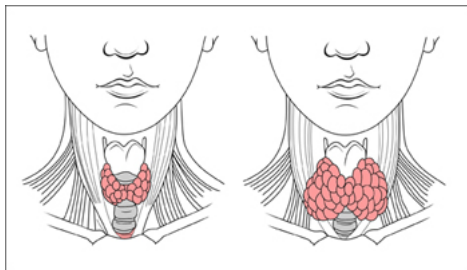


# Another disambiguation of the Russo-Williamson thesis

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Causality in the Sciences,  
7–9th June, 2017

# Radiotherapy and Goiters



## ORIGINAL INVESTIGATION

### Stimulation With 0.3-mg Recombinant Human Thyrotropin Prior to Iodine 131 Therapy to Improve the Size Reduction of Benign Nontoxic Nodular Goiter

*A Prospective Randomized Double-blind Trial*

Viveque Eggsgaard Nielsen, MD; Steen Joop Bonnema, MD, PhD; Henrik Boel-Jørgensen, MD; Peter Grøbe, MD; Laszlo Hegedüs, MD, DSc

## The More General Problem

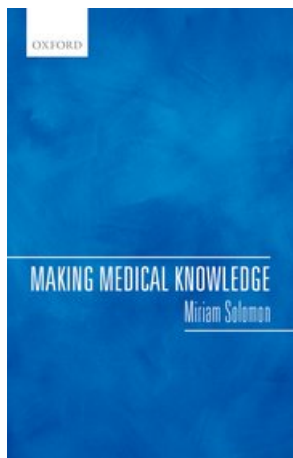
### The Problem of Masking:

*“You have found one link from C to E, but you do not know what other links there may be. Suppose you have found a link by which C increases E. There may still be another link, a route by which C reduces E. . . . The operation of one mechanism might mask or hide the operation of the other.” [Illari, 2011, 145–146]*

In order to establish a causal hypothesis in medicine, it's not enough to establish a particular relevant mechanism.

- This involves distinguishing between a **component effect** and a **net effect** [Hitchcock, 2001]. In the case of establishing treatment effects, the relevant hypothesis concerns the **net effect**.

## Masking in Practice



- Miriam Solomon has provided an account of the controversy regarding the benefits of screening for breast cancer with mammography in women within certain age ranges [Solomon, 2015, 210–217].
- In such cases, it looks like failing to solve the problem of masking may be leading to interventions that are not beneficial, and that often come with harmful side effects [Gøtzsche and Olsen, 2000].

## The Russo-Williamson Thesis

It is necessary also to establish the *existence* of a overall difference, in order to avoid *the problem of masking*:

*“It is uncontroversial that mechanistic evidence on its own cannot warrant a causal claim, as it may be the case that the purported cause, although prior to the effect and mechanistically connected to it, actually makes little or no [overall] difference to it” [Russo and Williamson, 2007, 162].*



# The Russo-Williamson Thesis

ORIGINAL ARTICLE

Endocrine Care—Brief Report

## **Recombinant Human Thyrotropin-Stimulated Radioiodine Therapy of Large Nodular Goiters Facilitates Tracheal Decompression and Improves Inspiration**

Steen J. Bonnema, Viveque E. Nielsen, Henrik Boel-Jørgensen, Peter Grupe, Peter B. Andersen,  
Lars Bastholt, and Laszlo Hegedus

### The Russo-Williamson Thesis:

*“In order to establish that A is a cause of B in medicine one normally needs to establish two things. First, that A and B are suitably correlated—typically, that A and B are probabilistically dependent, conditional on B’s other known causes. Second, that there is some underlying mechanism linking A and B that can account for the difference that A makes to B” [Clarke et al., 2014, 343].*

# Mechanistic Reasoning

However, Jeremy Howick has presented this radiotherapy case as a counterexample to the Russo-Williamson thesis [Howick, 2011a].

## Conditions on High Quality Mechanistic Reasoning:

- (1) Knowledge of mechanisms upon which the mechanistic reasoning is based is not incomplete; that is, the mechanisms linking the intervention with the outcome have been identified and their behavior under intervention established.
- (2) The probabilistic and complex nature of the mechanisms is explicitly considered when inferring from mechanisms to any claims that a particular intervention has a patient-relevant benefit. [Howick, 2011a, 937–938]

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An instance of reasoning that meets these conditions may overcome the problem of masking, simply because the problem of masking is the result of *incomplete* knowledge of all the relevant mechanisms and their complexity [Howick, 2011a, 934–937].



# Mechanistic Reasoning

## Exposing the Vanities—and a Qualified Defense—of Mechanistic Reasoning in Health Care Decision Making

Jeremy Howick<sup>†‡</sup>

Howick argues that the mechanistic reasoning in the radiotherapy case meets these conditions, and that the “[m]echanistic reasoning should therefore allow us to conclude that radiotherapy will improve respiratory function, at least in the longer term” [Howick, 2011a, 938].

## Mechanistic Reasoning

I think it is right that the later comparative clinical study was not required. However, it is not clear that this provides a counterexample to the Russo-Williamson thesis.

- Howick interprets the thesis as claiming that *“mechanistic reasoning is required alongside comparative clinical studies”* [Howick, 2011a, 930].

### A Disambiguation of the Russo-Williamson Thesis:

In fact, at least in this context, the thesis maintains only that in order to establish that an intervention causes some health outcome, it is necessary to establish both that there is a mechanism linking the intervention to the health outcome, and that the intervention makes an overall difference to the health outcome [Illari, 2011, 141–148].

# Mechanistic Reasoning

*International Studies in the Philosophy of Science*  
Vol. 25, No. 2, June 2011, pp. 139–157



## Mechanistic Evidence: Disambiguating the Russo–Williamson Thesis

Phyllis McKay Illari

According to the Russo-Williamson thesis, a causal hypothesis may be established by meeting the proposed conditions on high quality mechanistic reasoning, as long as meeting those conditions provides ***an alternative method*** for establishing that there is a mechanism by which the intervention makes an overall difference to the health outcome.

# Mechanistic Reasoning

However, it is likely that the best that can be done in terms of meeting the proposed conditions still falls short of providing a body of evidence that *establishes* that the intervention makes an overall difference to the health outcome [Howick, 2011b, 140–146]. (See also [Solomon, 2015, 123].)



# Mechanistic Reasoning

As a result, the radiotherapy case still looks like a counterexample to the Russo-Williamson thesis.

## The Radiotherapy Case:

It looks like a case in which the effectiveness of radiotherapy for breathing function is established even though there may still exist a mechanism by which the radiotherapy makes an overall negative difference to breathing function.

- In other words, it looks like a case in which a causal hypothesis is established even though it is not established that the cause makes an overall difference to its effect.

## Another Disambiguation

### Two Interpretations of the Russo-Williamson Thesis:

- (1) ***Demanding interpretation:*** The thesis may describe the constraints that a body of evidence must meet in order to provide a basis for establishing a causal hypothesis.
  - (2) ***Less demanding interpretation:*** The thesis may describe the constraints on the body of evidence that results after a causal hypothesis has come to be established.
- It all depends upon whether the thesis is concerned with the ***necessary preconditions*** for establishing a causal hypothesis.

## Another Disambiguation

In the radiotherapy case, the body of evidence upon which the causal hypothesis was established failed to establish that the radiotherapy makes an appropriate overall difference to respiratory function.

- According to *the demanding interpretation*, the case is a counterexample to the Russo-Williamson thesis.



## Another Disambiguation

However, in the radiotherapy case, even the limited body of evidence provided a basis for establishing the causal hypothesis that radiotherapy improves respiratory function [Howick, 2011a, 938].

- But as long as establishing the causal hypothesis thereby establishes that radiotherapy makes an overall difference to respiratory function, the case is consistent with ***the less demanding interpretation*** of the Russo-Williamson thesis.






## Another Disambiguation

### The Restricted Reach of the Russo-Williamson Thesis:




The thesis says something about the consequences of having established a causal hypothesis, namely, that it is also established that there is a mechanism by which the cause makes an overall difference to its effect. But it seems to say little about the conditions that a body of evidence must meet in order for it to play a role in establishing a causal hypothesis.

Although this restricted reach allows the thesis to avoid certain counterexamples, it comes at the cost of making the thesis less informative.




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