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Assessing the severity of short-term side-effects to a well-known tablet

Submission date	Recruitment status	[X] Prospectively registered
10/02/2015	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/02/2015	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
13/11/2019	Other	

Plain English summary of protocol

Background and study aims
The nocebo effect is the flip side to the well-known placebo effect. This is where taking a dummy tablet such as a sugar pill can lead to the development of side effects or worsening of symptoms because of negative expectations. This nocebo effect is thought to be one of the reasons why many people report side effects to medications. This study aims to deliver an intervention to reduce the nocebo effect and therefore the number of side effects reported to medications. As a secondary aim we also want to determine which type of participants are more likely to experience nocebo effects.

Who can participate?
People can participate if they are male or female, over 18 years of age, healthy, and an English speaker and writer.

What does the study involve?
First participants will fill in questionnaires about their demographics, recent symptoms and personality features/beliefs. They will then receive one of two patient information leaflets to read. Both leaflets have been adapted for a dummy tablet and follow the current guidelines. One leaflet will report side effect probability following current guidelines, such as “common side effects (More than 1 in 10 people will be affected)”. The other leaflet will report the probability of possible side effects more positively and use percentages, such as “uncommon side effects (80% of people will not be affected).” Half of the participants will receive the first leaflet and the other half will receive the second leaflet. After reading the leaflet they will then fill in questionnaires about their anxiety, expectations for developing side effects and the quality of the leaflet. After this they will take one dummy tablet and complete a series of standardised cognitive tests for one hour. Next they will complete the anxiety questionnaire again as well as a questionnaire to record the number and severity of any symptoms experienced, and guess at the tablet identity (as participants are not told it is a dummy tablet). Finally participants will be asked a series of qualitative questions to understand more about their symptom experience and their thoughts on the tablet. They will then be thanked for their participation and given their monetary reward. Once all data collection has taken place they will be emailed a full description of the study.

What are the possible benefits and risks of participating?
It is unlikely that participants will experience direct benefit from the research, but many people state that they gain benefit from contributing to research that has important consequences for current practices. Even though participants will only take a dummy tablet, due to their expectations from reading the patient information leaflet, they have a 25% chance of developing side effects. The side effects are listed on the patient information leaflet and are short lasting and common in everyday life, such as headache and nausea.

Where is the study run from?
The study will run from one centre, the NIHR/Wellcome Trust King's Clinical Research Facility (UK).

When is study starting and how long is it expected to run for?
November 2015 to February 2017.

Who is funding the study?
NIHR Health Protection Research Unit (UK).

Who is the main contact?
Rebecca Webster
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Contact information

Type(s)
Scientific

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Additional identifiers

Study information

Scientific Title
Preventing the nocebo effect in healthy volunteers: the influence of side-effect framing in patient information leaflets on symptom development

Study objectives

The nocebo effect is the flip side to the placebo phenomenon, whereby a therapeutically inert intervention can lead to the development of unwanted side effects or exacerbation of current symptoms, due to negative expectations of the intervention.

Hypothesis 1: Participants in the positive frame intervention will experience fewer and less severe side effects to the placebo than participants in the control group.

Hypothesis 2: Participants who score higher on the personality features that have been associated with the nocebo effect will be more likely to experience side effects than those who score lower on these measures.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Psychiatry, Nursing and Midwifery Research Ethics Subcommittee at King's College London, 18/12/2014, ref: PNM/14/15-62

Primary study design
Interventional

Study design
Randomised controlled trial

Study type(s)
Prevention

Health condition(s) or problem(s) studied
The nocebo effect

Interventions
We will conduct a randomised controlled trial in which healthy volunteers will be randomised to receive an intervention or control patient information leaflet for a placebo tablet, before taking the tablet.

Control arm
The control information leaflet is akin to the information leaflets seen in current practice, as guided by EU guidelines, Council Directive (2010) and MHRA (2005) recommendations. It has been adapted for a placebo tablet, so all information provided is accurate for a placebo. As participants are not told what the tablet is or what it does, certain sections of the patient information leaflet are concealed, these include the sections: 'What XXXXXXX is and what it is used for,' 'other medicines and XXXXXXX,' 'recommended doses,' and 'what XXXXXXX contains.' The possible side effects section of the control patient information leaflet follows current guidelines for describing their probability, e.g. "common side effects (More than 1 in 10 people will be affected)".

Intervention arm
The intervention information leaflet is exactly the same as the control, apart from what appears in section 4, 'possible side effects.' In the intervention patient information leaflet the probability of possible side effects is positively framed and presented in percentages e.g. "uncommon side effects (80% of people will not be affected)."

Intervention Type
Other

Primary outcome(s)
Effect of patient information leaflets on side effect reporting as assessed by the symptom report questionnaire delivered one hour following ingestion of the placebo.
1. Incidence of side effects - number of participants between the two conditions who experience side effects
2. Number of side effects - the sum of confirmed symptoms which are tablet attributed
3. Severity of side effects - sum of all symptom scores that are tablet attributed

Key secondary outcome(s)
Effect of personality features and personal beliefs on the number of side effects reported and /or the severity of side effects reported. This will be measured by delivering questionnaires at baseline that measure modern health worries, pessimism, somatizitation, anxiety, beliefs about medicines, perceived sensitivity to medicines, and somatosensory amplification to see if scores on these measures predict scores on the symptom report questionnaire delivered 1 hour following ingestion of the placebo.

Completion date
01/02/2017

Eligibility

Key inclusion criteria
1. Male or female
2. Over 18 years of age
3. Healthy
4. English speakers and writers

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
203

Key exclusion criteria
We will exclude participants:
1. With any chronic or acute illnesses which are currently causing symptoms
2. Who are pregnant, might be pregnant or are breastfeeding
3. Who list any allergies to any of the substances in the placebo tablet

4. Who have taken any painkillers within 4 hours before taking part in the study
5. Who have been drinking alcohol

Date of first enrolment
01/11/2015

Date of final enrolment
01/02/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR/Wellcome Trust King's Clinical Research Facility
1st Floor Cheyne Wing
King’s College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Sponsor information

Organisation
King’s College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	22/10/2018	13/11/2019	Yes	No