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The desensitisation of graphic health warning labels and their impact on smokers, non-smokers and patients with COPD in a London cohort

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ABSTRACT

Background Graphic Health Warning Labels (GHWL) are used in smoking prevention. There is a lack of evidence regarding their effectiveness in different subjects, including COPD patients. Investigating knowledge and attitudes may allow better implementation of future public health policies. We hypothesised that there are significant differences in perception of GHWL between normal subjects, smokers and patients with COPD.

Patients and Methods We enrolled 163 subjects (60 non-smokers, 53 smokers and 50 COPD patients). We performed case-controlled structured interviews (fifty items), showing ten different GHWL; these interviews recorded demographics, smoking history, plans to quit, smoking risk awareness, emotional response, processing and impact of GHWL on behaviour. Further, patients were asked to prioritise the treatment of prevention of five specific diseases caused by smoking.

Results Smokers, particularly with COPD, were less susceptible to GHWL than non-smokers. 53.4% of the subjects expressed fear when looking at GHWL, non-smokers (71.9%) more so than smokers (39.8%, $p<0.001$). COPD participants were less aware of consequences than non-COPD participants ($p<0.001$), and that included awareness for lung cancer ($p=0.001$). Diseases most associated with smoking were lung cancer (95%), mouth and throat cancer (90.2%) and heart disease (84.7%), with blindness least well known (23.9%). However, 'Blindness' was relatively prioritised to be treated or prevented, ahead of stroke and oral cancer.

Conclusion GHWL are most effective in non-smokers and a desensitisation was observed in smokers and COPD patients. As a consequence, a tailored and concerted public health approach to use such messages is required, and 'blindness' deserves to be mentioned in this context because of an unexpectedly high deterring impact.

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ARTICLE SUMMARY

Article focus

- To assess the impact of Graphic Health Warning Labels (GHWL) in non-smokers, smokers and patients with COPD within a London cohort.
- To quantify the desensitisation of GHWL within these cohorts and to analyse the awareness of important smoking related risks and the preventive impact of this knowledge.

Key messages

- GHWL are least effective in those that have greatest exposure to them, such as smokers and patients with COPD; other strategies should be explored to assist smoking cessation.
- Few studies have investigated the awareness of non-pulmonary smoking related risks on patients with COPD, or the relative effects on smoking behaviour; awareness of non-pulmonary risks is low.
- Blindness was the least well-known risk of smoking, although it has a high deterring impact in all groups.

Strengths and limitations of this study

- Data were collected directly from patient groups in an outpatient setting.
- Detailed assessments used structured interviews, designed following an internal peer review process amongst three tertiary teaching hospitals and one academic institution.
- COPD patients were more reluctant to take part in the interviews and a potential limitation was an unmatched COPD cohort which was older with more male subjects.

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INTRODUCTION

Tobacco use is one of four factors responsible for the majority of all worldwide deaths caused by non-communicable disease according to the World Health Organisation,[1] causing lung cancer and Chronic Obstructive Pulmonary Disease (COPD).[2, 3] Smoking cessation at any stage improves health outcomes, even in patients with advanced COPD [4] and although it is difficult to change smoking behaviour, public health campaigns featuring primary and secondary prevention influence smoking habits and public health in the long-term.[5]

Graphic Health Warning Labels (GHWL) have already been used over several years to promote smoking cessation and increase awareness of smoking related side-effects.[6] Various studies have described the efficacy of GHWL, which appear more effective than plain text only warning labels.[7-11] However, difficulties to encourage smoking cessation persist [12] and currently, despite all efforts to change this, more than 21% of the UK population continue to smoke.[13]

Awareness of smoking-related ill health

Knowledge of smoking-related diseases amongst smokers and non-smokers, including exposure to second-hand smoke, oral health, and various cancers differs significantly [10, 14] and even amongst medical students.[15] Whilst cardiovascular and respiratory risks are well acknowledged, other diseases, particularly blindness are less so.[16-20]

Graphic Health Warning Labels

Vardavas and colleagues [8] investigated the significant role GHWL might play in preventing smoking during early adolescence, a crucial period in which experimentation and addiction commonly occur.[21] Despite their efficacy, long-term exposure to such warnings may have a desensitising effect on attitudes towards smoking cessation.

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The present study aims to investigate differences in GHWL impact, and knowledge of smoking outcomes in smokers, non-smokers and patients with COPD; hypothesising decreased effect on those at increasing severity of smoking behaviour. Identifying the level of awareness of smoking-related ill health would facilitate a more tailored public health approach for utilisation of GHWL within future health policies.

PATIENTS AND METHODS

The study was approved by the local research ethics committee (reference number 12/NE/0013) and was performed at Guy´s & St Thomas´ NHS Foundation Trust, London, UK. Participants were recruited from respiratory outpatient clinics and respiratory rehabilitation programs, between the dates of May 2012 to February 2013.

A structured interview was designed to investigate the effectiveness of GHWL in the UK and to establish differences in the awareness and knowledge of smoking-related ill health between smokers, non-smokers and COPD patients. 163 participants were studied, including 60 non-smokers, 53 smokers and 50 COPD patients (FEV1/FVC<0.7; active smokers and ex-smokers).

Structured Interview

The interview contained 50 items based on those utilised by previous studies [18, 19, 32] and following an internal peer review process amongst three tertiary teaching hospitals and one academic institution (King`s College London, UK). We recorded demographics (5 items), smoking history (7 items) and asked patients how confident they would be about quitting smoking (1 item) if they wanted to. Questions further determined knowledge of health risks associated with smoking (7 items), including how harmful they believed smoking was to their

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health (on a scale of 1, "not harmful", to 10, "very harmful, death") and the motivational impact of the risks towards stopping or preventing from smoking (15 items). The following health risks were included:

1) Mouth and throat cancer

   Smoking cessation causes a 50% reduction in risk of oral cancer within 5 years.[22]

2) Lung cancer

   Approximately 90% of male lung cancer deaths and 75-80% of female lung cancer deaths in the US are caused by smoking each year.[23]

3) Heart disease

   Estimations attribute 40% of heart disease to smoking.[24]

4) Stroke

   Smoking could increase the risk of stroke by 2 to 4 fold.[25]

5) Blindness

   Estimations attribute smoking to approximately 20% of new blindness in people over the age of 50.[26]

Participants were then shown GHWL (n=10) followed by questions to ascertain their emotional response to those labels (3 items), depth of processing the content of the labels (6 items) and the impact of these labels on their own smoking behaviour (1 item). It was also assessed whether participants would stop smoking if they were to develop early signs of the diseases illustrated (5 items).

All interviews were conducted by specially trained interviewers with medical backgrounds; instructed to guide but not influence decision-making and to remain neutral. Training took place prior to data collection and at two-weekly intervals, for 15-20 minutes, to standardise the interview process and minimise investigator-led bias.

Sample Size Calculation

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Sample size calculation was performed based on a 95% confidence interval, an alpha of 0.05, with an estimated total London smoking population (1,280,000) and the proportion expected to be aware of the least known consequence condition chosen in the questionnaire (blindness) at 0.01 – 0.05. The result was that at least 50 subjects needed to be included in each arm of this study to achieve a power of 0.8.

Statistical analysis

Data was collected using MS Excel 2007 (Microsoft Corporation, Seattle/WA, USA), analysed using SPSS Statistics 21 (IBM, New York/NY, USA) and tested for a normal distribution using the Kolmogornov-Smirnoff test. χ-square tests were used to compare categorical data. Non-categorical data were analysed using unpaired t-tests if data were normally distributed, or Mann-Whitney non-parametric tests if they were non-normally distributed. A regression analysis was conducted, using binary logistic regression and multiple linear regression, and applied to the primary outcome measure of knowledge score (the number of smoking-related risks that each participant was aware of). The independent variables in the analysis were age, gender, sex, ethnicity, smoking status and COPD status. The data is presented as mean (standard deviation, SD), unless otherwise indicated. A level of significance was defined as $p<0.05$.

RESULTS

A total of 163 participants (54% male (m), age 52.4 (17.8) years) were included, with 60 non-smokers (38.3% m; age 41.4 (16.4) years), 53 non-COPD smokers (69.8% m, age 49.7 (13.1) years) and 50 COPD patients (56% m; age 68.6 (10.7) years). The group with non-smokers had more female participants than the group with smokers and the one with COPD patients. The group with COPD patients was older than the other two groups. The ethnic background of all participants was predominantly “White” (78%), followed by “Asian/Asian British” (10%) and “Black/Black British” (9%). (Table 1)

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Table 1

	All (N=163)	Non-smokers (N=60)	Smokers (non-COPD) (N=53)	COPD (N=50)	X^2 / one-way ANOVA (P value)
Age (range, years)	52.4 (18-90)	41.4(18-85)	49.7(24-74)	68.6(40-90)	<0.001
Sex (N, %) Male Female	88 (54%) 75(46%)	23(38.3%) 37(61.7%)	37(69.8%) 16(30.2%)	28(56%) 22(44%)	0.003
Ethnicity/N White	127 (77.9%)	42 (70.0%)	40 (75.5%)	45 (90.0%)	
Asian/ Asian British	17 (10.4%)	9 (15.0%)	7 (13.2%)	1 (2.0%)	0.074
Black/ Black British	14 (8.6%)	5 (8.3%)	4 (7.5%)	4 (8.0%)	
Mixed	3 (1.8%)	3 (5.0%)	0	0	

Awareness of smoking-related ill health

93.3% of non-COPD smokers stated that they had thought about the health risks associated with smoking compared to 75.0% of COPD smokers (p=0.097). Across all participants, greatest awareness was for lung cancer (95%), followed by mouth and throat cancer (90.2%), heart disease (84.7%) and stroke (71.2%). The lowest grade of awareness was found for blindness (23.9%) across the groups. Non-smokers had a significantly increased awareness of association between smoking and mouth and throat cancer (p=0.004) compared to smokers. COPD patients had a significantly decreased awareness of lung cancer (p=0.001), heart disease (p=0.012), stroke (p=0.001) and mouth and throat cancer (p<0.001) compared to the other groups. There was no significant difference between the groups in the awareness of blindness.

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Awareness of smoking consequences and future behaviour

Smokers were more motivated to quit smoking if they were to develop heart disease (89.7% *vs* 75%, p<0.001), stroke (82.8% *vs* 75%, p<0.001), blindness (89.7% *vs* 66.7%, p<0.001), mouth and throat cancer (93.1% *vs* 75%, p<0.001) or lung cancer (89.7% *vs* 83.3%, p<0.001) compared to COPD patients. Non-smokers scored similarly to COPD patients (9.4 (1.1) *vs* 8.7 (2.3) points, p=0.055) when asked about *'the harmfulness of smoking to health'*, but they scored higher than smokers (8.4 (1.5) points, p=0.004).

When given the choice to avoid one of five hypothetical conditions associated with smoking, smokers rated lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and finally stroke. Similarly, non-smokers ranked lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and stroke. COPD patients also ranked lung cancer highest, followed by blindness, heart disease, mouth and throat cancer and stroke. However, no significant differences existed between the ranks in the different subgroups.(Table 2)

When given the choice to hypothetically treat only one of the five smoking associated conditions, smokers ranked lung cancer first, followed by heart disease, blindness, stroke and lastly mouth and throat cancer. Non-smokers ranked lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and stroke. COPD patients ranked lung cancer highest, then blindness, heart disease, mouth and throat cancer and stroke. Compared to non-smokers, smokers were significantly more likely to seek hypothetical treatment for lung cancer compared to non-smokers (p=0.005), who were more likely to seek treatment for mouth and throat cancer (p=0.043).(Table 2)

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Table 2

	COPD (n=50)	Non-COPD (n=113)	p-value	Smokers (n=103)	Non-smokers (n=60)	p-value
1) *How harmful is smoking to health? (non-normal)* Mean (SD)	8.7 (2.3)	8.9 (1.4)	**0.564**	8.4 (1.5)	9.4 (1.1)	**0.004**
Awareness of smoking related side-effects: total score out of 5	3.06	3.92	**p<0.001**	3.58	3.83	**0.293**
Awareness of Heart Disease as related to smoking (%)	74.0	89.4	**0.012**	85.9%	82.8	**0.598**
Awareness of Stroke as related to smoking (%)	54.0	78.8	**0.001**	69.7	73.4	**0.607**
Awareness of Blindness as related to smoking (%)	18.0	26.5	**0.238**	23.2	25.0	**0.796**
Awareness of Mouth and Throat Cancer as related to smoking (%)	72.0	98.2	**<0.001**	84.8	98.4	**0.004**
Awareness of Lung Cancer as related to smoking (%)	88.0	99.1	**0.001**	93.9	98.4	**0.167**
2) *If you could Prevent only one of Heart Disease, Stroke, Blindness, Mouth and Throat Cancer and Lung Cancer, which would you choose? (% choosing each option)*	[Rank 1-5]					[rank sum]
Heart Disease (%)	14.0 [3]	24.8 [2]	**0.122**	18.4 [2]	26.7 [2]	**0.203** [9]
Stroke (%)	8.0 [5]	8.0 [5]	**0.994**	7.8 [5]	8.3 [5]	**0.951** [20]
Blindness (%)	18.0 [2]	15.0 [3]	**0.634**	17.5 [3]	13.3 [3]	**0.927** [11]
Mouth and Throat Cancer (%)	12.0 [4]	8.8 [4]	**0.533**	8.7 [4]	11.7 [4]	**0.699** [16]
Lung Cancer (%)	48.0 [1]	41.6 [1]	**0.447**	46.6 [1]	38.3 [1]	**0.210** [4]
3) *If you could seek treatment for only one of the following conditions, which would you choose? (%)*	[Rank 1-5]					[rank sum]
Heart Disease	18.0 [3]	24.8 [2]	**0.341**	21.2 [2]	25.0 [2]	**0.572** [9]
Stroke	4.0 [5]	7.1 [5]	**0.450**	5.1 [4]	7.8 [5]	**0.473** [19]
Blindness	20.0 [2]	19.5 [3]	**0.937**	17.2 [3]	23.4 [3]	**0.325** [11]
Mouth and Throat Cancer	6.0 [4]	8.0 [4]	**0.658**	4.0 [5]	12.5 [4]	**0.043** [17]
Lung Cancer	52.0 [1]	38.9 [1]	**0.120**	51.5 [1]	29.7 [1]	**0.005** [4]

***Statistically significant values are highlighted in grey. In sections 2 and 3, ranks of each condition are given in brackets in columns 1,2,4 and 5, with sum of ranks in brackets in column 6 to allow comparison.**

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Response and processing of GHWL

Amongst all participants, 53.4% of patients experienced fear after viewing pictures of GHWL, 78.5% of participants expressed disgust; 28.8% would actively avoid labels if they saw them in public. Non-smokers experienced more fear when looking at GHWL (71.9%) compared to smokers (39.8%; $p<0.001$); there was no significant difference in expressing disgust between smokers and non-smokers.(Table 3).

GHWL would have been more sufficient to prevent or stop smoking in non-smokers than smokers ($p<0.001$). Non-smokers were more likely than smokers to think about the warning messages on cigarette packaging ($p=0.006$) and talk about the warning labels to others ($p<0.001$). COPD patients were less likely to avoid looking at GHWL compared to the other groups ($p=0.016$), to read the packaging less often ($p<0.001$), and to do so less carefully ($p=0.010$). They were less likely to think about the messages ($p=0.001$), talk to others about warning labels ($p<0.001$), think about warning labels when they were not in sight ($p<0.023$) or to keep a warning label at home as a reminder ($p=0.013$). No significant differences existed between COPD and non-COPD groups when comparing whether the warning labels were sufficient motivation to stop smoking ($p=0.240$).(Table 3).

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Table 3

Initial response to GHWLs	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=103)	Non-smokers (n=60)	**p-value**
...Fear? (%)	48.0	55.8	**0.360**	39.8	71.9	**<0.001**
...Disgust? (%)	76.0	79.6	**0.601**	72.8	82.8	**0.284**
Ever avoided looking at GHWLs? (%)	16.0	34.5	**0.016**	27.2	29.7	**0.846**
Are the warning labels sufficient motivation for you to stop smoking (if a current smoker) or not start smoking (if a non- or ex-smoker)? (%)	44.0	54.0	**0.240**	35.4	75.0	**<0.001**
16) Processing of GHWLs	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=103)	Non-smokers (n=60)	**p-value**
Packaging processing response						
a) How carefully have you ever read the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.9 (1.1)	2.4 (1.3)	**0.010**	2.4 (1.4)	2.1 (1.1)	**0.493**
b) How often do you read the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.6 (1.0)	2.5 (1.3)	**<0.001**	2.5 (1.5)	2.1 (1.1)	**0.064**
c) How often have you thought about the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.9 (1.3)	2.7 (1.3)	**0.001**	2.2 (1.2)	2.8 (1.5)	**0.006**
General processing response						
d) Have you ever talked to others about the warning labels on cigarette packaging? (1 = never, 5 = very often)	1.5 (1.1)	2.5 (1.4)	**<0.001**	1.8 (1.1)	2.7 (1.5)	**<0.001**
e) How often have you thought about the warning messages on cigarette packages when there has been no pack in sight? (1 = never, 5 = very often)	1.5 (0.9)	1.9 (1.2)	**0.023**	1.6 (1.0)	2.0 (1.3)	**0.112**
f) How often have you kept a warning label from a cigarette pack? (1 = never, 5 = very often)	1.0 (0.3)	1.4 (1.0)	**0.013**	1.2 (0.8)	1.3 (0.8)	**0.995**

***Statistically significant values are highlighted in grey**

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In terms of age and sex of participants, female subjects were more likely to experience fear compared to male participants (p=0.002), but not disgust or active avoidance of labels. They were also more likely to stop smoking following exposure to the labels (p=0.002) and more likely to think about GHWL messages when they are not in sight (p=0.023). Those who experienced fear were younger (p=0.037), as were those who would actively avoid looking at labels (p=0.008). (Table 4) Increase in age was also significantly correlated with a decrease in depth of processing of labels (r= -0.386, p<0.0000001), including a decrease in carefully reading GHWL (r= -0.315, p<0.0001), paying less close attention to them (r= -0.351, p<00001), less often thinking about the labels (r= -0.375, p<0.000001), including when they aren't in sight (r=-0.201, p<0.010) and talking about them less (r= -0.31, p<0.0001).(Table 5)

Table 4

Emotional response to warning labels	Male - Yes	Female - Yes	X^2	Mean age: Yes	Mean age: No	**t-test (2-tailed)**
Fear	37/88	50/75	**0.002**	50.0	55.6	**0.044**
Disgust	66/88	62/75	**0.235**	51.3	57.1	**0.112**
Avoidance	21/88	26/75	**0.129**	47.0	54.8	**0.008**
Sufficient to stop from smoking	35/88	48/75	**0.002**	51.5	53.9	**0.381**

***Statistically significant values are highlighted in grey**

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Table 5

	(1+2) Depth of processing total	1) Package processing total	2) General processing Total
Age (r)	-0.386	-0.393	-0.276
p-value	<0.000001	<0.000001	<0.001
male (mean)	11.739	6.761	4.977
female (mean)	12.589	7.096	5.493
t-test (2 tailed)	0.323	0.559	0.217
Package processing response:			
	16a) Carefully	16b) Close attention	16c) Thought about
Age (r)	-0.315	-0.351	-0.375
p-value	<0.0001	<0.00001	<0.000001
male (mean)	2.193	2.239	2.33
female (mean)	2.247	2.26	2.589
t-test (2 tailed)	0.788	0.915	0.312
General processing response:			
	16f) Talked about	16g) Thought about	16h) Kept a label
Age (r)	-0.31	-0.201	-0.094
p-value	<0.0001	0.010	0.232
male (mean)	2.114	1.58	1.284
female (mean)	2.329	2	1.219
t-test (2 tailed)	0.315	0.023	0.651

***Statistically significant values are highlighted in grey**

The regression analysis to understand whether there were independent predictors of knowledge or awareness of smoking-related consequences revealed no significant association with the overall knowledge score of respondents age (p=0.333), gender (p=0.079), race (p=0.552) and smoking status (p=0.756)).

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DISCUSSION

Our study revealed that most people are aware of smoking-related risks of ill health. Graphic Health Warning Labels evoke an emotional response of fear and disgust in the majority of participants, particularly in non-smokers, females and younger participants. Awareness is high when it comes to the association between lung cancer, heart disease, mouth and throat cancer and smoking, whilst it is very low to recognise the association between blindness and smoking. Indeed one study at a British district general hospital found only 9.5% of patients older than 18 could associate blindness with smoking, whilst other disease including lung cancer (92.2%), heart disease (87.6%) and stroke (70.6%) were higher in comparison;[27] despite up to 20% of new blindness being attributed to smoking.[26] It is therefore remarkable that participants would rather try to avoid or treat blindness, should they ever develop it from smoking, than oral and throat cancer or even stroke. The response of COPD patients to the processing of information expressed in the GHWL revealed a desensitisation effect which needs to be considered when using such messages in public health campaigns.

Awareness of smoking consequences and impact on future behaviour

Various studies have outlined an increased awareness of smoking-related respiratory complications in COPD patients.[27-32] 86% of smokers with COPD acknowledged the benefits of monitoring lung function of heavy smokers to increase awareness of the detrimental effects of smoking.[31] In contrast, our study found that COPD patients had a decreased awareness of smoking-related consequences compared to non-COPD patients with regards to heart disease, stroke, mouth and throat cancer, and lung cancer. Smokers scored significantly lower than non-smokers when asked to rank how harmful smoking is to their health and had a decreased awareness of mouth and throat cancer as a consequence of smoking.

Some patients with COPD mentioned that they failed to see an association between their smoking habits and their health problems and were unconvinced of smoking-related risks.

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COPD patients were less likely to give up smoking compared to non-COPD current smokers if they developed any of the proposed diseases, as were smokers compared to non-smokers.

The role of awareness for "blindness" in the context of public health campaigns

Smoking-related lung cancer, heart disease, mouth and throat cancer and stroke are well publicised and recognised; these factors are used not only in public health campaigns on GHWL but they are also included in campaigns via printed media and TV advertising;[33-34] this awareness is reflected across all the patient groups studied.

Blindness, however, is the least well-known smoking-related risk in our study, but all participants were highly motivated to prevent and treat blindness (ranked 2nd or 3rd in all groups following lung cancer and heart disease). Previous studies have also found blindness to be a better motivational message towards smoking prevention [17-19] than conventional messages. In comparison to non-smokers, smokers have a lower level of understanding of certain smoking-related health risks including macular degeneration, cataract and oral diseases.[16, 17, 20] Previous studies found that teenagers were more motivated to consider smoking cessation when becoming aware of risks for blindness over other conditions, such as heart disease and lung cancer.[18] Given this, an increased emphasis on blindness in this context could have the potential to motivate and encourage smoking cessation.[17] Countries such as Australia where various studies have shown an increased awareness of smoking-related eye disease [37] have effective public health promoting strategies in place to comprehensively include these risk factors.

Desensitisation, reduced effectiveness of GHWL and future interventions

GHWL appear to lose efficacy in patients that are consistently and longer exposed to these messages. Unfortunately, those are the cohorts of patients that these labels are primarily targeted at, particularly long-term smokers and COPD patients who still smoke. There has to be a balance between sensible use of GHWL and an expected desensitisation effect over time.

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Therefore, specific health message should be targeted at these cohorts over defined periods or re-organised with specific and regular campaigns to avoid a desensitisation effect. The knowledge that additional factors that are less well-known (e.g. blindness) could have similar effects on public health as well-established risks associated with smoking (e.g. lung cancer, heart disease) provides the chance to alternate with different diseases featuring on GHWL.

Indeed, different approaches to promote smoking cessation are still required. It has recently been considered whether plain packages should be introduced, preventing the use of illusory packaging techniques as a means of attracting consumers.[38] Evidence around plain packaging is currently based on indirect studies [39-43] and whilst Australia is the first to sell tobacco products adopting such packaging [44, 45] the UK government had considered to introduce such a policy [46] but has currently rejected it.

Other motivational factors and smoking cessation

Stimuli for smoking cessation in ex-smokers include healthcare professional's advice, family request, and financial incentives.[19] GHWL that focus specifically on the effects of passive smoking may be emotionally salient and therefore provide some motivation to stop smoking. However, advertising financial benefits of smoking cessation via GHWL on packaging is unlikely to be a viable option.

Limitations

The respondents interviewed came from a hospital setting in outpatients and pulmonary rehabilitation courses and, therefore, a selection bias will have influenced the outcome of our study. Further, the COPD cohort tended to be older, with more male subjects, whereas the non-smoker group consisted of proportionally more females. However, the numbers used in the analysis were taken from a reasonably large dataset and represent consistent results amongst all groups which are in line with previous findings. Group differences therefore may have influenced some outcomes but they will not have invalidated the general message.

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In addition, recruiting COPD patients proved to be difficult because patients were more reluctant to take part in this kind of research. It is likely that the true aversion to GHWL might have been even greater amongst unselected COPD patients.

The content of GHWL was challenged in some interviews. All warning labels were shown together, despite some evoking more of a response than others in terms of fear and disgust and this might have lead to a greater emotional response to GHWL than showing isolated pictures. It remains to be determined whether some GHWL have more success in the use to prevent smoking than others.

Conclusion

The use of GHWL is an important and useful deterrent in the primary and secondary prevention of smoking, it has also the potential to stop people from starting to smoke. Prolonged exposure to GHWL may cause desensitisation and other strategies using intermittent application of different features on GHWL within health campaigns need to be employed to maintain their efficacy. Blindness has to be mentioned as a specific factor because there is low awareness of its association with smoking whilst having an unexpectedly strong impact on the emotional response when used in the context of GHWL. The evidence provided by our research is needed more than ever to continue to develop sufficient public health campaigns to deter from smoking, because plain packaging has been currently rejected as public health policy in the UK. Health care policies should focus on improving the lack of awareness of smoking-related diseases, especially in those with chronic smoking behaviour. Timing the exposure of specific messages used in GHWL should be considered to avoid desensitisation and tailor public health campaigns.

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Contributorship

CR designed the study, designed and adapted data collection tools, set up research teams in Singapore (Singapore arm, data not yet available) and London, obtained ethical approval, monitored data collection and data collection training, collected data, revised and oversaw formation of the literature review, analysed data and wrote and revised literature review, analysis and discussion sections of the paper. He is the first guarantor. B-MC collected data, made significant contribution to analysis and wrote proportions of analysis and discussion section. PD made significant contribution to data collection and reviewing paper. SS performed initial literature search and literature review. BS collected data and aided in elements of data analysis section. MB made significant contribution to data collection and reviewing the paper. AD was vital in statistical analysis plan, analysis sections and so tailoring discussion sections. JS is second guarantor. He oversaw data collection in the London arm, established, enabled and supervised undertaking of the project in the London

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site; facilitated formation of the London research team; safeguarded data collected and was responsible for overlooking, guiding and re-drafting the eventual manuscript prior to submission.

Competing interests and funding

There are no competing interests or external sources of funding in the undertaking of this project or production of the given manuscript.

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APPENDIX

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SMOKING QUESTIONNAIRE

1. Personal particulars:

Initials: _____

2. Age: _____ years

3. Sex: Male/ Female

4. Race:
[Please tick or if 'other' write on the line provided]

Asian or Asian British
- ☐ Bangladeshi
- ☐ Pakistani
- ☐ Indian
- ☐ Other _____

Black or Black British
- ☐ African
- ☐ Caribbean
- ☐ Other _____

Chinese or Chinese British
- ☐ Chinese
- ☐ Other _____

Mixed
- ☐ White and Asian
- ☐ White and Caribbean
- ☐ White and Black African
- ☐ Other _____

White
- ☐ Irish
- ☐ Northern Irish
- ☐ English
- ☐ Scottish
- ☐ Welsh
- ☐ Other _____

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5. Occupation:

- ☐ Legislators, senior officials and managers
- ☐ Professionals
- ☐ Clerical workers
- ☐ Service workers and shop and market sales workers
- ☐ Agricultural and fishery workers
- ☐ Production craftsmen and related workers
- ☐ Plant and machine operators and assemblies
- ☐ Cleaners, labourers and related workers
- ☐ Military
- ☐ Unemployed
- ☐ Student

6. Cigarette smoking status: Current smoker/ ex-smoker/ non-smoker

If current smoker, please proceed to question 7.

If ex-smoker, please proceed to question 8.

If non-smoker, please proceed to question 9.

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QUESTION 7 - CURRENT SMOKERS

a) How long have you smoked for?

_____

b) On average, how many cigarettes do you smoke a day?

_____

c) Have you ever considered giving up smoking? **YES / NO**

IF YES

d) Have any of the following motivated you to give up smoking?
(Multiple choices possible)

- ☐ Health
- ☐ Financial savings
- ☐ Family request
- ☐ Health professional's advice
- ☐ Media (magazines/ newspapers/ TV commercial / radio)
- ☐ Internet
- ☐ Peer advice
- ☐ Graphic health warnings (cigarette packs)

Other: _____

e) How many attempts have you made at giving up smoking?

f) On a scale of 1 – 10, how confident are you about giving up smoking when you when you want?

0 1 2 3 4 5 6 7 8 9 10

Not confident Very confident

g) Have you even thought about the health risks associated with smoking? **YES/NO**

IF YES

h) On a scale of 0 – 10, how often do you think about the health risks associated with smoking?

0 1 2 3 4 5 6 7 8 9 10

Not at all Very often

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Please proceed to question 9.

QUESTION 8 - EX-SMOKERS

a) How long ago did you give up smoking?

b) How many cigarettes did you smoke a day?

c) How many years did you smoke for?

d) How many attempts did you make to stop smoking, including the last?

e) What was your motivation for stopping smoking? (Multiple choices possible)

- ☐ Health
- ☐ Financial savings
- ☐ Family request
- ☐ Health professional's advice
- ☐ Media (magazines/ newspapers/ TV commercial / radio)
- ☐ Internet
- ☐ Peer advice
- ☐ Graphic health warnings (cigarette packs)

Others: _____

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QUESTION 9

How harmful do you think smoking is to health in general?

0	1	2	3	4	5	6	7	8	9	10
Not harmful										Very harmful (death)

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General awareness of smoking and disease

10. Do you believe the following diseases are related to smoking?

Heart disease	**YES / NO / NOT SURE**
Stroke	**YES / NO / NOT SURE**
Blindness	**YES / NO / NOT SURE**
Mouth and throat cancer	**YES / NO / NOT SURE**
Lung cancer	**YES / NO / NOT SURE**

11. Which disease would you like to prevent if it were possible to prevent only one?

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

12. Which disease would you seek treatment for if it were possible to treat only one?

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

If smoker, please proceed to question 13.

If ex- or non-smoker, please proceed to question 14.

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QUESTION 13

Imagine that all the conditions below have the same risk of occurrence. Rank the following conditions from 1 to 5 in order of how much motivation each provides towards you stopping smoking, with 1 being most feared, and 5 being the least feared.

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

QUESTION 14

Imagine the following conditions all have the same risk of occurrence. Rank the following conditions from 1 to 5 in order of how much each motivates you to not start smoking, with 1 being most feared, and 5 being the least feared.

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

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Attitudes toward graphic health warning labels on cigarette packs

15. Emotional response to warning labels

a) Did you experience any fear when looking at the warning labels? **YES / NO**

b) Did you experience any disgust when looking at the warning labels? **YES / NO**

c) Have you ever actively avoided looking at the warning labels in public? **YES / NO**

16. Depth of processing

Please score the following questions on a scale of 1 to 5 using this guide:
1=not at all/never; 2=once; 3=sometimes; 4=often; 5=all the time/a lot

Package messages (outside)

a) How carefully have you ever read the messages on the outside of cigarette packets? 1 2 3 4 5

b) How often have you read or paid close attention to the messages on the outside of packages? 1 2 3 4 5

c) How often have you thought about what the warnings on the outside of packages have to say? 1 2 3 4 5

General

d) Have you ever talked about the warning labels with other smokers or non-smokers? 1 2 3 4 5

e) Have you ever thought about the warnings or what they had to say when a cigarette pack wasn't in sight? 1 2 3 4 5

f) Have you ever kept a warning label to serve as a reminder of the effects of smoking on health? 1 2 3 4 5

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Impact of graphic health warning labels on smoking behaviour

If current smoker, please proceed to question 17.

If ex- or non-smoker, please proceed to question 18.

17. Current smoker

Do you feel the labels are a sufficient motivation for you to stop smoking? **YES / NO**

Would you stop smoking if you developed early signs of the following disease?

Heart disease	**YES / NO**
Stroke	**YES / NO**
Blindness	**YES / NO**
Mouth and throat cancer	**YES / NO**
Lung Cancer	**YES / NO**

Rank the conditions in order of how much motivation each provides towards you stopping smoking, with 1 being most feared, and 5 being the least feared.

Heart disease

Stroke

Blindness

Mouth and throat cancer

Lung Cancer

18. Ex- or non-smokers

Do you feel the labels are a sufficient motivation to prevent you from starting smoking? **YES / NO**

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STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **[page 2]**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **[page 2]**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **[page 4]**
Objectives	3	State specific objectives, including any prespecified hypotheses **[page 5]**
Methods		
Study design	4	Present key elements of study design early in the paper **[page 5]**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **[page 5]**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls **[page 5]**
		(*b*) For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **[page 5-6]**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **[page 5-6]**
Bias	9	Describe any efforts to address potential sources of bias **[page 6]**
Study size	10	Explain how the study size was arrived at **[page 6-7]**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **[page 7]**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **[page 7]**
		(*b*) Describe any methods used to examine subgroups and interactions **[page 7]**
		(*c*) Explain how missing data were addressed **[n/a]**
		(*d*) If applicable, explain how matching of cases and controls was addressed **[n/a]**
		(*e*) Describe any sensitivity analyses **[n/a]**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **[page 7]**
		(b) Give reasons for non-participation at each stage **[n/a]**
		(c) Consider use of a flow diagram **[n/a]**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **[page 7]**
		(b) Indicate number of participants with missing data for each variable of interest **[n/a]**
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure **[page 8]**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

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	adjusted for and why they were included **[page 7-14]**
	(*b*) Report category boundaries when continuous variables were categorized **[n/a]**
	(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **[n/a]**

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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **[page 13]**
Discussion		
Key results	18	Summarise key results with reference to study objectives **[page 15]**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **[17-18]**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **[18]**
Generalisability	21	Discuss the generalisability (external validity) of the study results **[18]**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **[19]**

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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BMJ Open

A cross-sectional survey investigating the desensitisation of graphic health warning labels and their impact on smokers, non-smokers and COPD patients in a London cohort

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Primary Subject Heading:	Smoking and tobacco
Secondary Subject Heading:	Public health, Respiratory medicine, Health policy
Keywords:	PREVENTIVE MEDICINE, PUBLIC HEALTH, Chronic airways disease < THORACIC MEDICINE, Emphysema < THORACIC MEDICINE

SCHOLARONE™
Manuscripts

A cross-sectional survey investigating the desensitisation of graphic health warning labels and their impact on smokers, non-smokers and COPD patients in a London cohort

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ABSTRACT

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Objectives There is a lack of evidence regarding the effectiveness of GHWL in different subjects, including COPD patients. Investigating knowledge and attitudes may allow better implementation of future public health policies. We hypothesised significant differences in GHWL impact between non-smokers, smokers and COPD patients; with decreased efficacy in those groups who are longer and more frequently exposed to them.

Participants and setting 163 subjects (54% male, aged 21-80) including 60 non-smokers, 53 smokers and 50 COPD patients (Gold stage II-IV), attending London respiratory outpatient clinics, participated in case-controlled surveys (fifty items).

Outcome measures Ten different GHWL were shown and demographics, smoking history, plans to quit, smoking risk awareness, emotional response, processing and impact of GHWL on behaviour were recorded. Patients were further asked to prioritise the hypothetical treatment or prevention of five specific smoking-related diseases.

Results Smokers, in particular those with COPD, were less susceptible to GHWL than non-smokers; 53.4% of all subjects expressed fear when looking at GHWL, non-smokers (71.9%) more so than smokers (39.8%, $p<0.001$). COPD participants were less aware of the consequences than non-COPD participants ($p<0.001$), including an awareness of lung cancer ($p=0.001$). Lung cancer (95%), oral cancer (90.2%), heart disease (84.7%) and stroke (71.2%) were correctly associated with smoking, whilst blindness was least associated (23.9%). However blindness was prioritised over oral cancer, stroke and in COPD patients also over heart disease when subjects were asked about hypothetical treatment or prevention.

Conclusion GHWL are most effective in non-smokers and a desensitisation effect was observed in smokers and COPD patients. As a consequence, a tailored and concerted public health approach to use such messages is required and 'blindness' deserves to be mentioned in this context because of an unexpectedly high deterring impact.

ARTICLE SUMMARY

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Article focus

- To assess the impact of Graphic Health Warning Labels (GHWL) in non-smokers, smokers and patients with COPD within a London cohort.
- To quantify the desensitisation of GHWL within these cohorts and to analyse the awareness of important smoking related risks and the preventive impact of this knowledge.

Key messages

- GHWL are least effective in those that have greatest exposure to them, such as smokers and patients with COPD due to desensitisation; additional strategies should be explored to assist smoking cessation further.
- Awareness of the non-pulmonary risks of smoking are low and few studies have investigated the awareness of patients with COPD, or the relative effects of GHWL on smoking behaviour in these groups.
- Blindness was the least well-known risk of smoking, despite a high deterring impact in all groups.

Strengths and limitations of this study

- Detailed assessments used structured surveys, designed following an internal peer review process amongst three tertiary teaching hospitals and one academic institution.
- COPD patients were more reluctant to take part in the research and a more substantial aversion to GHWL may have been masked in this group. Further, the COPD cohort was older and had more male subjects than the other groups.
- Data were collected directly from patient groups in an outpatient setting and generalisability to the wider population may be limited.

INTRODUCTION

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Tobacco use is one of four factors responsible for the majority of all worldwide deaths caused by non-communicable disease, according to the World Health Organisation.[1] It causes lung cancer and Chronic Obstructive Pulmonary Disease (COPD).[2, 3] Smoking cessation at any stage improves health outcomes, even in patients with advanced COPD [4] and, although it is difficult to change smoking behaviour, public health campaigns featuring primary and secondary prevention influence smoking habits and public health in the long-term.[5]

Graphic Health Warning Labels (GHWL) have been used over several years to promote smoking cessation and increase awareness of smoking related side-effects.[6] Whilst various studies have described their efficacy, which appears to be more effective than text-only labels,[7-11] difficulties persist to encourage smoking cessation.[12] Despite all efforts and whilst the government supports a comprehensive tobacco plan (Table 1),[13] more than 21% of the UK population continue to smoke.[14]

Table 1: Government tobacco plan [13]

Table 1 showing the six-part governmental tobacco control plan for England
1) Stopping promotion of tobacco
2) Making tobacco less affordable
3) Effective regulation of tobacco products
4) Helping tobacco users to quit
5) Reducing exposure to second hand smoke
6) Effective communications for tobacco control

Awareness of smoking-related ill

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health

Knowledge of smoking-related diseases amongst smokers and non-smokers, including exposure to second-hand smoke, oral health, and various types of cancer differs significantly,[10, 15] even amongst medical students.[16] While cardiovascular and respiratory risks are well acknowledged this is not true for other diseases, particularly for blindness.[17-21]

COPD and Graphic Health Warning Labels

Vardavas and colleagues [8] investigated the significant role GHWL might play in preventing smoking during early adolescence, a crucial period in which experimentation and addiction commonly occur.[22] Despite their efficacy, long-term exposure to such warnings may have a desensitising effect on attitudes towards smoking cessation.

Desensitisation to GHWL could have the greatest impact in patients with COPD because they are exposed long term to the efforts of public health campaigns. Indeed older smokers are also reported to demonstrate less interest in quitting smoking [23] and they more often attribute symptoms to the effect of ageing or a non-medical cause [24]. A reduced respiratory symptom attribution to smoking would lead to a reduced likelihood to quit [25]. COPD is also associated with a higher prevalence of depression, poor memory, decreased attention [26] and mild cognitive impairment [27, 28]. These factors may reduce the cognitive impact GHWL have on smoking cessation and warrant further investigation.

The present study aims to investigate differences in GHWL impact, and knowledge of smoking outcomes in smokers, non-smokers and patients with COPD; we hypothesised a decreased efficacy on subjects with increased exposure to smoking. Identifying individual responses may facilitate a more tailored public health approach for the utilisation of GHWL in future health policies.

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PATIENTS AND METHODS

The study was approved by the local research ethics committee (reference number 12/NE/0013) and was performed at Guy´s & St Thomas´ NHS Foundation Trust, London, UK. Prior to participation informed and written consent was obtained for all subjects. Inclusion criteria were: fluent English, respiratory department outpatients, age 21-80 years, both genders, smokers, non-smokers and ex-smokers, as well as COPD patients (GOLD stage II-IV) with a pre-diagnosed condition. Patients who were unable to communicate, understand or view the GHWL or consent form were excluded.

163 participants were studied, including 60 non-smokers, 53 smokers and 50 COPD patients (smokers and non-smokers, see online supplement table E1 and E2). A structured survey was designed to investigate the awareness of smoking risks and the effectiveness of GHWL within these groups.

Structured Survey

The survey contained 50 items based on those utilised by previous studies.[19, 20, 29] These items were included following an internal peer review process amongst three tertiary teaching hospitals and one academic institution (King`s College London, UK; the survey is available in the appendix and more details can be found in the online supplement). The following health risks were included:

1) Mouth and throat cancer

   Smoking cessation causes a 50% reduction in risk of oral cancer within 5 years.[30]

2) Lung cancer

   Approximately 90% of male lung cancer deaths and 75-80% of female lung cancer deaths in the US are caused by smoking each year.[31]

3) Heart disease

   Estimations attribute 40% of heart disease to smoking.[32]

4) Stroke

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Smoking could increase the risk of stroke by 2 to 4 fold.[33]

5) Blindness

Estimations attribute smoking to approximately 20% of new blindness in people over the age of 50.[34]

Participants were then shown GHWL (n=10) and their responses were recorded. More details about this can be found in the online supplement. The surveys were conducted by investigators with medical background who were instructed to remain neutral and not to influence decision making. Training took place prior to data collection and at two-weekly intervals, lasting 15-20 minutes, to standardise the interview process and minimise investigator-led bias.

Statistical analysis

Sample size calculations revealed that at least 50 subjects were required in each arm of the study to achieve a power of 0.8 (for more details on the sample size calculation please refer to the online supplement). Data were collected using MS Excel 2007 (Microsoft Corporation, Seattle/WA, USA); they were analysed using SPSS Statistics 21 (IBM, New York/NY, USA) and tested for a normal distribution using the Kolmogornov-Smirnoff test. χ-square tests were used to compare categorical data. Non-categorical data were analysed using unpaired t-tests, if data were normally distributed, or Mann-Whitney non-parametric tests if they were non-normally distributed. A regression analysis was conducted, using binary logistic regression and multiple linear regression, and applied to the primary outcome measure of knowledge score (the number of smoking-related risks that each participant was aware of). The independent variables in the analysis were age, gender, sex, ethnicity, smoking status and COPD status. Data are presented as mean (standard deviation, SD), unless otherwise indicated. A level of significance was defined as $p<0.05$.

RESULTS

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A total of 163 participants (54% male (m), age 52.4 (17.8) years) were included, with 60 non-smokers without airway disease (38.3% m; age 41.4 (16.4) years), 53 smokers without airway disease (69.8% m, age 49.7 (13.1) years) and 50 COPD patients (56% m; age 68.6 (10.7) years); this group contained smokers and non-smokers (please refer to the online supplement, table E1 and E2). The group with non-smokers had more female participants than the group with smokers and the one with COPD patients. The COPD group was older than the other two groups. The ethnic background of all participants was predominantly "White" (79%), followed by "Asian/Asian British" (10%) and "Black/Black British" (9%).(Table 2)

	All (N=163)	**Non-smokers (non-COPD) (N=60)**	**Smokers (non-COPD) (N=53)**	**COPD (N=50)**	**X^2 / one-way ANOVA (P value)**
Age in years (range)	52.4 (18-90)	41.4(18-85)	49.7(24-74)	68.6(40-90)	<0.001
Sex (N, %) **Male** **Female**	88 (54%) 75(46%)	23 (38%) 37 (62%)	37 (70%) 16 (30%)	28 (56%) 22 (44%)	0.003
Ethnicity/N **White**	129 (79%)	43 (72%)	41 (77%)	45 (90%)	
Asian/ Asian British	17 (10%)	9 (15%)	7 (13%)	1 (2%)	0.074
Black/ Black British	14 (9%)	5 (8%)	5 (9%)	4 (8%)	
Mixed	3 (2%)	3 (5%)	0 (0%)	0 (0%)	

Table 2: Participants demographics, revealing mean age (with range), number of participants according to gender (%) and ethnicity (%) for all groups.

Awareness of health risks associated with smoking

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93.3% of non-COPD smokers stated that they had thought about the health risks associated with smoking compared to 75.0% of COPD smokers (p=0.097). Across all participants, the greatest awareness was for lung cancer (95.0%), followed by mouth and throat cancer (90.2%), heart disease (84.7%) and stroke (71.2%). Blindness was least well known (23.9%). Non-smokers revealed an increased awareness of associations between smoking and mouth and throat cancer (p=0.004) compared to smokers (Figure 1). COPD patients expressed a decreased awareness of lung cancer (p=0.001), heart disease (p=0.012), stroke (p=0.001) and mouth and throat cancer (p<0.001) compared to the other groups (Figure 2). There was no significant difference between the groups in the awareness of blindness.

Figure 1 inserts here.

Figure 2 inserts here.

Impact of smoking consequences on future behaviour

Smokers were more motivated to quit smoking if, hypothetically, they were to develop heart disease (89.7% *vs* 75.0%, p<0.001), stroke (82.8% *vs* 75.0%, p<0.001), blindness (89.7% *vs* 66.7%, p<0.001), mouth and throat cancer (93.1% *vs* 75.0%, p<0.001) or lung cancer (89.7% *vs* 83.3%, p<0.001) compared to COPD patients. Non-smokers scored similarly to COPD patients (9.4 (1.1) *vs* 8.7 (2.3) points, p=0.055) when asked about *'the harmfulness of smoking to health'*, but they scored higher than current smokers (8.4 (1.5) points, p=0.004; Table 3).

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=99)	Non-smokers (n=64)	**p-value**
***1)** How harmful is smoking to health? (non-normal)* Mean (SD)	8.7 (2.3)	8.9 (1.4)	**0.564**	8.4 (1.5)	9.4 (1.1)	**0.004**
Awareness of smoking related side-effects: total score out of 5. Mean (SD)	3.1 (1.4)	3.9 (1.0)	**p<0.001**	3.6 (1.2)	3.8 (1.1)	**0.293**
Awareness of Heart Disease	74.0	89.4	**0.012**	85.9	82.8	**0.598**

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as related to smoking (%)						
Awareness of Stroke as related to smoking (%)	54.0	78.8	**0.001**	69.7	73.4	**0.607**
Awareness of Blindness as related to smoking (%)	18.0	26.5	**0.238**	23.2	25.0	**0.796**
Awareness of Mouth and Throat Cancer as related to smoking (%)	72.0	98.2	**<0.001**	84.8	98.4	**0.004**
Awareness of Lung Cancer as related to smoking (%)	88.0	99.1	**0.001**	93.9	98.4	**0.167**

Table 3: Awareness of smoking consequences. Item 1 showing each group's response (1-10) of the perceived harmfulness of smoking to health (mean (SD)), number of known smoking related consequences from 1-5 (mean (SD)), and total number (%) in each group that was aware of the smoking consequence. *Statistically significant results are highlighted in grey.*

When given the choice to avoid one of five hypothetical conditions associated with smoking, smokers rated lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and finally stroke. Similarly, non-smokers ranked lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and stroke. COPD patients ranked lung cancer highest, followed by blindness, heart disease, mouth and throat cancer and stroke. However, no significant differences existed between the ranks in the different subgroups.(Table 4 and online supplement Table E3)

When subject had to choose to hypothetically treat only one of these five smoking associated conditions, smokers ranked most commonly lung cancer first, followed by heart disease, blindness, stroke and lastly mouth and throat cancer. Non-smokers most commonly ranked lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and stroke. COPD patients most commonly ranked lung cancer highest, followed by blindness, heart disease, mouth and throat cancer and stroke. Compared to non-smokers, smokers were significantly more likely to seek hypothetical treatment for lung cancer compared to non-

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smokers (p=0.005) who were more likely to seek treatment for mouth and throat cancer (p=0.043).(Table 4 and online supplement Table E4)

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=99)	Non-smokers (n=64)	**p-value**
If you could Prevent or Treat only one of Heart Disease, Stroke, Blindness, Mouth and Throat Cancer and Lung Cancer, which would you choose? (% choosing each option)	[Rank 1-5]					[Overall rank 1-5]
Heart Disease (%)	16.0 [3]	24.8 [2]	**0.078**	19.7 [2]	25.8 [2]	**0.196** [2]
Stroke (%)	6.0 [5]	7.5 [5]	**0.621**	6.6 [5]	7.8 [5]	**0.668** [5]
Blindness (%)	19.0 [2]	17.3 [3]	**0.704**	16.7 [3]	19.5 [3]	**0.509** [3]
Mouth and Throat Cancer (%)	9.0 [4]	8.4 [4]	**0.860**	6.6 [5]	11.7 [4]	**0.105** [4]
Lung Cancer (%)	50.0 [1]	40.3 [1]	**0.102**	49.5 [1]	33.6 [1]	**0.005** [1]

Table 4: showing the number (%) of each group that would hypothetically prevent or treat the named condition if they could choose only one from the given list. Ranks of each condition [1-5] are stated in columns 1, 2, 4 and 5 with overall rank [1-5] in column 6. Table 4 is a composite score of table E3 (if you can prevent only one named disease) and table E4 (if you could treat only one named disease) which are available in the online supplement. *Statistically significant results are highlighted in grey.*

Response and processing of GHWL

Amongst all participants, 53.4% of patients experienced fear after viewing pictures of GHWL, 78.5% of participants expressed disgust; 28.8% would actively avoid labels if they saw them in public. Smokers experienced less fear when looking at GHWL (71.9%) compared to non-smokers (39.8%; p<0.001; Figure 3). There was no significant difference in avoiding GHWL or feelings of disgust between smokers and non-smokers (Table 4). COPD patients experienced less fear, disgust and were less likely to avoid looking at GHWL

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compared to other groups (p=0.016; Figure 4), but only avoidance reached the level of statistical significance. (Table 5)

Figure 3 inserts here.

Figure 4 inserts here.

GHWL would have been more sufficient to prevent or stop smoking in non-smokers than smokers (p<0.001). Non-smokers were more likely than smokers to think about the warning messages on cigarette packaging (p=0.006) and talk about the warning labels to others (p<0.001; online supplement, Figure E1). COPD patients read the packaging less often (p<0.001), less carefully (p=0.010), they were less likely to think about the messages (p=0.001), talk to others about warning labels (p<0.001), think about warning labels when they were not in sight (p<0.023) or were less likely to keep a warning label at home as a reminder (p=0.013; online supplement, Figure E2). No significant differences existed between COPD and non-COPD groups when comparing whether the warning labels were sufficient motivation to stop smoking (p=0.240; Table 5).

Initial response to GHWLs	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=103)	Non-smokers (n=60)	**p-value**
...Fear? (%)	48.0	55.8	**0.360**	39.8	71.9	**<0.001**
...Disgust? (%)	76.0	79.6	**0.601**	72.8	82.8	**0.284**
Ever avoided looking at GHWLs? (%)	16.0	34.5	**0.016**	27.2	29.7	**0.846**
Are the warning labels sufficient motivation for you to stop smoking (if a current smoker) or not start smoking (if a non- or ex-	44.0	54.0	**0.240**	35.4	75.0	**<0.001**

smoker)? (%)						
Processing of GHWLs						
Packaging processing response						
a) How carefully have you ever read the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.9 (1.1)	2.4 (1.3)	**0.010**	2.4 (1.4)	2.1 (1.1)	**0.493**
b) How often do you read the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.6 (1.0)	2.5 (1.3)	**<0.001**	2.5 (1.5)	2.1 (1.1)	**0.064**
c) How often have you thought about the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.9 (1.3)	2.7 (1.3)	**0.001**	2.2 (1.2)	2.8 (1.5)	**0.006**
General processing response						
d) Have you ever talked to others about the warning labels on cigarette packaging? (1 = never, 5 = very often)	1.5 (1.1)	2.5 (1.4)	**<0.001**	1.8 (1.1)	2.7 (1.5)	**<0.001**
e) How often have you thought about the warning messages on cigarette packages when there has been no pack in sight? (1 = never, 5 = very often)	1.5 (0.9)	1.9 (1.2)	**0.023**	1.6 (1.0)	2.0 (1.3)	**0.112**
f) How often have you kept a warning label from a cigarette pack? (1 = never, 5 = very often)	1.0 (0.3)	1.4 (1.0)	**0.013**	1.2 (0.8)	1.3 (0.8)	**0.995**

Table 5: Emotional response and processing of GHWL, indicating the number of participants (%) that responded with fear, disgust, avoidance and the number (%) motivated to stop smoking. Also, the mean (SD) processing of GHWL (1-5) over two items (packaging and general processing response). *Statistically significant values are highlighted grey.*

In terms of age and sex of the participants, female subjects were more likely to experience fear compared to male participants (p=0.002), but not disgust or active avoidance of labels. They were also more likely to stop smoking following exposure (p=0.002) and more likely to think about GHWL messages when they were not in sight (p=0.023). Those who experienced fear were younger (p=0.037), as were those who would actively avoid looking at labels

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(p=0.008; Table 6). An increased age was significantly correlated with a decrease in depth of processing of labels (r= -0.386, p<0.001), older subjects exhibited a decreased level of attention to detail when reading GHWL (r= -0.315, p<0.001), they payed less attention to them (r= -0.351, p<0.001), they were less often thinking about the labels (r= -0.375, p<0.001), also when GHWL were not in sight (r=-0.201, p<0.010) and they talked less about them (r= -0.31, p<0.001; Table 7).

Emotional response to warning labels	Male - Yes	Female - Yes	**X^2**	Mean age of those who said 'Yes'	Mean age of those who said 'No'	**t-test (2-tailed)**
Fear	37/88	50/75	**0.002**	50.0 (18.3)	55.6 (16.7)	**0.044**
Disgust	66/88	62/75	**0.235**	51.3 (17.4)	57.1 (18.7)	**0.112**
Avoidance	21/88	26/75	**0.129**	47.0 (16.1)	54.8 (18.0)	**0.008**
Sufficient to stop from smoking	35/88	48/75	**0.002**	51.5 (18.4)	53.9 (16.9)	**0.381**

Table 6: Age and gender differences in the response to GHWL, showing differences in gender (total number) and age (mean (SD)) in the emotional response to GHWL and motivation to stop smoking. *Statistically significant values are highlighted grey.*

	Total package (P) processing response	**Total general (G) Processing response**	**Overall depth of processing (P+G)**
Age (r)	-0.393	-0.276	-0.386
p-value	<0.001	<0.001	<0.001
Mean score - **Male**	6.8 (3.5)	5.0 (2.5)	11.7 (5.2)
Mean score - **Female**	7.1 (3.5)	5.5 (2.7)	12.6 (5.6)

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Gender t-test p-value (2 tailed)	0.559	0.217	0.323
Breakdown of package (P) processing response:			
	Paid close attention	Thought about labels	Carefully read
Age (r)	-0.351	-0.375	-0.315
p-value	<0.001	<0.001	<0.001
Mean score – **Male**	2.2 (1.3)	2.3 (1.3)	2.2 (1.3)
Mean score – **Female**	2.3 (1.3)	2.6 (1.4)	2.2 (1.2)
Gender t-test p-value (2 tailed)	0.915	0.312	0.788
Breakdown of general (G) processing response:			
	Thought about when not in sight	Kept a label as a reminder	Talked to others about labels
Age (r)	-0.201	-0.094	-0.31
p-value	0.010	0.232	<0.001
Mean score – **Male**	1.6 (1.0)	1.3 (0.9)	2.1 (1.3)
Mean score – **Female**	2.0 (1.3)	1.2 (0.8)	2.3 (1.4)
Gender t-test p-value (2 tailed)	0.023	0.651	0.315

Table 7: Age and gender differences in the processing of GHWL**,** showing Pearson's correlation with age and mean (SD) gender scores (1-10), in package processing (3-items) and general processing (3-items) of the warning labels. The overall processing is shown in the third column. *Statistically significant values are highlighted grey.*

The regression analysis to understand whether there were independent predictors of knowledge or awareness of smoking-related consequences revealed no significant association with the overall knowledge score of the respondent`s age (p=0.333), gender (p=0.079), race (p=0.552) or smoking status (p=0.756).

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DISCUSSION

Patients with COPD exhibit a decreased response to Graphic Health Warning Labels, an effect that can be referred to as desensitisation, whilst non-smokers and smokers without airway disease responded better. The use of GHWL evoked an emotional response of fear and disgust in the majority of participants, particularly in non-smokers, in females and in younger participants.

The effect of desensitisation can be defined as a process where repeated exposure results in habituation of a cognitive, emotional and physiological response. Psychological research has shown that novel events are processed more extensively than common events [35, 36] and whilst some papers discuss desensitisation as a possible mechanism for a decreased impact of GHWL,[37, 38] it has largely been described in relation to graphic video game imagery and violence.[39]

Awareness of smoking consequences and impact on future behaviour

Various studies have outlined an increased awareness of smoking-related respiratory complications in COPD patients.[29, 34, 40-43] In contrast, our study found that COPD patients had a decreased awareness of consequences compared to non-COPD patients and were less likely to quit if they developed any of the diseases; the same was true when smokers were compared to non-smokers. Smokers also scored significantly lower than non-smokers when asked how harmful smoking was to their health and they had a decreased awareness of mouth and throat cancer.

The awareness of "blindness" and its role in public health campaigns

Blindness was the least well-known smoking-related risk despite all participants being highly motivated to prevent and treat it (ranked 2nd or 3rd in all groups, following lung cancer and heart disease). Up to 20% of all subjects with new onset of blindness are attributed to

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smoking [44] and previous studies have found it more motivational than conventional messages in smoking prevention [18-20].

Smoking-related lung cancer, heart disease, mouth and throat cancer and stroke are well recognised and publicised in printed media and TV advertising.[34, 45] This awareness is reflected across all study groups. However, it has been established that current smokers have a lower understanding of other risks including macular degeneration, cataracts and oral diseases compared to non-smokers.[17, 18, 21] In one study, less than 10% of patients older than 18 years were able to associate blindness with smoking.[34]

A study from Australia has shown an increased awareness of smoking-related eye disease due to public health strategies [46] and an increased emphasis on blindness in this context could have the potential to motivate and encourage smoking cessation.[18]

Future implications

GHWL appear to lose efficacy with increased exposure. Unfortunately this limits the extensive use for the primary target groups, in particular long-term smokers and COPD patients. A balance between the use of GHWL and the observed desensitisation effects need to be considered. Therefore, specific health messages should be targeted at these cohorts over defined periods and re-organised with regular campaigns to avoid desensitisation. The knowledge that less well-known risks (e.g. blindness) could have a similar impact as more well-known risks of smoking (e.g. lung cancer, heart disease) provides the chance to alternate features of different diseases on GHWL in concerted public health campaigns.

Indeed different approaches to promote smoking cessation are still required. Over the last few years it has been considered whether plain packages should be introduced, preventing the use of illusory packaging techniques as a means of attracting consumers.[47] Evidence around plain packaging is currently based on indirect studies [48-52] and whilst Australia is the first

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country to sell tobacco products adopting this policy [53, 54] the UK government, following consideration of such an approach,[13] has currently rejected a proposal.

Limitations

The respondents in this study came from a hospital setting in respiratory and outpatient departments and therefore a selection bias might have influenced some of the outcomes of our survey; the generalisability of our data should therefore be considered with caution. Several GHWL were shown to participants within a short time period and this could have caused a greater emotional response than showing single pictures.

Further, the COPD cohort tended to be older, with more male subjects, whereas the non-smoker group consisted of proportionally more females. The numbers used in the analysis however were taken from a reasonably large dataset and represent consistent results amongst all groups, in line with previous findings. The smoking history was variable between subjects in the COPD group as it included current smokers and also non-smokers. This could have impacted on and limited our results with regard to the COPD group (see online supplement, Table E1).

COPD patients were more reluctant to take part in this survey and it is likely that a true aversion to GHWL might have been underestimated. In addition, although Hammond et al. [11] demonstrated that smoking cessation was related to high cognitive processing of labels, intention to quit smoking was investigated here rather than actual behaviour change. Future research may need to investigate the achieved rate of smoking cessation following GHWL exposure; also the link between intention and actual change of smoking behaviour.

Whilst desensitisation is one explanation for our findings, it is possible that COPD patients demonstrate an ambivalence towards risks to support their own self-esteem.[55] This would suppress anxiety associated with a fear of the consequences of smoking [56] and portray itself

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as a 'don't care' attitude. Leventhal [57] postulated that fear messages may lead to two competing processes, either a 'danger control' or, in the case of our COPD cohort, a 'fear control' response. Indeed where fear-based approaches have been used to reduce illicit drug rates, increased rates of drug abuse were described post intervention.[58] Further qualitative work will help understand these specific responses better.

Conclusion

Prolonged exposure to GHWL may cause desensitisation, in particular to COPD patients and current smokers. To maintain their efficacy, other strategies using the intermittent application of different features need to be employed within concerted health campaigns. Blindness has to be mentioned as a specific factor because it leads to a strong emotional response in the context of GHWL.

The evidence provided by our research is required to continue to develop successful public health campaigns, in particular because plain packaging has currently been rejected as public health policy in the UK. These campaigns should focus on improving the lack of awareness of smoking-related diseases, especially in those with chronic smoking behaviour. The timing of exposure to specific GHWL messages should be considered to avoid desensitisation. Future qualitative research is required to explore thoughts and beliefs in order to successfully support primary and secondary smoking cessation interventions.

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Contributorship

CR designed the study, designed and adapted data collection tools, set up research teams in Singapore (Singapore arm, data not yet available) and London, obtained ethical approval, monitored data collection and data collection training, collected data, revised and oversaw formation of the literature review, analysed data and wrote and revised literature review, analysis and discussion sections of the paper. He is the first guarantor. B-MC collected data, made significant contribution to analysis and wrote proportions of analysis and discussion section. PD made significant contribution to data collection and reviewing paper. SS performed initial literature search and literature review. BS collected data and aided in elements of data analysis section. MB made significant contribution to data collection and reviewing the paper. AD was vital in statistical analysis plan, analysis sections and so tailoring discussion sections. JS is second guarantor. He oversaw data collection in the London arm, established, enabled and supervised undertaking of the project in the London

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site; facilitated formation of the London research team; safeguarded data collected and was responsible for overlooking, guiding and re-drafting the eventual manuscript prior to submission.

Competing interests and funding

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Data Sharing Statement

Extra data is available on emailing the corresponding author [c.ratneswaran@gmail.com]. This includes the raw data collected if necessary and is available to researchers looking to further investigate the scope of the current project.

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Figure legends

Figure 1: Awareness of smoking-related consequences (smokers *vs* non-smokers), showing the differences in number of respondents (%). *Significant differences are marked (** p<0.01).*

Figure 2: Awareness of smoking-related consequences (COPD *vs* non-COPD), showing the differences in number of respondents (%). *Significant differences are marked (* p<0.05 ** p<0.01 *** P<0.001).*

Figure 3: Emotional response to GHWL (smokers *vs* non-smokers)**,** showing the difference in respondents (%) experiencing fear, disgust and avoidance after GHWL exposure. *Statistically significant differences are marked (*** p<0.001).*

Figure 4: Emotional response to GHWL (COPD *vs* non-COPD), showing the difference in respondents (%) experiencing fear, disgust and avoidance after GHWL exposure. *Statistically significant differences are marked (* p<0.05).*

Supplementary Files

Appendix

Table E1 COPD and non-COPD patients grouped into smokers and non-smokers

Table E2 Non-smokers smoking history

Table E3: Smoking consequences to be prevented

Table E4: Smoking consequence to be treated

Supplemental Figures

Figure E1: GHWL processing (Smokers and non-Smokers)

Figure E2: GHWL processing (COPD and non-COPD)

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APPENDIX

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SMOKING QUESTIONNAIRE

1. Personal particulars:

Initials: _____

2. Age: _____ years

3. Sex: Male/ Female

4. Race:
[Please tick or if 'other' write on the line provided]

Asian or Asian British
- ☐ Bangladeshi
- ☐ Pakistani
- ☐ Indian
- ☐ Other _____

Black or Black British
- ☐ African
- ☐ Caribbean
- ☐ Other _____

Chinese or Chinese British
- ☐ Chinese
- ☐ Other _____

Mixed
- ☐ White and Asian
- ☐ White and Caribbean
- ☐ White and Black African
- ☐ Other _____

White
- ☐ Irish
- ☐ Northern Irish
- ☐ English
- ☐ Scottish
- ☐ Welsh
- ☐ Other _____

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5. Occupation:

- ☐ Legislators, senior officials and managers
- ☐ Professionals
- ☐ Clerical workers
- ☐ Service workers and shop and market sales workers
- ☐ Agricultural and fishery workers
- ☐ Production craftsmen and related workers
- ☐ Plant and machine operators and assemblies
- ☐ Cleaners, labourers and related workers
- ☐ Military
- ☐ Unemployed
- ☐ Student

6. Cigarette smoking status: Current smoker/ ex-smoker/ non-smoker

If current smoker, please proceed to question 7.

If ex-smoker, please proceed to question 8.

If non-smoker, please proceed to question 9.

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QUESTION 7 - CURRENT SMOKERS

a) How long have you smoked for?

_____

b) On average, how many cigarettes do you smoke a day?

_____

c) Have you ever considered giving up smoking? **YES / NO**

IF YES

d) Have any of the following motivated you to give up smoking?
(Multiple choices possible)

- ☐ Health
- ☐ Financial savings
- ☐ Family request
- ☐ Health professional's advice
- ☐ Media (magazines/ newspapers/ TV commercial / radio)
- ☐ Internet
- ☐ Peer advice
- ☐ Graphic health warnings (cigarette packs)

Other: _____

e) How many attempts have you made at giving up smoking?

f) On a scale of 1 – 10, how confident are you about giving up smoking when you when you want?

0 1 2 3 4 5 6 7 8 9 10

Not confident Very confident

g) Have you even thought about the health risks associated with smoking? **YES/NO**

IF YES

h) On a scale of 0 – 10, how often do you think about the health risks associated with smoking?

0 1 2 3 4 5 6 7 8 9 10

Not at all Very often

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Please proceed to question 9.

QUESTION 8 - EX-SMOKERS

a) How long ago did you give up smoking?

b) How many cigarettes did you smoke a day?

c) How many years did you smoke for?

d) How many attempts did you make to stop smoking, including the last?

e) What was your motivation for stopping smoking? (Multiple choices possible)

- ☐ Health
- ☐ Financial savings
- ☐ Family request
- ☐ Health professional's advice
- ☐ Media (magazines/ newspapers/ TV commercial / radio)
- ☐ Internet
- ☐ Peer advice
- ☐ Graphic health warnings (cigarette packs)

Others: _____

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QUESTION 9

How harmful do you think smoking is to health in general?

0	1	2	3	4	5	6	7	8	9	10
Not harmful										Very harmful (death)

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General awareness of smoking and disease

10. Do you believe the following diseases are related to smoking?

Heart disease	**YES / NO / NOT SURE**
Stroke	**YES / NO / NOT SURE**
Blindness	**YES / NO / NOT SURE**
Mouth and throat cancer	**YES / NO / NOT SURE**
Lung cancer	**YES / NO / NOT SURE**

11. Which disease would you like to prevent if it were possible to prevent only one?

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

12. Which disease would you seek treatment for if it were possible to treat only one?

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

If smoker, please proceed to question 13.

If ex- or non-smoker, please proceed to question 14.

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QUESTION 13

Imagine that all the conditions below have the same risk of occurrence. Rank the following conditions from 1 to 5 in order of how much motivation each provides towards you stopping smoking, with 1 being most feared, and 5 being the least feared.

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

QUESTION 14

Imagine the following conditions all have the same risk of occurrence. Rank the following conditions from 1 to 5 in order of how much each motivates you to not start smoking, with 1 being most feared, and 5 being the least feared.

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

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Attitudes toward graphic health warning labels on cigarette packs

15. Emotional response to warning labels

a) Did you experience any fear when looking at the warning labels? **YES / NO**

b) Did you experience any disgust when looking at the warning labels? **YES / NO**

c) Have you ever actively avoided looking at the warning labels in public? **YES / NO**

16. Depth of processing

Please score the following questions on a scale of 1 to 5 using this guide:
1=not at all/never; 2=once; 3=sometimes; 4=often; 5=all the time/a lot

Package messages (outside)

a) How carefully have you ever read the messages on the outside of cigarette packets? 1 2 3 4 5

b) How often have you read or paid close attention to the messages on the outside of packages? 1 2 3 4 5

c) How often have you thought about what the warnings on the outside of packages have to say? 1 2 3 4 5

General

d) Have you ever talked about the warning labels with other smokers or non-smokers? 1 2 3 4 5

e) Have you ever thought about the warnings or what they had to say when a cigarette pack wasn't in sight? 1 2 3 4 5

f) Have you ever kept a warning label to serve as a reminder of the effects of smoking on health? 1 2 3 4 5

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Impact of graphic health warning labels on smoking behaviour

If current smoker, please proceed to question 17.

If ex- or non-smoker, please proceed to question 18.

17. Current smoker

Do you feel the labels are a sufficient motivation for you to stop smoking? **YES / NO**

Would you stop smoking if you developed early signs of the following disease?

Heart disease	**YES / NO**
Stroke	**YES / NO**
Blindness	**YES / NO**
Mouth and throat cancer	**YES / NO**
Lung Cancer	**YES / NO**

Rank the conditions in order of how much motivation each provides towards you stopping smoking, with 1 being most feared, and 5 being the least feared.

Heart disease

Stroke

Blindness

Mouth and throat cancer

Lung Cancer

18. Ex- or non-smokers

Do you feel the labels are a sufficient motivation to prevent you from starting smoking? **YES / NO**

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Online Supplement

A cross-sectional survey investigating the desensitisation of graphic health warning labels and their impact on smokers, non-smokers and COPD patients in a London cohort

Culadeeban Ratneswaran, Ben Chisnall, Panagis Drakatos, Sukhanthan Sivakumar, Bairavie Sivakumar, Miriam Barrecheguren, Abdel Douiri, Joerg Steier

Patients & Methods

Table E1 COPD and non-COPD patients grouped into smokers and non-smokers

	COPD	Non-COPD	Total
Smokers	46	53	99
Non-smokers	4	60	64
Total	50	113	163

Table E1: Cross-tabulation of the number of COPD and non-COPD patients grouped into smokers and non-smokers, including the total number of participants in each group: non-smokers, smokers, non-COPD and COPD.

Table E2 Non-smokers smoking history

	Never smokers	Quit >2yrs	Quit <2yrs
Non-smokers	60	4	0

Table E2: Smoking history of the non-smokers into never-smokers, recent quitters (<2 years) and quitters for > 2 years.

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Structured survey – items before GHWL exposure

We recorded demographics (5 items), smoking history (7 items) and asked patients how confident they would be about quitting smoking (1 item) if they wanted to. Questions further determined knowledge of health risks associated with smoking (7 items), including how harmful they believed smoking was to their health (on a scale of 1, "not harmful", to 10, "very harmful, death") and the motivational impact of the risks towards stopping or preventing from smoking (15 items). The following health risks were included: mouth and throat cancer, lung cancer, heart disease, stroke and blindness.

Structured survey – items following GHWL exposure

Their emotional response (3 items), depth of content processing (6 items), impact on their smoking behaviour (1 item) and whether they would stop smoking if they developed early signs of the diseases illustrated (5 items) were recorded.

Statistical analysis – sample size calculation

Sample size calculation was performed based on a 95% confidence interval, an alpha of 0.05, with an estimated total London smoking population (1,280,000) and the proportion expected to be aware of the least known consequence condition chosen in the questionnaire (blindness) at 0.01 – 0.05.

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Results

Table E3: Smoking consequences to be prevented

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=103)	Non-smokers (n=60)	**p-value**
If you could Prevent only one of Heart Disease, Stroke, Blindness, Mouth and Throat Cancer and Lung Cancer, which would you choose? (% choosing each option)	[Rank 1- 5]					[Overall rank 1-5]
Heart Disease (%)	14.0 [3]	24.8 [2]	**0.122**	18.4 [2]	26.7 [2]	**0.203** [2]
Stroke (%)	8.0 [5]	8.0 [5]	**0.994**	7.8 [5]	8.3 [5]	**0.951** [5]
Blindness (%)	18.0 [2]	15.0 [3]	**0.634**	17.5 [3]	13.3 [3]	**0.927** [3]
Mouth and Throat Cancer (%)	12.0 [4]	8.8 [4]	**0.533**	8.7 [4]	11.7 [4]	**0.699** [4]
Lung Cancer (%)	48.0 [1]	41.6 [1]	**0.447**	46.6 [1]	38.3 [1]	**0.210** [1]

Table E3: showing the number (%) of each group that would hypothetically prevent the named condition if they could choose only one from the given list. Ranks of each condition [1-5] are stated in columns 1, 2, 4 and 5 with overall rank [1-5] in column 6. Table E3 and E4 form the composite score for table 4. *There were no statistically significant differences.*

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Table E4: **Smoking consequence to be treated**

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=103)	Non-smokers (n=60)	**p-value**
If you could seek treatment for only one of the following conditions, which would you choose? (%)	[Rank 1- 5]					[rank sum]
Heart Disease	18.0 [3]	24.8 [2]	**0.341**	21.2 [2]	25.0 [2]	**0.572** [2]
Stroke	4.0 [5]	7.1 [5]	**0.450**	5.1 [4]	7.8 [5]	**0.473** [5]
Blindness	20.0 [2]	19.5 [3]	**0.937**	17.2 [3]	23.4 [3]	**0.325** [3]
Mouth and Throat Cancer	6.0 [4]	8.0 [4]	**0.658**	4.0 [5]	12.5 [4]	**0.043** [4]
Lung Cancer	52.0 [1]	38.9 [1]	**0.120**	51.5 [1]	29.7 [1]	**0.006** [1]

Table E4: showing the number (%) of each group that would hypothetically treat the named condition if they could choose only one from the given list. Ranks of each condition [1-5] are stated in columns 1, 2, 4 and 5 with overall rank [1-5] in column 6. Table E3 and E4 form the composite score for table 4. *Statistically significant differences are highlighted in grey.*

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Figure E1: GHWL processing (Smokers and non-Smokers)

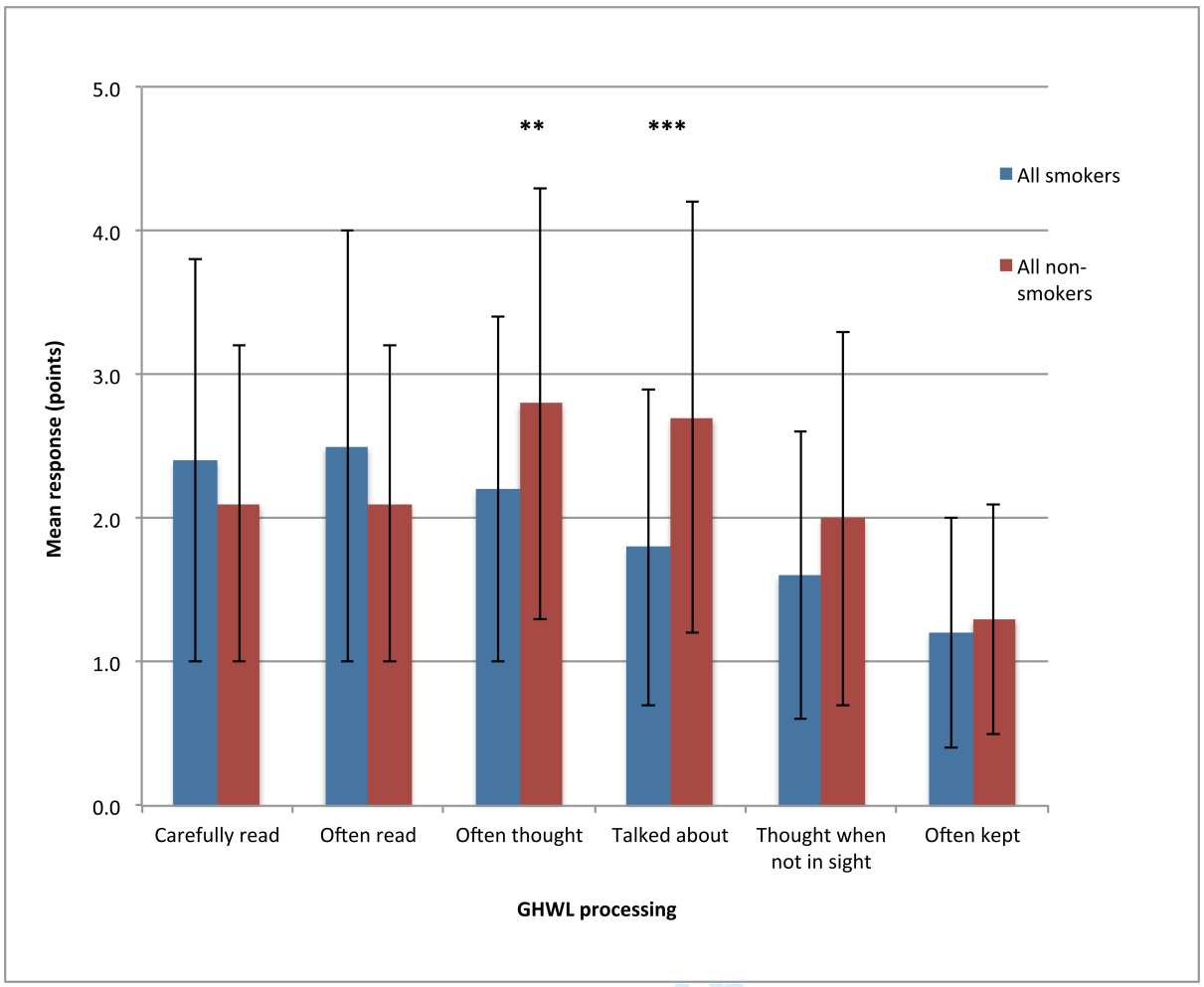

Figure E1: Processing of GHWL (smokers *vs* non-smokers), showing the mean difference (1-5) between smokers and non-smokers. Error bars indicate the standard deviation. *Statistically significant differences are marked (**p<0.01 *** p<0.001).*

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Figure E2: GHWL processing (COPD and non-COPD)

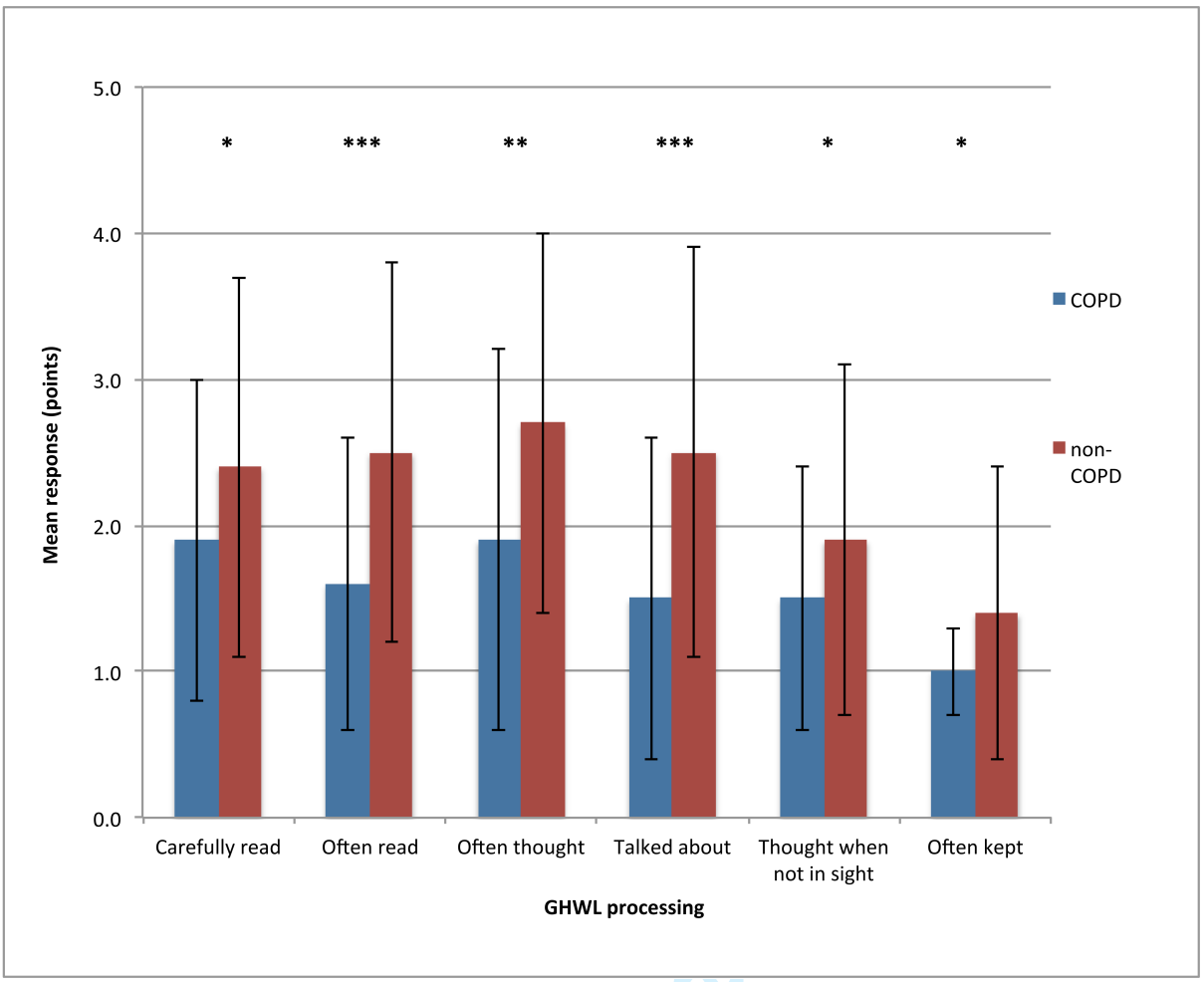

Figure E2: Processing of GHWL (COPD *vs* non-COPD), showing the mean difference in (1-5) between COPD and non-COPD. Error bars indicate the standard deviation. *Statistically significant differences are marked (* p<0.05 ** p<0.01 *** p<0.001).*

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STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **[page 2]**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **[page 2]**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **[page 4]**
Objectives	3	State specific objectives, including any prespecified hypotheses **[page 5]**
Methods		
Study design	4	Present key elements of study design early in the paper **[page 6]**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **[page 6]**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls **[page 6]**
		(*b*) For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **[page 6-7]**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **[page 6-7]**
Bias	9	Describe any efforts to address potential sources of bias **[page 6-7]**
Study size	10	Explain how the study size was arrived at **[page 7 and online supplement page 2]**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **[page 7]**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **[page 7 and online supplement page 2]**
		(*b*) Describe any methods used to examine subgroups and interactions **[page 7-8]**
		(*c*) Explain how missing data were addressed **[n/a]**
		(*d*) If applicable, explain how matching of cases and controls was addressed **[n/a]**
		(*e*) Describe any sensitivity analyses **[n/a]**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **[page 8]**
		(b) Give reasons for non-participation at each stage **[n/a]**
		(c) Consider use of a flow diagram **[n/a]**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **[page 8]**
		(b) Indicate number of participants with missing data for each variable of interest **[n/a]**
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure **[page 8]**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

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		adjusted for and why they were included **[page 8-17]**
		(*b*) Report category boundaries when continuous variables were categorized **[n/a]**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **[n/a]**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **[page 8-17]**
Discussion		
Key results	18	Summarise key results with reference to study objectives **[page 18]**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **[20]**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **[21]**
Generalisability	21	Discuss the generalisability (external validity) of the study results **[20]**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **[23]**

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*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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A cross-sectional survey investigating the desensitisation of graphic health warning labels and their impact on smokers, non-smokers and COPD patients in a London cohort

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ABSTRACT

Objectives There is a lack of evidence regarding the effectiveness of GHWL in different subjects, including COPD patients. Investigating knowledge and attitudes may allow better implementation of future public health policies. We hypothesised significant differences in GHWL impact between non-smokers, smokers and COPD patients; with decreased efficacy in those groups who are longer and more frequently exposed to them.

Participants and setting 163 subjects (54% male, aged 21-80) including 60 non-smokers, 53 smokers and 50 COPD patients (Gold stage II-IV), attending London respiratory outpatient clinics, participated in case-controlled surveys (fifty items).

Outcome measures Ten different GHWL were shown and demographics, smoking history, plans to quit, smoking risk awareness, emotional response, processing and impact of GHWL on behaviour were recorded. Patients were further asked to prioritise the hypothetical treatment or prevention of five specific smoking-related diseases.

Results Smokers, in particular those with COPD, were less susceptible to GHWL than non-smokers; 53.4% of all subjects expressed fear when looking at GHWL, non-smokers (71.9%) more so than smokers (39.8%, $p<0.001$). COPD participants were less aware of the consequences than non-COPD participants ($p<0.001$), including an awareness of lung cancer ($p=0.001$). Lung cancer (95%), oral cancer (90.2%), heart disease (84.7%) and stroke (71.2%) were correctly associated with smoking, whereas blindness was least associated (23.9%). However blindness was prioritised over oral cancer, stroke and in COPD patients also over heart disease when subjects were asked about hypothetical treatment or prevention.

Conclusion GHWL are most effective in non-smokers and a desensitisation effect was observed in smokers and COPD patients. As a consequence, a tailored and concerted public health approach to use such messages is required and 'blindness' deserves to be mentioned in this context because of an unexpectedly high deterring impact.

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ARTICLE SUMMARY

Article focus

- To assess the impact of Graphic Health Warning Labels (GHWL) in non-smokers, smokers and patients with COPD within a London cohort.
- To quantify the desensitisation of GHWL within these cohorts and to analyse the awareness of important smoking related risks and the preventive impact of this knowledge.

Key messages

- GHWL are least effective in those that have greatest exposure to them, such as smokers and patients with COPD due to desensitisation; additional strategies should be explored to assist smoking cessation further.
- Awareness of the non-pulmonary risks of smoking are low and few studies have investigated the awareness of patients with COPD, or the relative effects of GHWL on smoking behaviour in these groups.
- Blindness was the least well-known risk of smoking, despite a high deterring impact in all groups.

Strengths and limitations of this study

- Detailed assessments used structured surveys, designed following an internal peer review process amongst three tertiary teaching hospitals and one academic institution.
- COPD patients were more reluctant to take part in the research and a more substantial aversion to GHWL may have been masked in this group. Further, the COPD cohort was older and had more male subjects than the other groups.
- Data were collected directly from patient groups in an outpatient setting and generalisability to the wider population may be limited.

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INTRODUCTION

Tobacco use is one of four factors responsible for the majority of all worldwide deaths caused by non-communicable disease, according to the World Health Organisation.[1] It causes lung cancer and Chronic Obstructive Pulmonary Disease (COPD).[2, 3] Smoking cessation at any stage improves health outcomes, even in patients with advanced COPD [4] and, although it is difficult to change smoking behaviour, public health campaigns featuring primary and secondary prevention influence smoking habits and public health in the long-term.[5]

Graphic Health Warning Labels (GHWL) have been used over several years to promote smoking cessation and increase awareness of smoking related side-effects.[6] Various studies have described their efficacy, which appears to be more effective than text-only labels,[7-11] but difficulties still persist to encourage smoking cessation.[12] Despite all efforts and a comprehensive government tobacco plan (Table 1),[13] more than 21% of the UK population continue to smoke.[14]

Table 1: Government tobacco plan [13]

Table 1 showing the six-part governmental tobacco control plan for England
1) Stopping promotion of tobacco
2) Making tobacco less affordable
3) Effective regulation of tobacco products
4) Helping tobacco users to quit
5) Reducing exposure to second hand smoke
6) Effective communications for tobacco control

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Awareness of smoking-related ill health

Knowledge of smoking-related diseases amongst smokers and non-smokers, including exposure to second-hand smoke, oral health, and various types of cancer differs significantly,[10, 15] even amongst medical students.[16] While cardiovascular and respiratory risks are well acknowledged this is not true for other diseases, particularly for blindness.[17-21]

COPD and Graphic Health Warning Labels

Vardavas and colleagues [8] investigated the significant role GHWL might play in preventing smoking during early adolescence, a crucial period in which experimentation and addiction commonly occur.[22] Despite their efficacy, long-term exposure to such warnings may have a desensitising effect on attitudes towards smoking cessation.

Desensitisation to GHWL could have the greatest impact in patients with COPD because they are exposed long term to the efforts of public health campaigns. Indeed older smokers are also reported to demonstrate less interest in quitting smoking [23] and they more often attribute symptoms to the effect of ageing or a non-medical cause [24]. A reduced respiratory symptom attribution to smoking would lead to a reduced likelihood to quit [25]. COPD is also associated with a higher prevalence of depression, poor memory, decreased attention [26] and mild cognitive impairment [27, 28]. These factors may reduce the cognitive impact GHWL have on smoking cessation and warrant further investigation.

The present study aims to investigate differences in GHWL impact, and knowledge of smoking outcomes in smokers, non-smokers and patients with COPD; we hypothesised a decreased efficacy on subjects with increased exposure to smoking. Identifying individual responses may facilitate a more tailored public health approach for the utilisation of GHWL in future health policies.

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PATIENTS AND METHODS

The study was approved by the local research ethics committee (reference number 12/NE/0013) and was performed at Guy´s & St Thomas´ NHS Foundation Trust, London, UK. Prior to participation informed and written consent was obtained for all subjects. Inclusion criteria were: fluent English, respiratory department outpatients, age 21-80 years, both genders, smokers, non-smokers and ex-smokers, as well as COPD patients (GOLD stage II-IV) with a pre-diagnosed condition. Patients who were unable to communicate, understand or view the GHWL or consent form were excluded.

163 participants were studied, including 60 non-smokers, 53 smokers and 50 COPD patients (smokers and non-smokers, see online supplement table E1 and E2). A structured survey was designed to investigate the awareness of smoking risks and the effectiveness of GHWL within these groups.

Structured Survey

The survey contained 50 items based on those utilised by previous studies.[19, 20, 29] These items were included following an internal peer review process amongst three tertiary teaching hospitals and one academic institution (King`s College London, UK; the survey is available in the appendix and more details can be found in the online supplement). The following health risks were included:

1) Mouth and throat cancer

   Smoking cessation causes a 50% reduction in risk of oral cancer within 5 years.[30]

2) Lung cancer

   Approximately 90% of male lung cancer deaths and 75-80% of female lung cancer deaths in the US are caused by smoking each year.[31]

3) Heart disease

   Estimations attribute 40% of heart disease to smoking.[32]

4) Stroke

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Smoking could increase the risk of stroke by 2 to 4 fold.[33]

5) Blindness

Estimations attribute smoking to approximately 20% of new blindness in people over the age of 50.[34]

Participants were then shown GHWL (n=10) and their responses were recorded. More details about this can be found in the online supplement. The surveys were conducted by investigators with medical background who were instructed to remain neutral and not to influence decision making. Training took place prior to data collection and at two-weekly intervals, lasting 15-20 minutes, to standardise the interview process and minimise investigator-led bias.

Statistical analysis

Sample size calculations revealed that at least 50 subjects were required in each arm of the study to achieve a power of 0.8 (for more details on the sample size calculation please refer to the online supplement). Data were collected using MS Excel 2007 (Microsoft Corporation, Seattle/WA, USA); they were analysed using SPSS Statistics 21 (IBM, New York/NY, USA) and tested for a normal distribution using the Kolmogornov-Smirnoff test. χ-square tests were used to compare categorical data. Non-categorical data were analysed using unpaired t-tests, if data were normally distributed, or Mann-Whitney non-parametric tests if they were non-normally distributed. A regression analysis was conducted, using binary logistic regression and multiple linear regression, and applied to the primary outcome measure of knowledge score (the number of smoking-related risks that each participant was aware of). The independent variables in the analysis were age, gender, sex, ethnicity, smoking status and COPD status. Data are presented as mean (standard deviation, SD), unless otherwise indicated. A level of significance was defined as $p<0.05$.

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RESULTS

A total of 163 participants (54% male (m), age 52.4 (17.8) years) were included, with 60 non-smokers without airway disease (38.3% m; age 41.4 (16.4) years), 53 smokers without airway disease (69.8% m, age 49.7 (13.1) years) and 50 COPD patients (56% m; age 68.6 (10.7) years); this group contained smokers and non-smokers (please refer to the online supplement, table E1 and E2). The group with non-smokers had more female participants than the group with smokers and the one with COPD patients. The COPD group was older than the other two groups. The ethnic background of all participants was predominantly "White" (79%), followed by "Asian/Asian British" (10%) and "Black/Black British" (9%).(Table 2)

	All (N=163)	**Non-smokers (non-COPD) (N=60)**	**Smokers (non-COPD) (N=53)**	**COPD (N=50)**	**X^2 / one-way ANOVA (P value)**
Age in years (range)	52.4 (18-90)	41.4(18-85)	49.7(24-74)	68.6(40-90)	<0.001
Sex (N, %) **Male** **Female**	88 (54%) 75(46%)	23 (38%) 37 (62%)	37 (70%) 16 (30%)	28 (56%) 22 (44%)	0.003
Ethnicity/N **White**	129 (79%)	43 (72%)	41 (77%)	45 (90%)	
Asian/ Asian British	17 (10%)	9 (15%)	7 (13%)	1 (2%)	0.074
Black/ Black British	14 (9%)	5 (8%)	5 (9%)	4 (8%)	
Mixed	3 (2%)	3 (5%)	0 (0%)	0 (0%)	

Table 2: Participants demographics, revealing mean age (with range), number of participants according to gender (%) and ethnicity (%) for all groups.

Awareness of health risks associated with smoking

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93.3% of non-COPD smokers stated that they had thought about the health risks associated with smoking compared to 75.0% of COPD smokers (p=0.097). Across all participants, the greatest awareness was for lung cancer (95.0%), followed by mouth and throat cancer (90.2%), heart disease (84.7%) and stroke (71.2%). Blindness was least well known (23.9%). Non-smokers revealed an increased awareness of associations between smoking and mouth and throat cancer (p=0.004) compared to smokers (Figure 1). COPD patients expressed a decreased awareness of lung cancer (p=0.001), heart disease (p=0.012), stroke (p=0.001) and mouth and throat cancer (p<0.001) compared to the other groups (Figure 2). There was no significant difference between the groups in the awareness of blindness.

Figure 1 inserts here.

Figure 2 inserts here.

Impact of smoking consequences on future behaviour

Smokers were more motivated to quit smoking if, hypothetically, they were to develop heart disease (89.7% *vs* 75.0%, p<0.001), stroke (82.8% *vs* 75.0%, p<0.001), blindness (89.7% *vs* 66.7%, p<0.001), mouth and throat cancer (93.1% *vs* 75.0%, p<0.001) or lung cancer (89.7% *vs* 83.3%, p<0.001) compared to COPD patients. Non-smokers scored similarly to COPD patients (9.4 (1.1) *vs* 8.7 (2.3) points, p=0.055) when asked about *'the harmfulness of smoking to health'*, but they scored higher than current smokers (8.4 (1.5) points, p=0.004; Table 3).

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=99)	Non-smokers (n=64)	**p-value**
***1)** How harmful is smoking to health? (non-normal)* Mean (SD)	8.7 (2.3)	8.9 (1.4)	**0.564**	8.4 (1.5)	9.4 (1.1)	**0.004**
Awareness of smoking related side-effects: total score out of 5. Mean (SD)	3.1 (1.4)	3.9 (1.0)	**p<0.001**	3.6 (1.2)	3.8 (1.1)	**0.293**
Awareness of Heart Disease	74.0	89.4	**0.012**	85.9	82.8	**0.598**

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as related to smoking (%)						
Awareness of Stroke as related to smoking (%)	54.0	78.8	**0.001**	69.7	73.4	**0.607**
Awareness of Blindness as related to smoking (%)	18.0	26.5	**0.238**	23.2	25.0	**0.796**
Awareness of Mouth and Throat Cancer as related to smoking (%)	72.0	98.2	**<0.001**	84.8	98.4	**0.004**
Awareness of Lung Cancer as related to smoking (%)	88.0	99.1	**0.001**	93.9	98.4	**0.167**

Table 3: Awareness of smoking consequences. Item 1 showing each group's response (1-10) of the perceived harmfulness of smoking to health (mean (SD)), number of known smoking related consequences from 1-5 (mean (SD)), and total number (%) in each group that was aware of the smoking consequence. *Statistically significant results are highlighted in grey.*

When given the choice to avoid one of five hypothetical conditions associated with smoking, smokers rated lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and finally stroke. Similarly, non-smokers ranked lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and stroke. COPD patients ranked lung cancer highest, followed by blindness, heart disease, mouth and throat cancer and stroke. However, no significant differences existed between the ranks in the different subgroups.(Table 4 and online supplement Table E3)

When subjects had to choose to hypothetically treat only one of these five smoking associated conditions, smokers most commonly ranked lung cancer first, followed by heart disease, blindness, stroke and lastly mouth and throat cancer. Non-smokers most commonly ranked lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and stroke. COPD patients most commonly ranked lung cancer highest, followed by blindness, heart disease, mouth and throat cancer and stroke. Compared to non-smokers, smokers were significantly more likely to seek hypothetical treatment for lung cancer compared to non-

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smokers (p=0.005) who were more likely to seek treatment for mouth and throat cancer (p=0.043).(Table 4 and online supplement Table E4)

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=99)	Non-smokers (n=64)	**p-value**
If you could Prevent or Treat only one of Heart Disease, Stroke, Blindness, Mouth and Throat Cancer and Lung Cancer, which would you choose? (% choosing each option)	[Rank 1-5]					[Overall rank 1-5]
Heart Disease (%)	16.0 [3]	24.8 [2]	**0.078**	19.7 [2]	25.8 [2]	**0.196** [2]
Stroke (%)	6.0 [5]	7.5 [5]	**0.621**	6.6 [5]	7.8 [5]	**0.668** [5]
Blindness (%)	19.0 [2]	17.3 [3]	**0.704**	16.7 [3]	19.5 [3]	**0.509** [3]
Mouth and Throat Cancer (%)	9.0 [4]	8.4 [4]	**0.860**	6.6 [5]	11.7 [4]	**0.105** [4]
Lung Cancer (%)	50.0 [1]	40.3 [1]	**0.102**	49.5 [1]	33.6 [1]	**0.005** [1]

Table 4: showing the number (%) of each group that would hypothetically prevent or treat the named condition if they could choose only one from the given list. Ranks of each condition [1-5] are stated in columns 1, 2, 4 and 5 with overall rank [1-5] in column 6. Table 4 is a composite score of table E3 (if you can prevent only one named disease) and table E4 (if you could treat only one named disease) which are available in the online supplement. *Statistically significant results are highlighted in grey.*

Response and processing of GHWL

Amongst all participants, 53.4% of patients experienced fear after viewing pictures of GHWL, 78.5% of participants expressed disgust; 28.8% would actively avoid labels if they saw them in public. Smokers experienced less fear when looking at GHWL (71.9%) compared to non-smokers (39.8%; p<0.001; Figure 3). There was no significant difference in avoiding GHWL or feelings of disgust between smokers and non-smokers (Table 4). COPD patients experienced less fear, disgust and were less likely to avoid looking at GHWL

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compared to other groups (p=0.016; Figure 4), but only avoidance reached the level of statistical significance. (Table 5)

Figure 3 inserts here.

Figure 4 inserts here.

GHWL would have been more sufficient to prevent or stop smoking in non-smokers than smokers (p<0.001). Non-smokers were more likely than smokers to think about the warning messages on cigarette packaging (p=0.006) and talk about the warning labels to others (p<0.001; online supplement, Figure E1). COPD patients read the packaging less often (p<0.001), less carefully (p=0.010), they were less likely to think about the messages (p=0.001), talk to others about warning labels (p<0.001), think about warning labels when they were not in sight (p<0.023) or were less likely to keep a warning label at home as a reminder (p=0.013; online supplement, Figure E2). No significant differences existed between COPD and non-COPD groups when comparing whether the warning labels were sufficient motivation to stop smoking (p=0.240; Table 5).

Initial response to GHWLs	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=103)	Non-smokers (n=60)	**p-value**
...Fear? (%)	48.0	55.8	**0.360**	39.8	71.9	**<0.001**
...Disgust? (%)	76.0	79.6	**0.601**	72.8	82.8	**0.284**
Ever avoided looking at GHWLs? (%)	16.0	34.5	**0.016**	27.2	29.7	**0.846**
Are the warning labels sufficient motivation for you to stop smoking (if a current smoker) or not start smoking (if a non- or ex-	44.0	54.0	**0.240**	35.4	75.0	**<0.001**

smoker)? (%)						
Processing of GHWLs						
Packaging processing response						
a) How carefully have you ever read the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.9 (1.1)	2.4 (1.3)	**0.010**	2.4 (1.4)	2.1 (1.1)	**0.493**
b) How often do you read the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.6 (1.0)	2.5 (1.3)	**<0.001**	2.5 (1.5)	2.1 (1.1)	**0.064**
c) How often have you thought about the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.9 (1.3)	2.7 (1.3)	**0.001**	2.2 (1.2)	2.8 (1.5)	**0.006**
General processing response						
d) Have you ever talked to others about the warning labels on cigarette packaging? (1 = never, 5 = very often)	1.5 (1.1)	2.5 (1.4)	**<0.001**	1.8 (1.1)	2.7 (1.5)	**<0.001**
e) How often have you thought about the warning messages on cigarette packages when there has been no pack in sight? (1 = never, 5 = very often)	1.5 (0.9)	1.9 (1.2)	**0.023**	1.6 (1.0)	2.0 (1.3)	**0.112**
f) How often have you kept a warning label from a cigarette pack? (1 = never, 5 = very often)	1.0 (0.3)	1.4 (1.0)	**0.013**	1.2 (0.8)	1.3 (0.8)	**0.995**

Table 5: Emotional response and processing of GHWL, indicating the number of participants (%) that responded with fear, disgust, avoidance and the number (%) motivated to stop smoking. Also, the mean (SD) processing of GHWL (1-5) over two items (packaging and general processing response). *Statistically significant values are highlighted grey.*

In terms of age and sex of the participants, female subjects were more likely to experience fear compared to male participants (p=0.002), but not disgust or active avoidance of labels. They were also more likely to stop smoking following exposure (p=0.002) and more likely to think about GHWL messages when they were not in sight (p=0.023). Those who experienced fear were younger (p=0.037), as were those who would actively avoid looking at labels

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(p=0.008; Table 6). An increased age was significantly correlated with a decrease in depth of processing of labels (r= -0.386, p<0.001), older subjects exhibited a decreased level of attention to detail when reading GHWL (r= -0.315, p<0.001), they paid less attention to them (r= -0.351, p<0.001), they were less often thinking about the labels (r= -0.375, p<0.001), also when GHWL were not in sight (r=-0.201, p<0.010) and they talked less about them (r= -0.31, p<0.001; Table 7).

Emotional response to warning labels	Male - Yes	Female - Yes	X^2	Mean age of those who said 'Yes'	Mean age of those who said 'No'	**t-test (2-tailed)**
Fear	37/88	50/75	**0.002**	50.0 (18.3)	55.6 (16.7)	**0.044**
Disgust	66/88	62/75	**0.235**	51.3 (17.4)	57.1 (18.7)	**0.112**
Avoidance	21/88	26/75	**0.129**	47.0 (16.1)	54.8 (18.0)	**0.008**
Sufficient to stop from smoking	35/88	48/75	**0.002**	51.5 (18.4)	53.9 (16.9)	**0.381**

Table 6: Age and gender differences in the response to GHWL, showing differences in gender (total number) and age (mean (SD)) in the emotional response to GHWL and motivation to stop smoking. *Statistically significant values are highlighted grey.*

	Total package (P) processing response	**Total general (G) Processing response**	**Overall depth of processing (P+G)**
Age (r)	-0.393	-0.276	-0.386
p-value	<0.001	<0.001	<0.001
Mean score - **Male**	6.8 (3.5)	5.0 (2.5)	11.7 (5.2)
Mean score - **Female**	7.1 (3.5)	5.5 (2.7)	12.6 (5.6)

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Gender t-test p-value (2 tailed)	0.559	0.217	0.323
Breakdown of package (P) processing response:			
	Paid close attention	Thought about labels	Carefully read
Age (r)	-0.351	-0.375	-0.315
p-value	<0.001	<0.001	<0.001
Mean score – **Male**	2.2 (1.3)	2.3 (1.3)	2.2 (1.3)
Mean score – **Female**	2.3 (1.3)	2.6 (1.4)	2.2 (1.2)
Gender t-test p-value (2 tailed)	0.915	0.312	0.788
Breakdown of general (G) processing response:			
	Thought about when not in sight	Kept a label as a reminder	Talked to others about labels
Age (r)	-0.201	-0.094	-0.31
p-value	0.010	0.232	<0.001
Mean score – **Male**	1.6 (1.0)	1.3 (0.9)	2.1 (1.3)
Mean score – **Female**	2.0 (1.3)	1.2 (0.8)	2.3 (1.4)
Gender t-test p-value (2 tailed)	0.023	0.651	0.315

Table 7: Age and gender differences in the processing of GHWL**,** showing Pearson's correlation with age and mean (SD) gender scores (1-10), in package processing (3-items) and general processing (3-items) of the warning labels. The overall processing is shown in the third column. *Statistically significant values are highlighted grey.*

The regression analysis to understand whether there were independent predictors of knowledge or awareness of smoking-related consequences revealed no significant association with the overall knowledge score of the respondent`s age (p=0.333), gender (p=0.079), race (p=0.552) or smoking status (p=0.756).

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DISCUSSION

Patients with COPD exhibit a decreased response to Graphic Health Warning Labels, an effect that can be referred to as desensitisation, whereas non-smokers and smokers without airway disease responded better. The use of GHWL evoked an emotional response of fear and disgust in the majority of participants, particularly in non-smokers, in females and in younger participants.

The effect of desensitisation can be defined as a process where repeated exposure results in habituation of a cognitive, emotional and physiological response. Psychological research has shown that novel events are processed more extensively than common events [35, 36] and although some papers discuss desensitisation as a possible mechanism for a decreased impact of GHWL,[37, 38] it has largely been described in relation to graphic video game imagery and violence.[39]

Awareness of smoking consequences and impact on future behaviour

Various studies have outlined an increased awareness of smoking-related respiratory complications in COPD patients.[29, 34, 40-43] In contrast, our study found that COPD patients had a decreased awareness of consequences compared to non-COPD patients and were less likely to quit if they developed any of the diseases; the same was true when smokers were compared to non-smokers. Smokers also scored significantly lower than non-smokers when asked how harmful smoking was to their health and they had a decreased awareness of mouth and throat cancer.

The awareness of "blindness" and its role in public health campaigns

Blindness was the least well-known smoking-related risk despite all participants being highly motivated to prevent and treat it (ranked 2nd or 3rd in all groups, following lung cancer and heart disease). Up to 20% of all subjects with new onset of blindness are attributed to

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smoking [44] and previous studies have found it more motivational than conventional messages in smoking prevention [18-20].

Smoking-related lung cancer, heart disease, mouth and throat cancer and stroke are well recognised and publicised in printed media and TV advertising.[34, 45] This awareness is reflected across all study groups. However, it has been established that current smokers have a lower understanding of other risks including macular degeneration, cataracts and oral diseases compared to non-smokers.[17, 18, 21] In one study, less than 10% of patients older than 18 years were able to associate blindness with smoking.[34]

A study from Australia has shown an increased awareness of smoking-related eye disease due to public health strategies [46] and an increased emphasis on blindness in this context could have the potential to motivate and encourage smoking cessation.[18]

Future implications

GHWL appear to lose efficacy with increased exposure. Unfortunately this limits the extensive use for the primary target groups, in particular long-term smokers and COPD patients. A balance between the use of GHWL and the observed desensitisation effects need to be considered. Therefore, specific health messages should be targeted at these cohorts over defined periods and re-organised with regular campaigns to avoid desensitisation. The knowledge that less well-known risks (e.g. blindness) could have a similar impact as more well-known risks of smoking (e.g. lung cancer, heart disease) provides the chance to alternate features of different diseases on GHWL in concerted public health campaigns.

Indeed different approaches to promote smoking cessation are still required. Over the last few years it has been considered whether plain packages should be introduced, preventing the use of illusory packaging techniques as a means of attracting consumers.[47] Evidence around plain packaging is currently based on indirect studies [48-52] and whilst Australia is the first

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country to sell tobacco products adopting this policy [53, 54] the UK government, following consideration of such an approach,[13] has currently rejected a proposal.

Limitations

The respondents in this study came from a hospital setting in respiratory and outpatient departments and therefore a selection bias might have influenced some of the outcomes of our survey; the generalisability of our data should therefore be considered with caution. Several GHWL were shown to participants within a short time period and this could have caused a greater emotional response than showing single pictures.

Further, the COPD cohort tended to be older, with more male subjects, whereas the non-smoker group consisted of proportionally more females. The numbers used in the analysis however were taken from a reasonably large dataset and represent consistent results amongst all groups, in line with previous findings. The smoking history was variable between subjects in the COPD group as it included current smokers and also non-smokers. This could have impacted on and limited our results with regard to the COPD group (see online supplement, Table E1).

COPD patients were more reluctant to take part in this survey and it is likely that a true aversion to GHWL might have been underestimated. In addition, although Hammond et al. [11] demonstrated that smoking cessation was related to high cognitive processing of labels, intention to quit smoking was investigated here rather than actual behaviour change. Future research may need to investigate the achieved rate of smoking cessation following GHWL exposure; also the link between intention and actual change of smoking behaviour.

Desensitisation is one explanation for our findings, however, it is possible that COPD patients demonstrate an ambivalence towards risks to support their own self-esteem.[55] This would suppress anxiety associated with a fear of the consequences of smoking [56] and portray itself

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as a 'don't care' attitude. Leventhal [57] postulated that fear messages may lead to two competing processes, either a 'danger control' or, in the case of our COPD cohort, a 'fear control' response. Indeed where fear-based approaches have been used to reduce illicit drug rates, increased rates of drug abuse were described post intervention.[58] Further qualitative work will help understand these specific responses better.

Conclusion

Prolonged exposure to GHWL may cause desensitisation, in particular to COPD patients and current smokers. To maintain their efficacy, other strategies using the intermittent application of different features need to be employed within concerted health campaigns. Blindness has to be mentioned as a specific factor because it leads to a strong emotional response in the context of GHWL.

The evidence provided by our research is required to continue to develop successful public health campaigns, in particular because plain packaging has currently been rejected as public health policy in the UK. These campaigns should focus on improving the lack of awareness of smoking-related diseases, especially in those with chronic smoking behaviour. Further, the timing of exposure to specific GHWL messages needs to be considered to avoid desensitisation. Future qualitative research is required to explore thoughts and beliefs of chronic smokers and COPD patients, to understand any ambivalence towards smoking consequences and to explore underlying reasons. A more tailored approach will help to support effective primary and secondary prevention and smoking cessation interventions.

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Contributorship

CR designed the study, designed and adapted data collection tools, set up research teams in Singapore (Singapore arm, data not yet available) and London, obtained ethical approval, monitored data collection and data collection training, collected data, revised and oversaw formation of the literature review, analysed data and wrote and revised literature review, analysis and discussion sections of the paper. He is the first guarantor. B-MC collected data, made significant contribution to analysis and wrote proportions of analysis and discussion section. PD made significant contribution to data collection and reviewing paper. SS performed initial literature search and literature review. BS collected data and aided in elements of data analysis section. MB made significant contribution to data collection and reviewing the paper. AD was vital in statistical analysis plan, analysis sections and so

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tailoring discussion sections. JS is second guarantor. He oversaw data collection in the London arm, established, enabled and supervised undertaking of the project in the London site; facilitated formation of the London research team; safeguarded data collected and was responsible for overlooking, guiding and re-drafting the eventual manuscript prior to submission.

Competing interests and funding

The main sponsor of the study was King's College London School of Medicine. There are no competing interests or additional external sources of funding in the undertaking of this project or production of the manuscript.

Data Sharing Statement

Extra data is available on emailing the corresponding author [c.ratneswaran@gmail.com]. This includes the raw data collected if necessary and is available to researchers looking to further investigate the scope of the current project.

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Figure legends

Figure 1: Awareness of smoking-related consequences (smokers *vs* non-smokers), showing the differences in number of respondents (%). *Significant differences are marked (** p<0.01).*

Figure 2: Awareness of smoking-related consequences (COPD *vs* non-COPD), showing the differences in number of respondents (%). *Significant differences are marked (* p<0.05 ** p<0.01 *** P<0.001).*

Figure 3: Emotional response to GHWL (smokers *vs* non-smokers)**,** showing the difference in respondents (%) experiencing fear, disgust and avoidance after GHWL exposure. *Statistically significant differences are marked (*** p<0.001).*

Figure 4: Emotional response to GHWL (COPD *vs* non-COPD), showing the difference in respondents (%) experiencing fear, disgust and avoidance after GHWL exposure. *Statistically significant differences are marked (* p<0.05).*

Supplementary Files

Appendix

Table E1 COPD and non-COPD patients grouped into smokers and non-smokers

Table E2 Non-smokers smoking history

Table E3: Smoking consequences to be prevented

Table E4: Smoking consequence to be treated

Supplemental Figures

Figure E1: GHWL processing (Smokers and non-Smokers)

Figure E2: GHWL processing (COPD and non-COPD)

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A cross-sectional survey investigating the desensitisation of graphic health warning labels and their impact on smokers, non-smokers and COPD patients in a London cohort

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ABSTRACT

Objectives There is a lack of evidence regarding the effectiveness of GHWL in different subjects, including COPD patients. Investigating knowledge and attitudes may allow better implementation of future public health policies. We hypothesised significant differences in GHWL impact between non-smokers, smokers and COPD patients; with decreased efficacy in those groups who are longer and more frequently exposed to them.

Participants and setting 163 subjects (54% male, aged 21-80) including 60 non-smokers, 53 smokers and 50 COPD patients (Gold stage II-IV), attending London respiratory outpatient clinics, participated in case-controlled surveys (fifty items).

Outcome measures Ten different GHWL were shown and demographics, smoking history, plans to quit, smoking risk awareness, emotional response, processing and impact of GHWL on behaviour were recorded. Patients were further asked to prioritise the hypothetical treatment or prevention of five specific smoking-related diseases.

Results Smokers, in particular those with COPD, were less susceptible to GHWL than non-smokers; 53.4% of all subjects expressed fear when looking at GHWL, non-smokers (71.9%) more so than smokers (39.8%, $p<0.001$). COPD participants were less aware of the consequences than non-COPD participants ($p<0.001$), including an awareness of lung cancer ($p=0.001$). Lung cancer (95%), oral cancer (90.2%), heart disease (84.7%) and stroke (71.2%) were correctly associated with smoking, whereas~~ilst~~ blindness was least associated (23.9%). However blindness was prioritised over oral cancer, stroke and in COPD patients also over heart disease when subjects were asked about hypothetical treatment or prevention.

Conclusion GHWL are most effective in non-smokers and a desensitisation effect was observed in smokers and COPD patients. As a consequence, a tailored and concerted public health approach to use such messages is required and 'blindness' deserves to be mentioned in this context because of an unexpectedly high deterring impact.

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ARTICLE SUMMARY

Article focus

- To assess the impact of Graphic Health Warning Labels (GHWL) in non-smokers, smokers and patients with COPD within a London cohort.
- To quantify the desensitisation of GHWL within these cohorts and to analyse the awareness of important smoking related risks and the preventive impact of this knowledge.

Key messages

- GHWL are least effective in those that have greatest exposure to them, such as smokers and patients with COPD due to desensitisation; additional strategies should be explored to assist smoking cessation further.
- Awareness of the non-pulmonary risks of smoking are low and few studies have investigated the awareness of patients with COPD, or the relative effects of GHWL on smoking behaviour in these groups.
- Blindness was the least well-known risk of smoking, despite a high deterring impact in all groups.

Strengths and limitations of this study

- Detailed assessments used structured surveys, designed following an internal peer review process amongst three tertiary teaching hospitals and one academic institution.
- COPD patients were more reluctant to take part in the research and a more substantial aversion to GHWL may have been masked in this group. Further, the COPD cohort was older and had more male subjects than the other groups.
- Data were collected directly from patient groups in an outpatient setting and generalisability to the wider population may be limited.

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INTRODUCTION

Tobacco use is one of four factors responsible for the majority of all worldwide deaths caused by non-communicable disease, according to the World Health Organisation.[1] It causes lung cancer and Chronic Obstructive Pulmonary Disease (COPD).[2, 3] Smoking cessation at any stage improves health outcomes, even in patients with advanced COPD [4] and, although it is difficult to change smoking behaviour, public health campaigns featuring primary and secondary prevention influence smoking habits and public health in the long-term.[5]

Graphic Health Warning Labels (GHWL) have been used over several years to promote smoking cessation and increase awareness of smoking related side-effects.[6] ~~Whilst~~ ~~v~~Various studies have described their efficacy, which appears to be more effective than text-only labels,[7-11] but difficulties still persist to encourage smoking cessation.[12] Despite all efforts and a ~~whilst the government supports a~~ comprehensive government tobacco plan (Table 1),[13] more than 21% of the UK population continue to smoke.[14]

Table 1: Government tobacco plan [13]

Table 1 showing the six-part governmental tobacco control plan for England
1) Stopping promotion of tobacco
2) Making tobacco less affordable
3) Effective regulation of tobacco products
4) Helping tobacco users to quit
5) Reducing exposure to second hand smoke
6) Effective communications for tobacco control

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Awareness of smoking-related ill health

Knowledge of smoking-related diseases amongst smokers and non-smokers, including exposure to second-hand smoke, oral health, and various types of cancer differs significantly,[10, 15] even amongst medical students.[16] While cardiovascular and respiratory risks are well acknowledged this is not true for other diseases, particularly for blindness.[17-21]

COPD and Graphic Health Warning Labels

Vardavas and colleagues [8] investigated the significant role GHWL might play in preventing smoking during early adolescence, a crucial period in which experimentation and addiction commonly occur.[22] Despite their efficacy, long-term exposure to such warnings may have a desensitising effect on attitudes towards smoking cessation.

Desensitisation to GHWL could have the greatest impact in patients with COPD because they are exposed long term to the efforts of public health campaigns. Indeed older smokers are also reported to demonstrate less interest in quitting smoking [23] and they more often attribute symptoms to the effect of ageing or a non-medical cause [24]. A reduced respiratory symptom attribution to smoking would lead to a reduced likelihood to quit [25]. COPD is also associated with a higher prevalence of depression, poor memory, decreased attention [26] and mild cognitive impairment [27, 28]. These factors may reduce the cognitive impact GHWL have on smoking cessation and warrant further investigation.

The present study aims to investigate differences in GHWL impact, and knowledge of smoking outcomes in smokers, non-smokers and patients with COPD; we hypothesised a decreased efficacy on subjects with increased exposure to smoking. Identifying individual responses may facilitate a more tailored public health approach for the utilisation of GHWL in future health policies.

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PATIENTS AND METHODS

The study was approved by the local research ethics committee (reference number 12/NE/0013) and was performed at Guy´s & St Thomas´ NHS Foundation Trust, London, UK. Prior to participation informed and written consent was obtained for all subjects. Inclusion criteria were: fluent English, respiratory department outpatients, age 21-80 years, both genders, smokers, non-smokers and ex-smokers, as well as COPD patients (GOLD stage II-IV) with a pre-diagnosed condition. Patients who were unable to communicate, understand or view the GHWL or consent form were excluded.

163 participants were studied, including 60 non-smokers, 53 smokers and 50 COPD patients (smokers and non-smokers, see online supplement table E1 and E2). A structured survey was designed to investigate the awareness of smoking risks and the effectiveness of GHWL within these groups.

Structured Survey

The survey contained 50 items based on those utilised by previous studies.[19, 20, 29] These items were included following an internal peer review process amongst three tertiary teaching hospitals and one academic institution (King`s College London, UK; the survey is available in the appendix and more details can be found in the online supplement). The following health risks were included:

1) Mouth and throat cancer

   Smoking cessation causes a 50% reduction in risk of oral cancer within 5 years.[30]

2) Lung cancer

   Approximately 90% of male lung cancer deaths and 75-80% of female lung cancer deaths in the US are caused by smoking each year.[31]

3) Heart disease

   Estimations attribute 40% of heart disease to smoking.[32]

4) Stroke

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Smoking could increase the risk of stroke by 2 to 4 fold.[33]

5) Blindness

Estimations attribute smoking to approximately 20% of new blindness in people over the age of 50.[34]

Participants were then shown GHWL (n=10) and their responses were recorded. More details about this can be found in the online supplement. The surveys were conducted by investigators with medical background who were instructed to remain neutral and not to influence decision making. Training took place prior to data collection and at two-weekly intervals, lasting 15-20 minutes, to standardise the interview process and minimise investigator-led bias.

Statistical analysis

Sample size calculations revealed that at least 50 subjects were required in each arm of the study to achieve a power of 0.8 (for more details on the sample size calculation please refer to the online supplement). Data were collected using MS Excel 2007 (Microsoft Corporation, Seattle/WA, USA); they were analysed using SPSS Statistics 21 (IBM, New York/NY, USA) and tested for a normal distribution using the Kolmogornov-Smirnoff test. χ-square tests were used to compare categorical data. Non-categorical data were analysed using unpaired t-tests, if data were normally distributed, or Mann-Whitney non-parametric tests if they were non-normally distributed. A regression analysis was conducted, using binary logistic regression and multiple linear regression, and applied to the primary outcome measure of knowledge score (the number of smoking-related risks that each participant was aware of). The independent variables in the analysis were age, gender, sex, ethnicity, smoking status and COPD status. Data are presented as mean (standard deviation, SD), unless otherwise indicated. A level of significance was defined as $p<0.05$.

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RESULTS

A total of 163 participants (54% male (m), age 52.4 (17.8) years) were included, with 60 non-smokers without airway disease (38.3% m; age 41.4 (16.4) years), 53 smokers without airway disease (69.8% m, age 49.7 (13.1) years) and 50 COPD patients (56% m; age 68.6 (10.7) years); this group contained smokers and non-smokers (please refer to the online supplement, table E1 and E2). The group with non-smokers had more female participants than the group with smokers and the one with COPD patients. The COPD group was older than the other two groups. The ethnic background of all participants was predominantly "White" (79%), followed by "Asian/Asian British" (10%) and "Black/Black British" (9%).(Table 2)

	All (N=163)	**Non-smokers (non-COPD) (N=60)**	**Smokers (non-COPD) (N=53)**	**COPD (N=50)**	**X^2 / one-way ANOVA (P value)**
Age in years (range)	52.4 (18-90)	41.4(18-85)	49.7(24-74)	68.6(40-90)	<0.001
Sex (N, %) **Male** **Female**	88 (54%) 75(46%)	23 (38%) 37 (62%)	37 (70%) 16 (30%)	28 (56%) 22 (44%)	0.003
Ethnicity/N **White**	129 (79%)	43 (72%)	41 (77%)	45 (90%)	
Asian/ Asian British	17 (10%)	9 (15%)	7 (13%)	1 (2%)	0.074
Black/ Black British	14 (9%)	5 (8%)	5 (9%)	4 (8%)	
Mixed	3 (2%)	3 (5%)	0 (0%)	0 (0%)	

Table 2: Participants demographics, revealing mean age (with range), number of participants according to gender (%) and ethnicity (%) for all groups.

Awareness of health risks associated with smoking

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93.3% of non-COPD smokers stated that they had thought about the health risks associated with smoking compared to 75.0% of COPD smokers (p=0.097). Across all participants, the greatest awareness was for lung cancer (95.0%), followed by mouth and throat cancer (90.2%), heart disease (84.7%) and stroke (71.2%). Blindness was least well known (23.9%). Non-smokers revealed an increased awareness of associations between smoking and mouth and throat cancer (p=0.004) compared to smokers (Figure 1). COPD patients expressed a decreased awareness of lung cancer (p=0.001), heart disease (p=0.012), stroke (p=0.001) and mouth and throat cancer (p<0.001) compared to the other groups (Figure 2). There was no significant difference between the groups in the awareness of blindness.

Figure 1 inserts here.

Figure 2 inserts here.

Impact of smoking consequences on future behaviour

Smokers were more motivated to quit smoking if, hypothetically, they were to develop heart disease (89.7% *vs* 75.0%, p<0.001), stroke (82.8% *vs* 75.0%, p<0.001), blindness (89.7% *vs* 66.7%, p<0.001), mouth and throat cancer (93.1% *vs* 75.0%, p<0.001) or lung cancer (89.7% *vs* 83.3%, p<0.001) compared to COPD patients. Non-smokers scored similarly to COPD patients (9.4 (1.1) *vs* 8.7 (2.3) points, p=0.055) when asked about *'the harmfulness of smoking to health'*, but they scored higher than current smokers (8.4 (1.5) points, p=0.004; Table 3).

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=99)	Non-smokers (n=64)	**p-value**
***1)** How harmful is smoking to health? (non-normal)* Mean (SD)	8.7 (2.3)	8.9 (1.4)	**0.564**	8.4 (1.5)	9.4 (1.1)	**0.004**
Awareness of smoking related side-effects: total score out of 5. Mean (SD)	3.1 (1.4)	3.9 (1.0)	**p<0.001**	3.6 (1.2)	3.8 (1.1)	**0.293**
Awareness of Heart Disease	74.0	89.4	**0.012**	85.9	82.8	**0.598**

as related to smoking (%)						
Awareness of Stroke as related to smoking (%)	54.0	78.8	**0.001**	69.7	73.4	**0.607**
Awareness of Blindness as related to smoking (%)	18.0	26.5	**0.238**	23.2	25.0	**0.796**
Awareness of Mouth and Throat Cancer as related to smoking (%)	72.0	98.2	**<0.001**	84.8	98.4	**0.004**
Awareness of Lung Cancer as related to smoking (%)	88.0	99.1	**0.001**	93.9	98.4	**0.167**

Table 3: Awareness of smoking consequences. Item 1 showing each group's response (1-10) of the perceived harmfulness of smoking to health (mean (SD)), number of known smoking related consequences from 1-5 (mean (SD)), and total number (%) in each group that was aware of the smoking consequence. *Statistically significant results are highlighted in grey.*

When given the choice to avoid one of five hypothetical conditions associated with smoking, smokers rated lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and finally stroke. Similarly, non-smokers ranked lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and stroke. COPD patients ranked lung cancer highest, followed by blindness, heart disease, mouth and throat cancer and stroke. However, no significant differences existed between the ranks in the different subgroups.(Table 4 and online supplement Table E3)

When subject had to choose to hypothetically treat only one of these five smoking associated conditions, smokers ~~ranked~~ most commonly ranked lung cancer first, followed by heart disease, blindness, stroke and lastly mouth and throat cancer. Non-smokers most commonly ranked lung cancer highest, followed by heart disease, blindness, mouth and throat cancer and stroke. COPD patients most commonly ranked lung cancer highest, followed by blindness, heart disease, mouth and throat cancer and stroke. Compared to non-smokers, smokers were significantly more likely to seek hypothetical treatment for lung cancer compared to non-

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smokers (p=0.005) who were more likely to seek treatment for mouth and throat cancer (p=0.043).(Table 4 and online supplement Table E4)

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=99)	Non-smokers (n=64)	**p-value**
If you could Prevent or Treat only one of Heart Disease, Stroke, Blindness, Mouth and Throat Cancer and Lung Cancer, which would you choose? (% choosing each option)	[Rank 1-5]					[Overall rank 1-5]
Heart Disease (%)	16.0 [3]	24.8 [2]	**0.078**	19.7 [2]	25.8 [2]	**0.196** [2]
Stroke (%)	6.0 [5]	7.5 [5]	**0.621**	6.6 [5]	7.8 [5]	**0.668** [5]
Blindness (%)	19.0 [2]	17.3 [3]	**0.704**	16.7 [3]	19.5 [3]	**0.509** [3]
Mouth and Throat Cancer (%)	9.0 [4]	8.4 [4]	**0.860**	6.6 [5]	11.7 [4]	**0.105** [4]
Lung Cancer (%)	50.0 [1]	40.3 [1]	**0.102**	49.5 [1]	33.6 [1]	**0.005** [1]

Table 4: showing the number (%) of each group that would hypothetically prevent or treat the named condition if they could choose only one from the given list. Ranks of each condition [1-5] are stated in columns 1, 2, 4 and 5 with overall rank [1-5] in column 6. Table 4 is a composite score of table E3 (if you can prevent only one named disease) and table E4 (if you could treat only one named disease) which are available in the online supplement. *Statistically significant results are highlighted in grey.*

Response and processing of GHWL

Amongst all participants, 53.4% of patients experienced fear after viewing pictures of GHWL, 78.5% of participants expressed disgust; 28.8% would actively avoid labels if they saw them in public. Smokers experienced less fear when looking at GHWL (71.9%) compared to non-smokers (39.8%; p<0.001; Figure 3). There was no significant difference in avoiding GHWL or feelings of disgust between smokers and non-smokers (Table 4). COPD patients experienced less fear, disgust and were less likely to avoid looking at GHWL

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compared to other groups (p=0.016; Figure 4), but only avoidance reached the level of statistical significance. (Table 5)

Figure 3 inserts here.

Figure 4 inserts here.

GHWL would have been more sufficient to prevent or stop smoking in non-smokers than smokers (p<0.001). Non-smokers were more likely than smokers to think about the warning messages on cigarette packaging (p=0.006) and talk about the warning labels to others (p<0.001; online supplement, Figure E1). COPD patients read the packaging less often (p<0.001), less carefully (p=0.010), they were less likely to think about the messages (p=0.001), talk to others about warning labels (p<0.001), think about warning labels when they were not in sight (p<0.023) or were less likely to keep a warning label at home as a reminder (p=0.013; online supplement, Figure E2). No significant differences existed between COPD and non-COPD groups when comparing whether the warning labels were sufficient motivation to stop smoking (p=0.240; Table 5).

Initial response to GHWLs	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=103)	Non-smokers (n=60)	**p-value**
...Fear? (%)	48.0	55.8	**0.360**	39.8	71.9	**<0.001**
...Disgust? (%)	76.0	79.6	**0.601**	72.8	82.8	**0.284**
Ever avoided looking at GHWLs? (%)	16.0	34.5	**0.016**	27.2	29.7	**0.846**
Are the warning labels sufficient motivation for you to stop smoking (if a current smoker) or not start smoking (if a non- or ex-	44.0	54.0	**0.240**	35.4	75.0	**<0.001**

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smoker)? (%)						
Processing of GHWLs						
Packaging processing response						
a) How carefully have you ever read the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.9 (1.1)	2.4 (1.3)	**0.010**	2.4 (1.4)	2.1 (1.1)	**0.493**
b) How often do you read the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.6 (1.0)	2.5 (1.3)	**<0.001**	2.5 (1.5)	2.1 (1.1)	**0.064**
c) How often have you thought about the warning messages on cigarette packaging? (1 = never, 5 = very often)	1.9 (1.3)	2.7 (1.3)	**0.001**	2.2 (1.2)	2.8 (1.5)	**0.006**
General processing response						
d) Have you ever talked to others about the warning labels on cigarette packaging? (1 = never, 5 = very often)	1.5 (1.1)	2.5 (1.4)	**<0.001**	1.8 (1.1)	2.7 (1.5)	**<0.001**
e) How often have you thought about the warning messages on cigarette packages when there has been no pack in sight? (1 = never, 5 = very often)	1.5 (0.9)	1.9 (1.2)	**0.023**	1.6 (1.0)	2.0 (1.3)	**0.112**
f) How often have you kept a warning label from a cigarette pack? (1 = never, 5 = very often)	1.0 (0.3)	1.4 (1.0)	**0.013**	1.2 (0.8)	1.3 (0.8)	**0.995**

Table 5: Emotional response and processing of GHWL, indicating the number of participants (%) that responded with fear, disgust, avoidance and the number (%) motivated to stop smoking. Also, the mean (SD) processing of GHWL (1-5) over two items (packaging and general processing response). *Statistically significant values are highlighted grey.*

In terms of age and sex of the participants, female subjects were more likely to experience fear compared to male participants (p=0.002), but not disgust or active avoidance of labels. They were also more likely to stop smoking following exposure (p=0.002) and more likely to think about GHWL messages when they were not in sight (p=0.023). Those who experienced fear were younger (p=0.037), as were those who would actively avoid looking at labels

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(p=0.008; Table 6). An increased age was significantly correlated with a decrease in depth of processing of labels (r= -0.386, p<0.001), older subjects exhibited a decreased level of attention to detail when reading GHWL (r= -0.315, p<0.001), they ~~payed~~paid less attention to them (r= -0.351, p<0.001), they were less often thinking about the labels (r= -0.375, p<0.001), also when GHWL were not in sight (r=-0.201, p<0.010) and they talked less about them (r= -0.31, p<0.001; Table 7).

Emotional response to warning labels	Male - Yes	Female - Yes	X^2	Mean age of those who said 'Yes'	Mean age of those who said 'No'	**t-test (2-tailed)**
Fear	37/88	50/75	**0.002**	50.0 (18.3)	55.6 (16.7)	**0.044**
Disgust	66/88	62/75	**0.235**	51.3 (17.4)	57.1 (18.7)	**0.112**
Avoidance	21/88	26/75	**0.129**	47.0 (16.1)	54.8 (18.0)	**0.008**
Sufficient to stop from smoking	35/88	48/75	**0.002**	51.5 (18.4)	53.9 (16.9)	**0.381**

Table 6: Age and gender differences in the response to GHWL, showing differences in gender (total number) and age (mean (SD)) in the emotional response to GHWL and motivation to stop smoking. *Statistically significant values are highlighted grey.*

	Total package (P) processing response	**Total general (G) Processing response**	**Overall depth of processing (P+G)**
Age (r)	-0.393	-0.276	-0.386
p-value	<0.001	<0.001	<0.001
Mean score - **Male**	6.8 (3.5)	5.0 (2.5)	11.7 (5.2)
Mean score - **Female**	7.1 (3.5)	5.5 (2.7)	12.6 (5.6)

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Gender t-test p-value (2 tailed)	0.559	0.217	0.323
Breakdown of package (P) processing response:			
	Paid close attention	Thought about labels	Carefully read
Age (r)	-0.351	-0.375	-0.315
p-value	<0.001	<0.001	<0.001
Mean score – **Male**	2.2 (1.3)	2.3 (1.3)	2.2 (1.3)
Mean score – **Female**	2.3 (1.3)	2.6 (1.4)	2.2 (1.2)
Gender t-test p-value (2 tailed)	0.915	0.312	0.788
Breakdown of general (G) processing response:			
	Thought about when not in sight	Kept a label as a reminder	Talked to others about labels
Age (r)	-0.201	-0.094	-0.31
p-value	0.010	0.232	<0.001
Mean score – **Male**	1.6 (1.0)	1.3 (0.9)	2.1 (1.3)
Mean score – **Female**	2.0 (1.3)	1.2 (0.8)	2.3 (1.4)
Gender t-test p-value (2 tailed)	0.023	0.651	0.315

Table 7: Age and gender differences in the processing of GHWL**,** showing Pearson's correlation with age and mean (SD) gender scores (1-10), in package processing (3-items) and general processing (3-items) of the warning labels. The overall processing is shown in the third column. *Statistically significant values are highlighted grey.*

The regression analysis to understand whether there were independent predictors of knowledge or awareness of smoking-related consequences revealed no significant association with the overall knowledge score of the respondent`s age (p=0.333), gender (p=0.079), race (p=0.552) or smoking status (p=0.756).

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DISCUSSION

Patients with COPD exhibit a decreased response to Graphic Health Warning Labels, an effect that can be referred to as desensitisation, whereas~~ilst~~ non-smokers and smokers without airway disease responded better. The use of GHWL evoked an emotional response of fear and disgust in the majority of participants, particularly in non-smokers, in females and in younger participants.

The effect of desensitisation can be defined as a process where repeated exposure results in habituation of a cognitive, emotional and physiological response. Psychological research has shown that novel events are processed more extensively than common events [35, 36] and although~~whilst~~ some papers discuss desensitisation as a possible mechanism for a decreased impact of GHWL,[37, 38] it has largely been described in relation to graphic video game imagery and violence.[39]

Awareness of smoking consequences and impact on future behaviour

Various studies have outlined an increased awareness of smoking-related respiratory complications in COPD patients.[29, 34, 40-43] In contrast, our study found that COPD patients had a decreased awareness of consequences compared to non-COPD patients and were less likely to quit if they developed any of the diseases; the same was true when smokers were compared to non-smokers. Smokers also scored significantly lower than non-smokers when asked how harmful smoking was to their health and they had a decreased awareness of mouth and throat cancer.

The awareness of "blindness" and its role in public health campaigns

Blindness was the least well-known smoking-related risk despite all participants being highly motivated to prevent and treat it (ranked 2nd or 3rd in all groups, following lung cancer and heart disease). Up to 20% of all subjects with new onset of blindness are attributed to

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smoking [44] and previous studies have found it more motivational than conventional messages in smoking prevention [18-20].

Smoking-related lung cancer, heart disease, mouth and throat cancer and stroke are well recognised and publicised in printed media and TV advertising.[34, 45] This awareness is reflected across all study groups. However, it has been established that current smokers have a lower understanding of other risks including macular degeneration, cataracts and oral diseases compared to non-smokers.[17, 18, 21] In one study, less than 10% of patients older than 18 years were able to associate blindness with smoking.[34]

A study from Australia has shown an increased awareness of smoking-related eye disease due to public health strategies [46] and an increased emphasis on blindness in this context could have the potential to motivate and encourage smoking cessation.[18]

Future implications

GHWL appear to lose efficacy with increased exposure. Unfortunately this limits the extensive use for the primary target groups, in particular long-term smokers and COPD patients. A balance between the use of GHWL and the observed desensitisation effects need to be considered. Therefore, specific health messages should be targeted at these cohorts over defined periods and re-organised with regular campaigns to avoid desensitisation. The knowledge that less well-known risks (e.g. blindness) could have a similar impact as more well-known risks of smoking (e.g. lung cancer, heart disease) provides the chance to alternate features of different diseases on GHWL in concerted public health campaigns.

Indeed different approaches to promote smoking cessation are still required. Over the last few years it has been considered whether plain packages should be introduced, preventing the use of illusory packaging techniques as a means of attracting consumers.[47] Evidence around plain packaging is currently based on indirect studies [48-52] and whilst Australia is the first

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country to sell tobacco products adopting this policy [53, 54] the UK government, following consideration of such an approach,[13] has currently rejected a proposal.

Limitations

The respondents in this study came from a hospital setting in respiratory and outpatient departments and therefore a selection bias might have influenced some of the outcomes of our survey; the generalisability of our data should therefore be considered with caution. Several GHWL were shown to participants within a short time period and this could have caused a greater emotional response than showing single pictures.

Further, the COPD cohort tended to be older, with more male subjects, whereas the non-smoker group consisted of proportionally more females. The numbers used in the analysis however were taken from a reasonably large dataset and represent consistent results amongst all groups, in line with previous findings. The smoking history was variable between subjects in the COPD group as it included current smokers and also non-smokers. This could have impacted on and limited our results with regard to the COPD group (see online supplement, Table E1).

COPD patients were more reluctant to take part in this survey and it is likely that a true aversion to GHWL might have been underestimated. In addition, although Hammond et al. [11] demonstrated that smoking cessation was related to high cognitive processing of labels, intention to quit smoking was investigated here rather than actual behaviour change. Future research may need to investigate the achieved rate of smoking cessation following GHWL exposure; also the link between intention and actual change of smoking behaviour.

~~Whilst d~~Desensitisation is one explanation for our findings, however, it is possible that COPD patients demonstrate an ambivalence towards risks to support their own self-esteem.[55] This would suppress anxiety associated with a fear of the consequences of smoking [56] and

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portray itself as a 'don't care' attitude. Leventhal [57] postulated that fear messages may lead to two competing processes, either a 'danger control' or, in the case of our COPD cohort, a 'fear control' response. Indeed where fear-based approaches have been used to reduce illicit drug rates, increased rates of drug abuse were described post intervention.[58] Further qualitative work will help understand these specific responses better.

Conclusion

Prolonged exposure to GHWL may cause desensitisation, in particular to COPD patients and current smokers. To maintain their efficacy, other strategies using the intermittent application of different features need to be employed within concerted health campaigns. Blindness has to be mentioned as a specific factor because it leads to a strong emotional response in the context of GHWL.

The evidence provided by our research is required to continue to develop successful public health campaigns, in particular because plain packaging has currently been rejected as public health policy in the UK. These campaigns should focus on improving the lack of awareness of smoking-related diseases, especially in those with chronic smoking behaviour. Further, t~~T~~he timing of exposure to specific GHWL messages ~~should~~ needs to be considered to avoid desensitisation. Future qualitative research is required to explore thoughts and beliefs ~~within~~of chronic smokers and COPD patients.~~,~~ ~~This may~~to ~~demonstrate~~understand any ambivalence towards smoking consequences and to~~,~~ explore~~ing~~ underlying reasons. ~~, in order and~~ A more tailored approach ~~so~~will help to ~~to successfully~~ support effective primary and secondary prevention and smoking cessation interventions.

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Contributorship

CR designed the study, designed and adapted data collection tools, set up research teams in Singapore (Singapore arm, data not yet available) and London, obtained ethical approval, monitored data collection and data collection training, collected data, revised and oversaw formation of the literature review, analysed data and wrote and revised literature review, analysis and discussion sections of the paper. He is the first guarantor. B-MC collected data, made significant contribution to analysis and wrote proportions of analysis and discussion section. PD made significant contribution to data collection and reviewing paper. SS performed initial literature search and literature review. BS collected data and aided in elements of data analysis section. MB made significant contribution to data collection and

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reviewing the paper. AD was vital in statistical analysis plan, analysis sections and so tailoring discussion sections. JS is second guarantor. He oversaw data collection in the London arm, established, enabled and supervised undertaking of the project in the London site; facilitated formation of the London research team; safeguarded data collected and was responsible for overlooking, guiding and re-drafting the eventual manuscript prior to submission.

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Data Sharing Statement

Extra data is available on emailing the corresponding author [c.ratneswaran@gmail.com]. This includes the raw data collected if necessary and is available to researchers looking to further investigate the scope of the current project.

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Figure legends

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Figure 1: Awareness of smoking-related consequences (smokers *vs* non-smokers), showing the differences in number of respondents (%). *Significant differences are marked (** p<0.01).*

Figure 2: Awareness of smoking-related consequences (COPD *vs* non-COPD), showing the differences in number of respondents (%). *Significant differences are marked (* p<0.05 ** p<0.01 *** P<0.001).*

Figure 3: Emotional response to GHWL (smokers *vs* non-smokers)**,** showing the difference in respondents (%) experiencing fear, disgust and avoidance after GHWL exposure. *Statistically significant differences are marked (*** p<0.001).*

Figure 4: Emotional response to GHWL (COPD *vs* non-COPD), showing the difference in respondents (%) experiencing fear, disgust and avoidance after GHWL exposure. *Statistically significant differences are marked (* p<0.05).*

Supplementary Files

Appendix

Table E1 COPD and non-COPD patients grouped into smokers and non-smokers

Table E2 Non-smokers smoking history

Table E3: Smoking consequences to be prevented

Table E4: Smoking consequence to be treated

Supplemental Figures

Figure E1: GHWL processing (Smokers and non-Smokers)

Figure E2: GHWL processing (COPD and non-COPD)

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APPENDIX

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SMOKING QUESTIONNAIRE

1. Personal particulars:

Initials: _____

2. Age: _____ years

3. Sex: Male/ Female

4. Race:
[Please tick or if 'other' write on the line provided]

Asian or Asian British
- ☐ Bangladeshi
- ☐ Pakistani
- ☐ Indian
- ☐ Other _____

Black or Black British
- ☐ African
- ☐ Caribbean
- ☐ Other _____

Chinese or Chinese British
- ☐ Chinese
- ☐ Other _____

Mixed
- ☐ White and Asian
- ☐ White and Caribbean
- ☐ White and Black African
- ☐ Other _____

White
- ☐ Irish
- ☐ Northern Irish
- ☐ English
- ☐ Scottish
- ☐ Welsh
- ☐ Other _____

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5. Occupation:

- ☐ Legislators, senior officials and managers
- ☐ Professionals
- ☐ Clerical workers
- ☐ Service workers and shop and market sales workers
- ☐ Agricultural and fishery workers
- ☐ Production craftsmen and related workers
- ☐ Plant and machine operators and assemblies
- ☐ Cleaners, labourers and related workers
- ☐ Military
- ☐ Unemployed
- ☐ Student

6. Cigarette smoking status: Current smoker/ ex-smoker/ non-smoker

If current smoker, please proceed to question 7.

If ex-smoker, please proceed to question 8.

If non-smoker, please proceed to question 9.

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QUESTION 7 - CURRENT SMOKERS

a) How long have you smoked for?

_____

b) On average, how many cigarettes do you smoke a day?

_____

c) Have you ever considered giving up smoking? **YES / NO**

IF YES

d) Have any of the following motivated you to give up smoking?
(Multiple choices possible)

- ☐ Health
- ☐ Financial savings
- ☐ Family request
- ☐ Health professional's advice
- ☐ Media (magazines/ newspapers/ TV commercial / radio)
- ☐ Internet
- ☐ Peer advice
- ☐ Graphic health warnings (cigarette packs)

Other: _____

e) How many attempts have you made at giving up smoking?

f) On a scale of 1 – 10, how confident are you about giving up smoking when you when you want?

0 1 2 3 4 5 6 7 8 9 10

Not confident Very confident

g) Have you even thought about the health risks associated with smoking? **YES/NO**

IF YES

h) On a scale of 0 – 10, how often do you think about the health risks associated with smoking?

0 1 2 3 4 5 6 7 8 9 10

Not at all Very often

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Please proceed to question 9.

QUESTION 8 - EX-SMOKERS

a) How long ago did you give up smoking?

b) How many cigarettes did you smoke a day?

c) How many years did you smoke for?

d) How many attempts did you make to stop smoking, including the last?

e) What was your motivation for stopping smoking? (Multiple choices possible)

- ☐ Health
- ☐ Financial savings
- ☐ Family request
- ☐ Health professional's advice
- ☐ Media (magazines/ newspapers/ TV commercial / radio)
- ☐ Internet
- ☐ Peer advice
- ☐ Graphic health warnings (cigarette packs)

Others: _____

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QUESTION 9

How harmful do you think smoking is to health in general?

0	1	2	3	4	5	6	7	8	9	10
Not harmful										Very harmful (death)

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General awareness of smoking and disease

10. Do you believe the following diseases are related to smoking?

Heart disease	**YES / NO / NOT SURE**
Stroke	**YES / NO / NOT SURE**
Blindness	**YES / NO / NOT SURE**
Mouth and throat cancer	**YES / NO / NOT SURE**
Lung cancer	**YES / NO / NOT SURE**

11. Which disease would you like to prevent if it were possible to prevent only one?

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

12. Which disease would you seek treatment for if it were possible to treat only one?

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

If smoker, please proceed to question 13.

If ex- or non-smoker, please proceed to question 14.

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QUESTION 13

Imagine that all the conditions below have the same risk of occurrence. Rank the following conditions from 1 to 5 in order of how much motivation each provides towards you stopping smoking, with 1 being most feared, and 5 being the least feared.

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

QUESTION 14

Imagine the following conditions all have the same risk of occurrence. Rank the following conditions from 1 to 5 in order of how much each motivates you to not start smoking, with 1 being most feared, and 5 being the least feared.

Heart disease	☐
Stroke	☐
Blindness	☐
Mouth and throat cancer	☐
Lung cancer	☐

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Attitudes toward graphic health warning labels on cigarette packs

15. Emotional response to warning labels

a) Did you experience any fear when looking at the warning labels? **YES / NO**

b) Did you experience any disgust when looking at the warning labels? **YES / NO**

c) Have you ever actively avoided looking at the warning labels in public? **YES / NO**

16. Depth of processing

Please score the following questions on a scale of 1 to 5 using this guide:
1=not at all/never; 2=once; 3=sometimes; 4=often; 5=all the time/a lot

Package messages (outside)

a) How carefully have you ever read the messages on the outside of cigarette packets? 1 2 3 4 5

b) How often have you read or paid close attention to the messages on the outside of packages? 1 2 3 4 5

c) How often have you thought about what the warnings on the outside of packages have to say? 1 2 3 4 5

General

d) Have you ever talked about the warning labels with other smokers or non-smokers? 1 2 3 4 5

e) Have you ever thought about the warnings or what they had to say when a cigarette pack wasn't in sight? 1 2 3 4 5

f) Have you ever kept a warning label to serve as a reminder of the effects of smoking on health? 1 2 3 4 5

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Impact of graphic health warning labels on smoking behaviour

If current smoker, please proceed to question 17.

If ex- or non-smoker, please proceed to question 18.

17. Current smoker

Do you feel the labels are a sufficient motivation for you to stop smoking? **YES / NO**

Would you stop smoking if you developed early signs of the following disease?

Heart disease	**YES / NO**
Stroke	**YES / NO**
Blindness	**YES / NO**
Mouth and throat cancer	**YES / NO**
Lung Cancer	**YES / NO**

Rank the conditions in order of how much motivation each provides towards you stopping smoking, with 1 being most feared, and 5 being the least feared.

Heart disease

Stroke

Blindness

Mouth and throat cancer

Lung Cancer

18. Ex- or non-smokers

Do you feel the labels are a sufficient motivation to prevent you from starting smoking? **YES / NO**

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Online Supplement

A cross-sectional survey investigating the desensitisation of graphic health warning labels and their impact on smokers, non-smokers and COPD patients in a London cohort

Culadeeban Ratneswaran, Ben Chisnall, Panagis Drakatos, Sukhanthan Sivakumar, Bairavie Sivakumar, Miriam Barrecheguren, Abdel Douiri, Joerg Steier

Patients & Methods

Table E1 COPD and non-COPD patients grouped into smokers and non-smokers

	COPD	Non-COPD	Total
Smokers	46	53	99
Non-smokers	4	60	64
Total	50	113	163

Table E1: Cross-tabulation of the number of COPD and non-COPD patients grouped into smokers and non-smokers, including the total number of participants in each group: non-smokers, smokers, non-COPD and COPD.

Table E2 Non-smokers smoking history

	Never smokers	Quit >2yrs	Quit <2yrs
Non-smokers	60	4	0

Table E2: Smoking history of the non-smokers into never-smokers, recent quitters (<2 years) and quitters for > 2 years.

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Structured survey – items before GHWL exposure

We recorded demographics (5 items), smoking history (7 items) and asked patients how confident they would be about quitting smoking (1 item) if they wanted to. Questions further determined knowledge of health risks associated with smoking (7 items), including how harmful they believed smoking was to their health (on a scale of 1, "not harmful", to 10, "very harmful, death") and the motivational impact of the risks towards stopping or preventing from smoking (15 items). The following health risks were included: mouth and throat cancer, lung cancer, heart disease, stroke and blindness.

Structured survey – items following GHWL exposure

Their emotional response (3 items), depth of content processing (6 items), impact on their smoking behaviour (1 item) and whether they would stop smoking if they developed early signs of the diseases illustrated (5 items) were recorded.

Statistical analysis – sample size calculation

Sample size calculation was performed based on a 95% confidence interval, an alpha of 0.05, with an estimated total London smoking population (1,280,000) and the proportion expected to be aware of the least known consequence condition chosen in the questionnaire (blindness) at 0.01 – 0.05.

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Results

Table E3: Smoking consequences to be prevented

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=103)	Non-smokers (n=60)	**p-value**
If you could Prevent only one of Heart Disease, Stroke, Blindness, Mouth and Throat Cancer and Lung Cancer, which would you choose? (% choosing each option)	[Rank 1- 5]					[Overall rank 1-5]
Heart Disease (%)	14.0 [3]	24.8 [2]	**0.122**	18.4 [2]	26.7 [2]	**0.203** [2]
Stroke (%)	8.0 [5]	8.0 [5]	**0.994**	7.8 [5]	8.3 [5]	**0.951** [5]
Blindness (%)	18.0 [2]	15.0 [3]	**0.634**	17.5 [3]	13.3 [3]	**0.927** [3]
Mouth and Throat Cancer (%)	12.0 [4]	8.8 [4]	**0.533**	8.7 [4]	11.7 [4]	**0.699** [4]
Lung Cancer (%)	48.0 [1]	41.6 [1]	**0.447**	46.6 [1]	38.3 [1]	**0.210** [1]

Table E3: showing the number (%) of each group that would hypothetically prevent the named condition if they could choose only one from the given list. Ranks of each condition [1-5] are stated in columns 1, 2, 4 and 5 with overall rank [1-5] in column 6. Table E3 and E4 form the composite score for table 4. *There were no statistically significant differences.*

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Table E4: **Smoking consequence to be treated**

	COPD (n=50)	Non-COPD (n=113)	**p-value**	Smokers (n=103)	Non-smokers (n=60)	**p-value**
If you could seek treatment for only one of the following conditions, which would you choose? (%)	[Rank 1- 5]					[rank sum]
Heart Disease	18.0 [3]	24.8 [2]	**0.341**	21.2 [2]	25.0 [2]	**0.572** [2]
Stroke	4.0 [5]	7.1 [5]	**0.450**	5.1 [4]	7.8 [5]	**0.473** [5]
Blindness	20.0 [2]	19.5 [3]	**0.937**	17.2 [3]	23.4 [3]	**0.325** [3]
Mouth and Throat Cancer	6.0 [4]	8.0 [4]	**0.658**	4.0 [5]	12.5 [4]	**0.043** [4]
Lung Cancer	52.0 [1]	38.9 [1]	**0.120**	51.5 [1]	29.7 [1]	**0.006** [1]

Table E4: showing the number (%) of each group that would hypothetically treat the named condition if they could choose only one from the given list. Ranks of each condition [1-5] are stated in columns 1, 2, 4 and 5 with overall rank [1-5] in column 6. Table E3 and E4 form the composite score for table 4. *Statistically significant differences are highlighted in grey.*

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Figure E1: GHWL processing (Smokers and non-Smokers)

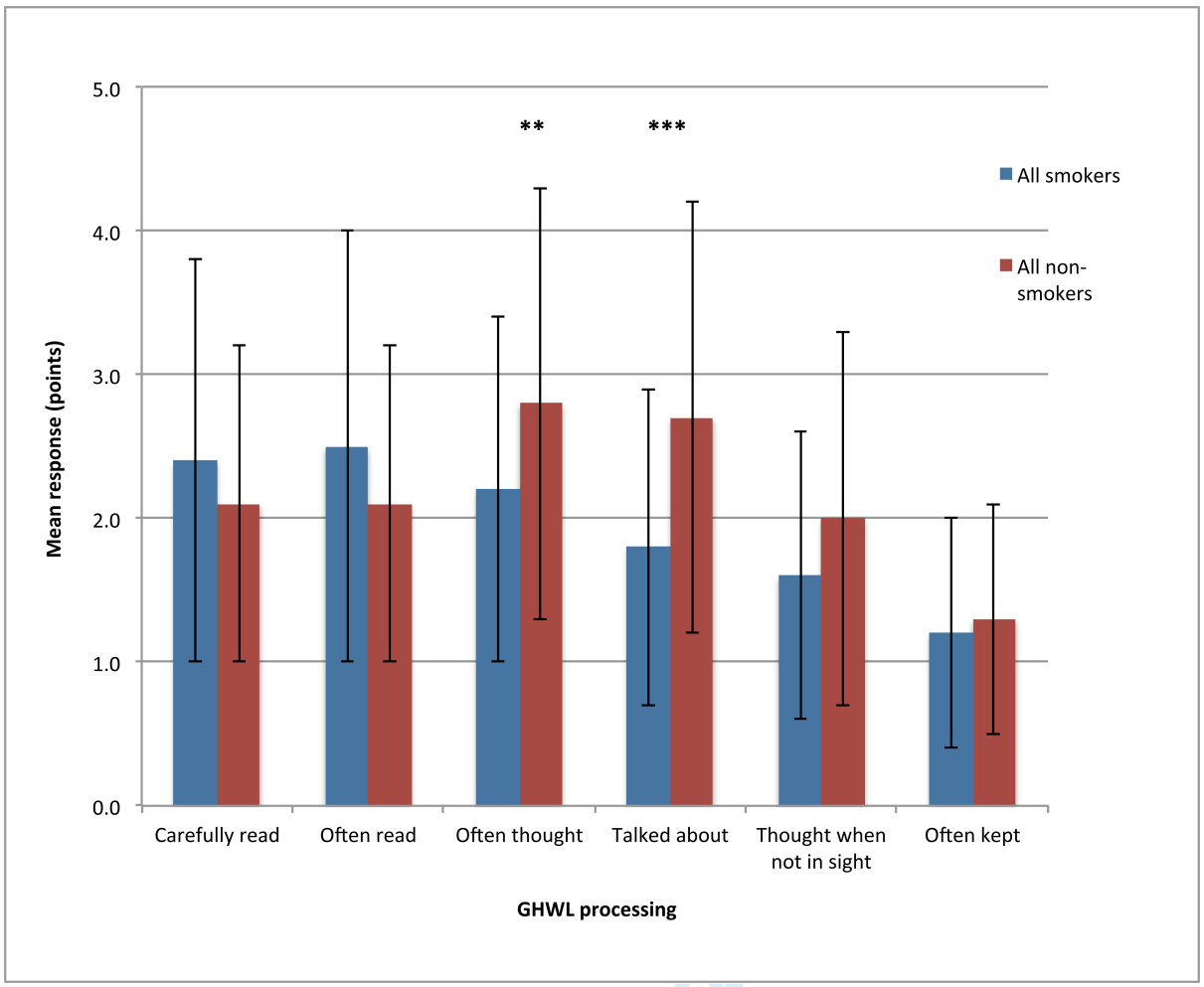

Figure E1: Processing of GHWL (smokers *vs* non-smokers), showing the mean difference (1-5) between smokers and non-smokers. Error bars indicate the standard deviation. *Statistically significant differences are marked (**p<0.01 *** p<0.001).*

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Figure E2: GHWL processing (COPD and non-COPD)

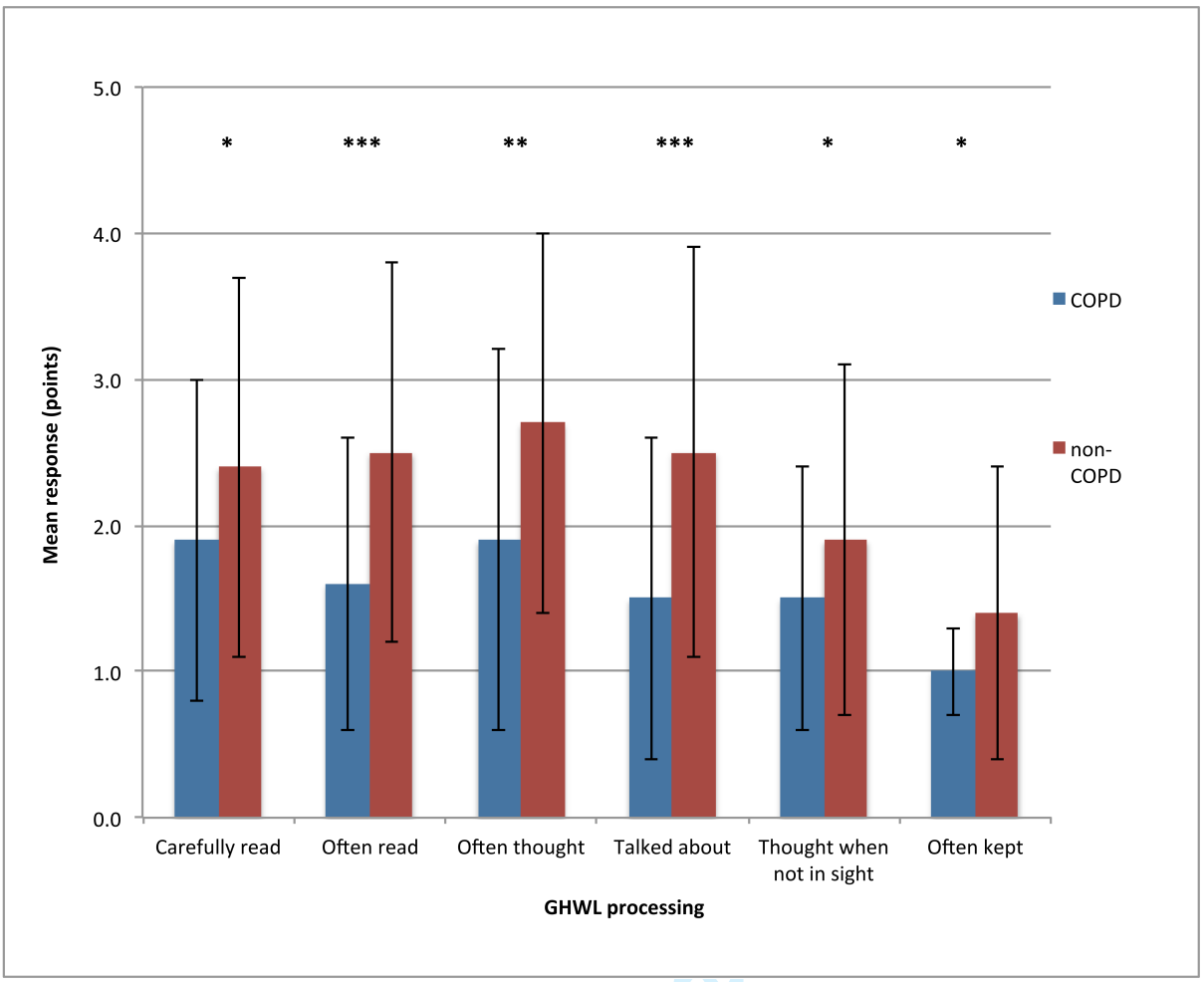

Figure E2: Processing of GHWL (COPD *vs* non-COPD), showing the mean difference in (1-5) between COPD and non-COPD. Error bars indicate the standard deviation. *Statistically significant differences are marked (* p<0.05 ** p<0.01 *** p<0.001).*

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STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **[page 2]**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **[page 2]**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **[page 4]**
Objectives	3	State specific objectives, including any prespecified hypotheses **[page 5]**
Methods		
Study design	4	Present key elements of study design early in the paper **[page 6]**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **[page 6]**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls **[page 6]**
		(*b*) For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **[page 6-7]**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **[page 6-7]**
Bias	9	Describe any efforts to address potential sources of bias **[page 6-7]**
Study size	10	Explain how the study size was arrived at **[page 7 and online supplement page 2]**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **[page 7]**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **[page 7 and online supplement page 2]**
		(*b*) Describe any methods used to examine subgroups and interactions **[page 7-8]**
		(*c*) Explain how missing data were addressed **[n/a]**
		(*d*) If applicable, explain how matching of cases and controls was addressed **[n/a]**
		(*e*) Describe any sensitivity analyses **[n/a]**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **[page 8]**
		(b) Give reasons for non-participation at each stage **[n/a]**
		(c) Consider use of a flow diagram **[n/a]**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **[page 8]**
		(b) Indicate number of participants with missing data for each variable of interest **[n/a]**
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure **[page 8]**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were

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		adjusted for and why they were included **[page 8-17]**
		(*b*) Report category boundaries when continuous variables were categorized **[n/a]**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **[n/a]**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **[page 8-17]**
Discussion		
Key results	18	Summarise key results with reference to study objectives **[page 18]**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **[20]**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **[21]**
Generalisability	21	Discuss the generalisability (external validity) of the study results **[20]**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **[23]**

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*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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