Limitations in Reporting "Benefit-Risk" Across Therapeutic Areas in Medical Device Literature

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BACKGROUND

- Throughout a medical product's life cycle, decisions about its use are evaluated as a balance between patients' anticipated benefits and risks.
- Both qualitative and quantitative methodologies have been developed to assess benefit-risk (Table 1); however, reporting of benefit-risk assessments by medical device researchers can often be vague.

Table 1. Benefit-Risk Methodologies Identified by the Innovative Medicines Initiative (IMI) Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium (PROTECT) Benefit-Risk Group[1]

Methodology	Brief Description	Example
Descriptive framework	Qualitative or semiquantitative guidelines to conduct benefit-risk assessment	FDA BRF, PrOACT-URL, BRAT
Quantitative framework	Quantitative methods of trading risks and benefits based on mathematical principles	MCDA
Metric indices	Indices used to define thresholds (cut points), health utility, or formal trade-offs between benefits and risks	Number needed to harm, quality-adjusted life-years, incremental net health benefit
Estimation	Infer benefit-risk tradeoff based on metrics, considering evidence, data, and assumptions	Indirect treatment comparison
Utility survey	Elicit utilities and preference values (not a formal benefit-risk assessment)	Discrete-choice experiment, conjoint analysis

BRAT = Benefit-Risk Action Team; BRF = benefit-risk framework; FDA = Food and Drug Administration, MCDA = multi-criteria decision analysis; PrOACT-URL = Problems, Objectives, Alternatives, Consequences, Trade-offs, Uncertainty, Risk attitudes, and Linked decisions.

OBJECTIVE

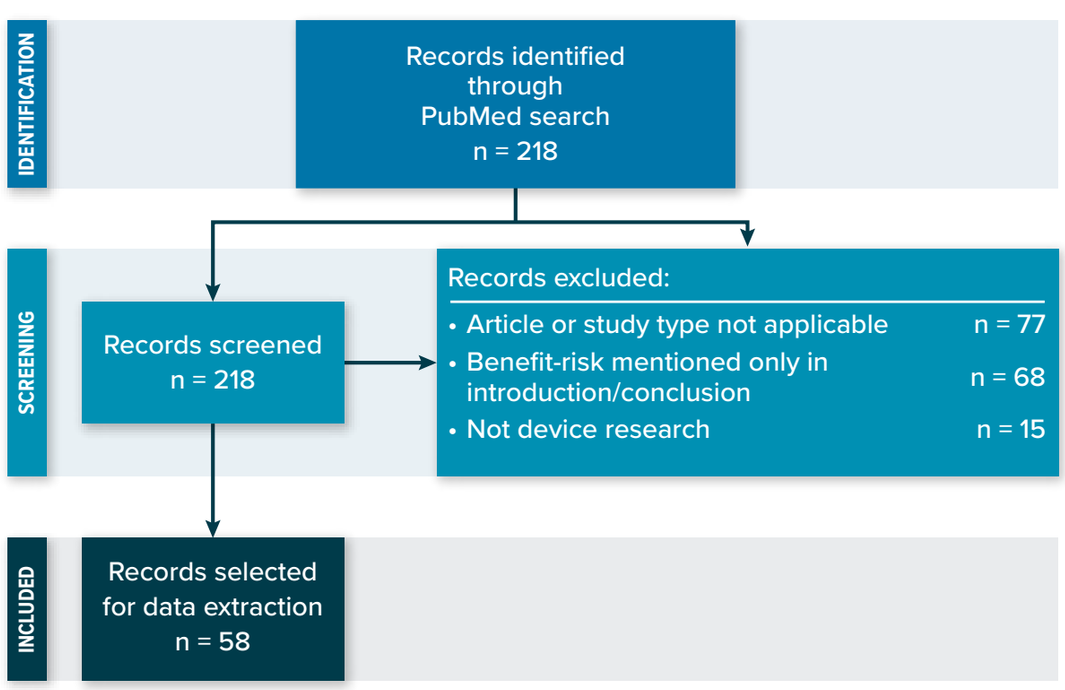
- This literature review aimed to evaluate the medical device literature and evaluate how benefit-risk is reported across therapeutic areas.

METHODS

- Using MeSH terms for a broad capture, PubMed was searched for English-language articles published between 2008 and 2017 in which IMI-PROTECT benefit-risk methodologies were employed for medical devices.
- Titles and abstracts were reviewed to identify relevant articles.
- For the articles selected for inclusion in the review, data were extracted from the abstract only.
- We analyzed the methodological framework used to describe differences in approaches across therapeutic areas.

RESULTS

Figure 1. PRISMA Flow Diagram for Article Screening



Therapeutic Areas

- Predominant therapeutic areas for the 58 selected articles were cardiovascular (CV, 50%) and oncology (10%). Less common other therapeutic areas (OTAs, 40%) included injury/poisoning/procedural complications (n = 4), endocrine disorders (n = 3), eye disorders (n = 3), nervous system disorders (n = 2), respiratory/thoracic/mediastinal disorders (n = 2), surgical/medical procedures (n = 2), musculoskeletal/connective tissue disorders (n = 2), gastrointestinal diseases (n = 1), blood/lymphatic system (n = 1), renal/urinary disorders (n = 1), and metabolism/nutrition disorders (n = 1).

Determining Methodology

- Due to the limited details described within the abstracts, benefit-risk methodology (e.g., PrOACT-URL, MCDA) had to be inferred for most of the abstracts (91%) or could not be determined (2%).
  - Of the 4 abstracts that sufficiently described methodology to define the benefit-risk framework, 3 were CV studies (10% of the 29 selected CV studies) and 1 was an OTA study (4% of all OTA studies).
  - No oncology study sufficiently described the benefit-risk methodology; the framework was inferred for all oncology studies.

Benefit-Risk Assessments

- Most abstracts (n = 44, 76%) used descriptive frameworks; 13 (22%) were quantitative (Figure 2 and Table 2). (The framework could not be determined for one abstract.)
  - Two of the 6 oncology studies (33%) described quantitative frameworks, compared with 5 of the 23 OTA studies (22%) and 6 of the 29 CV studies (21%).
- Five oncology studies (83%) used data from registries, cohorts, or chart reviews, which was more frequent than in CV (n = 21, 72%) and OTA (n = 13, 57%) studies. No oncology studies claiming to assess benefit-risk were randomized trials, while 20% of CV and 10% of OTA studies used randomized designs (Figure 2).
- The publication's target audience was most often clinicians and regulators for CV (66%) and OTA (57%) studies; for oncology studies, the audience was most often clinicians only (67%) (Figure 3).

Figure 2. Therapeutic Area and Type of Benefit-Risk Analysis Reported or Inferred (Left) and Therapeutic Area and Study Type (Right)

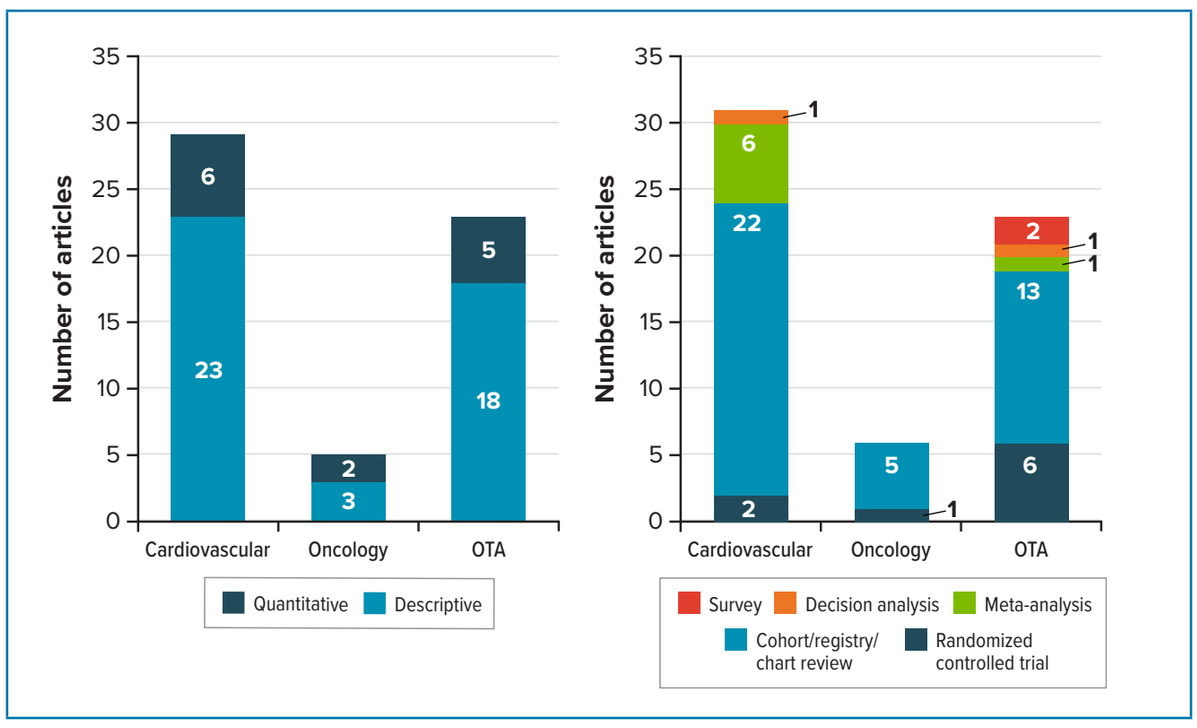
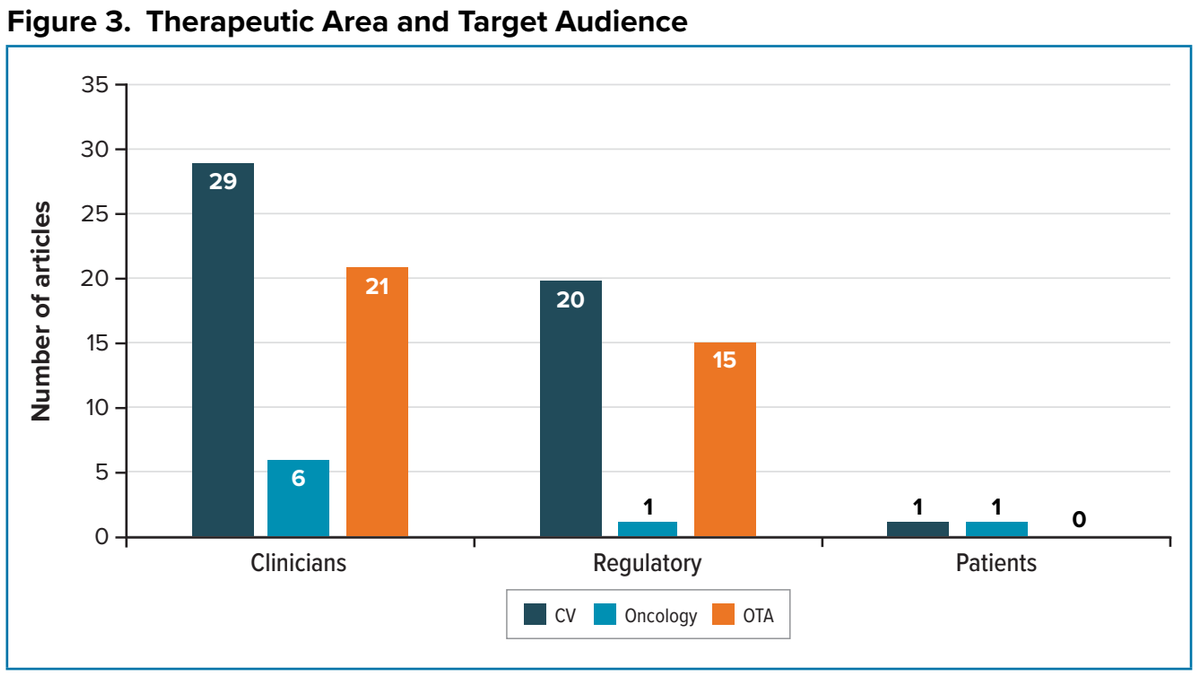


Table 2. Specific Frameworks by Therapeutic Area

	Framework	Total	CV	Oncology	OTAs
Descriptive frameworks	Unspecified framework	**40**	20	3	17
	PrOACT-URL	**3**	2	0	1
	ASF	**1**	1	0	0
Descriptive frameworks	Net clinical benefit	**5**	3	1	1
	MCDA	**4**	2	1	1
	Markov	**2**	0	0	2
	BLRA	**1**	0	0	1
	Decision tree	**1**	1	0	0
Unknown	Unknown	**1**	0	1	0

ASF = Ashby and Smith framework; BLRA = benefit-less-risk analysis.

Figure 3. Therapeutic Area and Target Audience



DISCUSSION

- This review of published articles' abstracts suggests that the term benefit-risk is used broadly across medical device publications, with little context given to methodology.
- Oncology studies most often employed quantitative frameworks.
- CV studies provided more study design information, were more often randomized (vs. nonrandomized) studies, and more often employed descriptive methodologies.

CONCLUSIONS

- The lack of detail included in article abstracts limits clarity regarding which benefit-risk assessment was conducted.
- Differences observed across therapeutic areas further limit interpretation.
- There is a need for improved standardization in reporting benefit-risk assessments for medical devices overall and across therapeutic areas to facilitate readers' understanding and interpretation of results.

REFERENCES

1. IMI-Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium (PROTECT) Benefit-Risk Website, Methods Classification. Available at: http://protectbenefitrisk.eu/methods.html. Accessed May 31, 2018.

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Presented at: 34th International Conference on Pharmacoepidemiology & Therapeutic Risk Management; August 22-26, 2018; Prague, Czech Republic