How Can Literature Reviews Inform Evidence Planning?

Teresa Wilcox, PhD, Senior Research Leader; Clark Paramore, MSPH, Senior Research Scientist, Health Economics and Epidemiology

If you're charged with creating a plan to gather the evidence you need to support a product, you know that evidence planning activities occur at a variety of levels within your organization. In some organizations, a cross-functional team will work together on a plan, and in this case, the evidence needs of various decision makers (represented by members of the team) can be considered together. In other organizations, each of the internal stakeholders has to create a separate plan specific to his or her area of responsibility. Regardless of who is doing the planning, the goal is to generate and communicate the best evidence to support the product. This package of evidence must meet decision-makers' requirements and expectations for demonstrating the product's value. Different decision-makers need to see different types of evidence; for example, regulators may focus on key endpoints for measuring treatment effect, while payers may focus on how the product addresses unmet needs in their population.

Fundamental components of a product's evidence package will come from a review of the scientific literature. For good reason, this is often the first step in developing an evidence plan, and a step that needs to be considered carefully to maximize its value. Traditionally, a literature review is commissioned for a specific research question at an ad-hoc time during the development process, such as when a publication is needed to define burden of illness. But literature reviews should be considered an integral part of the entire process as they can help with so many other types of evidence generation activities, including:

- Early in development, to characterize epidemiology of disease, understanding of current treatment patterns, burden of illness, and unmet needs
- Prior to full development, to systematically review the literature to inform the clinical development program, provide inputs for economic models, and refine understanding of evidence gaps
- In preparation for submissions, to refresh the systematic review to meet requirements for submissions, and derive inputs for indirect/mixed treatment comparisons
- Post-launch, to gather new evidence to inform ongoing promotional efforts

The principal goal of any evidence generation plan is to ensure that the appropriate evidence is delivered to the appropriate stakeholder (audience) at the right time, using the optimal scientific/methodological study designs and considering the constraints of timelines and budget. An evidence generation plan begins by assessing the landscape of the disease (or diseases) for which a product will be indicated. This landscape assessment takes into consideration types of information/data that are typically proprietary to a manufacturer including market share and prescription refill data, payer and provider research, advisory boards and primary research studies. Components of a landscape assessment can also be addressed with a review of the literature to investigate the following:

- Guidelines
- Unmet need associated with the condition
- Thresholds representing meaningful treatment effect
- Treatment patterns
- Health Technology Assessments (HTAs)
- Data currently supporting the value of competitors
- Evidence needs for the product to gain market access, including regulatory hurdles
- Evidence to differentiate the product from competitors
- Data gaps for the product

Informed by these data from the literature, a plan can be developed to bolster the evidence for the value proposition of the product with studies that will fill in the rest of the picture. For example, a drug that in published

studies offers no greater efficacy than current therapies, but is more easily administered and tolerable, should have adequate support from studies of patient-reported outcomes. A drug with a likely role as second-line or adjunct therapy that studies show also offers some efficacy against common comorbidities will benefit from studies conducted in comorbid populations. A therapy that is expensive, but easily distributed, may be more cost-effective in an economic model than an equally effective, inexpensive therapy with complex distribution and monitoring requirements.

With an understanding of the purpose of reviewing the published literature, it is possible to choose the right type of review to conduct.

- A systematic review is the "gold standard" for demonstrating the most comprehensive assessment of the evidence and a study in itself. This design finds every publication that meets a predefined set of inclusion and exclusion criteria. Because of its completeness, it is the optimal literature review design for submissions and for publication; for clinical topics, a meta-analysis may be possible and desirable to show efficacy and safety.
- When a review is being written to inform internal decision-makers, find model inputs, or populate a dossier, and not for submissions or publication, it may not be necessary to spend the time and money on a systematic review. A targeted or narrative review may yield the necessary information in a faster timeframe and with a smaller budget.
- A composite review, covering one narrow topic systematically and the rest of the topics of interest with a targeted/narrative approach, can save time and money over a full systematic review while still enabling some of its uses. The targeted/narrative portion of the review can be tailored to meet the budget and timeframe constraints of the project, while the systematic portion can be used for dissemination and submissions.

The proper review of the published literature done at the outset of an evidence generation plan will yield important guidance for the plan, which in turn will determine when to conduct additional literature reviews. Planning ahead allows efficiencies, because each literature review can gather information needed for multiple activities. For example, the review done at the beginning of value development can provide necessary background information such as epidemiology, current guidelines, current treatment patterns, and unmet needs. Another review done prior to construction of an economic model might inform choice of variables, derive model inputs, and yield cost and utilization data. During clinical use of a drug, pharmacovigilance studies can sweep the literature for reports of adverse effects and their circumstances.

Literature reviews are an integral component of any evidence generation plan. With 1) a clear description of unmet needs in the disease area, together with 2) a well-considered picture of how the product is likely to be able to contribute to reducing unmet needs (from the target product profile, value statements, and early clinical results), and 3) feedback provided by regulators, payers, HTA agencies, prescribers, and patients on the relative importance of each attribute (how the product reduces unmet needs), a manufacturer can then develop a focused and cost-effective evidence generation strategy.

For more information, please contact Teresa.Wilcox@evidera.com or Clark.Paramore@evidera.com.