Multimedia Appendix 1. E-tables.

E-table 1.search strategy

Search date 2014.9.25

*=wild word Adj=adjacent

Medline:

1. "blended learning" [Title/Abstract] OR "hybrid learning" [Title/Abstract] OR "integrated learning" [Title/Abstract] OR "computer-aided learning" [Title/Abstract] OR "hybrid training" [Title/Abstract] OR "integrated training" [Title/Abstract] OR "computer-aided training" [Title/Abstract] OR "integrated education" [Title/Abstract] OR "computer-aided education" [Title/Abstract] OR "computer-aided education" [Title/Abstract] OR "computer-aided education" [Title/Abstract] OR "integrated instruction" [Title/Abstract] OR "computer-aided instruction" [Title/Abstract] OR "blended teaching" [Title/Abstract] OR "integrated teaching" [Title/Abstract] OR "blended course" [Title/Abstract] OR "hybrid course" [Title/Abstract] OR "integrated course" [Title/Abstract] OR "computer-assisted course" [Title/Abstr

2.physician*[Title/Abstract] OR medic*[Title/Abstract] OR nurs*[Title/Abstract] OR pharmac*[Title/Abstract] OR dental[Title/Abstract] OR health*[Title/Abstract] OR cme[Title/Abstract]

3.compar* OR trial* OR evaluat* OR assess* OR effect* OR pretest* OR pre-test OR post-test OR post-test OR pre-interven* OR pre-intervention OR post-interven* OR post-intervention

4.1 AND 2 AND 3

Ovid Embase:

- 1.(blended OR hybrid OR integrated OR distributed OR computer-aided OR computer-assited) adj (learing OR training OR educat* OR instruct* OR teach* OR course*).ti,ab.
- 2.(physician*OR medic* OR nurs* OR pharmac* OR dental OR health* OR cme) .ab.
- 3.(compar* OR trial* OR evaluat* OR assess* OR effect* OR pretest* OR pre-test OR post-test OR post-test OR pre-intervention OR pre-intervention OR

postintervention OR post-intervention).af.

4. 4.1 AND 2 AND 3

Web of science

1.title: ("blended learning" OR "hybrid learning" OR "integrated learning" OR "computer-aided learning" OR "computer-assisted learning" OR "distributed learning" OR "hybrid training" OR "integrated training" OR "computer-aided training" OR "integrated education" OR "computer-aided education" OR "computer-assisted education" OR "distributed education" OR "integrated instruction" OR "computer-assisted instruction" OR "blended teaching" OR "integrated teaching" OR "computer-assisted teaching" OR "blended course" OR "hybrid course" OR "integrated course" OR "integrated course" OR "computer-assisted cour

2.subject: (physician*OR medic* OR nurs* OR pharmac* OR dental OR cme OR health*)

- 3. subject: (compar* OR trial* OR evaluat* OR assess* OR effect* OR pretest* OR pre-test OR post-test OR post-test OR preintervention OR pre-intervention OR post-intervention)
- 4. 1 AND 2 AND 3

CINAHL

- 1.Tl"blended learning" OR TI"hybrid learning" OR TI"integrated learning" OR TI"computer-aided learning" OR TI"integrated education" OR TI"computer-aided training" OR TI"integrated education" OR TI"computer-aided training" OR TI"computer-aided education" OR TI"computer-aided instruction" OR TI"computer-aided instruction" OR TI"computer-aided instruction" OR TI"blended teaching" OR TI"integrated teaching" OR AB"integrated course" OR TI"integrated course" OR AB"integrated course" OR AB"integrated training" OR AB"computer-aided training" OR AB"integrated education or OR AB"integrated educ
- 2. TI physician*OR TI medic* OR TI nurs* OR TI pharmac* OR TI dental OR TI health* OR TI cme OR AB physician* OR AB medic* OR AB nurs* OR AB pharmac* OR AB dental OR AB health* OR AB cme
- 3. compar* OR trial* OR evaluat* OR assess* OR effect* OR pretest* OR pre-test OR posttest* OR post-test OR pre-interven* OR pre-intervention OR post-intervention
- 4.1 AND 2 AND 3

ERIC

1 title:("blended learning" OR "hybrid learning" OR "integrated learning" OR "computer-aided learning" OR "computer-assisted learning" OR "distributed learning" OR "hybrid training" OR "integrated training" OR "computer-aided training" OR "integrated education" OR "computer-aided education" OR "computer-assisted education" OR "distributed education" OR "integrated instruction" OR "computer-assisted instruction" OR "blended teaching" OR "integrated teaching" OR "computer-aided teaching" OR "blended course" OR "hybrid course" OR "integrated course" OR "computer-assisted course" OR nurse oR pharmac* OR dental OR health* OR cme) AND (compar* OR trial* OR evaluat* OR assess* OR effect* OR pretest* OR pretest OR post-test OR preintervention OR pre-intervention OR post-intervention)

Sciencedirect

1.(ttl("blended learning") OR ttl("hybrid learning") OR ttl("integrated learning") OR ttl("computer-aided learning") OR ttl("computer-assisted learning") OR ttl("integrated training") OR ttl("computer-aided training") OR ttl("integrated education") OR ttl("computer-aided education") OR ttl("computer-aided education") OR ttl("computer-aided instruction") OR ttl("computer-aided instruction") OR ttl("computer-aided teaching") OR ttl("computer-aide

Cochrane Central

- 1. Title, Abstract, Keywords: ("blended learning" OR "hybrid learning" OR "integrated learning" OR "computer-aided learning" OR "computer-assisted learning" OR "computer-aided training" OR "integrated education" OR "computer-aided education" OR "computer-assisted education" OR "distributed education" OR "integrated instruction" OR "computer-aided instruction" OR "computer-assisted instruction" OR "blended teaching" OR "integrated teaching" OR "computer-aided teaching" OR "blended course" OR "hybrid course" OR "integrated course" OR "computer-assisted course")
- 2. Title, Abstract, Keywords: (physician*OR medic* OR nurs* OR pharmac* OR dental OR health* OR cme)
- 3. Search all text (compar* OR trial* OR evaluat* OR assess* OR effect* OR pretest* OR pre-test OR post-test OR post-test OR preintervention OR post-intervention OR post-intervention)
- 4. 1 AND 2 AND 3

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E-Table 3. Description of included publications

Section 1. Studies comparing blended learning with no intervention

Study	Design RCT/NRS)	Country	Participants no.(B/N)³; type	Topic	Study intervention(component or features)	Modality or technology	Intervention duration	Exercises	Interactivity	Discussion	Delay between posttest and course	Assessment(question type)	Conflict of interest		Funding from company	Quality score
Flys,2012	Pre- posttes t 1- group; NRS	Pana ma, Nicar agua, Domi nican Repu blic, and Guate mala	225; Doctors, nurses, psycholo gists, health administ rators, etc.	Principle s of HIV care and health systems	Online+on-site +projects	Moodle; on- site workshops	150 hour s (10 week s)	Present(cases, self-assessment)	High(essay s, group work)	Pre sen t	No dela y	Subjective (MCQ ,essays)	No		No	4
Puri,2010	Pre- posttes t, 2 groups ; NRS	India na	350/102; Dietetic students	Commun ication and counselin g skills	CAI+print resources	Internet- based site	1 week	Present(cases)	Low	Abs ent	No dela y	Objective(cannot tell)		No	No	6
Karaksha,2011	Posttes t, 2 groups ;RCT	Austr alia	23/17;Ph armacy students	Pharmac ology	CAL+lecture	CD, iSpring Pro 4.3.0.	24 hour s	Present(quiz,a ssessment)	Low	Abs ent	No dela y	Objective(MCQ)		No	No	4
Buchowski,2002	Pre- posttes t, 1 group; NRS	USA	80/78;Me dical students	Nutrition al Anemias and the Diabetes and Weight Manage ment	CAI+traditional	Aberrations in Glucose Metabolism modules	1 seme ster	Present(cases, self-assessment)	High(group work)	Abs ent	3 mon ths	Objective(cannot tell)		No	Yes	3
Wallen,2010	Pre- posttes t 1- group; NRS	USA	127;- nurses	Basic genetics	Web-based+face- toface	self-paced learning modules	<1 seme ster	Absent	Low	Abs ent	No dela y	Objective(problem-base questions)	d	No	No	3
Weaver,2014(a)	Pre- posttes	USA	60; Health	Health policy	e- learning+traditional	technology- driven	12 mont	Present(cases, self-	High(team- baased	Pre sen	No dela	Subjective(analysis,inte retation,inference,	erp	No	No	3

	t 1- group; NRS		students			combined platform, blackboard-uploaded virtual interactive lectures	hs	assessment)	assignment)	t	у	evaluation)			
Weaver,2014(b)	Pre- posttes t 1- group; NRS	USA	60; Health students	Health policy	e- learning+traditional	technology- driven combined platform, blackboard- uploaded virtual interactive lectures	mont hs	Present	High	Pre sen t	No dela y	Subjective(analysis,interp retation,inference, evaluation)	No	No	3
Riesen,2012	Pre- posttes t 1- group; NRS	Cana da	60;Healt h graduate s	Interprof essional competen cies	virtual face-to-face +traditional face-to- face+online	real-life simulation, virtual simulation, virtual debriefing and a didactic learning component. Web.Alive	2 days	Absent	High(discus sion group)	Pre sen t	No dela y	Subjective(self-report)	No	Yes	3
Cho,2014(a)	Pre- posttes t 1- group; NRS	South Korea	45; Nurses	Research ethic	Web-based online instruction + a off-line instruction(review of the core contents on the online program, case analysis, small group discussion and miscellaneous activities)	develope Analysis, Design, Developmen t, Implementa tion, and Evaluation (ADDIE) model	30 hour s	Present(cases	High(group discussion)	Pre sen t	No dela y	Objective(cannot tell)	No	No	3
Cho,2014(b)	Pre- posttes t 1- group; NRS	South Korea	69;Nursi ng students	Research ethic	Web-based online instruction + a off-line instruction(review of the core contents on the online program, case analysis, small group discussion and miscellaneous activities)	Analysis, Design, Developmen t, Implementa tion, and Evaluation (ADDIE) model	30 hour s	Present(cases	High(group discussion)	Pre sen t	No dela y	Objective(cannot tell)	No	No	3
Pereira,2008(a)	Pre- posttes t 1- group;	Cana da	14;Famil y medicine resident	Palliative care	Web-based learning+face-toface workshop	asynchrono us discussion forums, a	8 week s	Absent	High(group -based discussion)	Pre sen t	No dela y	Objective(MCQ)	No	No	4

	NRS		S			live audio									
						and text- based									
						online									
						synchronou s									
						session(Cen tra); online modules (Macromedi									
						a Breeze)									
Pereira,2008(b)	Pre- posttes t 1- group; NRS	Cana da	16;Famil y medicine resident s	Palliative care	Web-based learning+face-toface workshop	asynchrono us discussion forums a live audio- and text- based online synchronou s session(Cen tra); online modules (Macromedi a Breeze)	8 week s	Absent	High(group -based discussion)	Pre sen t	No dela y	Objective(MCQ)	No	No	4
Karamizadeh,2011 (a)	Pre- posttes t 1- group; NRS	Iran	10;Medic al students	Medical training	E-learning+class session	Multimedia compact disk	4 week s	Absent	High(probl em solving session)	Abs ent	2-4 wee ks dela	Objective(cannot tell)	No	No	3
Karamizadeh,2011 (b)	Pre- posttes t 1- group; NRS	Iran	40;Exter n	Medical training	E-learning+class session	Multimedia compact disk	4 week s	Absent	High(probl em solving session)	Abs ent	2-4 wee ks dela y	Objective(cannot tell)	No	No	3
Karamizadeh,2011 (c)	Pre- posttes t 1- group; NRS	Iran	19;Inter n	Medical training	E-learning+class session	Multimedia compact disk	4 week s	Absent	High(probl em solving session)	Abs ent	2-4 wee ks dela y	Objective(cannot tell)	No	No	3
Karamizadeh,2011 (d)	Pre- posttes t 1- group; NRS	Iran	38; Resident	Medical training	E-learning+class session	Multimedia compact disk	4 week s	Absent	High(probl em solving session)	Abs ent	2-4 wee ks dela y	Objective(cannot tell)	No	No	3
Karamizadeh,2011	Pre-	Iran	6;Assista	Medical	E-learning+class	Multimedia	4	Absent	High(probl	Abs	2-4	Objective(cannot tell)	No	No	3

(e)[1][1][21][1]	posttes t 1- group; NRS		nt professor	training	session	compact disk	week s		em solving session)	ent	wee ks dela y				
Chandler,2008	Pre- posttes t 1- group; NRS	USA	817;Publ ic health workers	Emergen cy prepared ness	Web-based+on-the- job+face-to-face; downloadable homework assignment	Website; downloadab le template	2 days	Absent	High(requir ed for response)	Pre sen t	No dela y	Objective(MCQ)	No	No	3
Baumlin 2006	Posttes t, 2 group; RCT	USA	40/50; Clinical medical students	Lung cancer	Web tutorial +traditional	Internet tutor, repetition	1- 4wee ks	Present(case)	Low(case)	Pre sen t	No dela y	Objective(cannot tell)	No	No	3
Cragun, 2005	Pre- posttes t, 1 group; NRS	USA	39/15Nu rsing students	Genetics	Web tutorial +face- to-face lecture	Web tutorial	1 day	Present(case- based problem)	Low	Abs ent	No dela y	Objective(MCQ, true or false question)	No	No	3

Section 2.Studies comparing blended learning with non-blended learning

Study	Design RCT/NRS)	Country	Comparison intervention	Participants no.(B/Nª); type	Topic	Study intervention(component or features)	Modality or technology	Duration	Exercises	Interactivity	Discussion	courseDelay between posttest and	Assessment(question type)	Conflict of interest:	,	Quality score
Kulier, 2012	Pre- posttes t 2 groups ;RCT	7 LMICs (Argen tina, Brazil, Democ ratic Repub lic of the	Tradition al teaching	123/81; Postgraduat e trainees	Reproductiv e Health	E- learning+F2F	recorded video, specialist database	8 week s	Present(questio ns, assignments)	High(Feedb ack on assignments)	Abs ent	4 we eks	Objective(MCQ)	No	No	6

Kavadella,2012	Pre- posttes t 2 group; RCTs	Congo, India, Philip pines, South Africa, Thaila nd). Greece	Conventio nal face to face methodolo gy	24/22; Undergradu ate	Oral radiology	F2F + online	E-learning platform Web -based tools include self- graded tests and quizzes, online discussion groups	0.5 year	Present(self- graded tests and quizzes)	High(self- graded tests and quizzes, online discussion groups)	Pre sent	No del ay	Objective(dichoto mal :yes/no)	No	No	4
Lancaster,2011	Pre- posttes t, 1 group; NRS	USA	Tradition al	97; Second professional year students	Pharmacy curriculum	online self- directed study +in-class active learning	Blackboard online hosting service	1 seme ster	Present(quiz	High(quiz, group discussion)	Pre sent	No del ay	Objective(Choice question)	No	No	3
Sowan,2013	Posttes t, 2 groups ; RCT	Jordan	Tradition al format	105/105; undergradu ate nursing students	Scientific research in nursing	Web- based+interacti ve F2F	Blackboard and Tegrity systems	1 seme ster	Present(questio ns, assignments)	High (questions, assignments)	Pre sent	No del ay	Objective(open- ended questions)	No	No	5
Makhdoom,2013	Posttes t, 2 groups ;RCT	Saudi Arabia	face-to- face	60/61; Medical students	Family medicine course	E- learning+F2F	Electronic course management system	10 week s	Absent	High(intera ct with tutors)	Pre sent	No del ay	Objective(MCQ)	No	No	5
Lancaster,2012	Posttes t, 2 groups ;RCT	USA	Tradition al in-class	29/23; Graduate	Pharmacoth erapeutics course	Oline+F2F	Griffin Lapel Microphone, Articulate Presenter '09, electronic Blackboardhos ting website	1 year	Present(assign ment, question and answer sessions)	High (assignment , question and answer session ,question and answer sessions)	Pre sent	No del ay	Objective(Cannot tell)	No	No	4
Dankbaar,2014(a)	Posttes t, 2 groups ;NRS	Nether lands	Tradition al course	31/16; Nurse in postgraduat e	Acute and intensive care	Online material+F2F lecture	Web lectures	11 days	Present (examples and exercises)	Low(exampl es and exercises with feedback)	Abs ent	No del ay	Objective(MCQ)	No	No	5
Dankbaar,2014(b)[2][2][22][2]	Posttes t, 2 groups ;NRS	Nether lands	Tradition al course	31/16; Nurse in postgraduat e	Acute and intensive care	Online material+F2F lecture	Web lectures	11 days	Present (examples and exercises)	Low(exampl es and exercises with feedback)	Abs ent	No del ay	Objective(MCQ)	No	No	5

Dankbaar,2014(c)	Posttes t, 2 groups ;NRS	Nether lands	Tradition al course	31/16; Nurse in postgraduat e	Acute and intensive care	Online material+F2F lecture	Web lectures	11 days	Present (examples and exercises)	Low(exampl es and exercises with feedback)	Abs ent	No del ay	Objective(MCQ)	No	No	5
Mangione,1991(a)	Pre- posttes t, 2 groups ;RCT	USA	Computer- assisted instructio n	13/9; Medical students	Cardiac auscultation	Self-schedule CAI + small- group seminar	HEARTLAB platform,	12 week s	Absent	Low	Abs ent	No del ay	Objective(choice question)	No	No	4
Mangione,1991(b)	Pre- posttes t, 2 groups ;RCT	USA	Tutorial instructio n	13/13; Medical students	Cardiac auscultation	Self-schedule CAI + small- group seminar	HEARTLAB platform,	12 week s	Absent	Low	Abs ent	No del ay	Objective(choice question)	No	No	4
Shomaker, 2002(a)	Pre- osttest, 2 groups ; RCT	USA	traditiona I	24/24;medic al students	parasitology	computer program + lectures	interactive text	2 week s	Present(questio ns)	Low(questio ns)	Abs ent	No del ay	Objective(MCQ or slides)	No	No	5
Shomaker, 2002(b)	Pre- posttes t, 2 groups ; RCT	USA	e-learning	24/17; medical students	parasitology		interactive text	2 week s	Present(questio ns)	Low(questio ns)	Abs ent	No del ay	Objective(MCQ or slides)	No	No	5
Stewart,2013	Posttes t, 2 groups ; RCT	Austra lia	standard teaching	34/37; Medical students	Newborn	Online module+standa rd programme	PENSKE Baby Check Learning module	8 week s	Absent	Low	Abs ent	No del ay	Objective(Cannot tell)	No	No	4
Mahnken,2011(a)	Pre- posttes t, 2 groups ; RCT	Germa ny	Tradition al learning	32/32; Medical students	Radiology	E- learning+intern ship(F2F)	Electronic cases	1 week	Present (cases and expert feedback, question-and- answer	High (cases and expert feedback, question- and-answer)	Abs ent	No del ay	Objective(Cannot tell)	No	No	4
Mahnken,2011(b)	Pre- posttes t, 2 groups ; RCT	Germa ny	Tradition al learning	32/32; Medical students	Radiology	E- learning+intern ship(F2F)	Electronic cases	1 week	Present (cases and expert feedback, question-and- answer	High (cases and expert feedback, question- and-answer)	Abs ent	No del ay	Objective(Cannot tell)	No	No	4
Sung, 2008	Pre- posttes t, 2 groups ;NRS	Korea	Face to face instructio n	24/26; Nurses	Medical administrati on	Web-based matirilas +_face-to-face instruction	Web-based e- learning program	10 mont hs	Present(quizzes with feedback, clinical cases)	High (quizzes with feedback, clinical cases, active interaction between tutors and students)	Abs ent	No del ay	Objective(Cannot tell)	No	No	5
Woltering,2009	Posttes	Germa	traditiona	74/71;	Model	Online	multimedia	2	Present(questio	High(online	Pre	No	Objective(MCQ)	No	No	6

	t, 2 groups ;NRS	ny	l PBL	Medical students	Curriculum Medicine	learning+stude nts' Meeting+tutore d final session	case vignette, Group-Wiki, The virtual clinical order entry system, bulletin board	week s	ns, cases)	collaboratio n including comments of the tutor)	sent	del ay				
Karaksha,2011(a)	Posttes t, 2 groups ; RCT	Austra lia	CAI	23/22; Pharmacy students	Pharmacolo gy	Lecture+CAI	iSpring Pro 4.3.0, Blackboard, CD.	24H	Present (quiz, questions,multi ple choice)	High(quiz, multiple choice essay questions)	Abs ent	No del ay	Objective(MCQ)	No	No	5
Karaksha,2011(b)	Posttes t, 2 groups ; RCT	Austra Iia	Lecture	23/13; Pharmacy students	Pharmacolo gy	Lecture+CAI	iSpring Pro 4.3.0, Blackboard, CD.	24H	Present (quiz, questions,multi ple choice)	High(quiz, multiple choice essay questions)	Abs ent	No del ay	Objective(MCQ)	No	No	5
Lowe,2001(a)	Posttes t, 2 groups ;NRS	UK	lecture and seminar	39/46; Undergradu ate dental students	Index of Orthodontic treatment need	CAL programme+se minar	Internet web- authoring package	1 week	Present(self- assessment)	High(multi media design with interactive comment)	Pre sent	No del ay	Objective(cases)	No	No	5
Lowe,2001(b)	Posttes t, 2 groups ;NRS	UK	lecture and seminar	39/46; Undergradu ate dental students	Index of Orthodontic treatment need	CAL programme+se minar	Internet web- authoring package	1 week	Present (self- assessment)	High(multi media design with interactive comment)	Pre sent	No del ay	Objective(cases)	No	No	5
Hilger, 1996	Pre- posttes t, 2 groups ; RCT	USA	traditiona I	45/32;medic al students	Streptococca I Pharyngitis	CAI program +clerkship	Online tutorial, case simulation	4 week s	Present (case simulation,self- assessment)	High(discus sion with feedback)	Pre sent	No del ay	Objective(MCQ. True or false)	No	No	5
Hic,2013[3][3] [23][3]	Posttes t, 2 groups ;NRS	Austra lia	Didactic learning	34/27; Graduate medical students	Evidence based practice (EBP)	Tutorial sessions+web- site learning	Monash University Iibrary website	1 day	Present (patient- basedPresentat ion)	High(group work, patient- based Presentatio n)	Pre sent	No del ay	Objective(MCQ)	Ye s	No	5
Daunt, 2013(a)	posttes t, 2 groups ;NRS	UK	traditiona I	162/168;med ical students	geriatric medicine	CAL package + traditional teaching	Xerte open access platform, Storyboards	4 week s	Present(case,	High(case, interactive session)	Pre sent	No del ay	Objective(true or false, choice question, extended matching question)	No	No	3
Daunt, 2013(b)	posttes t, 2 groups ;NRS	UK	traditiona I	92/67;medic al students	geriatric medicine	CAL package + traditional teaching	Xerte open access platform, Storyboards	8 week s	Absent	Low	abs ent	No del ay	Objective(true or false, choice question, extended matching question)	No	No	3
Morales,2012[4] [4][24][4]	Posttes t, 2 groups	Spain	document s and books	22/22; Physiothera py second-	Physiothera py degree course	on-campus training+ website	ECOFISIO website	1 seme ster	Present(self- assessment)	Low(self- assessment)	Abs ent	No del ay	Objective(MCQ)	No	No	5

	; RCT			year degree students		training										
Raupach,2010	Pre- posttes t, 2 groups ; RCT	Germa ny	Tradition al learning	40/34; Medical students	Cardio- respiratory curriculum	Online module+traditi onal curriculum	web-based learning management system	6 week s	Present(test with feedback)	High(test with feedback)	Pre sent	No del ay	Objective(MCQ)	No	No	5
Carbonaro,2008	Pre- posttes t, 2 groups ; RCT	Canad a	face to face	22/22;Stude nt	Health science program	E- learning+F2F interprofession al team course		5 week s	Present(giving/ receiving feedback, consensus decision- making)	High(giving/ receiving feedback, consensus decision- making, Group discussions, problem solving)	Pre sent	No del ay	Subjective(canno t tell)	No	No	5
Pereira,2007	Posttes t, 2 groups ;NRS	Spain	Tradition al teaching	65/65;Stude nts	Human anatomy	Online learning+semin ars	Computerised materials	45 class hour s	Present(interac tive multiple- choice, short- answer self- assessment test problem solving activities)	High(intera ctive multiple-choice, short-answer sel f-assessment test	Pre sent	No del ay	Objective(MCQ, short answer question, practical question)	No	No	4
Devitt,2001	Pre- posttes t, 2 group; nrss	Austra lia	Lecture	85/20; Medical students	Ophthalmol ogy	Lecture+e- learning	Medici software	2 week s	Present(cases)	Low	Abs ent	No del ay	Objective(MCQ)	No	No	5
Mukti,2005	Posttes t, 2 groups ; RCT	Malay sia	Tradition al collaborati ve learning	101/85;Unde rgraduate students	Animal diversity œurse	lecture + Online collaborative learning	Online web sites	1 seme ster	Present(group project)	High(collab orative learning, group working)	Pre sent	No del ay	Objective(MCQ)	No	No	5
Kiviniemi,2014	Posttes t 2- group; NRS	USA	traditiona I learning	38/28; Public health graduate student	Public health	Online lecture presentation +didactic lecture	web	3 week s	Absent	High(active learning activity)	Pre sent	No del ay	Objective(MCQ, short answer question)	No	No	3
Hsu,2011(a)	Pre- posttes t, 2 groups ;NRS	Taiwa n	traditiona I learning	113/88; Nursing students	Nursing ethics	web-based teaching/learni ng module+ classroom lectures	web-based module(videos, PowerPoint files)	17 week s	Present(questio ns and comments)	High(excha nge ideas, questions and comments)	Pre sent	No del ay	Objective(cannot tell)	No	No	4
Hsu,2011(b)	Pre- posttes t, 2 group;	Taiwa n	traditiona I learning	113/88; Nursing students	Nursing ethics	web-based teaching/learni ng module+ classroom	web-based module(videos, PowerPoint files)	17 week s	Present(questio ns and comments)	High(excha nge ideas, questions and	Pre sent	No del ay	Subjective(canno t tell)	No	No	4

	NRSs					lectures				comments)						
Kaveevivitchai,2 009	Pre- posttes t, 2 group; RCT s	Thaila nd	traditiona I learning	40/40;Nursi ng students	Anatomy and physiology	CAL multimedia+tra ditional lecture	interactive CAL multimedia	2 days	Present(questio ns, case scenarios)	High(questi ons, case scenarios)	Pre sent	No del ay	Objective(MCQ)	No	No	5
Kumrow,2005	Posttes t 2- group; NRS	USA	traditiona I learning	18/15; Graduate nursing students	Health care economic policy and managemen t	Online instruction(50%)+traditional in- classface-to- face(50%)	Web-based	>1 seme ster	Absent	Low	Abs ent	No del ay	Subjective(self- report)	No	No	3
Howerton,2004(a)	Pre- posttes t, 2 groups ; RCT	USA	traditiona I learning	25/24; Dental students	Dental radiology	Interactive CD +lecture	Director 8 authoring software	2 week s	Present(exercis es)	High(exercis es, interactive presentatio n)	Abs ent	we eks	Objective(cannot tell)	No	No	4
Howerton,2004(b)	Pre- posttes t, 2 groups ; RCT	USA	e-learning	25/26; Dental students	Dental radiology	Interactive CD +lecture	Director 8 authoring software	2 week s	Present(exercis es)	High(exercis es, interactive presentatio n)	Abs ent	2 we eks	Objective(cannot tell)	No	No	4
Fleetwood,2009	Posttes t 2- group; RCT	USA	traditiona I learning	89/84;Medic al students	Bioethics course	Web-based program+lectur es +small-group discussions	MedEthEx Online System	8 week s	Present case, questions with feedback	High(questi ons with feedback g roup discussions)	Pre sent	3 we eks	Objective(MCQ)	No	No	4
Mars,1996	Pre- posttes t, 2 groups ;NRS	Durba n	traditiona I learning	34/34; Medical students	histology	CAI module+	onscreen "patient"	3 week s	Present(self- assessment questions	High (self- assessment questions ,asking and answering questions)	Abs ent	No del ay	Objective(cannot tell)	No	No	4
Gadbury- Amyot,2012	Posttes t 2- group; NRS	USA	traditiona I learning	309/300; Dental and dental hygiene students	Oral Histology	CAI+lecture	Software sta ndard interactions	>1 seme ster	Present(questio ns, self- assessment)	High(intera ctive multimedia)	Abs ent	No del ay	Objective(cannot tell)	No	No	5
Perkins,2010	Pre- posttes t, 2 groups ; RCT	UK	traditiona I learning	275/276; Medical students	Life support	Face-to-face course +e- learning	Microsim programme on a CD	4 week s	Absent	Low(Feedba ck on experiences)	Abs ent	No del ay	Objective(MCQ)	Ye s	No	5
Strickland,2008[6][6][26][6]	Pre- posttes t, 2 groups	Germa n	traditiona I learning	8/6; Health professions student	Respiratory Care	Course materials via Internet +face- to-face	Cannot tell	1 seme ster	Absent	Low	Abs ent	No del ay	Objective(cannot tell)	No	No	3

	;NRS					interaction										
Rouse,2000(a)	Pre- posttes t, 2 groups ; RCT	USA	traditiona I learning	20/26; Nursing Students	Pediatric nursing	computer- assisted instruction +traditional class room lecture	CD-ROM, computer	>1 seme ster	Absent	Low	Abs ent	No del ay	Objective(MCQ)	No	No	5
Rouse,2000(b)	Pre- posttes t, 2 groups ; RCT	USA	e-learning	20/26; Nursing Students	Pediatric nursing	computer- assisted instruction +traditional class room lecture	CD-ROM, computer	>1 seme ster	Absent	Low	Abs ent	No del ay	Objective(MCQ)	No	No	5
Gagnon2013	Posttes t 2- group; RCT	Canad a	traditiona I learning	52/50; Nursing undergradu ates	Critical reading of scientific articles	Internet-based tutorials +in- class sessions;	interactive, Internet-based modules	1 seme ster	Present(small- group exercises, quizzes)	High(lass discussion, small-group exercises, quizzes.)	Pre sent	No del ay	Objective(MCQ, open-ended questions)	No	No	5
Boynton,2007	Posttes t 2- group; NRS	USA	traditiona I learning	98/107; Dental students	Pediatric Behavior Managemen t	Internet-based instructional tool+lectures	web-based instructional tool	6 week s	Absent	High(essay question)	Pre sent	No del ay	Objective(MCQ, short essay)	No	No	3
Lamb,2011	Pre- posttes t, 2 groups ;NRS	Urugu ay	e-learning	36/30; Health professional s	Tobacco Cessation Skills	Face-toface + online activitie	EviMed system	3 mont hs	Present(cases)	High(cases, wiki-type collaborativ e activity group- discussion workshops)	Pre sent	No del ay	Objective(cannot tell)	No	No	3
Raupach, 2009	Posttes t, 2 groups ; RCT	Germa ny	traditiona I	72/73; medical students	Clinical reasoning	online module + course	web-based collaborative teaching module	6 week s	Present(cases)	High(small group discussions)	Pre sent	No del ay	Objective(MCQ)	No	No	5
Sherman, 2012	Pre- posttes t, 2 groups ; RCT	USA	traditiona I	35/33;nurses	critical care pharmacolog y	interactive module+discuss ion session	interactive learning modules delivered via the hospital's learning management system	1 day	Absent	Low	Pre sent	No del ay	Objective(MCQ)	No	No	5
Gerdprasert,201 0	Pre- posttes t, 2 groups ; RCT	Thaila nd	traditiona I	42/43;nursin g students	mechanism of labour	web-based learning +conventional lecture	Web-site	2 week s	Presnt(case scenarios, formative questions and exercises)	High(eb- board for posting questions and discussion between students— students	Pre sent	No del ay	Objective(MCQ. True or false question, interctive question)	No	No	5

Wahlgren,2006	Posttes t, 2 groups ; RCT	Swede n	traditiona I	28/85; medical students	dermatology and venereology	conventional teaching +computerised interactsimulat ion system	computer programming	17 days	Present(cases,q uexstions)	and students— teacher) High(cases, question, extensive feedback)	Pre sent	No del ay	Objective(diagno sis)	No	No	4
Farrell.2006	Pre- posttes t, 2 groups ; RCT	Austra Iia	traditiona I	35/41; nursing students	pharmacolog ical and clinical contextual knowledge	Mobile Handheld computers+clini cal practice	Hewlett Packard PDAs (HP iPAQ Pocket Pc h5500)	3 week s	Absent	Low	Abs ent	No del ay	Objective(MCQ)	No	No	5
Taradi,2004	Posttes t, 2 groups ; RCT	Croati a	traditiona I	37/84; medical students	acid-base physiology	Online+face-to- face	A Webenvironme nt created by using the commercially available Web Course Tools (WebCT)	5 week s	Present(self- testing, exercises, quiz)	High(group ∞llaboratio ns)	Pre sent	No del ay	Objective(MCQ, true/false, matching, calculated, short answer, and written paragraph questions)	No	No	4
Eskenazi, 2010	Pre- posttes t, 2 groups ;NRS	Brasil	traditiona I	41/37;	oral health	Internet-based training p	Cannot tell	3 mont hs	Present(case)	Low(case)	abs ent	No del ay	Objective(cannot tell)	No	No	4

a. no.(B/N) means number of participants in blended learning versus number of participants in no intervention or non-blended learning.

E-Table 4. Quality of included studies

Section 1. Studies comparing blended learning to no intervention

Author, year	Representative intervention group	Comparison group selected from same community	Comparability of cohorts	Blinded outcome assessment	Follow-up adequate	Score
Flys, 2012	Yes	No	Controlled for baseline	Yes	Yes	4
Purl, 2010	Yes	Yes	Controlled for learning outcome and other	Yes	Yes	6
Karaksha, 2011	Yes	Yes	Randomized	Yes	Yes	4
Buchowski, 2002	Yes	No	Controlled for baseline	No	Yes	3
Wallen,2010	Yes	No	Controlled for baseline	No	Yes	3
Weaver,2014(a)	Yes	No	Controlled for baseline	No	Yes	3

Weaver,2014(b)	Yes	No	Controlled for baseline	No	Yes	3
Riesen,2012	Yes	No	Controlled for baseline	No	Yes	3
Cho,2014(a)	Yes	No	Controlled for age	No	Yes	3
Cho,2014(b)	Yes	No	Controlled for age	No	Yes	3
Pereira,2008(a)	Yes	No	Controlled for baseline	Yes	Yes	4
Pereira,2008(b)	Yes	No	Controlled for baseline	Yes	Yes	4
Karamizadeh,2011(a)	Yes	No	Controlled for baseline	No	Yes	3
Karamizadeh,2011(b)	Yes	No	Controlled for baseline	No	Yes	3
Karamizadeh,2011(c)	Yes	No	Controlled for baseline	No	Yes	3
Karamizadeh,2011(d)	Yes	No	Controlled for baseline	No	Yes	3
Karamizadeh,2011(e)	Yes	No	Controlled for baseline	No	Yes	3
Chandler,2008	Yes	No	Controlled for baseline	No	Yes	3
Baumlin 2006	Yes	No	Randomized	No	Yes	3
Cragun, 2005	Yes	No	No	Yes	Yes	3

Section 2.Studies comparing blended learning to non-blended learning

Author, year	Representative intervention group	Comparison group selected from same community	Comparability of cohorts	Blinded outcome assessment	Follow-up adequate	Score
Kulier, 2012	Yes	Yes	Randomized, allocation concealed	Yes	Yes	6
Kavadella, 2012	Yes	Yes	Randomized	No	Yes	4
Lancaster, 2011	Yes	No	Controlled for other	Yes	No	3
Sowan, 2013	Yes	Yes	Randomized, allocation concealed	No	Yes	5
Makhdoom, 2013	Yes	Yes	Randomized	Yes	Yes	5
Lancaster, 2012	Yes	Yes	Randomized	No	Yes	4
Dankbaar, 2014(a)	Yes	Yes	Controlled for age and other	No	Yes	5
Dankbaar, 2014(b)	Yes	Yes	Controlled for age and other	No	Yes	5
Dankbaar, 2014(c)	Yes	Yes	Controlled for age and other	No	Yes	5
Mangione, 1991(a)	Yes	Yes	Randomized	No	Yes	4
Mangione,1991(b)	Yes	Yes	Randomized	No	Yes	4
Stewart, 2013	Yes	Yes	Randomized	No	Yes	4
Mahnken, 2011(a)	Yes	Yes	Randomized	No	Yes	4
Mahnken, 2011(b)	Yes	Yes	Randomized	No	Yes	4
Sung, 2008	Yes	Yes	Controlled for baseline and other	No	Yes	5
Woltering, 2009	Yes	Yes	Controlled for learning and baseline	Yes	Yes	6
Karaksha, 2011(a)	Yes	Yes	Randomized	Yes	Yes	5
Karaksha, 2011(b)	Yes	Yes	Randomized	Yes	Yes	5
Lowe, 2001(a)	Yes	Yes	Controlled for other	Yes	Yes	5
Lowe, 2001(b)	Yes	Yes	Controlled for other	Yes	Yes	5

Ilic, 2013	Yes	Yes	Controlled for other	Yes	Yes	5
Morales, 2012	Yes	Yes	Randomized	Yes	Yes	5
Raupach, 2010	Yes	Yes	Randomized	Yes	Yes	5
Carbonaro, 2008	Yes	Yes	Randomized, allocation concealed	No	Yes	5
Pereira, 2007	Yes	Yes	Controlled for learning and baseline	No	Yes	4
Devitt, 2001	Yes	Yes	Controlled for other	Yes	Yes	5
Mukti, 2005	Yes	Yes	Randomized	Yes	Yes	5
Kiviniemi,2014	Yes	Yes	Controlled for other	No	No	3
Hsu, 2011(a)	Yes	Yes	Controlled for other	No	Yes	4
Hsu, 2011(b)	Yes	Yes	Controlled for other	No	Yes	4
Kaveevivitchai,2009	Yes	Yes	Randomized	Yes	Yes	5
Kumrow,2005	Yes	Yes	No	No	Yes	3
Howerton,2004(a)	Yes	Yes	Randomized	No	Yes	4
Howerton,2004(b)	Yes	Yes	Randomized	No	Yes	4
Fleetwood,2009	Yes	Yes	Randomized	No	Yes	4
Mars,1996	Yes	Yes	Controlled for other	No	Yes	4
Gadbury-Amyot,2012	Yes	Yes	Controlled for age and other	No	Yes	5
Perkins,2010	Yes	Yes	Randomized	Yes	Yes	5
Strickland,2008	Yes	Yes	No	No	Yes	3
Rouse, 2000(a)	Yes	Yes	Randomized	Yes	Yes	5
Rouse, 2000(b)	Yes	Yes	Randomized	Yes	Yes	5
Gagnon,2013	Yes	Yes	Randomized	Yes	Yes	5
Boynton,2007	Yes	Yes	No	No	Yes	3
Lamb,2011	Yes	Yes	No	No	Yes	3
Raupach, 2009	Yes	Yes	Randomized	Yes	Yes	5
Sherman, 2012	Yes	Yes	Randomized	Yes	Yes	5
Gerdprasert,2010	Yes	Yes	Randomized	Yes	Yes	5
Wahlgren,2006	Yes	Yes	Randomized	No	Yes	4
Farrell.2006	Yes	Yes	Randomized	Yes	Yes	5
Taradi,2004	Yes	Yes	Randomized	No	Yes	4
Shomaker, 2002(a)	Yes	Yes	Randomized	Yes	Yes	5
Shomaker, 2002(b)	Yes	Yes	Randomized	Yes	Yes	5
Hilger, 1996	Yes	Yes	Randomized	Yes	Yes	5
Daunt, 2013(a)	Yes	Yes	No	No	Yes	3
Daunt, 2013(b)	Yes	Yes	No	No	Yes	3
Eskenazi, 2010	Yes	Yes	No	No	Yes	3

E-Table 5: GRADE evidence profile

Section 1: Studies comparing blended learning with no intervention

	Quality assessment N							Effect		Quality
No. and design	No. and design Risk of bias Inconsistency Indirectness Imprecisio					Х	Υ	Relative	Absolut	I
of study				n	consideration					I

					s				
Knowledge score									
2 randomized	No serious	No serious	No serious	Seriousa	No	63	67	SMD .59(.001-	 ⊕⊕⊕○
trials	risk of bias	inconsistency	indirectness					1.64)	moderate
18 non-	No serious	No serious	No serious	No serious	Large effect	2006	1861	SMD 1.49(1.11-	 ⊕⊕⊕○
randomized	risk of bias	inconsistency	indirectness	imprecisio	size ^b			1.87)	moderate
trials				n					

a. Sample size is small, and 95%CI is wide.

b. Effect size (1.49) is large.

Section 2. Studies comparing blended learning to non-blended learning

		Quality	assessment			No	o of	Effect		Qualit
						partic	ipants			у
No and design of	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	X	Υ	Relative	Absolu	
study					considerations				t	
Knowledge score										
31 randomized	Seriousª	No serious	No serious	No serious	Reporting biasb	1358	1359	SMD . 75(.38-		⊕⊕0
trials		inconsistency	indirectness	imprecision				1.12)		0
										low
25 non-	No serious	No serious	No serious	No serious	Large effect sizec,	1451	1270	SMD .87(.56-		⊕⊕0
randomized	risk of bias	inconsistency	indirectness	imprecision	reporting bias ²			1.05)		0
trials										low

a. Allocation concealed was not described in 28 studies.

- b. Reporting bias was found.
- c. The effect size .87(.56-1.05) was large.

E-Table 6. Standard knowledge score and source

Section 1. Studies comparing blended learning to no intervention

	Intervention			Control		Source
No.	Standard	Standard	No.	Standard	Standard SD	
	Mean SD			Mean		

Flys, 2012	225	90.3	10.71	225	70.9	16.84	Mean,95%CI
Purl, 2010	350	44.33	1.07	102	41.87	1.93	Mean, SD
Karaksha, 2011	23	66.96	23.82	17	45.88	18.39	Mean, SD
Buchowski, 2002	14	73	12	14	31	7	Mean, SD
Wallen,2010	16	56.39	20.02	16	37.09	16	Mean, SD
Weaver,2014(a)	80	76.81	13.43	78	74.13	13.33	Mean, average SD
Weaver,2014(b)	58	74.45	13.43	127	76.03	13.33	Mean, average SD
Riesen,2012	60	84.43	6.54	60	82.1	6.96	Mean, SD
Cho,2014(a)	60	79.2	16.6	60	64.8	13.4	Mean, SD
Cho,2014(b)	60	77.2	12	60	53.4	10	Mean, SD
Pereira,2008(a)	69	78	9.5	69	60.5	13.2	Mean, SD
Pereira,2008(b)	45	80	1.25	45	46.25	15	Mean, SD
Karamizadeh,2011(a)	6	100	11	6	80	11	Mean, SD
Karamizadeh,2011(b)	38	69	24	38	49	19	Mean, SD
Karamizadeh,2011(c)	19	85	22	19	44	15	Mean, SD
Karamizadeh,2011(d)	40	86	16	40	42	19	Mean, SD
Karamizadeh,2011(e)	10	70	31	10	42	14	Mean, SD
Chandler,2008	817	94.25	8.07	817	72.17	16.31	Mean, SD
Baumlin 2006	40	72.8	13.43	50	68.2	13.33	Mean, average SD
Cragun, 2005	39	74	13.5	15	62	13.5	Mean, SD

Section 2. Studies comparing blended learning to non-blended learning

		Intervention			Control		Source
	No.	Standard	Standard	No.	Standard	Standard SD	
		Mean	SD		Mean		
Kulier, 2012	123	69.52	5.95	81	61.45	6.20	Mean,95%CI
Kavadella, 2012	24	80.88	13.82	22	68.64	13.90	Mean, SD
Lancaster, 2011	97	84.09	8.98	97	65.15	10.14	Mean, average SD
Sowan, 2013	105	78.00	5.50	105	70.00	8.50	Mean, SD
Makhdoom, 2013	60	71.69	12.31	61	66.02	11.82	Mean, SD
Lancaster,2012	29	96.60	1.90	23	92.70	3.80	Mean, SD
Dankbaar, 2014(a)	31	80.00	2.00	16	80.00	3.00	Mean, SD

Dankbaar, 2014(b)	31	76.00	2.00	16	75.00	3.00	Mean, SD
Dankbaar, 2014	31	73.00	2.00	16	68.00	3.00	Mean, SD
Mangione, 1991(a)	13	78.50	18.28	13	70.00	22.28	Mean, SD
Mangione, 1991(b)	13	78.50	18.28	9	62.50	19.85	Mean, SD
Shomaker, 2002(a)	24	44.60	8.98	24	51.00	10.14	Mean, average SD
Shomaker, 2002(b)	24	44.60	8.98	17	51.20	10.14	Mean, average SD
Stewart, 2013	34	75.00	12.25	37	67.50	11.75	Mean, SD
Mahnken, 2011(a)	32	72.90	12.30	32	69.00	12.40	Mean, SD
Mahnken, 2011(b)	32	87.70	12.80	32	69.00	12.40	Mean, SD
Sung, 2008	24	82.21	8.75	26	67.92	7.17	Mean, SD
Woltering, 2009	74	63.20	14.08	71	55.76	12.28	Mean, SD
Karaksha, 2011(a)	23	66.96	23.82	13	54.55	26.32	Mean, SD
Karaksha, 2011(b)	23	66.96	23.82	22	41.54	22.30	Mean, SD
2e, 2001(a)	39	31.80	15.20	46	25.00	16.70	Mean, SD
2e, 2001(b)	39	50.30	14.00	46	50.20	17.40	Mean, SD
Hilger, 1996	45	78.40	8.98	32	73.40	10.14	Mean, average SD
Ilic, 2013	34	40.53	18.00	27	45.13	22.40	Mean, SD
Daunt, 2013(a)	92	92.00	8.98	67	85.10	10.14	Mean, average SD
Daunt, 2013(b)	162	84.20	8.98	168	68.40	10.14	Mean, average SD
Morales, 2012	22	72.30	6.20	22	74.20	8.10	Mean, SD
Raupach, 2010	40	84.80	1.30	34	79.50	1.40	Mean, SD
Carbonaro, 2008	22	32.44	7.33	22	34.00	10.67	Mean, SD
Pereira, 2007	65	63.00	13.00	65	50.00	16.00	Mean, SD
Devitt, 2001	85	61.67	1.11	20	45.00	2.50	Mean, SD
Mukti, 2005	101	61.77	9.98	85	45.38	11.66	Mean, SD
Kiviniemi,2014	38	93.92	2.45	28	91.76	4.95	Mean, SD
Hsu, 2011(a)	113	80.28	10.84	88	81.96	10.56	Mean, SD
Hsu, 2011(b)	113	66.41	8.46	88	68.11	8.73	Mean, SD
Kaveevivitchai, 2009	40	61.10	6.23	40	59.43	7.83	Mean, SD
Kumrow, 2005	18	97.15	2.56	15	94.78	3.37	Mean, SD
Howerton, 2004(a)	25	84.40	9.28	24	82.50	12.07	Mean, SD

Howerton, 2004(b)	25	84.40	9.28	26	75.00	7.07	Mean, SD
Fleetwood, 2009	89	83.00	5.00	84	83.00	5.00	Mean, SD
Mars, 1996	34	65.60	8.98	34	60.70	10.14	Mean, average SD
Gadbury-Amyot, 2012	309	95.75	10.00	300	92.00	12.75	Mean, SD
Perkins, 2010	275	84.50	11.58	276	84.92	11.50	Mean, SD
Strickland, 2008	8	86.00	8.98	6	85.00	10.14	Mean, average SD
Rouse, 2000(a)	20	77.30	11.50	26	66.20	11.60	Mean, SD
Rouse, 2000(b)	20	77.30	11.50	26	74.00	11.00	Mean, SD
Gagnon, 2013	52	17.20	0.90	50	14.50	0.60	Mean, SD
Boynton, 2007	98	78.22	7.67	107	74.72	12.56	Mean, SD
Lamb, 2011	36	83.10	2.80	30	75.30	17.20	Mean, SD
Raupach, 2009	73	74.00	10.00	72	74.00	9.60	Mean, SD
Sherman, 2012	35	89.7	5.16	33	88.30	6.79	Mean, SD
Gerdprasert, 2010	42	71.90	9.59	43	87.93	5.76	Mean, SD
Wahlgren, 2006	28	88.80	9.38	85	87.50	10.00	Mean, SD
Farrell, 2006	35	50.66	8.98	41	45.34	10.14	Mean, average SD
Taradi, 2004	37	71.69	1.83	84	61.33	1.03	Mean, SD
Eskenazi, 2010	41	33.30	8.98	37	30.30	10.14	Mean, average SD

E-table 7. PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on
			heading
TITLE			
on	1	Antenatal depressive symptoms and the risk of preeclampsia or operative deliveries: A meta-analysis	Title (page 1)
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Abstract (page 2-3)
INTRODUCTION			

Rationale	3	Describe the rationale for the review in the context of what is already known.	Introduction (page 4)
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Introduction (page 4-5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Methods: Eligibility criteria (page 5-6)
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Methods: Data sources (page 6)
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Methods: e-table 1 (supplemental document)
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Methods: Study selection (page 6-7)
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Methods: Data extraction (page 7)

Section/topic	#	Checklist item	Reported on Heading
METHODS (cont.)			
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Methods: Data extraction (page 7)
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Methods: Quality Assessment(pa ge 7-8)

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Methods: Data
Cummary measures		Otate the principal summary measures (e.g., risk ratio, difference in means).	Synthesis(page 9)
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²) for each meta-analysis.	Methods: Data Synthesis(page 9)
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Methods: Data Synthesis(page 9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.)	Methods: Data Synthesis(page 9)
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Results: Study selection and Figure 1 (page 9-10)
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Results: Table 1 (page 11-12) and e-table 3 (supplemental document)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Results: Study quality(page 12-13)
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Results: Figure 2 (page 14) and Figure 4 (page 18),

			and e-table 6 (supplemental document)
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Results: Figure 2 (page 14) and Figure 4 (page 18)
Section/topic	#	Checklist item	Reported on Heading
RESULTS (cont.)			<u> </u>
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Results: Figure 3(page 15) and Figure 5 (page 19)
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Results: Table 2 (page 16- 17)and Table 3 (page 20-21)
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Discussion (page 22-24)
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Limitations and strengths (page 24-25)
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Conclusion (page 26-27)
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Acknowledgem ents (page 27)

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