



# Validating Questionnaires

As we all know from political polls, the answer you get depends very much on the question you ask. In order for a questionnaire to be useful, the data it produces must be trustworthy, i.e., we must know that the results are meaningful and can be applied more generally than to just the sample tested. Proving that trustworthiness for questionnaires involving subjective clinical endpoints is not trivial, and ensuring that the resulting data reflect the “truth” has spawned an entire field of study. This article will provide some insight into what that process entails and why it is important.

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The term “validation” has a variety of meanings in clinical research, the first and most obvious being the assessment of computer systems to ensure they function as expected. “Validation” is also the process by which any data collection instrument, including questionnaires, is assessed for its dependability. Validating questionnaires is somewhat challenging as they usually evaluate subjective measures, meaning they can be influenced by a range of factors that are hard to control. In other words, a blood pressure machine can be assessed for accuracy and calibrated to ensure consistent readings. Obviously the SF-36 quality of life questionnaire cannot be similarly assessed. That said,



there are ways to evaluate the value of, or validate, a questionnaire. Validation involves establishing that the instrument produces reliable and true data.

There are a number of ways to define this, some of which are outlined below:

**Reliability:** the degree to which a questionnaire will produce the same result if administered again, or the “test-retest” concept. It is also a measure of the degree to which a questionnaire can reflect a true change.

**Validity:** the degree to which a questionnaire reflects reality. There are a number of different facets to validity.

**External validity:** the ability to make generalizations about a population beyond that of the sample tested.

**Internal validity:** the degree to which questions within an instrument agree with each other, i.e., that a subject will respond to similar questions in a similar way. It also affects the likelihood of producing false positives and false negatives.

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# Fun Pharma Facts

Did you know?

“Eat! Eat! Eat! And always stay thin!” That is, if you are willing to house a wriggling tapeworm in your bowels.

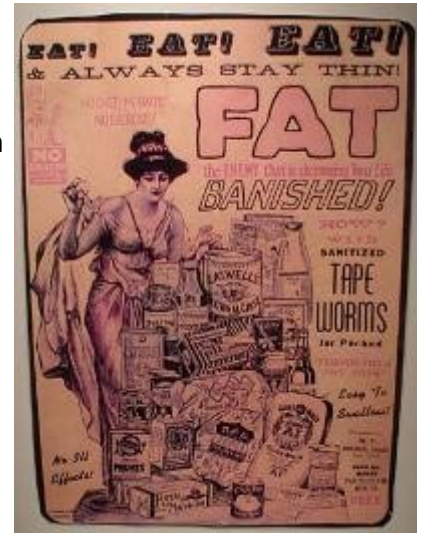
Advertisements for tapeworm pills first emerged in the 1920s. The Tapeworm Diet involved the intentional consumption of tapeworm eggs. You get to keep your trim figure, while the tapeworm gets most of the nourishment you consume.

Does the Tapeworm Diet Work?

This is the question that some people are most interested and in terms of weight loss, yes, the tape worm diet does appear to have some success with quick and significant weight loss. But not only does tapeworm infestation have its own serious health effects, and this really does mean serious, it can also cause abdominal distention, not exactly the look most dieters are going for. Which, when you think about it is an obvious side effect from having a 20 foot long worm curled up in your intestines.

While this diet should have died a long time ago, it made on appearance on the Tyra Banks show in 2009. The aim was not to promote the tapeworm diet, it was quite the opposite. A group of dieters spoke of their experiences and a doctor brought samples of some flat long tapeworms to the show and discussed the worm while the audience and Tyra Banks squirmed.

Courtesy of the Tyra Banks show and the Museum of Quackery



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**Sensitivity:** the degree to which the instrument can identify a true positive, e.g., accurately identify a person who does have the condition.

**Specificity:** similar to sensitivity, this is the degree to which the instrument can identify a true negative, e.g., correctly identify the people who do not have the disease. Sensitivity and specificity are another side of the coin from internal validity.

**Statistical validity:** this is related to internal validity, and assesses whether the differences in the questionnaire results between patient groups can appropriately be subjected to statistical tests of significance.

“Validity” is not an absolute quality. It’s a continuum, with a questionnaire being valid to a certain degree in certain circumstances, and researchers must decide what degree of validity is considered sufficient, preferably before the validation study is run. The above categories also suggest that there are types of validity that relate to the internal validity of the questionnaire (are similar questions answered similarly), others that relate to the ability of the questionnaire to determine a given state in a patient (e.g., that it varies in alignment with the severity of the condition), and still others that involve the validity of comparing different groups on the basis of the questionnaire. Each type of validity is distinct, meaning that a questionnaire can have one kind of validity but not another. Because of that, a questionnaire can never really be fully “validated.” It can only be validated for x patient population, under y conditions, and so forth. This implies that it may not be appropriate, for example, to use a lymphoma quality of life questionnaire in a melanoma study if the questionnaire hasn’t been validated for that particular population, unless it has been shown to be applicable to cancer patients generally.

The validity of the results can be impacted by more than just the design of the questionnaire itself. Some questionnaires must be administered by individuals who have been trained in survey administration in general or that survey in particular. Others can be administered by any experienced clinician, or nurse, or indeed completed by the patient. If an otherwise valid questionnaire is administered by the wrong individual, the results are compromised. Similarly, some instruments must be used in their original published form, and changing the layout to create a CRF may compromise the results. Results can also be compromised if the questionnaire is not completed at the expected times (either time or day or relative to some other event) or in the right setting.



The process of validating an instrument varies depending upon what aspect(s) of validity are being assessed. Generally it involves running a study that is designed to determine a specific kind of validity, al-

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# A Transformative Year

Kit Howard talks about why she is joining the many women and men taking part in the Susan G. Komen 3-Day For The Cure walk this August.

"I joined the 3 day walk for two reasons. I am honoring my mother, several friends and others who had or have breast cancer, some of whom are still fighting, and sadly some of whom finally succumbed. One person dies every 69 seconds from this terrible disease.

"In addition, in May 2012 I turn 50. I am incredibly grateful that I have not been one of the unlucky ones to have had breast cancer. In the months between now and then, I intend to transform myself into the physical, psychological, professional, academic and financial person I want to be for my second half century so that I can continue to work to support the best clinical research we can do. This walk is the beginning of that commitment."

The Susan G. Komen 3-Day for the Cure® is a 60-mile walk over the course of three days. Net proceeds from the 3-Day for the Cure are invested in breast cancer research and community programs. If you would like to make a donation you may do so at <http://www.the3day.org> and search for Kit Howard.

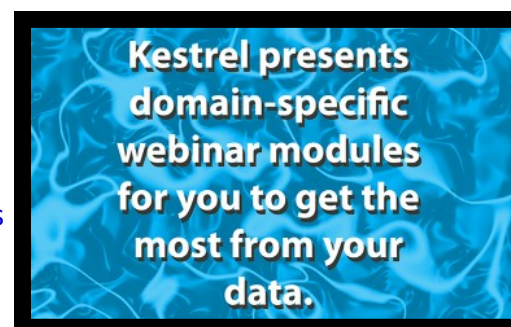


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**Description:** Adverse events are key data in virtually all clinical trials. Understanding the concepts and their application is critical to ensuring subject safety. This module explains the different types of AEs, the expected variables and how they should be structured. Elements of pre-approval drug and device studies are discussed.



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From time to time, Kestrel receives emails for employment opportunities and we decided some time ago that it would be a great idea to pass them along to our colleagues. If you can't benefit from this, but you know of someone who could, please forward them.

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**Senior Clinical Data Manager (CDM)** - We are looking for a highly motivated individual in the Detroit area to perform or coordinate all data management activities for government funded and commercial projects conducted in-house and outsourced in accordance with regulatory and company standards. The Senior CDM works with a project team made up of Project Management, Information Technology, Statistics and Data Management to ensure completion of project priorities in accordance with the study protocol and timeline. The Senior CDM also mentors clinical data management staff, oversees data entry staff and is available to assist the Data management department or assigned project teams when requested. For more information, please contact Kim Carney, Recruiter for Human Capital Staffing at [kcarey906@hotmail.com](mailto:kcarey906@hotmail.com)



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though it is sometimes possible to add a validation arm onto a trial with other primary objectives. One way to check the validity of a questionnaire is to compare its results with results from more objective measures. For example, a questionnaire assessing a patient’s perception of their chronic obstructive pulmonary disease (COPD) may be compared to measures of their lung function, and the results of each compared



between groups of healthy subjects and ill patients. If the instrument has appropriate specificity, sensitivity and discriminant validity, one should see a good correlation between the lung functions of the more severely ill patients and “worse” scores on the questionnaire. The degree to which the differences in the scores vary in alignment with the lung function tests across the healthy and ill subjects is the measure of the validity of the instrument at identifying patients who have COPD.

If this same questionnaire was developed in the US in English, and researchers wanted to use it in Italy, it would need to be translated into Italian. The Italian version would then have to be tested to see whether it varied with degree of illness in the way the English one did, or at least in a reliable and predictable fashion. Of course, there may be cultural differences that may require changing the content of the instrument. “Walking the length of a city block” is generally understood in the US, but the concept is meaningless in rural France.

Establishing longitudinal validation is particularly relevant to clinical trials, in that determining the degree to which the use of an instrument repeatedly in a study affects the instrument results. On the one hand, in order to be able to draw conclusions from the results, the same instrument should be used throughout the study. For that to work it must be longitudinally valid. There is a well documented test-retest effect, however. The first time a subject completes a given questionnaire the results are independent. After that, the subject is no longer naïve to the questions, and their answers in the second questionnaire may be influenced by their memory of their prior experience. Part of the process of validating instruments used over time is statistically evaluating that relationship.

**Fan Forum!**

“Kit Howard's experience and input has been invaluable in helping us to focus on the things that matter most and in organizing our efforts in a coherent way.”

**Dr. Mike Poole**  
After Wyeth’s implementation of Kestrel’s Data Lifecycle Plans®

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# Consultant's Corner

In every issue, we highlight members of our consulting community by listing their company's name, contact information and specialty. The goal is to present our readers with a resource to utilize if and when a consultant's expertise is needed.


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There are many cases in clinical research where no validated instrument exists for a given disease or population. That doesn't mean that the disease can't be assessed, or that questionnaires cannot be used. The protocol authors must decide how important that objective is to the study, and whether it is acceptable to have less trustworthy results for that objective. It suggests that unvalidated instruments should probably not be used for key efficacy or critical safety assessments until appropriate validation studies have been conducted. Alternatively, the company can consult with the regulatory au-

thorities to ensure their acceptance of the instrument prior to submission of the New Drug Application.

As with so much in clinical research, there are no black and white rules where it comes to assessing the reliability and validity of questionnaires. Each product development team must determine their study objectives and the best way of achieving those objectives. If that includes the use of questionnaires, they will need to assess what type and level of validation is sufficient for their purposes. As data managers, we can play a role in ensuring that those discussions happen before the study starts and it's too late to change.

**References**

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