TITLE: Is *hybrid*-PBL advancing teaching in biomedicine? A systematic review

AUTHORS: Rodrigo Jiménez-Saiz[a, b,§,*] & Domenico Rosace[b, c §]

[a]Department of Biochemistry and Molecular Biology, Chemistry School, Complutense University, Madrid, Spain. Email: r.jimenez.saiz@ucm.es

[b]McMaster Immunology Research Centre (MIRC), Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada. Email: jimenez@mcmaster.ca

[c]Applied Molecular Medicine Institute (IMMA), School of Medicine, CEU San Pablo University, Madrid, Spain. Email: domenico.rosace3@gmail.com

*Correspondence to: Dr. Rodrigo Jiménez-Saiz. Department of Biochemistry and Molecular Biology, Chemistry School, Complutense University, Ciudad Universitaria s/n, 28040 Madrid, Spain. Phone number: +34 91 394 4161. Email address: r.jimenez.saiz@ucm.es

[§]Equal contributions

Abstract

The impact of instructional guidance on learning outcomes in higher biomedical education is subject of intense debate. There is the teacher-centered or traditional way of teaching (TT) and, on the other side, the notion that students learn best under minimal guidance (problem-based learning, PBL). Although the benefits of PBL are well-known, there are aspects susceptible to improvement. Hence, a format merging TT and PBL (*hybrid*-PBL, h-PBL) may advance education in biomedical sciences. Here, we systematically reviewed studies that employed h-PBL in higher biomedical education compared to TT and/or pure PBL. We found that h-PBL resulted in better overall students' performance and perception than TT or pure PBL. These findings encourage more research on investigating the pedagogical benefits of h-PBL and posit an eclectic system in which the pedagogical tools from TT and PBL are used cooperatively in the best interest of the education and satisfaction of the students.

Keywords: hybrid problem-based learning; hybrid-PBL; biomedicine; systematic review; higher education.

Abbreviations: PBL, problem-based learning; h-PBL, hybrid problem-based learning; TT, traditional teaching;

Highlights (separate file)

- Studies on h-PBL in higher biomedical education were systemically reviewed.
- H-PBL resulted in better students' performance and perception than TT or pure PBL.
- These findings encourage further investigation of the pedagogical benefits of h-PBL.
- We posit an eclectic system where TT and PBL are used cooperatively.

1. Introduction

Education is a fundamental component of the decision-making process of every individual (and by extension of a society), which is essentially based on the acquisition and critical use of knowledge. Therefore, the method employed to educate (*i.e.* teach) profoundly impacts the social, cultural and professional endeavours of every person. On this note, there has been a heated debate on the impact of instructional guidance on learning outcomes (*e.g.* knowledge retention, critical thinking, communication and practical skills, etc.) for more than 50 years, particularly as it pertains to higher education (Kirschner, Sweller, & Clark, 2006; Strobel & Van Barneveld, 2009; Waldrop, 2015). On one side, there is the teacher-centered or traditional way of teaching (TT), in which there is direct instructional guidance on the concepts and procedures required by a given discipline; that is to say that there is direct transmission of knowledge from the instructor to the students. This modality of teaching often involves large-classes and lecture-based deliveries (H. Barrows, 2002; H. S. Barrows & Tamblyn, 1980). On the other side, there is the notion that students learn best in a minimally guided (or unguided) environment. This type of teaching is closer to an inductive reasoning, where one goes from an event to a conclusion that could, eventually, become a general statement. It was introduced in 1969, in the Medical Sciences program of McMaster University as Problem-based Learning (PBL) (Savery, 2006). PBL is defined as a learner-centered approach that empowers small groups of students to conduct research, integrate theory and practice, and apply knowledge and skills to develop a viable solution to a defined problem (H. S. Barrows & Tamblyn, 1980).

There is increasing advocacy towards the use of PBL in higher education in various fields, including biomedical sciences, under the premise that PBL is a (if not "the") superior way of teaching; indeed, to teach any other way may be even considered unethical (Waldrop, 2015). However, the evidence to support an absolutist view is debatable (Kirschner et al., 2006; Strobel & Van Barneveld, 2009). While it is plausible that PBL, or pedagogically comparable teaching methods (*e.g.* experiential,

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 November 2018 doi:10.20944/preprints201811.0344.v1

Peer-reviewed version available at BMC Medical Education 2019, 19; doi:10.1186/s12909-019-1673-0

discovery, inquiry-based learning), are pivotal for higher teaching (Waldrop, 2015), a number of studies have identified aspects of PBL that are susceptible to improvement (Hmelo-Silver, 2004; Houlden, Collier, Frid, John, & Pross, 2001; Kirschner et al., 2006). For example, PBL instructors often witness students that are stuck with a problem (Hmelo-Silver, 2004), which raises the need to tailor PBL to the knowledge of the students and complement it with guided sessions (*e.g.* lectures). Indeed, a vast majority of dental students in PBL-based programs from USA or Sweden wanted lectures, at least sometimes, regardless of their level of training (undergraduate students from 2nd to 5th year were asked) (Haghparast, Sedghizadeh, Shuler, Ferati, & Christersson, 2007), which indicates a need for more guidance. This suggests that lecture-based, guided sessions may be a useful teaching tool to fulfill certain deficiencies of the PBL-curriculum. In other words, that a *hybrid*-PBL (h-PBL) format that incorporates elements of TT and PBL may advance teaching and education in biomedical sciences.

The concept of h-PBL, understood as a combination of PBL and TT, is not unforeseen. In fact, it has been used in a number of biomedical programs that were transitioning from TT to PBL, in programs where TT is deeply rooted and the faculty members would not support a pure PBL system, and it has also been employed by instructors genuinely interested in investigating the learning outcomes of h-PBL (Callis et al., 2010; Carrio et al., 2016; Holaday & Buckley, 2008; Whelan, Mansour, & Farmer, 2002). While some studies have tested h-PBL in biomedical sciences, a comprehensive analysis and review of the data generated has not been performed, which makes it difficult to define accurately its pedagogical value. Here, we have conducted a systematic review of experimental studies that employed h-PBL in higher biomedical education compared to TT and/or pure PBL. Specifically, this review addresses the following question: does h-PBL in biomedical sciences result in superior marks and a better student's perception of the teaching and learning process?

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 November 2018 doi:10.20944/preprints201811.0344.v1

Peer-reviewed version available at BMC Medical Education 2019, 19; doi:10.1186/s12909-019-1673-0

2. Methods

This study was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to systematically and explicitly screen studies in a rigorous and unbiased manner (Moher, Liberati, Tetzlaff, Altman, & Group, 2009). The PRISMA flow diagram (**Fig. 1**) conveys the different phases of this systematic literature review from the number of records identified through to those included and excluded (with reasons). Data were collected from original research in higher education, in biomedical sciences, involving a h-PBL group and a TT and/or pure PBL group. Articles published in peer-reviewed academic journals between 1997 and January 2018 were examined. With the support of the staff from the Paul R. McPherson Institute for Leadership, Innovation, Excellence in Teaching at McMaster University (Hamilton, ON) databases were selected to find original research on h-PBL. A keyword search was conducted in 3 databases including ERIC, Web of Science and PubMed. The search terms were discussed and agreed upon by all authors to ensure relevant articles were located. For the purposes of this systematic review, the important search terms were: 'hybrid-problem-based learning', 'hybrid-PBL' and related terms. These search terms were applied for each of the 3 databases separately and records found were pooled using EndNote7.

Peer-reviewed version available at BMC Medical Education 2019, 19; doi:10.1186/s12909-019-1673-0

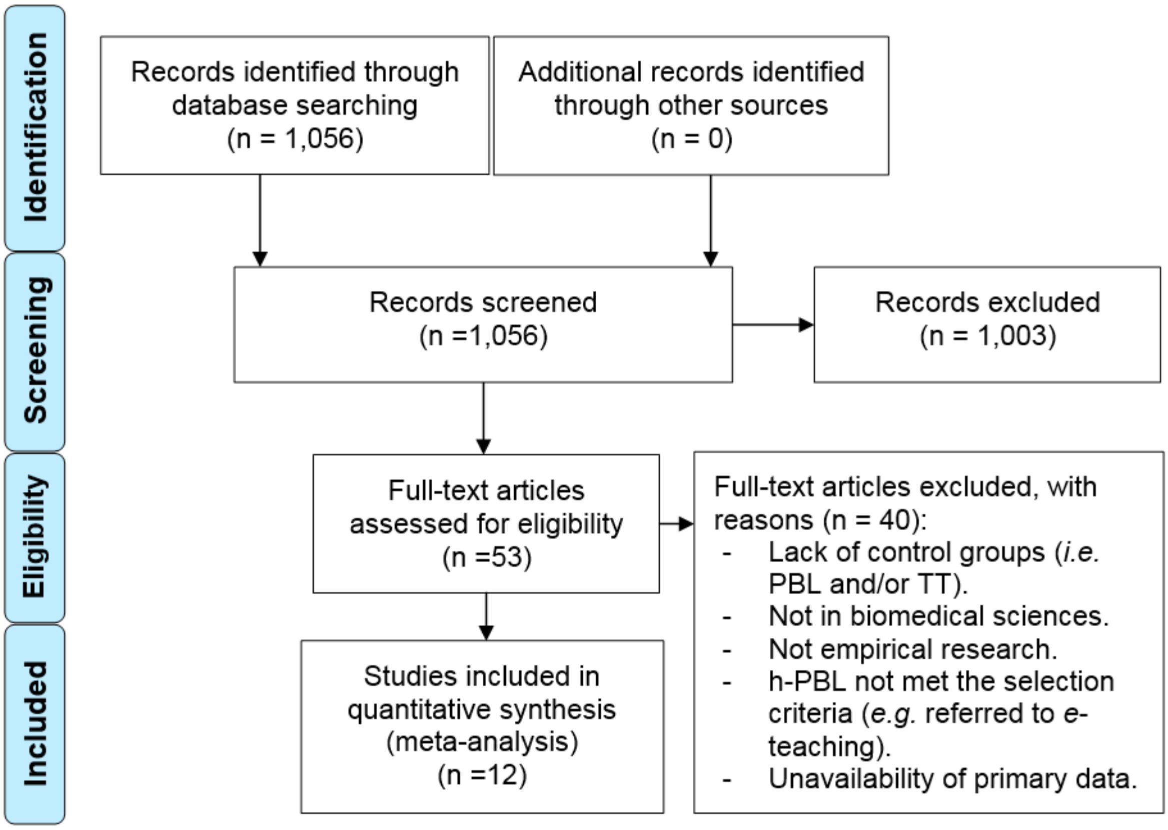

Fig. 1. PRISMA flow diagram demonstrating identification and screening stages and included articles.

The initial search of three databases identified 1,056 records (**Fig. 1**). These records were screened by reading the title and abstract. At this screening stage, records were excluded if they were (a) duplicates, (b) not in English, (c) not in higher education, (d) not in biomedical sciences (e) not original research. Following this initial screen, 53 records remained, which were then assessed for eligibility (**Fig. 1**). More detailed inclusion criteria were then applied to these articles. Articles were excluded for the aforementioned reasons, and also if they a) did not include control groups or b) the h-PBL system used was referring to *e*-teaching. After assessing the 53 full text articles, 12 articles fitting the eligibility criteria remained and these were analyzed in the review (**Table 1**).

Peer-reviewed version available at BMC Medical Education 2019, 19; doi:10.1186/s12909-019-1673-0

3. Results

3.1 Characterization of selected articles

The 12 original research studies on h-PBL in higher biomedical sciences that were selected for the analysis are summarized in **Table 1**.

Study	Country	Discipline	Groups	Total n number	Grades	Student's Perception
(Callis et al., 2010)	USA	Medicine	h-PBL, TT	71	Yes	Yes
(Carrió, Larramona, Baños, & Pérez, 2011)	Spain	Biology	h-PBL, TT	60	Yes	Yes
(Carrio et al., 2016)	Spain	Biology	h-PBL, TT	85	Yes	Yes
(Yan, Ma, Zhu, & Zhang, 2017)	China	Medicine	h-PBL, TT	273	Yes	Yes
(Yang et al., 2014)	China	Medicine	h-PBL, TT, PBL	127	Yes	Yes
(Gopalan & Klann, 2017)	USA	Physiology	h-PBL, TT	187	Yes	Yes
(Hartings, Fox, Miller, & Muratore, 2015)	USA	Chemistry	h-PBL, TT	300	Yes	Yes
(Chilkoti et al., 2016)	India	Medicine	h-PBL, TT	118	No	Yes
(Lian & He, 2013)	China	Medicine	h-PBL, TT	205	Yes	Yes
(Temple, Cresawn, & Monroe, 2010)	USA	Biology	h-PBL, TT	-	No	Yes
(Whelan et al., 2002)	Canada	Pharmacy	h-PBL, TT	64	Yes	Yes
(Gurpinar, Bati, & Tetik, 2011)	Turkey	Medicine	h-PBL, TT, PBL	547	No	Yes

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 November 2018 doi:10.20944/preprints201811.0344.v1

Peer-reviewed version available at BMC Medical Education 2019, 19; doi:10.1186/s12909-019-1673-0

The majority of articles were originated in the USA and China (34% and 25% respectively), followed by Spain (17%), and Canada, India and Turkey (8% each) (**Fig. 2**). At the continent level, 42% of the selected articles were from Asia and North America each, and 16% from Europe (**Fig. 2**).

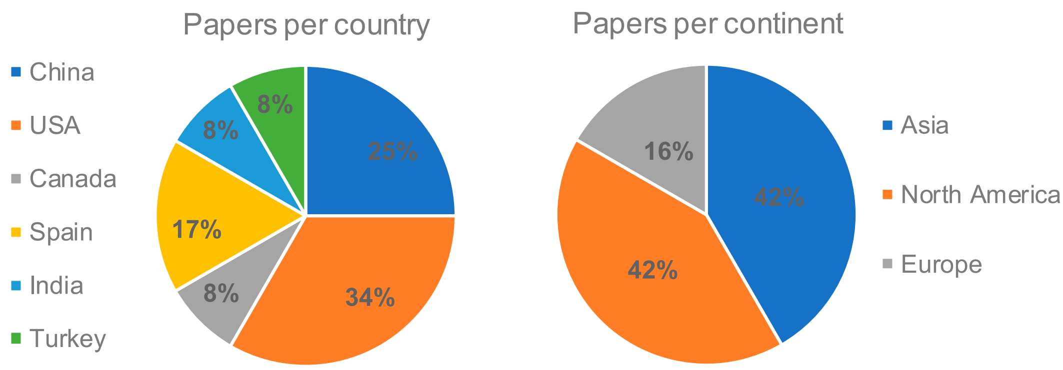

Fig. 2. Geographical characterization of the article selection.

Medicine was the discipline that prevailed in the selection (50%), followed by biology (25%), and physiology, chemistry and pharmacy (8% each) (**Fig. 3**). These data indicate that the findings of this systematic review are especially representative of the field of medicine in USA and China.

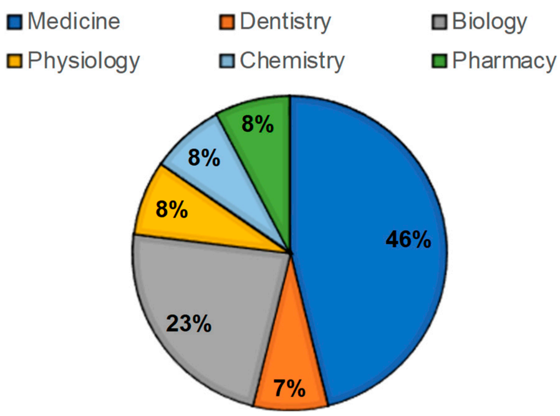

Fig. 3. Distribution of disciplines of the articles selected.

All the selected studies included an assessment of student performance that evaluated theoretical knowledge and/or problem-solving skills. Most of the studies compared 2 groups (10 articles, 83%), and 2 articles (17%) had the ideal design comparing the 3 groups of interest (h-PBL, pure PBL and TT). Furthermore, the selected articles for the present study compared h-PBL *vs* TT (9 articles, 75%)

Peer-reviewed version available at BMC Medical Education 2019, 19; doi:10.1186/s12909-019-1673-0

more often than h-PBL *vs* PBL (3 articles, 25%). This implies that the findings of this systematic review are more substantiated when comparisons between h-PBL and TT are made. Due to the limited number of studies comparing h-PBL *vs* PBL, or the 3 groups, these studies will be analyzed in more detail.

3.2 Students performance

Grades are usually taken as an indicator of student performance. To determine whether students in a h-PBL program performed better compared to TT and/or PBL, academic records were compared. Grading was assigned based on factual knowledge and/or problem-solving skills. To assess theoretical knowledge students belonging to different teaching methods performed a test that took place at the end of the semester, or the year, centered on basic science knowledge acquired during this time frame. The exams consisted of multiple-choice question, short-essay questions, or a combination of both. To assess problem-solving skills, students were to solve a problem-based or a case-study exam. Science comprehension, diagnosis, treatment, communication and hypothesis generation, among others, were evaluated.

Table 2. Characterization of the students' performance assessment method of the selection of original research on h-PBL in higher biomedical sciences.

Study	Factual Knowledge	Problem-solving skills
(Callis et al., 2010)	Yes	Yes
(Carrió et al., 2011)	Yes	No
(Carrio et al., 2016)	Yes	No
(Yan et al., 2017)	Yes	No
(Yang et al., 2014)	Yes	Yes
(Gopalan & Klann, 2017)	Yes	No
(Hartings et al., 2015)	No	Yes

 doi:10.20944/preprints201811.0344.v1

Peer-reviewed version available at *BMC Medical Education* **2019**, *19*; doi:10.1186/s12909-019-1673-0

(Lian & He, 2013)	Yes	Yes
(Whelan et al., 2002)	Yes	Yes

Eight out of the 12 articles selected (66%) analyzed student's theoretical knowledge and 5 (42%) of them assessed problem-solving skills (**Table 2**). Students in the h-PBL group obtained better theoretical results compared to TT (**Fig. 4A**). Six studies (75%) showed significantly better performance of students in the h-PBL compared to TT and 2 studies (25%) did not show significant differences. In these 2 studies (Carrió et al., 2011; Whelan et al., 2002), the students belonging to the h-PBL program had similar scores to the other experimental groups and did not show learning shortcomings. Interestingly, the study by Carriò *et al.* (Carrió et al., 2011), which compared 2nd year students educated with TT or hybrid-PBL, did not show significant differences in factual knowledge acquisition between both groups at that time. However, in a follow up study with the same cohort of students, upon completion of the degree (5 years), Carriò et *al.* (Carrio et al., 2016) reported that h-PBL students obtained higher marks than TT students, which suggests that h-PBL improved long-term retention of knowledge. In addition, students in the h-PBL group demonstrated better problem-solving skill performance compared to TT in 80% (4 out of 5) of the studies (**Fig. 4B**).

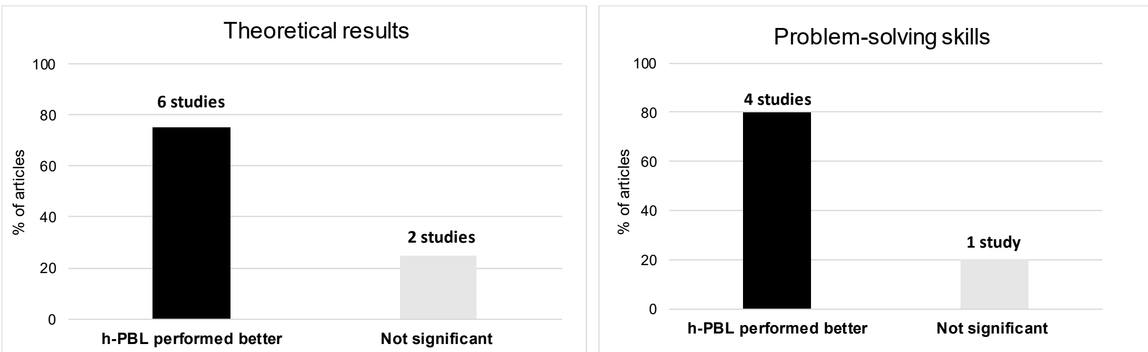

Fig. 4. Students performance in h-PBL compared to TT.

We found 2 studies comparing h-PBL and pure-PBL learning methods although only one compared student´s performance (Yang et al., 2014). This recent study was conducted by the Department of

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 November 2018 doi:10.20944/preprints201811.0344.v1

Peer-reviewed version available at BMC Medical Education 2019, 19; doi:10.1186/s12909-019-1673-0

Neurology at Sun Yat-Sen Memorial Hospital of China, with 127 students from a five-year undergraduate program that voluntarily participated. The aim of the authors was to introduce h-PBL in neurology and compare student´s performance to pure PBL and TT. The students were randomly assigned to each group and their performance was evaluated with a theoretical and a practical test at the end of the course. The test addressed the students' understanding of the fundamental concepts taught as well as the diagnosis and treatment for the diseases covered in the course. The practical test mainly evaluated the students' proficiency analyzing a medical case, formulating a hypothesis and a strategy for the physical examination. They found that the PBL group performed better in the practical test, while the theoretical test scores and the total scores of the h-PBL students were significantly higher than those of the other groups. Interestingly, the differences in scores were greater when comparing the results of the h-PBL *vs* the TT group.

Students perception

The perception of students was also analyzed as indicator of their satisfaction with the pedagogical method employed in the course. A questionnaire to investigate students' preference for either h-PBL, PBL or TT was performed after the course. The questionnaire evaluated the student satisfaction on four aspects: i) learning and understanding; ii) interest and motivation; iii) training one's personal abilities and satisfaction; and iv) confidence acquired with the teaching method. An example of the questions usually asked is given below:

(a) if you had the possibility to choose before the course, would you have opted for the PBL course/h-PBL course/TT course?

Peer-reviewed version available at BMC Medical Education 2019, 19; doi:10.1186/s12909-019-1673-0

(b) after the experience from the course, would you now opt for the h-PBL course if you had to choose again?

(c) which kind of teaching method is the more appropriate and supporting to achieve the key learning objectives planned at the beginning of the course?

In addition, students had the opportunity to comment on the contents of the tutorial, as well as express their opinions and suggestions to improve the course (Carrio et al., 2016; Hartings et al., 2015; Lian & He, 2013; Yang et al., 2014).

In the 12 articles analyzed, the students provided positive feedback and the questionnaires showed higher average scores for h-PBL than TT or pure PBL. In particular, the students were satisfied with the h-PBL format because they considered that this method helped them learn relatively complex and nonintuitive parts of the program more easily than with pure PBL. They also noted the cooperative work and informational skills (Carrio et al., 2016) and the ability of thinking indendently and critically (Hartings et al., 2015) as reinforcements of the acquired skills in h-PBL. In the study by Yang *et al.*, (Yang et al., 2014) the questionnaire conducted on the h-PBL and TT groups, showed that some students had negative feedback on pure PBL, which was mainly due to the difficulties had by the students to gain a comprehensive understanding of the subjects. On the other hand, the h-PBL method was widely accepted by the students, achieving 100% of satisfaction and preferences.

4. Discussion

The overarching goal of this systematic review was to advance higher education in biomedical sciences by questioning current views that promote the exclusive use of pure TT or PBL (Kirschner et al., 2006) (Strobel & Van Barneveld, 2009; Waldrop, 2015). We hypothesized that a h-PBL format that incorporates elements of TT and PBL may benefit the students pedagogically more than pure TT

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 November 2018 doi:10.20944/preprints201811.0344.v1

Peer-reviewed version available at BMC Medical Education 2019, 19; doi:10.1186/s12909-019-1673-0

or PBL alone. A systematic literature review was conducted to compare the performance and/or perceptions of students in a h-PBL *vs* TT and/or PBL format in higher biomedical sciences. Specifically, this review addressed the following question: does h-PBL in higher biomedical sciences result in superior marks and student's perception of the learning process?

Overall, this systematic review indicates that the use of h-PBL in higher biomedical sciences was superior compared to TT and pure-PBL. This is evidenced by the higher performance of the students in h-PBL as well as the level of student's satisfaction. The better performance of h-PBL students, compared to pure PBL students, may be due to the insufficient guidance often felt by PBL students, which causes anxiety, struggling with certain problems, absence of a higher understanding of the field, *etc.* (Haghparast et al., 2007; Hmelo-Silver, 2004; Houlden et al., 2001; Whelan et al., 2002). Expectedly, the differences observed between h-PBL and TT students were more pronounced than when comparing h-PBL and PBL. This is likely due to the pedagogical benefits of problem-solving activities, which empower rationalization and long-term retention of knowledge (Strobel & Van Barneveld, 2009).

While the results of this systematic review support the use of h-PBL in higher biomedical sciences over TT and PBL, the limited number of studies, particularly those directly comparing PBL and h-PBL, prevent us from giving strong recommendations. This systematic review is rather preliminary, but the findings clearly encourage more research on investigating the pedagogical benefits of h-PBL, and further studies in which PBL and h-PBL are directly compared and learning outcomes comprehensively analyzed.

There are additional aspects that are worth considering as they may have impacted the outcome of studies assessing the pedagogical value of h-PBL (and PBL). For example, how familiar the students are with the methodology may impact their predisposition towards it. More importantly, the training

Peer-reviewed version available at *BMC Medical Education* **2019**, *19*; doi:10.1186/s12909-019-1673-0

and expertise in PBL of the instructors participating in these studies need to be carefully evaluated when designing the studies (Pham, 2016). Instructors willing to investigate novel pedagogical methods often face the stagnation of other faculty members, their reluctance to prepare themselves to educate in a different format and a lack of pedagogical and human resources in their departments. For instance, some of the studies discussed here could not incorporate more than 20% of PBL teaching within the h-PBL program (Carrio et al., 2016; Carrió et al., 2011) because of the aforementioned reasons.

This leads us to a different question; what should be the flavor of a h-PBL course? In other words, how many teaching hours should be delivered as PBL? Probably the answer is that it depends! It depends on a number of variables including the background and number of the students, their level of conceptualization, and their progress, to mention a few. Therefore, the ability of the facilitator to perceive learning hurdles as they arise, and switch from one format to another is critical to maximize the potential benefits of h-PBL. This may be accomplished via regular assessment of students' progress in a manner that comprehensively informs of the learning outcomes.

In conclusion, our findings refute an absolutist view on teaching in higher biomedical sciences and rather posit an eclectic system in which the pedagogical tools from TT and PBL are used cooperatively and in the best interest of the education and satisfaction of the students.

Acknowledgements

We thank Drs. Manel Jordana and Cira Garcia de Durango, and Mrs. Melissa E. Gordon for critical review of the manuscript. We are grateful to the staff from the Paul R. McPherson Institute for Leadership, Innovation, Excellence in Teaching at McMaster University for assistance with the conceptualization and execution of the systematic review.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

References

Barrows, H. (2002). Is it truly possible to have such a thing as dPBL? *Distance Education, 23*(1), 119-122.

Barrows, H. S., & Tamblyn, R. M. (1980). *Problem-based learning: An approach to medical education*: Springer Publishing Company.

Callis, A. N., McCann, A. L., Schneiderman, E. D., Babler, W. J., Lacy, E. S., & Hale, D. S. (2010). Application of basic science to clinical problems: traditional vs. hybrid problem-based learning. *J Dent Educ, 74*(10), 1113-1124.

Carrio, M., Agell, L., Banos, J. E., Moyano, E., Larramona, P., & Perez, J. (2016). Benefits of using a hybrid problem-based learning curriculum to improve long-term learning acquisition in undergraduate biology education. *FEMS Microbiol Lett, 363*(15). doi:10.1093/femsle/fnw159

Carrió, M., Larramona, P., Baños, J. E., & Pérez, J. (2011). The effectiveness of the hybrid problem-based learning approach in the teaching of biology: a comparison with lecture-based learning. *Journal of Biological Education, 45*(4), 229-235. doi:10.1080/00219266.2010.546011

Chilkoti, G., Mohta, M., Wadhwa, R., Saxena, A. K., Sharma, C. S., & Shankar, N. (2016). Students' satisfaction to hybrid problem-based learning format for basic life support/advanced cardiac life support teaching. *Indian journal of anaesthesia, 60*(11), 821-826. doi:10.4103/0019-5049.193669

Gopalan, C., & Klann, M. C. (2017). The effect of flipped teaching combined with modified team-based learning on student performance in physiology. *Adv Physiol Educ, 41*(3), 363-367. doi:10.1152/advan.00179.2016

Gurpinar, E., Bati, H., & Tetik, C. (2011). Learning styles of medical students change in relation to time. *Adv Physiol Educ, 35*(3), 307-311. doi:10.1152/advan.00047.2011

Haghparast, N., Sedghizadeh, P. P., Shuler, C. F., Ferati, D., & Christersson, C. (2007). Evaluation of student and faculty perceptions of the PBL curriculum at two dental schools from a student perspective: a cross-sectional survey. *Eur J Dent Educ, 11*(1), 14-22. doi:10.1111/j.1600-0579.2007.00423.x

Hartings, M. R., Fox, D. M., Miller, A. E., & Muratore, K. E. (2015). A Hybrid Integrated Laboratory and Inquiry-Based Research Experience: Replacing Traditional Laboratory Instruction with a Sustainable Student-Led Research Project. *Journal of Chemical Education, 92*(6), 1016-1023. doi:10.1021/ed500793q

Hmelo-Silver, C. E. (2004). Problem-based learning: What and how do students learn? *Educational psychology review, 16*(3), 235-266.

Holaday, S. D., & Buckley, K. M. (2008). Addressing challenges in nursing education through a clinical instruction model based on a hybrid, inquiry-based learning framework. *Nurs Educ Perspect, 29*(6), 353-358.

Houlden, R. L., Collier, C. P., Frid, P. J., John, S. L., & Pross, H. (2001). Problems identified by tutors in a hybrid problem-based learning curriculum. *Acad Med, 76*(1), 81.

Kirschner, P. A., Sweller, J., & Clark, R. E. (2006). Why minimal guidance during instruction does not work: An analysis of the failure of constructivist, discovery, problem-based, experiential, and inquiry-based teaching. *Educational psychologist, 41*(2), 75-86.

Lian, J., & He, F. (2013). Improved performance of students instructed in a hybrid PBL format. *Biochem Mol Biol Educ, 41*(1), 5-10. doi:10.1002/bmb.20666

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Group, P. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. *Open Med, 3*(3), e123-130.

Pham, T. (2016). Student-centredness: Exploring the culturally appropriate pedagogical space in Vietnamese higher education classrooms using activity theory. *Australian Journal of Teacher Education (Online), 41*(1), 1.

Savery, J. R. (2006). Overview of problem-based learning: Definitions and distinctions. *Interdisciplinary Journal of Problem-based Learning, 1*(1), 3.

Strobel, J., & Van Barneveld, A. (2009). When is PBL more effective? A meta-synthesis of meta-analyses comparing PBL to conventional classrooms. *Interdisciplinary Journal of Problem-based Learning, 3*(1), 4.

Temple, L., Cresawn, S. G., & Monroe, J. D. (2010). Genomics and bioinformatics in undergraduate curricula: Contexts for hybrid laboratory/lecture courses for entering and advanced science students. *Biochem Mol Biol Educ, 38*(1), 23-28. doi:10.1002/bmb.20359

Waldrop, M. M. (2015). Why we are teaching science wrong, and how to make it right. *Nature, 523*(7560), 272-274. doi:10.1038/523272a

Whelan, A. M., Mansour, S., & Farmer, P. (2002). Outcomes-based integrated hybrid PBL curriculum. *American Journal of Pharmaceutical Education, 66*(3), 302-311.

Yan, Q., Ma, L., Zhu, L., & Zhang, W. (2017). Learning effectiveness and satisfaction of international medical students: Introducing a Hybrid-PBL curriculum in biochemistry. *Biochem Mol Biol Educ, 45*(4), 336-342. doi:10.1002/bmb.21046

Yang, L. H., Jiang, L. Y., Xu, B., Liu, S. Q., Liang, Y. R., Ye, J. H., & Tao, E. X. (2014). Evaluating team-based, lecture-based, and hybrid learning methods for neurology clerkship in China: a method-comparison study. *BMC Med Educ, 14*(1), 98. doi:10.1186/1472-6920-14-98