Academy of PHYSICAL MEDICINE

Broadcast Summary

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The Power of Placebo
With Jeremy Howick

About Jeremy Howick

- Oxford philosopher and medical researcher - has conducted groundbreaking studies about placebos and why unbiased experiments are needed.
- Degrees from Dartmouth College (USA), the London School of Economics, and the University of Oxford.
- Over 80 academic articles in journals such as the British Medical Journal, Annals of Internal Medicine, and the Lancet. His textbook – The Philosophy of Evidence-based Medicine spearheaded a new sub-discipline. Has also written for the Times, the Huffington Post, and The Conversation.
- Collaborates about placebo treatments and the need for rigorous evidence with the National Institutes of Health in the United States, the National Institutes of Health Research in the United Kingdom, the Canadian Institutes of Health Research, and Harvard University.
- Has won three teaching awards and appears regularly on television.
- Current director of the Empathy Programme at Oxford University

Placebo

- There are as many definitions of placebo as there are philosophers who have written about it. A placebo is about all context effects such as the empathy effect, positive message effect, sugar pill effect, sham surgery effect and so on.

- The common terms for honest placebo pills are open-label placebos or non-deceptive placebos.

- Placebos are considered by some to be unethical because:
    a) they do not work; and
    b) they are deceptive (i.e. require lying to patients)

- "Honest" placebos have been trialled for back pain, ADHD, depression pain and seem to be beneficial. The placebos were accompanied by a positive message.

- In placebo-controlled trials, there have been occasions where an ingredient is added to the placebo to mimic a side effect in the active drug. This addition may be undisclosed, but the trial report would indicate no difference in side effects.

- Different placebos for different conditions have different mechanisms. Some placebos are intended to activate the brain's reward mechanism which leads it to produce its own chemicals like dopamine and endorphins.

- The placebo effect is greater in a placebo which is more invasive:
    - Pills are the least invasive.
    - The placebo effect is greater for injections than pills; the placebo acupuncture is more effective than injections.
    - The effect is greater still in placebo surgery.

To give a dose of empathy:

- Use warm, empathic body language (e.g. looking at your watch is not empathic).
- Look at the patient instead of looking at a screen.
- Ask open-ended questions about what is really bothering them.
- Encourage patients to have positive expectations. Be honest with them.
- Sometimes a dose of empathy and a positive message will suffice for very mild pain, mild to moderate pain, anxiety or depression. In many cases, however, medical intervention will be needed.

Note: It is not recommended to replace evidence-based medical interventions with a placebo. However, adding a dose of empathy, a positive message and kindness definitely enhance

- Some drugs work by boosting/activating the body's natural processes at a general level. As to how they confound the placebo effect remains to be investigated/studied.

Placebo effect

- Research on the placebo effect has found it to be powerful but prescribing placebo pills encourages a pill-popping culture.

- The placebo effect can be induced without the pill. Two ways to do it:

    a) Give appropriately positive messages in order to enhance treatment, rehab programme etc

    b) Enhance the way empathy is expressed to patients. A dose of empathy works for pain and anxiety.

Nocebo effect

- The opposite of placebo effect where the pill gives a more negative effect than it otherwise would have. It is more powerful than the placebo effect.

- It should not be confused with misattribution. (E.g. 50% of the people who participated in a study reported having adverse events like nausea and headache after taking the placebo. Placebos cannot cause a *drug* side effect. Study participants may have had underlying conditions with symptoms which they report as adverse drug events. That was not a nocebo effect. That was misattribution).

- An ethical problem: patients warned that a placebo might cause GI side effects were 6 times more likely to experience those effects those who were not warned.

Subjective measure vs. objective measure

- Often, the placebo effect has more impact on subjective outcomes than objective.

- In some cases, patients go to the GP not because of some objective measure.

Placebo-controlled trial for asthma

- Three groups were involved. One group was with drug inhaler (salbutamol/albuterol); the other group was with placebo inhaler (no drugs induced); and the last group was with 'no treatment'.

- Two main outcomes: forced expiratory volume (FEV) – how much they can blow in one second (this was the objective measure); and function – how many stairs they can climb.

- Results: Both the placebo inhaler and drug inhaler were as good for the function of the patients compared to 'no treatment.' But the drug inhaler was better than the placebo inhaler for FEV.

- Argument: Asthma patients do not go to the GP because their FEV is abnormal. They go because they cannot climb up as many stairs as they would like to. Sometimes subjective measures are more important. Caveat: subjective reports are more susceptible to bias.

- A clinical outcome is one that improves morbidity and mortality. It is not clear how FEV improves morbidity such that it could definitely interpret is as a surrogate outcome.

Nocebo effect of statins

- Many of the adverse side effects/nocebo effects from statin therapy is because of the warnings that had been given to patients beforehand.

- In the placebo-controlled trials of statins, there was no significant difference in the rate of adverse event reported in the placebo group compared to the rate of adverse event reported in the statin group.

- The extent to which many people report muscle pain after taking statin is due to some information about its adverse effects. Oxford-led clinical trials are being conducted looking into how to minimise the effect of this misinformation.

- Another study looked into how many sites on Google talked about statin adverse events vis-à-vis how many people in that country reported statin adverse events. Results indicated that the more reports on the internet there are about adverse events of statins, the more people in that country actually report them.

Stress

- Chronic stress can exacerbate many health problems ranging from heart disease, mental health disorders, physical pain to sexual dysfunction, among others.

Sham surgery

- A placebo-controlled trial was administered on the Houston Rocket players in the US where one group underwent real arthroscopic surgery (i.e. small incision, lesion clean-up by scraping away pieces of bone or cartilage) while the other group underwent sham surgery/ minimally invasive surgery (i.e. small incision only).

- The results indicated that there was no difference between placebo surgery and real surgery.

- There were numerous sham surgery trials for knee pain, back pain, and shoulder pain. The sham surgery worked as well as the real surgery for these conditions.

- There are assertions that sham surgery is unethical i.e. making an incision is potentially harmful. However, if the actual more invasive real surgery does no better than a sham, it is the real surgery which is unethical.

- The clinical trials in the UK for shoulder pain was done such that instead of performing a sham surgery, the surgeons recommended not doing the procedure at all as a form of campaign for lowering the rates of invasive surgical procedures for shoulder pain.

- It can be argued that sham surgery is not a placebo because, unlike sugar pills, it requires an incision which induces the body's wound healing cascade.

- Sham manipulations in some cases seem to be just real manipulations but less intense in some way. It is arguably not the equivalent of a placebo where all active content is removed, leaving only lactose or sugar.

Oxford Empathy Programme

- One of its missions is to convince all healthcare professionals that they are a 'drug' i.e. they make the patients feel better because they are trusted.

- A study showed that when a GP sat down beside the patient in the hospital, compared to remaining standing up, the patient felt like there was more time when they were sat down.

Three groups and their take on the placebo effect:

a) Practitioners who appreciate the Empathy Programme for validating and quantifying the benefits of placebo effects, the benefits of empathy the same way the effects of drugs are quantified.

b) The practitioners who are sceptical before on the power of the placebo effect and were eventually convinced after being presented with evidence.

c) The practitioners who are radical sceptics saying – "placebo is all nonsense!"

- While one cannot patent a dose of empathy, the National Health Service in the UK and its equivalent elsewhere will be spending fewer funds by applying empathy or the placebo rather than investing in drugs/pills and surgeries.

Misconceptions

- There is a serious misconception about medicine – that the mind and body are separate.

- Just because the placebo can cure some people or make them feel better does not mean that the underlying condition is psychological.

- Nothing is just psychological. Even thoughts can be measured with a brain scan so nothing is 'just in the head'.

- Pain is complex. Back pain is rarely due just to a lesion in the lower back. It is often associated with different (behaviour) patterns and so on. If someone experiences back pain for example, and there is no longer lesion there, there remains some kind of neurological connection between the head, the brain, and the back. It might be misfiring on its own but it is not 'just in the head'.

- The fact that the placebo can help with addressing pain does not mean that the underlying problem is fake. It means the placebo effect is real and that mind and body are connected.

- Empathy involves understanding a patient individually and one cannot do that without taking some time to get to know them, what is bothering them and so on.

- Even if it does cause patients to come back more often, than they would if the GP was not as empathic, frequent visits with an empathic GP can perhaps prevent hospital admission or a mental health admission of patients.

- Evidence suggests that it is difficult to identify placebo responders. Non-deceptive or open-label placebos can still have an effect due to biopsychosocial factors.

Evidence for physical medicine

- There are systematic reviews including Cochrane Reviews which are viewed as the top level of evidence for the benefits of physical medicine.

- Osteopaths and chiropractors are very good at enhancing the placebo effect as they are good communicators, talking about the whole person, which is required for empathy. This might better be called a biopsychosocial approach to treatment than 'placebo effect'.

- Patients deserve to know all the information about the benefits of manual therapy. Practitioners should be honest about the potential harms while not inducing a nocebo effect.

- While there is a need to express all the information about the harms and benefits of manual therapy to patients, there is no need to spend twice as much time talking about the rare harms. It is in clinical trials where the Ethics Committee requires greater degree of details about the adverse effects.

Pragmatic randomized control trial

- An RCT which measures the result of a package of care (ie osteopathy or chiropractic appointment as a whole), rather than a single intervention (eg a manipulation).

On RCTs

- Trial study participants are sent with symptom questionnaire every week (i.e. list of symptoms include headache, nausea, shoulder pain, back pain, dizziness, etc).

- At some point in the week, they will have some kind of minor headache or other minor aches for some reason which they normally do not pay attention to. But with the symptom questionnaire, their attention was drawn to their symptoms and thus report them as adverse events.

- In some cases, study participants tend to suppress reporting of symptoms because they avoid feeling 'silly' for experiencing

Recommendations

- Do not just address the physical aspect as to overlook other components (eg emotional) might not give good results, leading in turn to drug prescription and possible dependency.

- Provide patients with information about the placebo in a way that does not actually cause harm. Causing harm unnecessarily is a violation of the ethical code.

- Reduce the stress build-up in patients by improving the physical context/environment in the physical therapy practice areas. Patients are often asked to undress to their underwear and they may be given the wrong environment in which to do that – makes them feel uncomfortable and therefore contributes to the nocebo effect.

- Find ways to help patients relax as this will enhance the placebo effect of the evidence-based therapeutic processes administered to them. Reducing patients' stress and anxiety will have an important effect on their wellbeing.

- Be honest to patients when they come for a physical checkup and there is nothing wrong with them. Sometimes patients immediately felt relaxed just by being in a trusted environment (E.g. doctor's clinic).

- Telling patients that there is nothing wrong with them is a very powerful message. Further reassure them, by telling them to come back in a few weeks to make sure that everything's been checked or give them a soft tissue work just to improve circulation, etc.

- Express the evidence in natural frequencies as patients tend to understand them better **E.g.** *"Out of 100 people who were given XX treatment, 95% would experience a benefit within YY days, however about X of them might have more pain or be at a greater risk of stroke"*.

- Always be nice to patients. This matters and is evidence-based. More than 150 years ago effective drugs were not that many, so all the doctor had was their kindness/empathy. They had continuity of care which is no longer true today.