Education By Chocolate Public Trials Protocol

CHOCOLATE CONSUMPTION TO IMPROVE SHORT-TERM COGNITIVE FUNCTION - A RANDOMIZED CONTROLLED TRIAL

ADMINISTRATION

TITLE AND PROTOCOL VERSION

Education By Chocolate to Improve Short-term Cognitive function; A Randomized Controlled Trial (Protocol version (01)
TRIAL REGISTRATION

This Education By Chocolate public trials protocol was supplied to all attendees at the lecture in which the trial was conducted, and copies were printed prior to the conduct of the trial and distributed at the end of the trial. It was published on the ThinkWell Website and the protocol was submitted for publication to clinical trials.gov.

FUNDING

This trial was funded by Amanda Burls who purchased the chocolate and arranged for all other equipment for the implementation of this trial to be available. The lecture theatre and TurningPoint software and clickers were provided by City University London.

ROLES AND RESPONSIBILITIES

<table>
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<tr>
<th>Names</th>
<th>Amanda Burls</th>
<th>Amy Price</th>
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<tr>
<td>Role</td>
<td>Principal Investigator</td>
<td>Co-investigator</td>
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Amanda Burls and Amy Price were responsible for the design of the trial. The analysis of the trial was automated using turning point software.

**INTRODUCTION**

Flavonoids are a group of polyphenolic compounds that occur widely in fruits, vegetables, tea, red wine, and chocolate. Cocoa and chocolate products have the highest concentration of flavonoids among commonly consumed foods. Chocolate is one of the most concentrated sources of the procyanidin flavonoids, catechin and epicatechin

“the concentration of polyphenols in milk chocolate is higher than in red wines and black or green teas. It is 20 times higher than in tomatoes, 2 times higher than in garlic, and over 3 times higher than in grapes.”
Cocoa flavonoids are absorbed and cleared from circulation relatively quickly. The concentration in plasma levels peaked at about one hour. If chocolate has been processed with alkali, known as Dutching, it will contain less flavanols.

**BACKGROUND AND RATIONALE**

The purpose of this trial is pedagogic. We have sought to use an intervention for this purpose that Bioflavonoids and polyphenols. The public trials protocol was distributed and published

**OBJECTIVES**

The objective is to show how the complexities inherent in a randomized controlled trial can be made simple, fun and used as a teaching tool for the public.

The objective within the trial is to test whether cognitive improvement occurs around 30 minutes after the ingesting dark chocolate.

**TRIAL DESIGN**

Placebo-controlled, single blind randomized controlled trial, the researchers are by blinded allocation the public are blinded to the purpose of the intervention.

**METHODS (PARTICIPANTS, INTERVENTIONS, AND OUTCOMES)**

**STUDY SETTING**

A public lecture setting based within a university
ELIGIBILITY CRITERIA

Inclusions
Anyone in attendance at the lecture who has no contraindications to eating chocolate and wishes to participate

Exclusions
Contraindications for chocolate consumption

INTERVENTIONS

Dark chocolate 72% cocoa solids, not alkali processed, a milk chocolate bar, and a white chocolate bar with no polyphenols. Bars were chosen for similarity in size and appearance to avoid external effects from bright coloured wrappers.

There are no criteria for discontinuing allocated interventions as this is not applicable for this short trial, however, participants are free to spit out or discontinue eating of the chocolate if they find it unpalatable.

Adherence was not monitored as it was anticipated that the time from agreement to participate to receiving the intervention was only seconds and was a one-off event. Participants will be asked not swap their chocolate.

Lecture attendees can enjoy the chocolate regardless of whether they choose to participate in the trial.

OUTCOME

Primary outcome
Accuracy on recall of a letter sequence test approximately half an hour after the consumption of chocolate.
Other Outcomes

Participants will be asked to record their mood on a scale of 0 to 9 at the end of the lecture with 0 being unhappy to 9 being the highest level of joy.

Participants will be asked their preference for chocolate dark milk or white to enable subgroup analysis of the results by participant preference.

SAMPLE SIZE

Estimated sample size using sealed envelope calculations at 95% confidence levels at 80% power. The sample size estimate is based on an accurate response for alphanumeric sequencing for 30% of the control group and 60% response for those assigned to dark chocolate.

RECRUITMENT

Participants were recruited to the lecture using social media including Twitter, Facebook, blogs, LinkedIn, e-mail, and inter-office memos. Announcements of the event were made on the ThinkWell website and through the City University London events page. Attendees were encouraged to invite others who may be interested.

ASSIGNMENT OF INTERVENTION (RCT ALLOCATION)

SEQUENCE GENERATION

Chocolate bars will be in opaque indistinguishable manila envelopes. These will be set up in random groups of 15 bars consisting of 5 dark, 5 milk and 5 white bars. The randomisation will be accomplished by putting the 15 envelopes into an opaque bag by one member of the research team and
mixing them up, another team member will blindly draw them out sequentially with distribution in 15 group blocks to participants. The same process will be used for each successive 15 group block.

Participants will be restricted to one envelope containing one piece of chocolate.

160 people booked to come to the lecture 48 hours prior to the lecture when the materials were being prepared. We anticipated that people changing their minds and a pending transportation strike would produce an attrition rate of ~50%. Despite anticipating an audience of 80 we prepared 150 envelopes to be on the safe side.

**ALLOCATION CONCEALMENT MECHANISM**

Participants were handed their envelopes on entry into the lecture theatre and asked not to open them until asked to do so.

**BLINDING (MASKING)**

Participants will not be blinded to the type of chocolate they consume.

**DATA COLLECTION, MANAGEMENT, AND ANALYSIS**

The primary analysis is dark chocolate compared to white chocolate. Milk chocolate has been included to enable the exploration of a dose-response, should chocolate be shown to be effective.

Intention to treat analysis will be automated by asking what kind of chocolate bar was in your envelope at the beginning of the trial which will be linked via the Turning Point response to the measurement of cognitive speed. Should any participants
have swapped their chocolate this will therefore not be taken into account when the answers are linked.

**DATA COLLECTION METHODS**

Data collection is automated using Turning Point 5.0 software and clickers to register and link participants’ responses.

**DATA MANAGEMENT**

All responses and a report will be saved at the end for inclusion in any published report of this trial.

**STATISTICAL METHODS**

We will look at the difference in the proportion of respondents accurately recording the correct final sequence of letters and the 95% CI of this difference.

Subgroup analyses will look at whether sex or chocolate preference has an effect. We will do a test for trends according to % cocoa solids in the intervention or control.

**MONITORING**

NA

**DATA MONITORING**

NA

**HARMS**

NA
AUDITING

NA

ETHICS AND DISSEMINATION

RESEARCH ETHICS APPROVAL

This protocol has ethics approval from The University of Oxford Central University Research Ethics Committee (CUREC) number- MSD-IDREC-CI-2013-17

PROTOCOL AMENDMENTS

NA

CONSENT OR ASSENT

Consent is by affirmation and the use of the clicker during the lecture and after the presentation of consent materials delivered orally and through a visual power point presentation. The participants will be told they can eat the chocolate whether or not they choose to participate in the trial. Consent will be in compliance with standards for good clinical practice and CUREC guidelines

CONFIDENTIALITY

Data is automatically anonymised and recorded.

DECLARATION OF INTERESTS

Amanda Burls and Amy Price have no conflicts of interest to declare except for the love of chocolate.
ACCESS TO DATA

All data is anonymised and collection and analysis through Turning Point software is automated. The key results will be made available during the lecture itself, immediately following completion of the letter sequence memory test. All data will be made available in publications arising from this research.

ANCILLARY AND POST-TRIAL CARE

NA. Although all participants will be offered the opportunity to join a moderated discussion forum where they can share their experiences.

DISSEMINATION POLICY

The research will be published in a peer-reviewed open access journal before July 2015. If peer-reviewed publication is not possible by this date, the paper will be made public through the ThinkWell website and by posting the same to FigShare and Mendeley.

APPENDIX

Standardized participant instructions
1. Actively reflect: what is your mood?
2. Open your envelope.
3. Clear your palate. Rub your tongue around your mouth and swallow. This is crucial in order to appreciate the subtleties of chocolate’s complex flavor.
4. Rub the chocolate briefly between your fingers to coax the flavour.
5. Break the piece in half. It should resonate with a resounding “SNAP!” and exhibit a fine gradient along the broken edge. This is quality stuff!
6. Smell the chocolate, especially at the break point. The aroma is an important component.
7. Place the chocolate on the tongue, and allow it to arrive at body temperature.
8. Observe the taste and texture. As the chocolate melts, concentrate on the flavors that are enveloping your tongue. Melting will release more volatile compounds for you to smell. Close your eyes, take note with your other senses.

References
Keen C. Chocolate: Food as medicine/medicine as food. J Amer Coll of Nutr. 2001. 20:90005 436S-439S. Available at: http://www.jacn.org/cgi/content/full/20/suppl_5/436S


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For more information see Education by Chocolate and Amanda Burls Inaugural Lecture