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## NEGLECTED ASPECT OF WHI STUDY

Since first publication in 2002, WHI has changed the way we think about and use HRT in the postmenopausal female [1]. The study has also been criticized and alternative explanations offered [2-4].

In 1934, Karl Popper published “The Logic of Scientific Discovery” (Logik der Forschung). Popper’s aim was to make a distinction between science and pseudo-science. He postulated that a theory that is not refutable by any conceivable event is nonscientific. A theory is refuted if it fails the “crucial experiment” [5]. Sometimes additional hypotheses (auxiliary hypotheses) are proposed to explain why the theory failed the crucial experiment, and to keep the original theory from rejection. This constitutes an immunizing stratagem (in the “Logic of Scientific Discovery” a conventionalist stratagem) [5;6]. Immunizing is not necessarily a bad thing. A well known example is the discovery of Neptune. Perturbations of Uranus’s orbits led to the hypothesis (auxiliary hypotheses) that there existed another planet, and not to a rejection of Newton laws. In 1843, John Couch Adams calculated the orbit of this planet. Urbain Jean Joseph Le Verrier made similar calculations and sent them to Johann Gottfried Galle in Berlin. On Sep. 23. 1846, Galle began to search for the new planet and found it after about an hour. The planet was baptized Neptune.

In this sense, the WHI study was the crucial experiment for the use of HRT in the postmenopausal female. The main question was whether HRT is a viable intervention for the primary prevention of chronic diseases. That question could be unambiguously answered. So, the crucial experiment was set. The answer was negative. Therefore, HRT failed the crucial experiment and the theory was rejected. Immediately, attempts to immunize the theory started. Auxiliary hypotheses were produced to defend the theory. In his “Logic of Scientific Discovery”, Karl Popper tried to delineate science from pseudo-science. He did not try to say when a theory is true or acceptable. Therefore, when HRT failed the crucial experiment it proved the scientific nature of the theory. Also, failing the crucial experiment led to an abundance of auxiliary hypotheses, to keep the theory alive. Reanalysis and alternative hypothesis improved our knowledge and the way we use hormone replacement therapy now [7,8].

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A bias against publishing negative results is wildly present [9;10]. A recent study has shown that a substantial number of large phase 3 trials presented at an international oncology meeting remain unpublished 5 years after presentation. Most of these studies have negative findings [11]. This kind of publication bias seriously impairs our understanding of the problem under examination. Besides, nonpublication breaks the contract that investigators made with the trial participants, funding agencies, and ethics boards [11]. In the “Logic of Scientific Discovery”, Popper stated that “Theory dominates the experimental work from its initial planning up to the finishing touches in the laboratory” [5]. Therefore, another possible reason for nonpublication of negative results is rejection of facts that do not fit the theory.

The WHI trial demonstrated a lot more than HRT influence on the postmenopausal female. It exposed all the elements of scientific study, and proved the importance of negative studies..

### **Reference List**

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