

Preventive health care using negative expectations increases risk over time



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Executive Summary

Preventive health care campaigns (smoking, cholesterol, high blood pressure, obesity, hay fever etc) likely *increase* risk and cause *additional* victims, contrary to the expectations.

This apparent absurdity *logically* follows from:

(1) the *understanding* that the placebo-effect is based on expectation, which can work two ways (positive and negative expectation)

(2) the *fact* that preventive health care policies essentially highlight the harm to be expected by e.g. smoking, eating fats, sugar, as it is considered the most effective to change the behavior

(3) the *fact* that there are always persons that do not change their behavior (e.g. keep on smoking), so that within this group the health care campaign reinforces the negative expectation: The more a cigarette is expected to kill, the more it will kill. The evil equivalent of “the more a drug is expected to cure, the more it will cure”.

This leads to the general inference that health care campaigns that stress the negative outcomes associated with bad habits will, while on one hand possibly reducing the size of the group at risk, on the other hand effectively increase *over time* the health risk itself within the group at risk.

Thus, risks of health hazards are not constant, but increased over time by health care campaigns because of increasing awareness of the health hazard associated with bad habits.

The understanding that expectation affects the probability of the outcome is well-accepted in pharmaceutical environments: the placebo-effect can be weakened or reinforced by management of suggestions, changing the effectiveness of the drug.

This dependency of the probability on the strength of expectation is however completely disregarded in the case of management of risk hazards, without any justification: The unjustified assumption of a constant risk over time justifies that health care campaigns only need to reduce the size of the group at risk (get smokers to quit smoking) to be effective. It thus completely disregards the increase in casualties due to increased risk within the group at risk, those that do not abandon the bad behavior.

Surely, if this prediction that risk increases over time due to campaigning is true, real-life data would have already exposed this truth?

First, you don't see what you don't expect, as the world-famous video on the selective attention test from Daniel Simons and Christopher Chabris shows. Few researchers look for stones falling upwards.

Second, if a risk would be found to unexpectedly increase, this would likely be classified as anomaly as not in line with the general understanding of a risk supposed to be constant. Interestingly, such anomalies have been observed in the past:

1. *Lung cancer risk with smokers (not with non-smokers) unexpectedly increased over time from the 1960s to the 1980s. This was unexpected as cigarette manufacturers had just implemented the filter to reduce lung cancer risk as they had been highly criticized for the health hazard caused by smoking. The negative placebo was not considered as possible explanation. More-over, lung cancer risk of female smokers has further increased from 2000 to 2010.*

2. *Hay fever risk increased from the 70s onwards, while it should have decreased as the pollen levels were highest in the 70s, decreasing till 1999.*

In both cases, the increase in risk went parallel with an increased public awareness (campaign), and the negative placebo-effect with its compelling logic was not considered as clarification.

The author hopes this paper will stimulate researchers to verify the claim.

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What is the placebo-effect?

If one takes a pill or one is subjected to a surgery, to which there is an expectation of a benefit (becoming better), that is shared by patient and environment (medical team), then this expectation (the improving) also materializes with a certain probability, even if the act itself is inert (not supposed to work: a placebo pill, a scam surgery). This is referred to as the placebo-effect or placebo response, and has been called the *power of belief*.

The strength of this placebo-effect strongly varies - in some studies 100% was reached. The core of the phenomenon is expectation/conditioning. One of the leading researchers, Benedetti, stresses that, as there are several operating mechanisms causing this placebo phenomenon, it is thus more correct to speak of placebo-effects in the plural.

Because of the significance of this effect, pharmaceutical companies have to demonstrate that new drugs work better than this placebo-effect.

What is the negative placebo-effect?

Much less known, but the core of our logic, is the negative placebo-effect, also called the nocebo-effect, or, as Helen Pilcher puts it "placebo's evil twin". In this case, one performs an act with a negative expectation (becoming ill) that, according to research, will also materialize with a certain probability : people can become ill just because of the negative expectation.

The negative placebo-effect is difficult to study for ethical reasons as one should not harm people while doing research.

Scientists in placebo-research (Irvin Kirsch, Shapiro, Steve Stewart-Williams, John Podd) state that, despite the difficulty to study, the positive and the negative placebo-effect are actually the same phenomenon: expectation/conditioning.

Scientists have been pointing out the relevance of the negative placebo-effect before:

The role of expectation, both positive and negative, is known since decades. Some examples:

1. *Robert A. Hahn in 1997* concluded in his paper "*The Nocebo Phenomenon: Concept, Evidence, and Implications for Public Health*":

"Second, and more immediately practical, if communication about pathological conditions may serve not only to describe, but in a sense, also to foster sickness by creating expectations, then we must be cautious in both public health communications and in clinical medicine. We need to know more about how health messages affect their audience. Such knowledge may enhance our ability to minimize the pathological consequences of negative messages. The placebo/nocebo phenomenon suggests that it may be healthier to err on the side of optimism than on the side of pessimism."

2. *Herbert Spiegel in 1997* "*Nocebo, the power of susceptibility*" recommended:

"to promote placebo effects and prevent the consequences of nocebo"

3. *F. Benedetti, M. Lanotte, L. Lopiano and L. Colloca in 2007* "*When words are painful: unraveling the mechanisms of the nocebo-effect*":

"All these findings underscore the important role of cognition in the therapeutic outcome, and suggest that nocebo and nocebo-related effects might represent a point of vulnerability both in the course of a disease and in the response to a therapy."

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The view that the placebo-effect is very promising but insufficiently understood and justifying more research, is strongly advocated by Benedetti - an authority in the field. He considers it will offer fundamental new understanding about the mind-body interactions that allow to improve health care, and stresses the importance of health care workers to be aware of the importance of expectation in the relation with the patient (see e.g. his 2011 book *The Patient's Brain*) - doctors that are less emphatic with their patients perform worse in curing.

The significance of the placebo-effect is also assessed in the more popular science press, such as in Michael Brooks book *13 things that don't make sense* (2008) and the New Scientist book *Nothing* (2013) that contains two entertaining articles, *Placebo Power* by Michael Brooks, and *When mind attacks body* by Helen Pilcher.

Entertaining Youtube video's on the nocebo-effect are Helen Pilcher's [The Nocebo Effect](#), and Grey's [This Video Will Hurt](#), the latter also referring to some mass psychogenic illness cases caused by the negative placebo-effect, highlighting the role of media communication.

Relation between placebo and anti-smoking campaigns?

Smokers perform an *act* (the smoking) with a *negative expectation* (higher risk to a number of diseases) that is *shared by an expert environment* (government, scientists, environment of the smoker). These look like the conditions that characterize the placebo-effect: referring smokers to the risks of smoking appears comparable to referring patients to the possibility to improvement to be expected by taking the pill.

Over the last decades, anti-smoking campaigns successfully *reduced* the number of smokers in several Western countries, but that is now *leveling*: one now has to deal with a hard core of smokers, of which the majority admits wanting to stop but not being able to. Anti-smoking measures currently fail in several countries to further reduce the number of smokers.

At the same time, anti-smoking campaigns and measures have become more intense, thus strengthening the negative expectation, the negative placebo-effect.

As this expectation of negative effects of smoking is frequently communicated in our society and considered to be scientifically very sound, it is reasonable to expect that the corresponding negative placebo-effect in the case of a smoker, will be higher than the average placebo-effect with drugs; especially considering the increase in frequency, intensity and credibility of the negative messages (smoking kills, pictures of tarred lungs, being reminded every time one leaves a room to smoke, ...).

Thus, the frequency of diseases amongst smokers could be expected to increase.

The reasoning also applies to *passive smoking*: As passive smoking was not considered unhealthy by science until around the early 1980s, the campaign spreading this news has increased the negative expectation, and thus the prevalence of diseases such as lung cancer with passive smokers could be expected to have increased since the 1980s.

This reasoning is shown in below figure 1:

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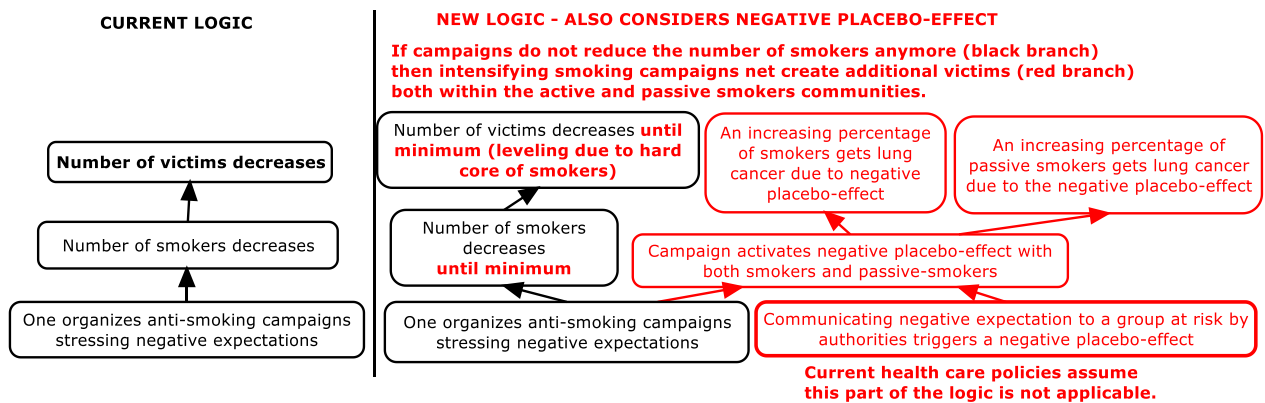


Figure 1: Logic with and without placebo-effect: placebo-effect adds additional victims

Generalisation from anti-smoking campaigns to any preventive health care campaign that emphasizes negative expectations

Figure 2 shows the generic logic for any preventive campaign stressing negative expectations.

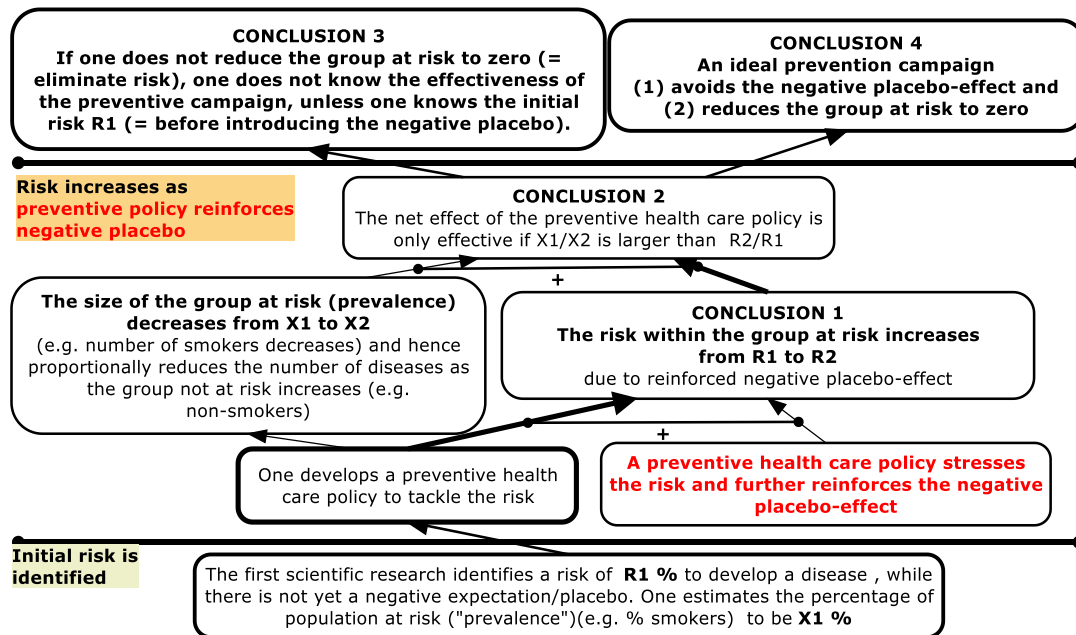


Figure 2. Logic showing how negative expectation increases the risk of negative health effects

Two key insights of this logic model are the following:

1. Health risks (smoking, cholesterol, obesity, ...) may not be fixed as generally assumed (!) but depend on frequency, intensity and credibility of the communication about the associated negative expectations (just like with the positive placebo-effect).
2. The actual risk assessments used by medical community may be placebo-inflated due to the expectation. The earliest risk assessments, as they are less placebo-inflated, will be a better indicator of the "natural risk", though not applicable anymore due to placebo-inflation. The risk assessment of health hazards is thus as difficult as the assessment of effectiveness of drugs : both are affected by the placebo-effect.

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Verification / falsification of the model:

Following Goldratt's rigorous Thinking Processes rule to check new proposed causes, in line with the scientific approach, through the ECE (effect-cause-effect) by predicting other effects from the same cause, this logic model allows to makes following new predictions:

1. All risks should appear to increase over time with frequency, intensity and credibility of preventive health care campaigns. The magnitude of this increase may vary strongly depending on the risk and expectation awareness in the same way positive placebo strongly varies and is rarely found to be zero.

As this prediction is against normal expectation, when observed, instead of considering negative placebo, one will attribute to (1) "available" clarifications (possible correlations), or (2) underestimation of past risk assessment, or (3) study outcome being anomalous.

Prediction: in general, all risks subject to preventive health care campaigns will appear to increase over time correlated with the intensity of negative communication.

2. The effect of a preventive health care campaign will be less than traditionally expected. Traditionally, one expects less victims proportional to the reduction in the size of the group at risk. E.g. 10% less smokers implies 10% less victims, while with the new logic, one needs to add the increase in risk within the group at risk due to the expectation,

Prediction: the reduction in number of victims due to preventive campaigns will in reality appear to be less than is expected from the reduction in size of group at risk

On the internet some evidence is available that appears in line with these predictions:

(1) **Smoking and lung cancer**

It was reported (<http://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf>) (page 185) that the risk of lung cancer within the smoking population has indeed increased unexpectedly, while cigarette redesign (implementation of filters) was assumed to actually decrease the risk based upon lower yields of machine-tested tar. Studies have subsequently attributed this increase to this changed cigarette design having unexpected negative effects. The same report identifies that for female smokers, lung cancer risk continued to rise through 2000-2010, long after the implementation of the cigarette redesign.

The placebo-effect may be a more consistent clarification for the observed increased risk. It is suggested to review data on risk of lung cancer with smokers in correlation with anti-smoking campaigns and measures (both active and passive).

(2) **Hay fever**

Risk of hay fever unexpectedly increased from the mid seventies onwards while the pollen levels were highest in the seventies and decreased till end of century. Current hypotheses put forward are pollution and the hygiene hypothesis. Negative placebo-effect due to increased communication through the media about pollen levels may be a more consistent clarification that was not considered or available at the time.

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It is now up to the scientific community to check the logic, available data and predictions. More specifically, it might be interesting to look e.g. into:

(1) *Cholesterol*

Levels have been decreasing from 1990 to 2010, so the number of victims due to cholesterol should have decreased. On the other hand, as communication about cholesterol has clearly increased, one can expect that the risk of cholesterol increased.

If victims due to too high cholesterol increased, this may be due to the placebo-effect.

(2) *Lung cancer and passive smoking*

As the risk of second hand smoke (passive smoking) only started to be communicated around the 1980s, data may exist that show an increase in lung cancer risk for passive smokers (e.g. non-smokers living with a smoker) in the period post 1980s as compared to the period before 1980s, all other factors such as air pollution being equal, due to the onset of this negative expectation through communication about passive smoking.

Meta-studies comparing several smoking-related diseases over longer periods in different countries with different health care policies and convictions, for active, passive and non-smokers, may allow to verify this prediction.

Important note

It is important to stress that this paper does not put into question that smoking (both active and passive) is bad for health. As has been excellently reported e.g. in Allan M. Brandt's book *The Cigarette Century* there is no doubt about the causal relation between smoking and e.g. lung cancer, and about the cigarette industry trying to hide this truth as long as possible! This also goes for the other health hazards referred to. The key point of the white paper is that the risk is, like with the use of drugs, also dependent on the communication about the risk.

Meantime, what to do with preventive health care campaigns while the judge is out?

Because of the *precautionary principle*, one should not disregard the negative placebo effect in preventive health care campaigns. This does not imply that one has to abandon these campaigns. It implies one should avoid emphasizing negative expectations.

In the case of smoking, in Western countries, this could be:

- improved facilitation to smokers that want to quit smoking (actually the majority),
- substantially higher prices (this has shown to work excellently)
- the promotion of physical fitness

However, according to WHO, the real challenge of reducing smoking victims is with developing countries, where smoking is on the rise: The current method of trying to discourage smokers actually may be very counterproductive as smoking prevalence increases.

It is interesting to note that with new drug development, government imposes double-blind clinical trials so as to assess drug effectiveness against placebo, so the placebo-effect is recognized as omnipresent (whatever the drug) and important enough to lead to directives.

If scientists confirm that the negative placebo-effect should be considered omnipresent in preventive health care campaigns, this should also imply law-enforced directives to avoid negative expectations or otherwise assess the balance of reduction in size of group at risk against the increased risk due to the campaign; this might also affect commercials.

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Negative placebo-effect also counters the development of new drugs

As the negative placebo-effect appears disregarded in preventive health care, the question arises whether this may also affect new drug development: Pharmaceutical companies have to demonstrate that new drugs work better than the placebo-effect, through so-called "double blind" clinical trial tests some of the patients get the real drug, and some get a placebo, and the person administering the drug does not know what patient gets what.

Reconsider now the need of pharmaceutical companies to score better than placebo. From traditional point of view, it looks attractive to avoid or minimize the placebo-effect as this should make it easier for the drug to score better than placebo: minimizing the placebo-effect should not affect the real drug result as it is based upon its chemical reactions: This would favor communication protocols for administering drugs that minimize expectation of the patient-doctor relation, so as to maximally rely on the chemical power of the drug.

Fabrizio Benedetti is one of the leading placebo-researchers, and well aware of issues with double-blind clinical trials. He compares the placebo-effect to the Heisenberg Principle in quantum physics: the observer unavoidably influences the outcome - in this case the health care provider influences the patient outcome. Benedetti states one never knows how effective a drug really is, as part of the effect of the real drug is caused by the expectation that causes also the placebo to work. He therefore proposes to assess the real power of drugs by excluding the expectation - such as *hidden administration* of drugs. In *hidden administration* studies, where effective drugs were administered without the patient knowing, these drugs appeared to be much less effective, *surprisingly*. This confirms that the effectiveness of a drug is *not* pure chemistry, but the combination of placebo-effect and chemistry. Thus, minimizing the placebo-effect in double-blind clinical trials should also reduce the effectiveness of the real drug.

This should not really come as a surprise: if in a double blind clinical trial test the placebo would score 30% and the real drug 40%, one should expect that within this 40%, 30% is contributed by the placebo, so eliminating this placebo component should reduce the effectiveness of the real drug significantly (though is not a mere subtraction).

Minimizing the placebo-effect implies that the positive placebo-effect with the real drug is minimized so overall effectiveness is lowered so larger test groups may be required to get statistically conclusive results: an undesirable effect caused by what looks like a desirable policy: *An increased probability that the real drug will not score better than placebo in double-blind clinical trials.*

It thus follows that a better strategy may actually be to go for protocols that strengthen the placebo-effect: as (1) these also strengthen the effectiveness of the real drug and (2) these minimize the effect of "negative expectation" on the real drug. As the placebo component plays a role in both the drug group and the control group, it becomes less likely that the drug would score less than the placebo group *if it really works also chemically.*

The fact that it came as a surprise that the working of real drugs was so reduced when expectation was eliminated, indicates the fundamental attribution error : one attributes its working entirely to its chemistry, and does not recognize the placebo-contribution.

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So, summarizing:

1. The effect of the real drug is inherently *variable*, not just chemistry but also depending on the associated expectation effect.
2. One must maximize the placebo-effect in double blind clinical trials, as this minimizes the impact of the negative expectation on the real drug - the positive placebo-effect is anyhow equal.
3. Doctors must be aware that part of the effectiveness of drugs is due to how they interface the client - this is one of the key messages Fabrizio Benedetti advocates amongst others in his book *The Patient's Brain*

The placebo-effect is an ally instead of a competitor to the real drug.

Conclusion

This white paper provides a logic model using factual knowledge about the placebo-effect, that suggests that it may have unintended undesirable effects on preventive health care policies, new drug development and drug administration in general.

In essence, this logic model states that risks of health hazards as well as effectiveness of drugs are *variable* and *influenced by expectation*.

Following suggestions result, considering the potential impact:

- (1) further investigation of the claims by assessing the presented logic and verifying the resulting predictions
- (2) dialogue between placebo-researchers and preventive health care policy makers on the relevance / irrelevance of the placebo-effect in health care campaigns, suggesting a more precautionary preventive health care policy. This dialogue may require support from cognitive psychologists to point out the thinking flaws related to the placebo-effect in current medical practice.
- (3) a more effective drug development policy by embracing the placebo-effect rather than considering it an enemy

About the author

Piet Holbrouck holds a Master in Physics (nuclear) from the University of Ghent and has been involved in innovation and high tech developments since 1986, in different roles such as project management, innovation management and CEO, in areas ranging from space and defense projects (development of instruments, avionics, small satellites, satellite navigation, electro-optical instruments) to home beer draught equipment. Since 2002 he is a free-lance consultant in innovation and project management. He was a visiting professor at UAMS from 2006 till 2010 with courses in Product Innovation and Entrepreneurship. He is currently in the process of rolling out the generic problem-solving and innovation toolbox Non Zero Ratio that uses logic to facilitate paradigm-changing innovation. NON ZERO RATIO, offering services in the area of innovation, strategy, business development and related project management.

For more information or further suggestions for research/dialogue on the case:

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