Playing with fire? Factors influencing risk willingness with the unlicensed fat burner drug 2,4-Dinitrophenol (DNP) in young adults

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Introduction

Efficient, but safe, pharmacological aids to weight loss is the holy grail of obesity research. From the public health point of view, it is concerning that hazards of the past seem to be a permanent or returning feature of today's off-street 'supplement' market, mainly through retail networks that fall outside standard safety regulations: the Internet [1]. 2,4-Dinitrophenol (DNP) was used until the late 1930s to treat obesity and was subsequently withdrawn owing to its severe toxicity[2]. However, industrial uses of DNP as a dye, wood preserver, herbicide and film-developer have remained in place over the years. Recently, DNP has resurfaced as a weight loss product in the supplement market as *Su/olfo Black, Nitro Kleenup* or *Caswell No.392,*[3] but also sold on the Internet or listed among the ingredients as *Aldifen, Chemox, Nitophen, Dinofan, Dinosan, Dnoc, Osmotox-, Fenoxyl-,* or *Tertosulphur PRB*. In parallel with the re-appearance of DNP as a weight-loss promoting agent, clinical presentations with DNP toxicity increased with associated high mortality worldwide[4-6]. Evidence from Internet forums and discussion boards suggests that DNP is widely used among bodybuilders to further reduce the often already low body fat percentage. To a lesser extent, DNP also appears to be in the repertoire of those with disordered eating, mainly restricted eaters and binge eaters, to counterbalance the calorie intake.

DNP is a fat burner that inhibits efficient energy (ATP) production in cells. Through uncoupling mitochondrial oxidative phosphorylation by facilitating proton transport across the mitochondrial membrane, DNP leads to rapid consumption of energy without generating ATP and consequently, to increased fat metabolism[3,4]. However, the weight-loss effect comes with serious, and in some cases potentially fatal, adverse side effects. These include hyperthermia (the leading cause of fatality with acute DNP toxicity) and cardiac arrest, but also diaphoresis, tachycardia, tachypnea; and cataracts with low dose chronic exposure[2-6].

With the persistent supply and popularity of DNP among bodybuilders and extreme dieters, regulatory efforts to prevent DNP use[7,8] are undermined by readily available retail options on the Internet. One alternative approach to mitigate health risks people willingly take with unknown, unlicensed and potentially dangerous substances is to devise end-user-centred, proactive public health policies. In order to do this, it is important to understand the factors that affect an individual's willingness to take the drug after acknowledgement of the adverse side effects. Therefore, the aims of this study were to examine the different risk levels individuals are willing to take with DNP for the desired results and to investigate psychosocial factors that may influence risk willingness.

Participants were recruited opportunistically through social networks with no specific inclusion/exclusion criteria for diet or weight. The final sample consisted of 150, mainly young, adults with mean age of 25.0 ± 5.4 years; age range 18-45 (88% being 30 years of age or younger); 50% male; 32.7% white, 15.3% black, 18.0% Asian, 12.7% mixed, 21.3% other ethnic background. The highest single proportion of the participants had an undergraduate degree (30.0%), followed by completed undergraduate Level 5 (26.7%), A-level/B-Tech (16.7%), GCSE (11.3%), postgraduate qualification (10.7%) and undergraduate Level 4 (4.7%).

The survey contained questions about satisfaction with weight and desired change (if not satisfied with current weight) and measured general risk propensity[9], global self-esteem[10] and DNP-specific risk willingness. Willingness to take risks with DNP was measured with three scenarios representing incremental levels of health risk: (i) guaranteed weight loss up to 8-10 kg in 2 months with no side

effect mentioned; (ii) as in (i) but some side effects including dehydration, headaches, sweating, discomfort, fever and/or flushed skin are known; and (iii) as in (i) but also aware that continual usage of DNP through a long period of time could cause death through abnormally high temperature (hyperthermia), high heart rate (tachycardia), excess sweating (diaphoresis) and rapid breathing (tachypnoea). The scenarios were individually rated on an 11-point scale which was anchored at 0 = not at all willing and 10 = very willing to take risk.

Past experience with weight-loss products (excluding meal replacements) was recorded as presence or absence. Self-reported satisfaction with current weight was assessed with a single question "Are you happy with your current weight?", with three answer options of 'Yes', 'No, I would like to lose weight' and 'No, I would like to gain weight' to cater for all possibilities. In case of 'No' answer, the magnitude of the discrepancy between current and desirable weights was recorded in incremental categories of 2kg, 4kg, 6kg, 10kg and > 10kg. Demographic information included age, sex, ethnicity and highest educational level. To create a single score to facilitate comparison, an overall score for DNP risk willingness was calculated by weighting the expressed level of willingness in the three scenarios by 1, 2 and 4 respectively in increasing order of risk severity, then adding the weighted scores together to form a scale with a theoretical range of 0 to 70 (Cronbach alpha = 0.781).

Weight satisfaction and past experience with weight-loss drugs other than DNP

Of the 150 participants, only 20.7% (23 males and 9 females) were happy with their current weight. A further 6.7% (8 males and 2 females) wanted to gain weight. The remaining 73.3% (44 males and 64 females) reported weight-loss as a desirable goal. Thirty-seven participants (24.7% of the sample; 15 female and 22 male) reported having previous experience with weight-loss drugs.

Based on sample characteristics, three distinct clusters were identified using two-step clustering with maximum likelihood method and Akaike's Information Criterion. Predictor variables for cluster membership, in decreasing order of importance, were: satisfaction with weight (1.00), having past experience with weight-loss drugs (0.92), magnitude and direction of desired weight change (0.90), general risk propensity (0.08) and global self-esteem (0.05). The obtained importance scores, which range between 0 and 1 reflecting relative importance (1 being very important), show that the key discriminating factor is the desired goal and the magnitude of weight change and having past experience with weight-loss drugs. Personality traits did not have discriminative power.

The first group (Cluster 1) contained 41 people (mean age = 24.59 ± 5.12 year; 73.2% male) who were mainly either satisfied with their weight (78.0%) or wanted to gain weight (9.8%). The majority (90.2%) had previous experience with weight-loss drugs and the average desired weight change, if any, was small (up to 2 kg). The largest group (Cluster 2) comprised of 75 people (mean age = 24.93 ± 6.12; 34.7% male) who all wanted to lose between 4 to 6 kgs of weight but none had previous experience with weight-loss drugs. The third distinct group (Cluster 3) formed with 33 people (mean age = 24.91 ± 4.09 years, 54.5% male) who all wanted to lose 6 kgs of weight or more and all had previous experience with weight-loss drugs. The difference in DNP risk willingness between the three clusters were statistically significant ($F(2,149) = 20.626$, $p < .001$), with Cluster 1 exhibiting the lowest overall willingness to use DNP (2.80±4.77), followed by Cluster 2 (12.73±13.66) with a highest level of expressed willingness in Cluster 3 (20.18±13.04). There was a notable variation in each group. The distribution of the willingness scores were skewed toward unwillingness in Clusters 1 and

2, but followed normal distribution in Cluster 3 (Kolmogorov-Smirnov tests with Lillefors correction, KS= 0.356, $p < .001$; 0.176, $p < .001$ and 0.137, $p = .121$, respectively).

DNP risk willingness

As expected, the overall DNP risk willingness decreased with the increase in health consequences: no side effects (4.83/10); some unpleasant but not fatal side effects (2.19/10) and potentially fatal side effects (0.59/10) for the full sample. However, desire to lose weight influenced people's willingness to take risk with DNP (Fig 1A). Detailed investigation further revealed a notable trend for gender (Fig 1B) and past experience (Fig 1C). Female participants appeared to be more vulnerable to DNP-risk ($t(129.8) = 2.981$, $p = .003$). Past experience facilitated higher willingness with DNP. The mediation effect (path model), which was tested using structural equation modeling with maximum likelihood estimation using AMOS v22, showed weak partial mediation of past experience on the relationship between desired weight loss and willingness to use DNP (using the weighted overall score). The regression weight from desired weight loss to willingness (B = 3.151 [standardised = .328]; SE = 0.777, $p < .001$) decreased but remained significant with past use interrupting the direct path (B = 2.902 [standardised B = .302], SE = 0.740, $p < .001$). The regression weights from past use to willingness was statistically significant (B = 9.269 [standardised B= .303]; SE = 2.261; $p < .001$). The similar regression weights from past use and desired weight change to DNP risk willingness suggest that the desired weight loss and having past experience exert equal influence on hypothetical willingness to take risks with DNP. (The relationship between desired weight loss and past use was small and non-significant.) Ethnicity or education did not have an effect on willingness ($F(4,145) = 0.506$, $p = .731$, $\eta^2 = .014$ and $F(5,144) = 1.140$, $p = .213$, $\eta^2 = .048$, respectively).

Relationship between demographics, personality traits and DNP risk willingness

General risk propensity only showed weak positive correlation (expressed as Spearman *r*s) with DNP risk willingness ($r = .242$, $p = .003$) and a non-significant relationship with desired weight change ($r = .115$, $p = .164$). Global self-esteem and age were independent of the DNP risk ($r = .134$, $p = .101$ and $r = -.009$, $p = .917$, respectively) or desired weight change ($r = .055$, $p = .502$; ; $r = -.054$, $p = .513$, respectively). A much stronger relationship was observed between DNP risk willingness and the desired weight change ($r = -.523$, $p < .001$). The negative correlation is explained by the coding: the more weight people wished to lose, the higher risk was that they were willing to take with DNP.

Discussion

The general trend if health consequences are known was negative because most participants were unwilling, to some degree, to take DNP. However, willingness showed an inverse relationship with the severity of the health consequences. Willingness to take risks with DNP, despite health warnings, appears to be influenced more by the desired goal (weigh-loss) and the magnitude of weight people wish to lose as well as having past experience with weight-loss drugs rather than their general risk-taking propensity or other psychosocial factors. Ethnicity or education did not have an effect on willingness. Possibly because of a highest level of weight dissatisfaction, female participants appear to be more vulnerable to DNP-risk. However, the highest level of willingness to take risks with DNP, an unlicensed and dangerous chemical, was reported in a group that was characterised by the large amount of desired weight loss and having past experience with weight-loss drugs, regardless of gender. With the caveat that hypothetical choices cannot be directly

extrapolated to actual decisions, it is notable that the willingness to use such a drug is present if health warnings are not known or potentially can be somehow discredited (e.g., used similar drugs before without problems, following 'expert advice' of those used the drug before or not exceeding recommended dose). This may be explained by compensatory belief mechanism, which warrant further investigation in exploring in relation to DNP or other health-risks associated with weight loss products and unlicensed substances.

Perspectives

Although the reported level of risk that people from the general population were willing to take was low, the willingness to take risks increased with the desired weight-loss and by having past experiences with weight-loss drug(s). Future studies should explore the level of willingness among specific populations such as bodybuilders and extreme dieters. Effective prevention should move beyond knowledge-based intervention (such as issuing health warnings regarding DNP) and tackle the motives behind the potentially risky behaviour with unknown or unlicensed drugs. To facilitate this, future investigation should focus on the cognitive process of conflicting information in the context of weight-related goals and past experiences, along with associated risk perception, compensatory belief mechanism (particularly in the light of the elevated risk willingness if past experience with similar drugs are available) and trust in information sources and purchase options.

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Ethical approval

Ethical approval was granted to the project by the Faculty Research Ethics Committee, Kingston University. Informed consent was implied by voluntarily completing and returning the anonymous questionnaire.

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Competing interests

None declared.

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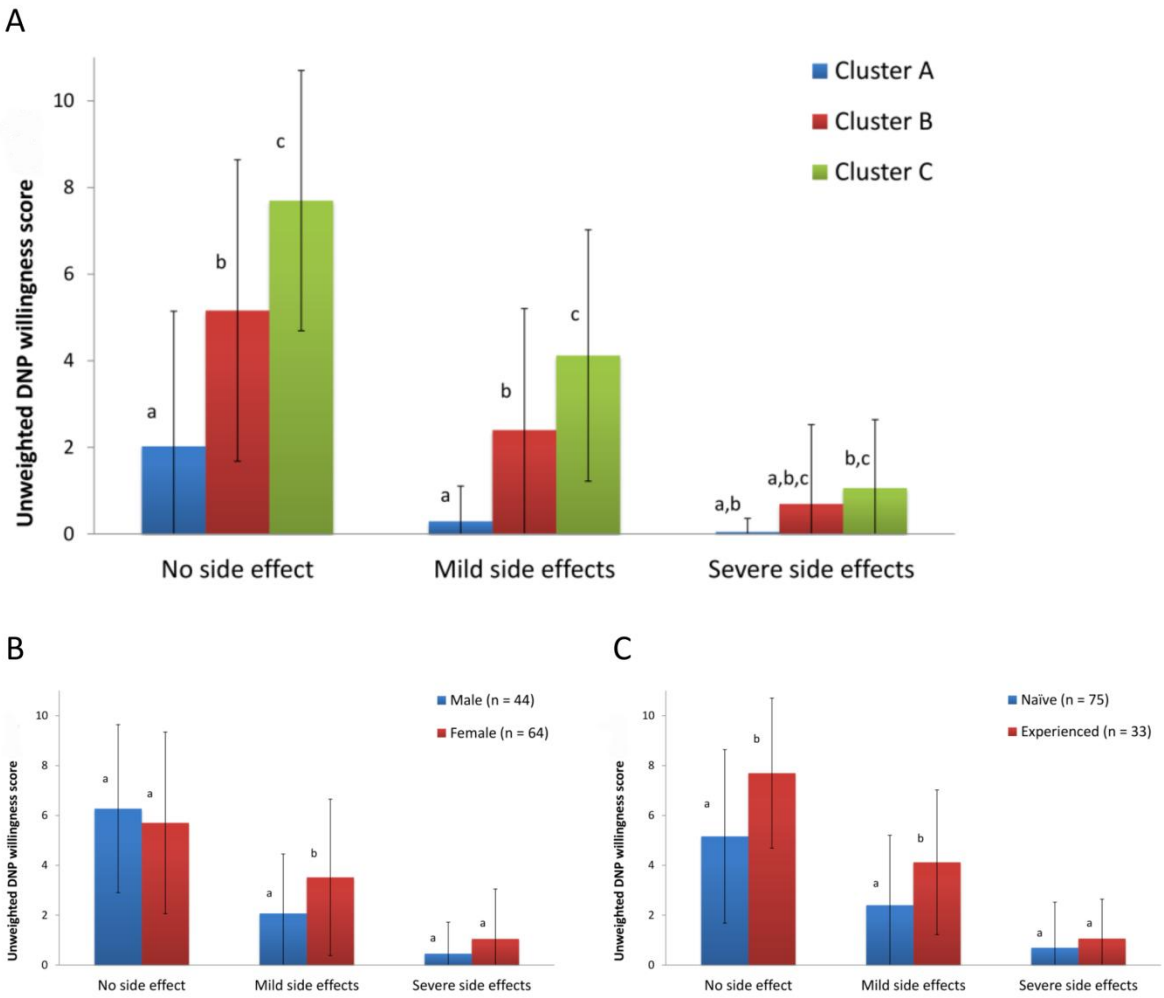

Fig 1: Level of willingness people are prepared to take with 2,4-Dinitrophenol (DNP) in the context of risk severity and participants' psychosocial characteristics. (A) Risk willingness with DNP in groups based on satisfaction with current weight, desired weight loss goal and past experience with weight-loss drugs in the full sample (n = 150) and (B) by gender and (C) experience in the subsample of participants desire weight loss (n = 108). Error bars represents standard deviations; different letters denote significant difference at $p < .05$.