EVERSANA®

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SINGLE-ARM DATA:

Turning Limitations into Strengths with Numbers

Randomized controlled trials (RCTs) are at the top of the evidence pyramid because they are designed to be unbiased. Unfortunately, for many medical devices, these types of studies are lacking. This is either because they are not required for 510K or post-market approval (PMA), or there are challenges with implementing a randomized study design. Clinical studies without a control group, otherwise known as single-arm studies, have become "the norm" for many device categories. For example, in the oncology space, there are hundreds of uncontrolled studies evaluating thermal ablation technologies! Drug-eluting stents are another category with a wealth of non-comparative data informing the coronary disease treatment space. However, any one of these individual studies alone may be viewed as biased, too small in sample, or minimally informative without a control group. How should medical device manufacturers therefore best make use of high volumes of single-arm data if they do not have adequate controlled studies?

The answer lies in the application of high-quality, state-of-the-art statistical techniques. The external control arm, where patient data from a separate registry or database are carefully matched with data from a single-arm study, is one solution. However, several other strong solutions can be applied, especially when a large volume of such studies have been published. In fact, many of these studies can be non-interventional and therefore observational in nature. The right statistical methods can leverage these to ensure a strong and robust real-world data set to inform regulatory or healthcare decision-making.

But what does this involve...?

A backbone of traditional systematic literature review (SLR) with meta-analysis is central to the solution. These methods are applied to single-arm data for a medical device, or device class, and its comparators, in a defined therapeutic area. Methods of PRISMA should be closely followed where possible with statistical techniques expanded for this unique focus. Of critical importance is the extraction of key patient characteristics to inform analyses that limit the impacts of confounding. Single-arm meta-analyses can be conducted as a first step to estimate approximate effect sizes, but particular care must be taken not to indirectly compare these estimates without statistical techniques. Various methods can then be applied to better understand device performance and leverage comparisons. These methods can include:

- Single-arm multivariate meta-regressions including treatment as a covariate
- Bayesian meta-analyses with treatment ranking
- Propensity-score matched simulated comparative studies

There is no one-size-fits-all approach! Methods of choice depend on many factors and careful evaluation of the approach is necessary to understand the right fit.

What are some examples of use-case scenarios?

- Conducting a comparison of technologies never compared in head-to-head trials
- Achieving a better understanding of which subgroups respond better to treatment
- Informing discussions with FDA on label expansion opportunities
- Creating awareness on wealth of data available for a device through publication
- Informing future trial design with pooled estimates for performance benchmarks

Why choose EVERSANA?

EVERSANA's Value & Evidence team has extensive experience conducting SLRs and meta-analyses, supporting strategy, and providing world-class statistical solutions. George Wright, Manager, HEOR, EVERSANA, Nicole Ferko, Vice President, EVERSANA, and Tim Disher, Senior Director, EVERSANA led several studies on this topic. Here are some examples:

- 2022 abstract and poster: P. Laeseke, C. Ng, N. Ferko, A. Naghi, G. Wright, Y. Zhang, I. Kalsekar, B. Laxmanan, S.K. Ghosh, M. Zhou, P. Szapary, and M. Pritchett. Overall Survival Associated with Image-guided Thermal Ablation (IGTA) and Stereotactic Body Radiation Therapy (SBRT) for Patients with Non-Small Cell Lung Cancer: A Systematic Review and Meta-Regression Analysis. Am J Respir Crit Care Med May 1, 2022, 205:A2354. https://www.atsjournals.org/doi/10.1164/ajrccm-conference.2022.205.1_MeetingAbstracts.A2354
- ATS 2023 abstract and poster: Rajaram, Q. Huang, R.Z. Li, U. Chandran, Y. Zhang, T. Amos, G.W.J. Wright, N.C. Ferko, I. Kalsekar. Recurrence-free survival (RFS) in Surgically-resected Non-small Cell Lung Cancer Patients – A Systematic Literature Review and Meta-analysis. May 19-20, 2023.
- CHEST 2022 abstract and podium presentation: A. Naghi, P.F. Laeseke, C.S.H. Ng, N. Ferko, Hall, G.W.J. Wright, Y.Y.Z. Zhang, I. Kalsekar, B. Laxmanan, S.K. Ghosh, M. Zhou, P.O. Szapary, M.A. Pritchett. Outcomes of Image-guided Thermal Ablation (IGTA) and Stereotactic Body Radiation Therapy (SBRT) for Patients with Pulmonary Metastases: A Systematic Review and Meta-Analysis. Chest 2022 162(4): Supplement A1626-A1627. https://journal.chestnet.org/article/S0012-3692(22)02724-6/fulltext
- SIO 2023 abstract and poster: A. Talenfeld, A. Lansing, N. Ferko, G. Wright, S. Ghosh, S. Raza, I. Kalsekar, I. Emam, Y. Zhang, T. McClure. A Comparison of Microwave Ablation and Cryoablation for the Treatment of Renal Cell Carcinoma: A Systematic Literature Review and Meta-Analysis. SIO January 19-23, 2023.
- Jaff MR, Nelson T, Ferko N et al. Endovascular Interventions for Femoropopliteal Peripheral artery Disease: A Network Meta-Analysis of Current Technologies. J Vasc Interv Radiol 2017; 12: 1617-1627. https://pubmed.ncbi.nlm.nih.gov/29031986/

Advanced statistical techniques are powerful and cost-effective tools for enhancing the evidence to support market access activities, messaging, and claims for medical devices where high-quality comparative data are limited. These tools need to be considered when generating evidence plans for medical devices. Ultimately, these methods allow stakeholders to be better informed for their decision-making to support the right treatment for optimizing patient care.