Review Article

Strategies for developing pre-clinical medical students' clinical reasoning based on illness script formation: a systematic review

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Clinical reasoning training in the pre-clinical phase has recently been considered important; however, when it comes to specific instructional methods for pre-clinical students, much is unknown. Thus, the aim of this review is to explore learning and teaching methods for pre-clinical students' clinical reasoning development based on illness script formation, their results, and strategies. A systematic review was conducted in accordance with the guidelines of the Association for Medical Education in Europe. The literature search was performed using the Cochrane Library, PubMed, EMBASE, Web of Science, and ERIC databases based on keywords, including "illness script*" AND ("medical student*" OR pre-clinical OR undergraduate). Then, 10 studies among the 91 studies were included in the final analysis. The quality of the selected studies was also appraised using the Medical Education Research Study Quality Instrument. Diverse teaching and learning methods were used to support the integration of biomedical and clinical knowledge working with patient cases, and their effects were assessed through diverse methods, including illness script richness and maturity, to learner responses. The effects of these interventions were effective in terms of the clinical reasoning development of pre-clinical students. Learning and teaching strategies were synthesized and described. This review found that explicit attempts to promote illness script formation with a structured program rather than informal training lead to positive results, and such formal clinical reasoning programs can provide smooth transition from pre-clinical to clinical experience.

Key Words: Clinical reasoning, Illness script, Pre-clinical, Teaching strategies, Medical education

Introduction

Clinical reasoning is a fundamental part of doctors' competencies, and an explicit curriculum for clinical reasoning should be incorporated at every level of medical school [1]. However, medical students do not usually receive this training until their clinical rotations. During their clinical rotations, medical students mostly learn clinical reasoning informally through experiential opportunities with irregular feedback [1-3]; however, the effectiveness of such traditional teaching methods is unclear [4].

Clinical reasoning training in the pre-clinical phase has recently been considered important. Instead of informal experiential learning with varying quality of supervision during clinical clerkships [5], the need for more structured explicit attempts to teach clinical

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reasoning before clinical rotations is rising. Medical schools want to address this issue by designing a clinical reasoning program for pre-clinical students [6,7], but it poses challenges as the best way to develop clinical reasoning is uncertain.

Charlin et al. [6] argued that illness script formation should be a focus in medical education in terms of clinical reasoning development. Schmidt and Mamede [3] suggested through a narrative review that the thinking process-oriented approach such as generic problem-solving skills, rather than the knowledge-oriented approach, is largely ineffective in teaching clinical reasoning. Clinical reasoning do not exist separately from the specific medical knowledge necessary to understand and diagnose a particular disease. Medical knowledge and how it is stored are essential for accurate diagnosis [2,8-10], and this combination is explained using the illness script theory [6,11].

Illness scripts are developed as a consequence of theoretical knowledge acquisition and accumulated clinical experience [6,12]. Clinicians represent diseases as illness scripts in their minds [6,12,13]. Highly experienced clinicians possess elaborate illness scripts as mental models that enable them to instantly compare, contrast, categorize, interpret, and store new information [14]. Illness scripts have three main components: enabling conditions (e.g., age, sex, occupation), faults (major real malfunctions), and consequences (complaints, signs, and symptoms) [15].

Medical students can build a limited repository of illness scripts during pre-clinical education [10]. During early medical training, students can develop mental structures that explain the causes and consequences of a disease, and through repeated application of this knowledge to patient problems, their mental structure is encapsulated into high-level simplified causal models that explain signs and symptoms. With repeated exposure to patient cases, their encapsulated knowledge is restructured as illness scripts [12,16]. As the illness script is updated and refined through experience and learning, the initial illness script becomes the key and framework for further development [6,17].

The implication of the illness script theory is that basic science should be taught pertinent to the development of encapsulating concepts, and biomedical and clinical knowledge should be taught by integrating teaching methods [16]. However, when it comes to specific instructional methods for pre-clinical students, much is unknown. Research regarding clinical reasoning development by focusing on illness script formation has recently been rising, but they have mostly targeted medical students during their clinical clerkships or above [6,7,18]. In addition, several systematic reviews have published methods to improve the clinical reasoning of undergraduate medical students [3,5,19], but none has been published regarding clinical reasoning development targeting pre-clinical medical students based on illness script formation. Thus, it is necessary and timely to conduct an in-depth analysis of such strategies to develop curriculum to foster preclinical medical students' clinical reasoning based on illness script formation.

This study aimed to fill the knowledge gap by offering a comprehensive answer to the following questions by systematically reviewing the latest pertinent studies. What methods were used to develop clinical reasoning for pre-clinical medical students based on illness script formation? What are the results in terms of developing clinical reasoning? What teaching and learning strategies are effective in terms of the clinical reasoning development of pre-clinical medical students based on illness script formation? This review could provide directions for effective educational applications and research on this emerging issue.

Methods

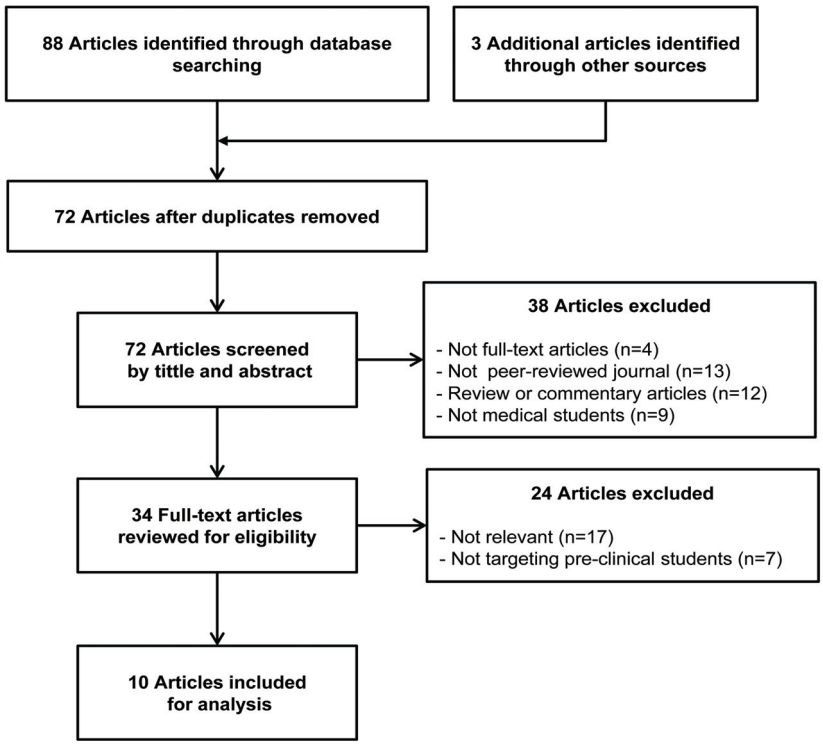
1. Literature search

This systematic review was conducted in accordance with the guidelines of the Association for Medical Education in Europe [20]. The initial literature search included peer-reviewed journal articles using the Cochrane Library, PubMed, EMBASE, Web of Science, and ERIC databases. The search strategies were based on keywords such as "illness script*" AND ("medical student*" OR pre-clinical OR undergraduate). Search strategies were performed on September 2021. The references of the included papers were also examined to identify additional relevant studies. The search strategy generated 91 studies, including 47 studies from PubMed, 25 studies from Web of Science, 11 studies from ERIC, five studies from Cochrane Library, and three additional articles identified through the reference check. After excluding 81 studies (19 duplicate searches and 62 studies that met the exclusion criteria), 10 studies were included in the final analysis. Fig. 1 shows the complete search and study selection strategies.

2. Exclusion and inclusion criteria

The inclusion criteria were as follows: (1) peer-reviewed; (2) full-text; (3) original research journal articles; (4) published in English; (5) focusing on developing clinical reasoning based on illness script formation; and (6) focusing on pre-clinical medical students. The exclusion criteria were as follows: (1) not peer-reviewed journal articles; (2) not published in English; (3) not full-text papers, such as conference papers; (4) not original research papers such as reviews and commentaries; (5) with illness script approaches used for assessment, such as script concordance tests, as this review focused on learning and teaching strategies;

Fig. 1. Flow Chart of the Article Selection Process



(6) studies in which participants were not medical students, such as nursing or veterinary students; and (7) studies with participants in their clinical clerkship or above. However, if the study included medical students during their clinical clerkship with pre-clinical students to compare among the groups and provided implications on the learning and teaching strategies for pre-clinical students, then the research was included for further analyses.

3. Literature analysis

Two researchers (the author and a research assistant) performed the search independently, and studies were selected after reviewing them against the inclusion and exclusion criteria. The screening process was first conducted according to the title and abstract, and full-text articles were reviewed for eligibility. All discrepancies were resolved through discussion until a consensus was reached. Once eligible articles were identified, full-text articles were reviewed again, and the following data were extracted: (1) study characteristics (e.g., author, publication year, country where the research was conducted, study design, course, or contents,); (2) participants; (3) methods; (4) measured variables; (5) results; and (6) learning and teaching strategies.

The quality of the selected studies was also appraised independently by the two researchers using the Medical Education Research Study Quality Instrument (MERSQI), which was designed to measure the quality of experimental, quasi-experimental, and observational studies [21]. MERSQI consists of 10 items covering six domains (study design, sampling, type of data, validity of the evaluation instrument, data analysis, and outcomes). The maximum score for each domain was 3. Any discrepancies were resolved through discussion.

Results

1. Study characteristics

The characteristics of each study are listed in Table 1. The 10 studies were published between 2012 and 2021. The number of publications has been increasing over the last 5 years: nine were published between 2016 and 2021, and one was published in 2012. Five studies were conducted in the United States, two in the Netherlands, one in Brazil, one in Iran, and one in New Zealand. The contents varied from late-onset asthma to emergency medicine. Seven studies employed a quasi-experimental design and included four within-subject posttest-only designs, two between-subject posttest-only designs, and one between-subject pre-posttest design. Meanwhile, two studies employed an experimental design (between-subject pre-posttest design), and one was an observational study (three groups).

2. Participants

The participants in six studies were from year 1 or 2 (Table 1). In three studies, they were from year 4 in the Netherlands, Brazil, and Iran. Medical schools in the Netherlands, New Zealand, and Brazil have a 6-year undergraduate curriculum, while Iran has a 7-year undergraduate curriculum. As medical school systems differ according to country and context, if the authors stated that the participants were in the pre-clinical part of the curriculum, these studies were regarded as targeting pre-clinical students. The last one studied three participant groups from years 2, 3, and 6 in New Zealand [7]. Although they included students from year 6 in their clinical clerkship, because its focus was on comparing how students at different stages of training were taking a history and it provided implications for pre-clinical

Table 1. Study Characteristics, Including Participants, Methods, Measured Variables, Results, and MERSQI Scores

Authors	Country	Study design	Participants	Course/content	Methods	Measured variables	Results	MERSQI score
Moghadami et al. [23] (2021)	Iran	Experimental design (pre-posttest, two groups)	100 students from year 4	Internal medicine	Illness script method - Taught clinical reasoning skills based on illness script method vs. clinical presentation methods (lecture) - Learned about three diseases during one workshop in small group settings (7 hours) - Helped students develop a correct problem representation and organize data into illness scripts	- Learner satisfaction - Knowledge test - SCT	- The illness script group scored significantly higher in the knowledge test and SCT compared to the control group. - The intervention was generally well-received by students.	13.5
Jackson et al. [26] (2020)	USA	Quasi-experimental design (posttest-only, one group)	278 students from year 1 for 2 years	Virology	Simulated clinic activity - Eight SP encounters for 2 hours - Rotated through eight SP encounters during which they collected patient histories, reviewed physical exam findings, and developed differential diagnoses and diagnostic plan - Instructor debriefed on the case afterward	- Students'activity evaluation	- Students rated the activity to be very effective for learning and providing opportunities to integrate microbiology and clinical skills.	7
Blunk et al. [4] (2019)	USA	Quasi-experimental design (pre-posttest, one group)	42 students from year 2	Psychiatry	Three integrated sessions - 2weeks, each for 2 hours, in small group (5–6) - Provided a clinical presentation (e.g., mood disorder), its associated basic science information, followed by the integration sessions beginning with an open discussion aiming at understanding symptoms, diagnosis, causes, and therapeutics. - Also participated in medical skills session every week; interviewed two SP with complex cases	- SCT	- Students' scores improved by 11% between the pre- and posttest. - After the integration sessions, there was no significant difference between the expert and students SCT scores.	13
Pinnock et al. [7] (2019)	New Zealand	Observational study (three groups)	23 students (7 from year 2, 10 from year 3, and 6 from year 6)	Late-onset asthma/ stable angina	History taking - With SP, two cases: simple and complex - Students were recruited via e-mail. - Post-consultation interview of how they were thinking during history taking	- The way students were taking a history and how they said they were thinking	-Students moved from generalized history taking by year 2 students to a more focused search based on possible diagnosis by year 3 students who knew the possible underlying causative disease and most of year 6 students.	8
Keemink et al. [10] (2018)	Netherlands	Quasi-experimental design (posttest-only, one group)	32 students from year 2	Case-based clinical reasoning course	CBCR - Nine sessions, meeting every 3–4 weeks - Peering teaching with a clinician moderator - Small group format (12–14 students) - Cases in a standard format covering all stage of clinical encounters - One case per session - CBCR cases vs. non-CBCR cases (similar diseases but not dealt with in the course)	- Illness script richness and maturity - Diagnostic performance - Course exam results	- Illness script richness and diagnostic performance for CBCR diseases were higher than those for non-CBCR diseases. - Relative contribution of the fault knowledge was lower but the enabling condition was higher in CBCR cases than in non-CBCR cases like in expert diagnostic reasoning process	10

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Table 1. (Continued)

Authors	Country	Study design	Participants	Course/content	Methods	Measured variables	Results	MERSQI score
Hennrikus et al. [22] (2018)	USA	Quasi-experimental design (posttest-only, one group)	300 students from year 1 for 2 years (each year, 150)	Basic science course	Metacognitive approach - 13-week long course with three methods (PBL, lecture, and metacognitive approach, every week) - Taught the basic science of the underlying disease - Metacognitive approach: 1 hour-review session, 1-hourpatient encounter (a patient with the disease discussed either in PBL or lecture spoke to the class), and illness script writing	- Course exams - National board exam - Written illness scripts analysis - Students'course feedback	- Students scored significantly higher on the metacognitive approach contents compared to lecture contents on the course and national board exams - A metacognitive approach created stronger conceptual knowledge frameworks.	11.5
Royan et al. [25] (2018)	USA	Quasi-experimental design (posttest-only, two groups)	171 students from year 2	Emergency medicine	CRE - Compared participating vs. nonparticipating students - Provided stepwise exposure to the clinical environment distinct from shadowing and without the performance pressure or formal grading - Asked students as a pair to evaluate patients, formulate a different diagnosis, and present the findings to their assigned faculty mentor - Faculty provided feedback - A longitudinal mentorship (8 months) - Encouraged to take a minimum of two 4-hour sessions per month	- Comprehensive clinical assessment (use SP and assess students' performance on 12 domains) - Student survey about this activity	- Students participated in an average of 10 sessions - Involvement in CRE increased scores on clinical assessment - Nearly all students (97%) reported that the program offered opportunities to enhance clinical skills, increased their comfort with patients, and better prepared them for their clinical years.	13.5
Peixoto et al. [24] (2017)	Brazil	Experimental design (pre-posttests, two groups)	39 students from year 4	Jaundice/ chest pain	Self-explanation - Diagnosed a set of eight clinical cases with vs. without self-explanation of pathophysiological mechanisms - Asked to explain aloud to themselves the pathophysiological mechanisms that underlie the patients' signs and symptoms.	- Previous knowledge and experience regarding the diseases to be discussed - Diagnostic accuracy of 10 cases	- Diagnostic performance of the self-explanation group on jaundice cases significantly improved but not on chest pain cases. - The positive effect of self-explanation depends on the disease sharing similar pathophysiological mechanisms.	12.5
Levin et al. [1] (2016)	USA	Quasi-experimental design (posttest-only, one group)	59 students from year 2	Renal system	Case-based illness script worksheet approach - Received the case with questions ahead of time and expected to come to the class prepared - Completed an illness script worksheet in class discussion in small groups (15 students) for 90–120 minutes - Facilitators provided feedback: adding missing information, highlighting key and differentiating features, guiding discussion, and debriefing after the session.	- Students' response regarding the course resources	- 80% of the students preferred the new framework compared to the traditional facilitator-led small group sessions.	6.5

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Table 1. (Continued)

Authors	Country	Study design	Participants	Course/content	Methods	Measured variables	Results	MERSQI score
Boshuizen et al. [27] (2012)	Netherlands	Quasi-experimental design (posttest-only, two groups)	31 students from year 4	Endocrinological problem	Learning from multiple cases with the same underlying pathophysiological process - Used two series of five cases with the same underlying pathophysiological process but with different presentation and cases (polycystic ovaries case vs. hyperprolactinemia cases) - Asked the students to diagnose, explain, and learn from each case (think-aloud)	- Progress of knowledge use over the cases - Learning from the case (pathophysiological explanation) - Knowledge development	- The students explicitly focused on variations in enabling conditions and consequences, which led to knowledge improvement, but the integration of biomedical knowledge into the fault components was hampered by the lack of knowledge and misconceptions.	10.5

MERSQI: Medical Education Research Study Quality Instrument, SCT: Script concordance test, SP: Standardized patient, CBCR: Case-based clinical reasoning, PBL: Problem-based learning, CRE: Clinical reasoning elective.

students' clinical reasoning development, this research was regarded as eligible for final analyses.

3. Methods

Diverse methods have been used to promote pre-clinical students' clinical reasoning through illness script formation. These methods include illness script method, simulated clinical activity, integrated session, history taking, case-based clinical reasoning, metacognitive approach, clinical reasoning elective program, self-explanation, case-based illness script worksheet approach, and learning from multiple cases with the same underlying pathophysiological process (Table 1). In all the studies included, teaching and learning methods were designed to support the integration of biomedical and clinical knowledge working with patient cases.

4. Measured variables and results

The effect of the interventions on pre-clinical students' clinical reasoning development was assessed through students' course feedback, script concordance test, course or national exams, history taking method, illness script richness and maturity, diagnostic performance, written illness script analysis, clinical assessment with standardized patients (SPs), and knowledge development (Table 1). Six studies found that their intervention was effective in developing pre-clinical students' diagnostic reasoning [4,10,22-25]. Two studies investigated only students' responses and reported very positive responses [1,26]. The remaining two studies reported that the whole-case approach for presenting patient data is effective for very novice students [7] and that learning from multiple cases with limited feedback from clinicians is insufficient for fostering illness script formation [27].

5. Leaning and teaching strategies

The learning and teaching strategies that have been demonstrated to be effective in improving the clinical reasoning of pre-clinical students are summarized in Table 2. The strategies were divided into three categories: learning and teaching settings, contents, and methods. Learning and teaching settings include a small group format, facilitators, and sufficient time for extensive discussion. As learning and teaching contents, all studies used patient cases that cover all stages of clinical encounters. Patient cases relevant to what the students are studying in other classes, increasing authenticity, multiple cases, and different approaches to presenting patient data according to the levels of training are also useful strategies in terms of contents. Regarding the methods, effective strategies include focusing on the integration of biomedical and clinical knowledge, emphasizing the application of basic science knowledge, providing a structured framework, direct illness script teaching, self-explanation, detailed and timely feedback, and stepwise exposure to clinical practices.

6. Study quality

The MERSQI scores of the 10 studies included in this review ranged from 6.5 to 13.5 (Table 1). The maximum total score of MERSQI was 18, and the maximum domain score was 3. The mean MERSQI (±standard deviation [SD]) score was 10.60±2.66. The mean domain score was highest for data analysis (2.8±0.42) and lowest for outcomes (1.35±0.24). In the study by Reed et al. [21], who developed MERSQI and applied it to 210 medical

Table 2. Effective Learning and Teaching Strategies for the Development of Preclinical Students' Clinical Reasoning Based on Illness Script Formation

	Effective learning and teaching strategies
Learning and teaching settings	Small group activity - 4–5 students per group [26] - With facilitators to provide guide for discussion and feedback [1,4,10,23,26] - Sufficient time for extensive discussion of all the relevant of clinical cases [10]
Learning and teaching contents	Clinical cases - Patient cases covering all the stages of clinical encounter in their usual sequence (history, physical examination, differential diagnosis, diagnostic testing, and management) [10] - Relevant to what students are currently studying in other classes [26] - More than one case at a time for repeated application of knowledge to encourage illness script development [10] - Increasing authenticity by presenting clinical cases through real or simulated patients [4,7,22,25,26] - Transitioning from the whole-case approach, a blended approach, to the serial-cue approach on presenting patients' data to students [7]
Learning and teaching methods	Integrated teaching - Focusing on the integration of biomedical and clinical knowledge [1,4,10,22-26] - Emphasis on the application of basic science to clinical cases instead of acquisition of new knowledge [10,26] - Providing a structured framework to formalize the clinical reasoning process for the integration of biomedical and clinical knowledge rather than informal training [4,22] - Direct illness script teaching method using worksheets; directly teaching illness scripts by helping students develop correct problem representation and organize data into illness script worksheets [1,23] - Self-explanation focusing on pathophysiological mechanism when diseases share similar pathophysiological processes and are unfamiliar or complex [24] - Detailed and timely feedback by think-aloud method [1,23,25,27] - Stepwise exposure to clinical practices; providing the clinical reasoning training opportunities without performance pressure or formal grading before traditional clinical clerkships [25]

education research published in peer-reviewed journals, the mean MERSQI (±SD) score was 9.95±2.34.

Discussion

Illness script construction and refinement of pre-clinical medical students come from the application of biomedical and clinical knowledge to clinical cases [6]. This raised educational issues concerning instructional methods. This review investigated the methods used to develop the pre-clinical students' clinical reasoning based on illness script formation, their results, and the useful strategies. Ten studies were included in this review. Almost all of these studies used integrated teaching methods focusing on the incorporation of biomedical and clinical knowledge with clinical cases and found that these interventions were effective in developing preclinical students' clinical reasoning based on illness script development. This indicate that before medical students enter their clinical rotations, they can benefit from clinical reasoning training based on illness script formation. In addition, Boshuizen et al. [27] found that illness script development does not automatically occur when students enter their clinical training. This study further supports why clinical reasoning training of preclinical students based on illness script formation is necessary. The methodological quality of the reviewed studies was above the mean value of the study by Reed et al. [21], and the lower quality of studies was due to the small number of participants and type of data (only self-assessed data).

The 10 studies reviewed employed diverse and effective teaching and learning methods and provided useful teaching and learning strategies for pre-clinical students to cultivate their clinical reasoning based on illness script formation. The strategies include three categories: learning and teaching settings, contents, and methods. First, regarding learning and teaching settings, five studies used small group settings to encourage the discussion among the group of students with their facilitators [1,4,10,23,26]. The focus of the programs for developing students' illness scripts should be on tuning and restructuring previously acquired knowledge instead of acquiring new knowledge for use in clinical contexts [10,26,28]. Then, the small discussion format is essential for students to apply their thoughts to clinical cases more freely and facilitators guiding the students' discussions and providing immediate and detailed feedback are also critical for their knowledge structure to become more elaborate. Moreover, sufficient time for extensive discussion of all relevant aspects of clinical cases is also recommended to promote illness script formation [10]. Group size also matters; Jackson et al. [26] suggested 4-5 students per group to prevent distraction and improve learning experience.

Regarding the learning and teaching contents, all studies used clinical cases as contents. Clinical cases that cover all stages of clinical encounters, including history, physical examination, differential diagnosis, diagnostic testing, and management, are useful for all the relevant aspects of developing illness scripts to be discussed [10]. Keemink et al. [10] also emphasized providing more than one case at a time for repeated application of knowledge. As repeated application of knowledge accelerates the tuning processes of the knowledge structure toward future use in practical situations, providing more than one case at a time can promote illness script development. Increasing the authenticity by presenting clinical cases through real or simulated patients offers learners engaging opportunities to practice the integration of biomedical and clinical knowledge [4,7,22,25,26]. Jackson et al. [26] developed a simulated virology clinic consisting of a series of eight SP encounters for

first-year students and showed that the students particularly appreciated how SPs brought the diseases to life in a memorable way that their classroom lectures and other learning materials could not provide. The application of basic science to human experiences in clinical contexts can create a stronger conceptual knowledge framework for students to integrate, store, retain, and retrieve knowledge [22]. Furthermore, a clinical case related to what the students were currently studying in the pre-clinical curriculum is useful, with an emphasis on independent learning [26].

On presenting patient data, the whole case format instead of a serial cue format for pre-clinical students is suggested based on the cognitive load theory [29]. Pinnock et al. [7] studied when the best time might be to introduce whole-case or serial-cue teaching approaches with students at different stages of training for history taking. In the former, the whole case is given to students, whereas in the latter, students are gradually given patient data, such as patient encounters at the doctor's office [3]. The results showed that in the early stages of their training, the students could not handle questioning and managing data simultaneously due to cognitive overload. The authors suggested transitioning from the whole case, a blended, to the serial-cue approach as clinical knowledge increases [7].

Regarding learning and teaching methods, almost all studies reviewed employed integrated teaching methods when working with clinical cases. In addition, because illness scripts develop from the application of biomedical and clinical knowledge to clinical cases, rather than the accretion of new knowledge, the emphasis should be on the application of previously acquired knowledge [10,16,26].

Integrated teaching should be structured to formalize the clinical reasoning processes. The systematic exposure of students to all essential components for the development of their illness scripts, rather than just focusing on correct patient diagnosis, is required [16]. For example, Blunk et al. [4] employed three integrated sessions, while Hennrikus et al. [22] employed the metacognitive approach. In the three integration sessions, the students were given a clinical presentation followed by the associated basic science information and then, three clinical cases to formulate diagnoses, causes, and therapeutics. The students also interviewed two SPs in complex cases. In the study by Hennrikus et al. [22], the students were taught basic science, and then, a patient with the disease spoke to the class. After that, students wrote illness scripts. The results indicated that both methods helped novice learners elaborate causal models, ultimately cultivating illness script formation and clinical reasoning.

A direct illness script teaching method that helps students develop correct problem representations and illness scripts is also useful in terms of the construction of pre-clinical students' illness scripts [1,23]. This approach explicitly teaches illness script construction with an illness script worksheet. Illness script building should start from the beginning of medical training as this script becomes the foundation for further development [6]. The illness script worksheet can serve as a scaffolding to facilitate this process. Self- explanation focusing on pathophysiological mechanisms can also foster the integration of biomedical and clinical knowledge, promoting illness script construction [24]. Self-explanation is a well-known strategy for training clinical reasoning [30]. From a slightly different perspective, Peixoto et al. [24] investigated whether self-explanation of the pathophysiological mechanism of diseases rather than about clinical knowledge can foster the pre-clinical students' clinical reasoning. They concluded that self-explanation of the pathophysiological mechanism of diseases can help activate biomedical

knowledge and create new links between biomedical and clinical knowledge, eventually leading to a more coherent mental representation. However, this positive effect works only in diseases with similar patho-physiological processes or in unfamiliar or complex diseases [24].

Timely and detailed feedback from the faculty is one of the most important strategies in developing clinical reasoning skills [1,5,23,25,27]. Feedback is regarded as effective in promoting reflective processes and enhancing learning [31]. Boshuizen et al. [27] explored what and how students learn from multiple cases with similar underlying problems and found that some students learn from multiple cases with limited feedback, but half of the students did not, particularly in the fault component of illness scripts. They concluded that unsupported case analyses from clinicians are insufficient for integrating biomedical knowledge into illness scripts. Providing timely and detailed feedback when students develop a correct problem representation, comparing and contrasting the findings, and organizing data appropriate for the illness script are essential in terms of illness script construction and clinical reasoning development.

Finally, stepwise exposure to clinical practice is an effective strategy [25]. Royan et al. [25] developed a clinical reasoning elective program to provide pre-clinical students an exposure to patients in the emergency department without performance pressure or formal grading before their clinical rotations. The students were expected to evaluate the patient in pair and present the findings to their faculty mentors. Royan et al. [25] found that the participating group showed an increased score in clinical assessment and overwhelmingly positive responses to this activity. The clinical training opportunities in a low-stakes environment before entering their clerkships provide pre-clinical students opportunities to practice the integration of basic science knowledge with patient cases in real contexts with sufficient feedback, ultimately facilitating structured and elaborate illness scripts.

Conclusion

This study systematically reviewed learning and teaching interventions, their results, and strategies for preclinical students' clinical reasoning development by facilitating illness script formation. The literature search strategy generated 91 studies and10 studies were selected for the final analysis. The results demonstrated that diverse teaching and learning methods were used to support the integration of biomedical and clinical knowledge working with patient cases, and their effects, assessed through diverse methods, were largely effective in terms of the clinical reasoning development of pre-clinical students. Acquiring clinical reasoning ability at every level of medical education is an essential learning goal [2]. This review suggests that explicit attempts to promote illness script formation with a structured program rather than informal training lead to positive results, and such formal clinical reasoning training programs could provide a smooth transition from pre-clinical to clinical experience. Research on pre-clinical students' clinical reasoning development by facilitating illness script formation has recently been rising, but more research is necessary to provide stronger evidence about this important issue. In addition, more randomized controlled studies using standardized assessment methods are recommended to add more convincing evidence.

This study has a few limitations. This study only included peer-reviewed and published journal articles in English. Gray literature and articles not in English and not in formal academic channels were excluded. In

addition, this review did not perform a meta-analysis due to the heterogeneity of the assessment methods of the studies, the rarity of randomized controlled trials, and the limited number of analyzed studies.

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