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A prospective observational study assessing the feasibility of measuring blood lead levels in New Zealand hunters eating meat harvested with lead projectiles

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ABSTRACT

There is no safe level of lead exposure. Correlations suggest that hunters harvesting wild game with lead bullets may be at risk of lead exposure through eating minute lead particles from shrapnel in their wild game. This feasibility study will determine if it is possible to conduct an interventional controlled, blinded study to evaluate if there is a causal relationship between meat harvested with lead bullets and elevated blood lead levels in those who consume the meat. This is an observational case crossover study and the primary outcome is blood lead levels. Individuals will have blood lead levels measured 2–4 days after eating one serving of meat harvested with lead bullets. At three potential washout periods these same individuals will have a subsequent blood lead level analysis. This observational study will provide the data necessary to determine the washout period and sample size for a prospective interventional study to evaluate if meat harvested with lead bullets raises blood-lead levels in those who consume the meat. This study has been approved by the Health and Disabilities Ethics Committees of New Zealand. *Trial registration:* NCT02775890.

1. Introduction

As lead is one of the few substances that does not have a safe level of exposure, it is important to minimize all exposure [1,2]. Hunters can use lead or lead-free bullets [3], and a vast majority choose to use lead bullets [4,5], primarily because of tradition and the belief that lead bullets are safe. Non-lead projectiles are considered premium ammunition [6], but they are not significantly more expensive in some world areas [7]. There is a correlation between hunters using lead projectiles and elevated lead blood levels [8–10], however a causal link is unestablished [11]. As lead-shot meat is sold globally, this potential lead contamination is a global health concern [12].

This is a clinical research protocol to determine the feasibility of assessing lead levels in hunters who use lead projectiles. This observational study will determine if it is possible to perform a subsequent interventional blinded controlled study of lead levels in hunters using lead or lead-free projectiles following consumption of self-harvested wild game. The hypothesis for the subsequent study is that minute lead particles from shrapnel dispersed through the animal during harvest are ingested and this exposure results in increased lead blood levels [3]. This current observational study will establish the sample size and washout period for the subsequent interventional study. This observational study will be conducted in compliance with the protocol, Good Clinical Practice Standards, associated regulations and institutional research requirements.

There are three biological compartments where unexcreted lead is stored: blood, soft tissue, and mineralising tissues. After absorption, lead is stored in the blood compartment with a half-life of 28 [13] – 36 [14] days. Lead rapidly disperses into soft tissues post-exposure and in soft-tissues it has a half-life of approximately 40 days [15]. The primary long term repository of lead in the body is mineralizing tissue in bones and teeth [16]. Importantly, these

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mineralizing tissue stores can be mobilized and increase lead levels in the blood. The long half-life of lead and the dynamic nature of storage with the various compartments present challenges in identifying causal relationships between lead exposure and blood lead levels.

This current study establishes the parameters necessary to assess whether hunters eating meat shot with lead projectiles have elevated blood lead levels. For this feasibility study, hunters will be asked to abstain from consuming meat harvested with lead projectiles for 7 days. After 7 days, hunters will provide a baseline blood sample. Hunters will then consume meat that was harvested with lead projectiles and provide an additional blood sample 2–4 days (the blood-lead level peak post exposure [17]) after consumption. Hunters will also provide subsequent blood samples at periods of 9, 18, and 27 days. During the 27 day period, hunters will not consume meat harvested with lead projectiles. (Fig. 1). We have chosen to use deer as the species for this study to reduce variation; New Zealand is the ideal place to conduct this study because of year-round hunting of deer [18]. This study design will allow for the development of a conditional linear effects model, which will account for the inherent correlation of longitudinal data that involves repeated measures on the same subject over a period of time. A conditional model will also be more robust to any missing data that may arise through the course of the study, which may also facilitate a reduction in the required number of subjects necessary for this feasibility study.

If this current observational study determines that an interventional study is feasible, the subsequent interventional study would randomize hunters into two groups: hunters using lead projectiles and hunters using non-lead projectiles. All hunters would undergo an initial wash-out period and then have baseline blood lead level recorded. Hunters in both cohorts would then eat the harvested meat and blood lead levels would be recorded 2–4 days after eating the self-harvested meat. Hunters would then repeat this process for a replication of 3 times during the year. After one year, the hunter would cross over to the other type of projectile and repeat the entire process again (Fig. 2). This case crossover study would be analyzed utilizing a conditional linear effects model to account for the correlative nature of longitudinal data involving repeated measures. Additionally, this model will allow for other factors to be included in the model, including time-dependent covariates. Additionally it would be possible to use isotope analysis to identify if the lead levels in the blood of participants were primarily from the environment or from the lead projectiles [10,19]. Fortunately, baseline blood lead levels in New Zealand are similar to levels in other developed countries [20] thus allowing a broad extrapolation of the data generated.

2. Material and methods

2.1. Study objectives

The primary objective of this observational study is to determine the washout period and sample size for a subsequent study measuring lead levels in hunters in New Zealand after eating wild game shot with lead projectiles. This primary objective will be accomplished through measuring lead levels in hunters who have recently eaten meat harvested from deer killed with lead projectiles and subsequently measuring blood lead levels of those same hunters after abstaining from eating meat harvested from deer killed with lead projectiles (Fig. 1).

The secondary objective is to determine the feasibility of a blinded controlled interventional trial comparing blood lead levels in hunters using lead and lead-free projectiles for harvesting wild game for consumption. Specifically, this aspect of feasibility will be determined by participant compliance during this feasibility study.

2.2. General study design

There are two periods of analysis for this study.

1. Hunters that within 2–4 days prior to blood being drawn have eaten self-harvested wild deer shot with lead projectiles; and
2. Hunters that have abstained from eating self-harvested wild deer shot with lead projectiles for specific periods of time.

Hunters in period 1 and period 2 are the same individuals; they will be consented for the study once they have harvested an animal and provide pictures of shot placement. In order to avoid bias, the investigator performing the data analyses and the laboratory staff will be blinded to the samples. The participants will know when they are submitting blood samples during the period while eating meat harvested with lead bullets and when they are submitting blood samples while abstaining from lead-harvested meat so they will not be blinded. Animals will be shot in the thorax (Fig. 3) and the hunter will provide photographs of the shot location. Hunters should process the animal according to their standard practice, including making of minced meat.

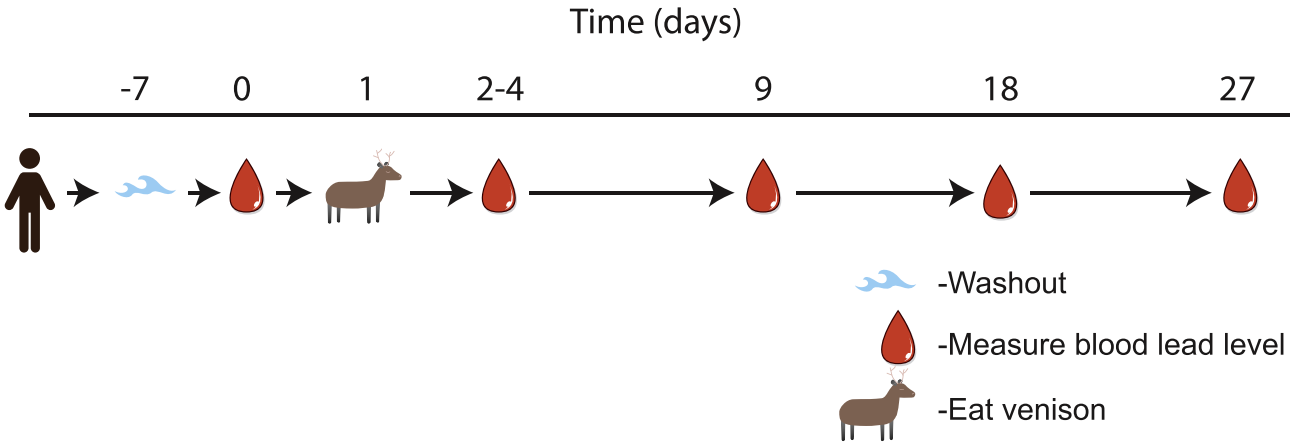

Fig. 1. Design of the current feasibility study. Participants in the current study will harvest deer with standard lead projectiles. A baseline lead measure, a measure immediately after eating the lead-shot meat, and measures at 9, 18 and 27 days. These blood lead levels will allow a model to be built determining appropriate sample size for each potential washout period.