Effective Health Care

Pathogen-Reduced Platelets for Thrombocytopenia

Results of Topic Selection Process & Next Steps

The nominator, the College of American Pathologists (CAP), is interested in a new evidence review on the cost-effectiveness of pathogen-reduced (PR) versus regular platelets for thrombocytopenic patients to inform the creation of guidelines.

Because limited original research addresses the nomination, a new review is not feasible at this time. No further activity on this nomination will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Number and Name: #0801 Pathogen-Reduced Platelets for Thrombocytopenia

Nomination Date: 06/29/2018

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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Background

Platelet transfusions are used to prevent and treat bleeding in patients with low levels of platelets (thrombocytopenia). Platelet components are at higher risk of bacterial infection compared to other blood products because they require a higher temperature for storage. In the U.S., 38 episodes of post-transfusion sepsis including four fatalities were reported after transfusion of platelets; although other studies have found rates that are 10 times higher.[1] Two types of pathogen-reduction (PR) technologies are commercially available, both of which use ultraviolet (UV) light in combination with either a synthetic psoralen compound (amotosalen) or riboflavin (vitamin B2) to reduce the number of pathogens. Only amotosalen has been approved for use in the U.S.

In 2016, the Food and Drug Administration (FDA) issued draft guidance on mitigating platelet bacterial contamination through the use of pathogen reduction systems and other strategies.[2] However, questions remain as to whether PR platelets are more effective than regular platelets at improving patient survival and reducing complications. A 2017 Cochrane review[1] found that PR platelets do not improve patient survival, bleeding, or risk of serious adverse events compared to regular platelets, and increase the risk of platelet refractoriness and platelet transfusions. The authors of this review recommended a cost-effectiveness analysis to determine whether any increase in costs from the use of PR systems would be offset by reduced need for bacterial screening, gamma irradiation, or increased shelf-life.

Nominator and Stakeholder Engagement

The College of American Pathologists (CAP) nominated this topic to inform the creation of guidelines outlining when to use PR versus regular platelet transfusions in thrombocytopenic patients. They are specifically interested in the upfront costs of PR platelets versus regular platelets as well as the costs associated with downstream events such as reduced complications, reduced need for additional bacterial screening, and extended shelf life.

Key Questions and PICOs

The key question for this nomination is:

1. What is the cost-effectiveness of pathogen-reduced platelets versus regular platelets for patients with thrombocytopenia?

To define the inclusion criteria for the key questions, we specify the population, interventions, comparators, and outcomes (PICOs) of interest (Table 1).

Table 1. Key Questions and PICOs

Key Questions	1. What is the cost-effectiveness of pathogen-reduced platelets versus regular platelets for patients with thrombocytopenia?
Population	Patients with thrombocytopenia
Interventions	Pathogen-reduced (PR) platelets
Comparators	Regular platelets
Outcomes	• Costs (e.g., costs associated with PR process, complications, need for subsequent infusions or irradiation) • Bleeding episodes • Mortality • Adverse events • Platelet count • Need for additional platelet infusion • Quality of life

Methods

We assessed nomination #0801 Pathogen-Reduction Platelets for Thrombocytopenia for priority for a systematic review or other Agency for Healthcare Research and Quality (AHRQ) EHC report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix A for detailed description of the criteria.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
4. Assess the *potential impact* a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years on the key questions of the nomination. See Appendix B for sources searched.

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a literature search in PubMed for the last five years. See Appendix C for the PubMed search strategy and link to the ClinicalTrials.gov search.

We reviewed all identified titles and abstracts for inclusion and classified identified studies by key question and study design to assess the size and scope of a potential evidence review.

Results

See Appendix A for detailed assessments of all Evidence-based Practice Center (EPC) program selection criteria.

Appropriateness and Importance

This is an appropriate and important topic. In the U.S., 38 episodes of post-transfusion sepsis including four fatalities were reported after transfusion of platelets; although other studies have found rates that are 10 times higher.[1] In 2016, the FDA issued draft guidance on the use of PR systems to reduce risk of bacterial infection in platelets.[2] This guidance is still under discussion as of July 2018.[3]

Desirability of New Review/Duplication

A new evidence review would not be duplicative of an existing review. Although a 2017 Cochrane review[1] found that PR platelets do not improve patient survival, bleeding, or risk of serious adverse events compared to regular platelets, the review did not cover costs. No other reviews on cost-effectiveness were identified.

See Table 2, Duplication column.

Impact of a New Evidence Review

A new systematic review may have moderate impact. Despite guidance by the FDA about the use of PR systems to reduce the risk of bacterial infections in platelet components, the recent Cochrane review calls into question whether PR platelets are more effective than regular platelets at improving patient outcomes. A cost analysis would provide insight on the extent to which PR platelets lead to decreased costs, which could inform decisions on when to use these systems in practice.

Feasibility of a New Evidence Review

A new evidence review is not feasible. The Cochrane review addressed the effects of PR systems on patient-important outcomes; therefore, the feasibility search focused on the costs associated with the use of these systems. Three studies of cost models and one retrospective analysis were identified. One U.S.-based cost model[4] assessed the costs of using PR technology to acquire, process and transfuse platelets, which included costs associated with platelet shelf-life and need for transfusions, irradiation, and bacterial testing. A second U.S.-based model[5] evaluated costs of PR technology by differing levels of implementation (use of 100% conventional platelets, 100% secondary rapid bacterial testing, 100% pathogen reduction, or 50% secondary rapid bacterial testing and 50% pathogen reduction). This model included costs associated with shelf-life, bacterial testing, and sepsis rates, among other downstream outcomes. A third Italy-based model[6] compared progressively increasing use of PR platelets (using both amotosalen and riboflavin systems) versus regular platelets, but did not include costs associated with infections or shelf-life. A fourth study,[7] a retrospective analysis, summarized the costs of using amotosalen in pathogen inactivation in one hospital. This study examined outcome such as allergic reactions and sepsis, as well as costs associated with shelf-life and bacterial testing. No ongoing studies identified from ClinicalTrials.gov address cost-effectiveness.

See Table 2, Feasibility column.

Table 2. Key Questions and Results for Duplication and Feasibility

Key Question	Duplication (8/2015-8/2018)	Feasibility (8/2013-8/2018)
KQ 1: Cost-effectiveness of PR vs. regular platelets	Total number of identified systematic reviews: 0	Size/scope of review Relevant Studies Identified: 2 • Cost models: 3[4-6] • Retrospective analysis: 1[7] ClinicalTrials.gov None identified.

Abbreviations: KQ=Key Question

Summary of Findings

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new evidence review would not be duplicative of an existing product. Although a 2017 Cochrane review thoroughly compared the benefits and risks of PR versus regular platelets, the review did not cover costs. No other reviews addressing cost-effectiveness were identified.
- Impact: A new systematic review has moderate impact potential.
- Feasibility: A new review is not feasible. We only identified four studies that evaluated cost-effectiveness of PR systems.

References

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5. Prioli KM, Karp JK, Lyons NM, Chrebtow V, Herman JH, Pizzi LT. Economic Implications of Pathogen Reduced and Bacterially Tested Platelet Components: A US Hospital Budget Impact Model. *Applied health economics and health policy.* 2018(Available at: https://www.ncbi.nlm.nih.gov/pubmed/?term=30062464).
6. Cicchetti A, Coretti S, Sacco F, et al. Budget impact of implementing platelet pathogen reduction into the Italian blood transfusion system. *Blood transfusion = Trasfusione del sangue.* 2018:1-7. Available at: https://www.ncbi.nlm.nih.gov/pubmed/?term=30201081.
7. Girona-Llobera E, Jimenez-Marco T, Galmes-Trueba A, et al. Reducing the financial impact of pathogen inactivation technology for platelet components: our experience. *Transfusion.* 2014;54(1. Available at: https://www.ncbi.nlm.nih.gov/pubmed/?term=23656485) .

Appendix A. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes, one type of pathogen-reduction (PR) system is available in the United States (amotosalen).
1b. Is the nomination a request for a systematic review?	Yes.
1c. Is the focus on effectiveness or comparative effectiveness?	Yes, the focus is on cost-effectiveness.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	In the U.S., 38 episodes of post-transfusion sepsis including four fatalities were reported after transfusion of platelets; although other studies have found rates that are 10 times higher.[1]
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes, the Food and Drug Administration (FDA) issued draft guidance on the use of PR systems to reduce risk of bacterial infection in platelets.[2] This guidance is still under discussion as of July 2018.[3]
2c. Represents important uncertainty for decision makers	Yes.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes.
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes, the appropriate use of normal platelets or pathogen-reduction platelets could reduce unnecessary costs, such as those associated with the PR process, complications, need for subsequent infusions or irradiation.
3. Desirability of a New Evidence Review/Duplication	
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	A new systematic review (SR) on the cost-effectiveness of PR vs regular platelets would not be duplicative. We identified no SRs addressing cost-effectiveness.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	FDA guidance exists on the use of PR systems, however there continue to be questions about whether PR systems lead to improvements in patient outcomes.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	There is no evidence that practice varies considerably from guidance.

Selection Criteria	Assessment
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	*Size/scope of review:* A new review is not feasible. Three studies of cost models[4-6] and a retrospective analysis[7] were identified. *ClinicalTrials.gov:* No ongoing clinical trials addressing cost-effectiveness were identified.

Abbreviations: AHRQ=Agency for Healthcare Research and Quality

Appendix B. Search for Evidence Reviews (Duplication)

Listed below are the sources searched, hierarchically

Primary Search
AHRQ: Evidence reports and technology assessments https://effectivehealthcare.ahrq.gov/; https://www.ahrq.gov/research/findings/ta/index.html; https://www.ahrq.gov/research/findings/evidence-based-reports/search.html
VA Products: PBM, and HSR&D (ESP) publications, and VA/DoD EBCPG Program https://www.hsrd.research.va.gov/publications/esp/
Cochrane Systematic Reviews http://www.cochranelibrary.com/
HTA (CRD database): Health Technology Assessments http://www.crd.york.ac.uk/crdweb/
PubMed Health http://www.ncbi.nlm.nih.gov/pubmedhealth/
Secondary Search
AHRQ Products in development https://effectivehealthcare.ahrq.gov/
VA Products in development https://www.hsrd.research.va.gov/publications/esp/
Cochrane Protocols http://www.cochranelibrary.com/
PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/

Appendix C. Search Strategy & Results (Feasibility)

PubMed Feasibility Search Searched on September 19, 2018

Concept	Search Strategy
Platelet Transfusions	(((((((("Platelet Transfusion"[Mesh]) OR ((platelet[Title]) AND (transfusion[Title] OR pathogen[Title] OR bacterial[Title] OR bacterially[Title] OR contamination[Title]))))
AND	
Economic Evaluation	(((((((value[Title]) OR budget[Title]) OR economic[Title]) OR (cost[Title] OR costs[Title])))) OR ((((("Value-Based Purchasing"[Mesh]) OR "Budgets"[Mesh]) OR ("Economics"[Mesh] OR "economics"[Subheading])) OR "Costs and Cost Analysis"[Mesh]))))
Limited to last five years	Filters: published in the last 5 years
SR N=3	Systematic[sb]
RCT N=7	(((((((groups[tiab])) OR (trial[tiab])) OR (randomly[tiab])) OR (drug therapy[sh])) OR (placebo[tiab])) OR (randomized[tiab])) OR (controlled clinical trial[pt])) OR (randomized controlled trial[pt])
Other N=27	

ClinicalTrials.gov:
https://clinicaltrials.gov/ct2/results?cond=&term=platelet+AND+pathogen&type=&rslt=&recrs=a&recrs=d&recrs=e&age_v=&gndr=&intr=platelet+AND+pathogen&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&strd_s=01%2F01%2F2013&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&lupd_s=&lupd_e=&sort=