SYSTEMATIC REVIEWS OF RISK FACTORS: METHODOLOGICAL CHALLENGES AND IMPLICATIONS FOR EVIDENCE REVIEWERS

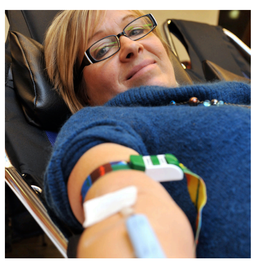
NELE S. PAUWELS[1], TESSA DIELTJENS[1], HANS VAN REMOORTEL[1], PHILIPPE VANDEKERCKHOVE[1,2] AND EMMY DE BUCK[1]

[1]CENTRE FOR EVIDENCE-BASED PRACTICE, BELGIAN RED CROSS-FLANDERS, MECHELEN, BELGIUM
[2]DEPARTMENT OF PUBLIC HEALTH AND PRIMARY CARE, CATHOLIC UNIVERSITY OF LEUVEN, LEUVEN, BELGIUM

AIM

To give an overview of the methodological challenges and implications related to the conduct of systematic reviews of risk factors.

Example §: Blood services play a critical role in healthcare by providing a safe, adequate and cost-effective supply of blood components. To achieve this, donors demonstrating certain characteristics which are considered to increase the risk of complications in either the donor or the transfusion recipient, are deferred. Therefore, systematic reviews examining risk factors for blood safety (e.g. hypotension, having tattoos, vaccination or blood disorder) are essential to set appropriate, up-to-date and evidence-based donor eligibility criteria. However, such reviews are challenging to conduct.



METHOD

Several challenges were encountered while developing a systematic review on the effect of pre-donation hypotension as a risk factor for whole blood donor adverse reactions. The challenges and implications for evidence reviewers when performing systematic reviews of risk factors are discussed here.

RESULTS

1 DEFINING THE REVIEW QUESTION AND STUDY SELECTION CRITERIA

Challenge: The review question does not completely fit the PICO format: "population", "intervention", "comparison" and "outcome", because it encompasses a risk factor instead of an intervention.

Implications for evidence reviewers: The review question should be adapted to encompass a risk factor.

Example §: In blood donors presenting for donation (population), does hypotension (risk factor) increase the risk of donor adverse events (outcome) when compared with normotension (comparison)?

2 SEARCHING AND SELECTING STUDIES, COLLECTING DATA

Challenge: Often there is selective reporting of statistically significant risk factors in the abstract of studies that investigate multiple risk factors, instead of reporting all risk factors.

Implications for evidence reviewers: The search strategy should include other risk factors than the factor of interest and general wording about risk factors. The search strategy may include general wording about the consequences of the risk factor of interest (optional). The search will reach high sensitivity but specificity will be negatively influenced.

Example §:

1. "Hypotension"[Mesh:NoExp] OR hypotens*[TIAB] OR "Arterial Pressure"[Mesh] OR "blood pressure"[TIAB] OR "systolic pressure"[TIAB] OR "diastolic pressure"[TIAB]	Terminology about the risk factor of interest
2. "first time"[TIAB] OR "Blood Volume"[Mesh:NoExp] OR "blood volume"[TIAB] OR "donor selection"[Mesh] OR "donation history"[TIAB] OR "donation status"[TIAB] OR "body weight"[Mesh:NoExp] OR "weight"[TIAB] OR "body mass index"[Mesh] OR "body mass index"[TIAB] OR "BMI"[TIAB]	Terminology about other reported risk factors than the factor of interest
3. "Risk"[Mesh:NoExp] OR "Risk Factors"[Mesh] OR risk factor*[TIAB] OR "Risk Assessment"[Mesh:NoExp] OR "predictive"[TIAB]	General wording about risk factors in general
4. "predonation"[TIAB] OR "pre donation"[TIAB] OR deferral*[TIAB] OR referral*[TIAB] OR inclusion*[TIAB] OR exclusion*[TIAB] OR "retention"[TIAB] OR retain*[TIAB] OR return*[TIAB]	Terminology about the consequences of the risk factor of interest (optional)
5. 1-4 OR	

3 ASSESSING RISK OF BIAS IN INCLUDED STUDIES

Challenge: The study designs used for risk factor analysis (e.g. cross-sectional studies) differ from experimental designs and are more prone to bias.

Implications for evidence reviewers: The body of evidence should be graded of lower quality, which reflects the confidence in our estimates of effect.

Example §: The level of evidence for hypotension as a risk factor for donor adverse events was low due to observational study designs, according to the GRADE approach.

4 PRESENTING RESULTS IN SUMMARY OF FINDINGS TABLES, INTERPRETING RESULTS AND DRAWING CONCLUSIONS

Challenge: Different approaches to control for confounding (e.g. by matching and/or by post-hoc statistical analysis) are being used. Additionally, there is often no control for appropriate confounding factors.

Implications for evidence reviewers: The results should be described in a narrative way because pooling of the data will often not be possible.

Example §: A multivariable regression analysis, accounting for multiple relevant confounding factors was performed in 2 out of 4 cross-sectional studies. Six case-control studies were identified yet they differed considerably in their design, because two studies did not control for confounding factors (either by matching or statistical analysis); one study was matched, but failed to include all relevant confounding factors in order to assess two relevant comparison groups; one study was inappropriately matched and two studies controlled for confounding by describing a statistical analysis.

CONCLUSION

The development of a systematic review about risk factors is prone to different methodological challenges including reporting issues, experimental flaws and statistical differences. This implies that systematically reviewing of risk factors is not only subjected to higher risk of bias but is also time- and cost-intensive.

Realized by the centre for EVIDENCE-BASED PRACTICE of the Belgian Red Cross-Flanders

References: § Pauwels NS, Cusack L, De Buck E, Compernolle V, Vandekerckhove P. *The effect of pre-donation hypotension on whole blood donor adverse reactions: a systematic review*. J Am Soc Hypertens 2014, 8(6):429-436.