteins from the ER are identified by a retention signal on its C-terminus that signals them to retrograde transport
Question	22	What is the signal that identifies ER resident proteins?
Question	23	Where is the signal that identifies a protein as part of the ER located?
Image	3	Traffic between the ER and the Golgi network
Flashcard	**10**	
Piece	15	The soluble ER resident proteins retention signal consists of 4 amino acids in KDEL sequence (Lys-Asp-Glu-Leu).
Question	24	What is the amino acid sequence of the retention signal of soluble ER resident proteins?
Piece	16	The KDEL sequence links specifically to the KDEL receptor, on the ERGIC or Golgi, which allows resident protein packaging in COPI coated vesicles for retrograde transport to the ER.
Question	25	To which receptor does the retention signal of the soluble proteins links to?
Question	26	Where does the retention signal binding to the soluble protein receptor occurs?
Question	27	In which vesicle type ER resident proteins are transported back to the ER?
Flashcard	**11**	
Piece	17	Transmembrane proteins retention signal consists of 2 lysine residues followed by other 2 other amino acids (KKXX). It links directly to COPI coated vesicles that allow the retrograde transport to the RE.
Question	28	What is the amino acid sequence of the transmembrane resident proteins?
Question	29	What is the type of vesicles that transmembrane resident proteins link to?
Flashcard	**12**	
Piece	18	Proteins and lipids coming to the Golgi-network from the ER are first transported to the ERGIC and then to the cis-Golgi network via COPI coated vesicles.
Question	30	Which are the structures in which proteins and lipids are passed to from the ER to the Golgi network?

Topic	**1.3**	**Metabolism of lipids and polysaccharides**
Flashcard	**13**	
Piece	19	In addition to glycoprotein processing, the Golgi network is also involved in the lipidic metabolism and in particular the synthesis of glycolipids and sphingomyelin.
Question	31	What other process is the Golgi network involved in addition to glycoprotein processing?
Flashcard	**14**	
Piece	20	Sphingomyelin results from the addition of a phosphorylcholine group to a ceramide molecule.
Question	32	What is the residue that produces sphingomyelin when added to ceramide?
Question	33	What is the residue that produces sphingomyelin when added phosphorylcholine group?
Question	34	Which molecules compose sphingomyelin?
Flashcard	**15**	
Piece	21	Glycoproteins result from the addition of carbohydrates to ceramide.
Question	35	How are glycolipids formed?
Question	36	What is the residue that produces glycolipids when added carbohydrates?
Flashcard	**16**	
Piece	22	In plants, the Golgi network is mainly involved in the synthesis of polysaccharides that form the nuclear wall.
Question	37	In which process is the Golgi network mostly involved in plants?
Topic	**2**	**Maturation of proteins by O-linked glycosylation**
Flashcard	**17**	
Piece	23	Another aspect of the processing of glycoproteins in the Golgi network consists of the addition of carbohydrates to the OH group on the serine and threonine residues present in specific peptidic sequences (O-linked glycosylation).
Question	38	What does the O-linked glycosylation process consists of?

Flashcard	**18**	
Piece	24	The O-linked glycosylation process is catalyzed by a series of glycosyltransferases that add firstly a n-acetylgalactosamine residue and after a variable number of carbohydrates, usually up to 10 residues.
Question	39	What are the proteins involved in the O-linked glycosylation process?
Question	40	What is the first residue added by the enzymes that catalyze the O-linked glycosylation process?
Piece	25	In some cases these residues are further modified by the addition of sulphate groups.
Question	41	What residues can be further added to the carbohydrates of the O-linked glycosylation matured proteins?
Flashcard	**19**	
Piece	26	Some cytosolic and nuclear proteins are processed by O-linked glycosylation.
Question	42	What are the final locations of the proteins processed by O-linked glycosylation?
Topic	**3**	**Maturation of proteins by n-linked glycosylation**
Flashcard	**20**	
Piece	27	One of the most important processes in the maturation of the glycoproteins in the Golgi network consists of the modification of the n-linked oligosaccharides added in the ER by an ordered sequence of reactions in each cistern. In the proteins destined to the plasmatic membrane or secretion, the first modification occurs via removal of 3 residues of mannose in the cis-Golgi network.
Question	43	What is the first modification that occurs in the proteins destined to the plasmatic membrane or secretion?
Question	44	Where does the first modification occur in the proteins destined to the plasmatic membrane or secretion?
Flashcard	**21**	
Piece	28	In the proteins destined to the plasmatic membrane, the second step occurs in the medial-Golgi network and consists of the removal of 2 residues of mannose and the addition of 3 residues of n-acetylglucosamine and fucose.
Question	45	What is the second modification that occurs in the proteins destined to the plasmatic membrane or secretion?
Question	46	Where does the second modification occur in the proteins destined to the plasmatic membrane or secretion?

Flashcard	**22**	
Piece	29	In the proteins destined to the plasmatic membrane, the last step takes place in the trans-Golgi network, and consists of the addition of 3 residues of galactose and the addition of n-acetylneuraminic acid to each galactose residue.
Question	47	What is the last modification that occurs in the proteins destined to the plasmatic membrane or secretion?
Question	48	Where does the last modification occur in the proteins destined to the plasmatic membrane or secretion?
Image	4	Processing of n-linked oligosaccharides in the Golgi complex cisterns
Flashcard	**23**	
Piece	30	The degree of processing of the n-linked oligosaccharides depends on: The structure of the proteins in the Golgi network The quantity of enzymes in the Golgi network
Question	49	What are the factors in which the degree of processing of the n-linked oligosaccharides depends?
Piece	31	In some cases the first processing reaction (removal of mannose residues) does not occur, which prevents the following addition of carbohydrate residues, leading to the formation of oligosaccharides rich in mannose instead of complex oligosaccharides that follow the full processing pathway.
Question	50	What type of error may occur in the processing pathway of the n-linked oligosaccharides?
Question	51	What type of molecules are formed in the case of first reaction errors?
Flashcard	**24**	
Piece	32	In the proteins destined to the lysosomes, phosphorylation of mannose residues in two sequenced reactions.
Question	52	What is the type of reaction that occurs in the proteins destined to the lysosomes?
Flashcard	**25**	
Piece	33	In the proteins destined to the lysosomes, the first reaction is catalyzed in the cis face by the enzyme n-acetylglucosamine phosphotransferase.
Question	53	What is the first modification in the proteins destined to the lysosomes?
Question	54	What is the enzyme responsible for the first modification that occurs in the proteins destined to the lysosomes?
Piece	34	The n-acetylglucosamine phosphotransferase transfers a group n-acetylglucosamine phosphate to the mannose residues of the lysosomal hydrolases.
Question	55	That is the molecule transferred by the n-acetylglucosamine phosphotransferase?
Question	56	What is the molecule that accepts the n-acetylglucosamine phosphate transferred by the enzyme n-acetylglucosamine phosphotransferase?

Flashcard	**26**	
Piece	35	The second reaction is catalyzed by a phosphodiesterase that removes the n-acetylglucosamine group, leaving behind a phosphorylated mannose residue.
Question	57	What is the second modification in the proteins destined to the lysosomes?
Question	58	What is the enzyme responsible for the second modification that occurs in the proteins destined to the lysosomes?
Flashcard	**27**	
Piece	36	Processing specificity of lysosomal proteins resides in the n-acetylglucosamine phosphotransferase enzyme, that catalyses the reaction of addition of n-acetylglucosamine phosphate.
Question	59	What is the molecule responsible for the specificity of the lysosomal protein processing?
Question	60	What is the reaction catalyzed by the n-acetylglucosamine phosphotransferase?
Piece	37	This enzyme recognizes a structural determinant present uniquely in the lysosomal proteins, named "signal patch", formed by the juxtaposition of amino acid sequences from different regions of the polypeptide chain, as illustrated in the picture.
Question	61	How is the structural determinant present only in the lysosomal proteins named?
Question	62	What is the lysosomal protein structure recognized by the enzyme n-acetylglucosamine phosphotransferase?
Question	63	What is the composition of the structural determinant present in the lysosomal proteins?
Image	5	Reckoning and processing of the lysosomal hydrolases by the n-acetylglucosamine phosphotransferase (GlcNAc phosphotransferase)