

The Increasing Use and Importance of RWE

A Q&A With Faith Davies, MD, MRCP, MRCPATH, FRCPATH



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The American Journal of Managed Care® (AJMC®): In general, how important is real-world evidence (RWE)?

DAVIES: RWE is becoming more and more important. I think it was often previously treated as soft data. At the moment it hasn't reached the same level of importance as randomized phase 3 studies, but it's clearly becoming more important, so much so that the regulatory authorities are now paying attention to it and are asking for it to help support the drugs' effectiveness in the general clinical setting.

AJMC®: How does RWE complement randomized clinical trial (RCT) data?

DAVIES: For RCT data, we are essentially looking to see the efficacy of the drug: "Can it work? Is it better than the previous standard therapy?" These kinds of studies are performed in a very controlled environment. I would argue that real-world data are different. Rather than asking, "Can it work?" RWE is asking, "Does it work? What's its effectiveness?" What happens in the general clinical setting? It is efficacy versus effectiveness. For cancer trials, it's generally a small percentage of patients who actually make it into a cancer study. It is somewhere less than 5% of patients, so we need to have some way of ensuring that the data we're taking from our clinical trials show how it actually works for the other 95% of patients who haven't had the opportunity to take part in those studies. I would argue that the question is, "Can it?" versus "Does it?"

It is definitely important to have both RWE and RCT data because of the 95% of patients who are not in the initial studies for various reasons. Some of our patients in clinic will be very similar to those patients in the initial studies, but many of them will have unfortunately been excluded for reasons that are common in general patient populations. It's important to know that the drug is effective in these excluded patients as well.

AJMC®: How widespread is the use of RWE at your institution?

DAVIES: I'm fortunate that my institution is making a real move forward to look at real-world data. There's a lot of background work going on at the moment to enable the IT [information technology] infrastructure to be able to work through electronic medical records (EMRs) in a research capacity that's HIPAA [Health Insurance Portability and Accountability Act] compliant and is not going to be causing any confidentiality breaches. To date, most of the existing real-world data have been collected via registry databases that people have developed; some of those have been academic registries while others have been clinical trial registries or registries developed by nonprofit organizations. Another good source of real-world data is billing and insurance claims databases.

To some extent, true real-world data are from the EMRs. There have previously been a lot of small studies, but I now think that many hospitals and academic institutions are embracing RWE and are embracing technology that enables people to determine how their own practice is comparing with randomized clinical trials and with other available data sets. I think that's a good thing.

It is a good auditing tool and it helps move research and patient care forward. It's always important to make sure that what you think you're doing is actually what you're doing and to know the outcome of your interventions.

AJMC®: How can RWE best be used?

DAVIES: Within my disease space, it is becoming increasingly used to aid patient and doctor decision-making and from a regulatory perspective. We are finding that the number of uses is increasing, and therefore having RWE available to the community and having it talked about are very important.

For example, a number of nonprofit patient organizations now offer patients the opportunity to put their data into a database. Patients can then search for other patients like them. For instance, if they're starting on a new regimen, they can search to see what other patients have experienced in terms of adverse effects and how they managed them. It's not just for physicians and pharmaceutical companies; the patient side of things is important too.

From a regulatory perspective, it's key because, unfortunately, many of our drugs are very expensive, so having real-world data enables a further judge of quality and value. The benefit of the drug for the patient is sometimes easier to see in a real-world data set because you can often look at changes in frequency, delays, and time on therapy. You can also look at tolerability with respect to how long a patient stays on the drug or whether the doses of the drug are changed. A great example of this is Velcade [bortezomib]. Originally, all the clinical studies have the dosing schedule as days 1, 4, 8, and 11 of a 21-day cycle; whereas in the real world, we use it once every week so that adverse effects for patients, such as neuropathy, are much less. The tolerability is much better, and the efficacy is much better. We therefore learn a lot from looking back at those real-world data as far as how we can best treat our patients. Getting the messages out there about its importance is good. For the regulatory authorities, thinking about RWE data in the same sphere as phase IV data, ie, additional data on safety and effectiveness, is key too.

AJMC®: Are there potential concerns regarding the use of RWE?

DAVIES: There's still some skepticism around the control and the authenticity of the data. The only potential way to overcome this is to start using it and to test it against known standards. I think of RWE like phase 4 clinical study data. We often learn a lot from phase 4 studies, especially about safety, whereas RWE is more about treatment effectiveness

in the wider population. RWE is important because we are taking a wider patient group into consideration, which may not be the ideal patient population that was placed in the clinical trial. We have patients in the real world who have comorbidities or other issues going on; we are embracing this because the real-world data may reflect the general patient population more so than that ideal RCT group.

AJMC®: What are some examples of how RWE can be useful in the RRMM population?

DAVIES: Patients with relapsed-refractory myeloma tend to be slightly older and often have comorbidities. There have now been a number of studies where [investigators] have used their registry data to say, "Looking through my registry data, how many of the patients in my EMRs would make it into one of the randomized clinical studies?" The reality is that anywhere between 20% and 60% of patients would not make it into one of those clinical studies. That is usually because of comorbidities; it might be performance status, cardiac issues, or kidney issues. Many of these comorbidities may not be high-grade or complicated, but they take many patients out of that standard category of trial patients.

In addition to patients being excluded from clinical trials based on comorbidities, a number of groups of patients are often not well represented in our clinical trials. Examples include patients who are frail and older or patients from racial minority populations. This highlights that some practical reasons such as travel or distance to the trial site and socioeconomic factors are just as important as comorbidities. In addition, we know that hypertension and diabetes are often higher in African Americans. While those are not an issue with trial entry per se, these conditions must be well controlled to be able to get into the clinical study. Therefore, this often makes it more difficult for patient groups such as African Americans or the elderly or frail population to enter into a trial.

Having RWE data are key because they guide everyday clinical practice more than just stating whether the treatment works. It's helpful for when you have a typical patient sitting in front of you in clinic to think, "What do the real-world data tell me? I know my clinical trial tells me this should work, but when I look at typical patients, is it going to work?" People are often afraid that the clinical trial data won't be reflected in the normal everyday situation. There are now quite a few studies showing that the drugs sometimes work better or at least equally effectively when you have them in this wider group than they do just with patient groups in the clinical trial. ♦