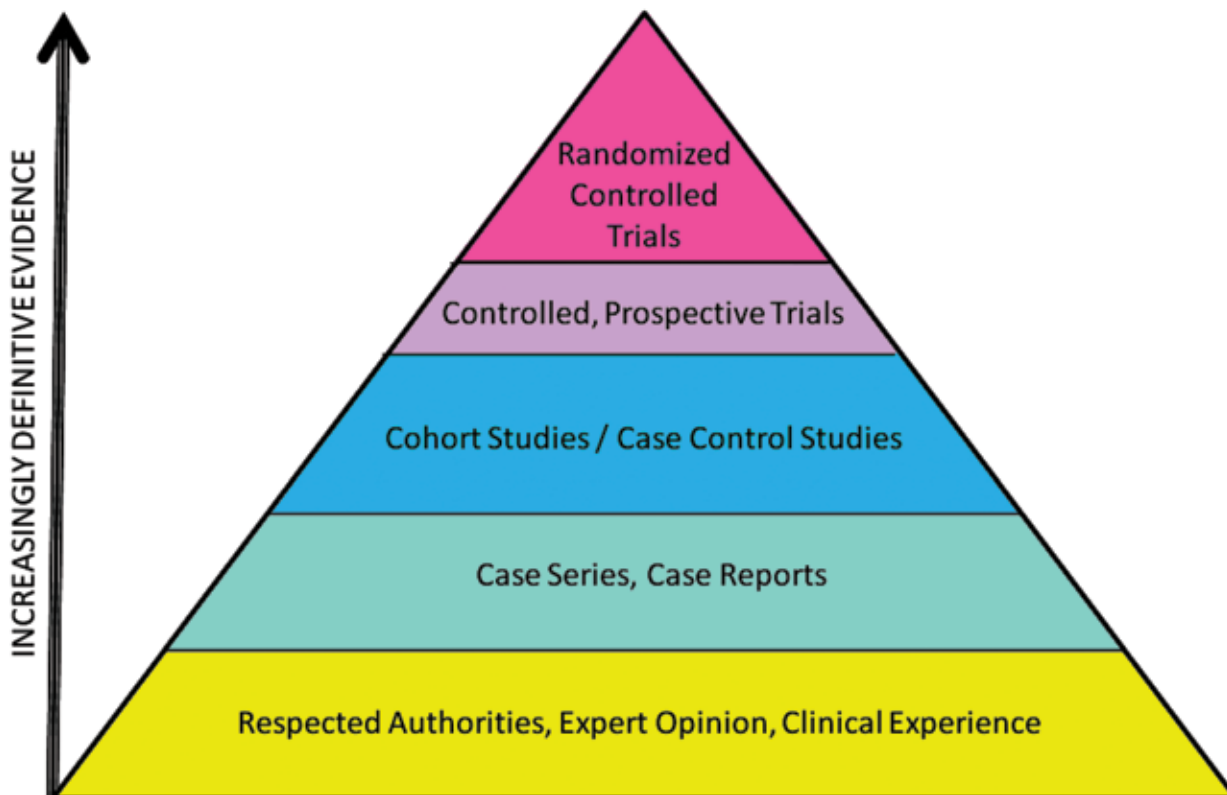


# LEVELS of EVIDENCE

By William Cavanagh

Not all evidence is created equal where the science of medicine is concerned. The U.S. Preventive Services Task Force, among others, has developed a set of guidelines that allow the categorization of information (or “evidence”) that is typically used to recommend for or against a specific path of treatment, diagnosis, screening, or related medical intervention.

These guidelines summarize “Levels of Evidence” of a scale of I to III, with Level II containing three sub-scales. These definitions allow for the evaluation of studies in such a way that some carry more weight than others.



- **Level I:** Evidence obtained from at least one properly designed randomized controlled trial.
- **Level II-1:** Evidence obtained from well-designed controlled trials without randomization.
- **Level II-2:** Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
- **Level II-3:** Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.
- **Level III:** Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

(From U.S. Preventive Services Task Force. 1996. *Guide to Preventive Services*. 2d ed. Baltimore, MD: Williams and Wilkens.)

# PCRI Insights

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## Prospective (“forward-looking”) study:

A study in which the key study elements, including hypotheses, the type of patients to be studied, the exact nature of the study treatment or diagnostic process, and the type of data analysis to be employed are all specified in advance of the study start. Data is collected as indicated in the study plan.

## Retrospective (“backward-looking”) study:

A study in which data is accumulated from existing records. With the exception of the retrospective case-control study, there is usually no control group for comparison; generally thought to be fraught with difficult-to-detect selection biases that weaken the inferences drawn from the data.

**Randomized trial:** A prospective study in which subjects who meet criteria for entry to the study (disease status, previous treatments, etc.) are assigned to a treatment arm or control arm on the basis of the flip of a coin, random number generator, or other randomization technique. Randomization prevents selection biases and other confounding factors from influencing the outcome of a study.

**Well-designed controlled trial:** A study that is conducted prospectively and that includes experimental (the process being studied) and control groups – but no randomization.

**Cohort study:** Typically a report detailing a large, consecutive group of subjects who all underwent the same intervention (treatment or diagnostic process); usually retrospective.

**Case-control study:** A retrospective study comparing a group of subjects who undergo a certain intervention (as with a cohort study) and a similar group who did not undergo the intervention, where each subject in the intervention group is “matched” to a subject in the control group on the basis of disease characteristics, previous treatments, etc.

**Time series / case series:** Generic terms for un-designed, small retrospective studies that describe the effects of a particular intervention but do not utilize controls or other techniques of more sophisticated studies.

What might surprise many prostate cancer patients is the fact that little, if any, of the evidence used to recommend treatment for localized prostate cancer achieves the status of Level I “proof”. Although few would question that interventions such as surgery, radiation, hormonal therapy, and cryotherapy benefit a significant proportion of prostate cancer patients, there has never been a study in the U.S. of the highest standard (the randomized controlled study) that demonstrates the case for intervention unequivocally. (The Prostate Cancer Intervention Versus Observation Trial [PIVOT<sup>1</sup>] is ongoing and its results will be closely watched).

We do, however, now have the results of two randomized controlled studies seeking to settle the vexing question over the value of screening healthy populations of men for prostate cancer using serum PSA testing. Although these studies are of historic significance in terms of providing “Level I” evidence to the debate, even the best-designed and intentioned study may fail to provide the foundation for crystal-clear conclusions (see “What Do We Know About PSA Screening Now That It’s 2009, page 2”).

1. Wilt TJ, Brawer MK, Barry MJ, et al. The prostate cancer versus observation trial: VA/NCI/AHRQ cooperative studies program #407 (PIVOT): design and baseline results of a randomized controlled trial comparing radical prostatectomy to watchful waiting for men with clinically localized prostate cancer. *Contemporary Clinical Trials* 30:81-87, 2009.