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No blank slates: Pre-existing schemas about pharmaceuticals predict memory for side effects

Monika K. Heller, Sarah C.E. Chapman and Rob Horne*

Research Department of Practice and Policy, University College London School of Pharmacy, London, UK

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Objectives: Attribution of symptoms as medication side effects is informed by pre-existing beliefs about medicines and perceptions of personal sensitivity to their effects (pharmaceutical schemas). We tested whether (1) pharmaceutical schemas were associated with memory (recall/recognition) for side effect information (2) memory explained the attribution of a common unrelated symptom as a side effect.
Design: In this analogue study participants saw the patient leaflet of a fictitious asthma drug listing eight side effects.
Main outcome measures: We measured recall and recognition memory for side effects and used a vignette to test whether participants attributed an unlisted common symptom (headache) as a side effect.
Results: Participants who perceived pharmaceuticals as more harmful in general recalled fewer side effects correctly ($r_{\text{Correct Recall}} = -.273$), were less able to differentiate between listed and unlisted side effects ($r_{\text{Recognition Sensitivity}} = -.256$) and were more likely to attribute the unlisted headache symptom as a side effect ($r_{\text{side effect attribution}} = .381$, $ps < .01$). The effect of harm beliefs on side effect attribution was partially mediated by correct recall of side effects.
Conclusion: Pharmaceutical schemas are associated with memory for side effect information. Memory may explain part of the association between pharmaceutical schemas and the attribution of unrelated symptoms as side effects.

Keywords: pharmaceutical schemas; memory; side effects; beliefs about medicines; questionnaire; perceived sensitivity to medicines scale

Introduction

Pharmaceutical medicines are fundamental to the management of most long-term conditions, but optimal treatment outcomes are compromised by side effects and non-adherence (Sabaté, 2003). Virtually all medicines can cause side effects, but not all the symptoms that patients attribute as medication side effects have a clear pharmacological grounding (Nestoriuc, Orav, Liang, Horne, & Barsky, 2010). Research on the nocebo effect shows for example that patients' expectations of side effects can increase side effect reporting even when patients are actually taking pharmacologically inactive

*Corresponding author. Email: r.horne@ucl.ac.uk
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placebo (Colloca & Miller, 2011; Faasse & Petrie, 2013). In addition, there is a clinical impression that some patient reported side effects may in fact be disease symptoms (Thiwan et al., 2009) or common symptoms (Barsky, Saintfort, Rogers, & Borus, 2002) that are falsely labelled as medication side effects.

Studies applying Leventhal's Common Sense Model (CSM) of self-regulation indicate that cognitive representations of illness and treatment play a key role in how patients appraise symptoms and make causal attributions (Baumann, Cameron, Zimmerman, & Leventhal, 1989; Cooper, Gellaitry, Hankins, Fisher, & Horne, 2009; Horne, 2003; Leventhal, Nerenz, & Straus, 1982). According to the CSM, cognitive representations of illness have five core dimensions: identity (e.g. disease label, representation of typical symptoms), cause of the illness, perceived control over the illness (e.g. responsiveness to pharmaceutical treatment) and the severity of illness consequences. These dimension influence emotional and cognitive responses to illness and coping behaviours. This model has been extended (Horne, 2003) to include cognitive representations of treatment, which have been shown to influence how patients cope with illness and engage with treatment. For example, medication adherence is influenced by cognitive representations of specific medicines (Horne et al., 2013) and more general 'background' beliefs about pharmaceuticals as a class of treatment (Horne, Parham, Driscoll, & Robinson, 2009; Horne, Weinman, & Hankins, 1999).

These background beliefs about medicines in general can be thought of as pharmaceutical schemas; how our ideas about pharmaceuticals are organised. Pharmaceutical schemas can be operationalised as ideas about medicines as objects (e.g. the degree to which they are generally harmful, beneficial, overused by doctors, etc. (Horne et al., 1999)) and beliefs about self in relation to medicines (e.g. beliefs about personal sensitivity to medicines (Horne et al., 1999)). Pharmaceutical schemas influence our evaluation of specific medicines (e.g. our perceptions of the treatment's value and risks). For example, people with more negative pharmaceutical schemas tend to report more concerns about potential harmful effects when considering a specific treatment (Horne et al., 1999, 2009).

A previous analogue study found that the misattribution of a common symptom as a side effect was influenced by individuals' cognitive representations of pharmaceutical treatment (Heller, Chapman & Horne, 2015). Individuals were more likely to misattribute an unrelated headache symptom as a side effect if they started out with more negative pharmaceutical schemas (perceiving pharmaceuticals to be generally harmful and less beneficial) and if they had stronger concerns about the medication.

In this paper we explore in more detail the psychological processes linking pharmaceutical schemas to the attribution of symptoms as side effects using an analogue design. The primary aim of the study is to investigate whether pharmaceutical schemas influence how individuals process and remember side effect information and whether this in turn affects side effect attribution. We hypothesise that the attribution of a symptom to a medication side effect will be more accurate when the patient has accurately remembered information they have been given about the specific side effects that are known to be associated with the particular medication.

Participants in this analogue online study saw the patient information leaflet of a fictitious asthma medication, with a list of side effects. Both recall and recognition memory for listed side effects was examined in this study. Recall involves the retrieval and reproduction of remembered information from memory while recognition memory relates

to the capacity to compare new information to information in memory (Zechmeister & Nyberg, 1982). Schemas have been shown to influence both recall and recognition (Graesser & Nakamura, 1984). For example in the Deese-Roedinger-McDermott-paradigm (Roediger & McDermott, 1995) individuals who were asked to recall a list of thematically related words (e.g. tired, dream, bed, duvet …) falsely recalled and recognised unlisted words (e.g. sleep, night) that were part of the activated schema.

Both recall and recognition could be important in the perception and attribution of symptoms as side effects: To recognise whether a new symptom (e.g. headache) is a side effect, patients need to compare it with the information they hold in memory about side effects, while recalling side effect information may influence whether patients expect to experience certain side effects.

As a secondary aim we explore whether including information about medication efficacy influences side effect attributions. Patient information leaflets tend to include mostly risk information (e.g. side effects, warnings about contraindications and interactions with other drugs), but rarely mention any benefits (e.g. efficacy information) (Kitching, 1990).

Research on risk perception suggests that people typically perceive products (including asthma and other prescription drugs (Slovic, Peters, Grana, Berger, & Dieck, 2007)) that offer greater benefits as less risky (Alhakami & Slovic, 1994). Making benefits more salient could thus be potentially effective in decreasing perceived risk and reducing the likelihood that unrelated symptoms are attributed as medication side effects. On the other hand there is a clinical impression that patients often perceive medicines as a two-edged sword, believing that greater potency of medicines comes at the price of greater adverse effects (Horne, 2003).

The following research questions and hypotheses were examined. In line with findings from a previous analogue study (Heller, Chapman & Horne, 2015) we hypothesised that individuals with more negative pre-existing pharmaceutical schemas (e.g. beliefs that medicines are generally harmful, high perceived sensitivity to their effects) would show an increased tendency to attribute an unrelated symptom (not listed in leaflet) as a side effect.

We further tested whether pre-existing negative pharmaceutical schemas influenced recall and recognition, as well as reading times for side effect information. Better memory for side effects from the leaflet was expected to reduce the likelihood that an unlisted symptom was attributed as a side effect.

In addition, we explored whether the inclusion of efficacy information had an effect on perceived risk and side effect attribution.

Method

Design

This analogue online study used a randomised between group design (efficacy information vs. no efficacy information).

Participants and recruitment

Adults (18 and over) with and without self-reported asthma were recruited via the Crowdflower crowdsourcing platform, from where they were directed to the Qualtrics

online study. Crowdflower allows subscribers to post surveys that are then completed by 'crowd workers' from online job boards (e.g. Amazon MTurk) for a small monetary reward (here $0.30). Only one survey submission from the same IP address (in this study or a related previous study (Heller, Chapman & Horne, 2015) was permitted to ensure independence of responses. This type of sampling has proved reliable in studies of decision-making and health (Buhrmester, Kwang, & Gosling, 2011; Ritter, Lorig, Laurent, & Matthews, 2004; Shapiro, Chandler, & Mueller, 2013).

Measures and materials

Beliefs about medicines questionnaire-general

The Beliefs about Medicines Questionnaire-General (BMQ-General) (Horne et al., 1999) assesses individuals' beliefs about pharmaceutical medicines as a class of treatment on three scales, containing four items each. General Harm assesses the degree to which pharmaceuticals are perceived to be essentially harmful, addictive substances that are best avoided (e.g. 'Medicines do more harm than good'). General Overuse assesses views about whether doctors place too much emphasis and trust on medicines (e.g. 'If doctors had more time with patients they would prescribe fewer medicines'). General Benefit captures perceptions of medicines as fundamentally beneficial (e.g. 'Medicines help many people to live better lives.').

Perceived sensitivity to medicines scale

The Perceived Sensitivity to Medicines Scale (PSM) (Horne et al., 2013) assesses beliefs about the self in relation to medicines; specifically about personal sensitivity to the positive and negative effects of medicines (e.g. 'My body overreacts to medicine.') with five scale items.

All BMQ and PSM items were rated on five-point Likert-type scales (from 1 = strongly disagree to 5 = strongly agree). Mean scale scores were computed by summing scale item scores and dividing the total by the number of scale items. Higher scale scores indicate higher endorsement of the scale construct. The BMQ and PSM scales have shown good reliability and validity in previous studies (Horne et al., 1999). Internal consistency of all scales in this study was good (Cronbach's αs > .75).

Demographics and self-reported asthma diagnosis

Participants indicated their age, gender, ethnicity, country of residence, and whether they had ever been diagnosed with asthma and previously taken asthma medication.

Asthma information

Participants read information about asthma, structured according to Leventhal's common sense model of illness representation (Diefenbach & Leventhal, 1996). It included information about asthma causes and triggers, symptoms and their episodic nature, likely consequences, and asthma management (see Heller, Chapman & Horne, 2015).

Molair patient information leaflets

Participants read one of two possible patient leaflets of the fictitious asthma medication Molair, modelled on the existing asthma drug Montelukast (see Figure 1). The Qualtrics block randomisation function was used to randomise participants to leaflet conditions.

- Both information leaflets provided information about Molair's mechanism of action (leukotriene receptor agonist) on the first page. Possible side effects (rash, dizziness; yellowing of the skin, itch, fatigue, abdominal pain, joint pain, muscle pain) were listed on a separate page. The order of side effects was randomised.
- The 'Efficacy information' leaflet contained an additional page outlining Molair's efficacy (based on a clinical trial of Montelukast (Virchow & Bachert, 2006)) presented before the side effect information: 'A recent clinical trial (with 5855 asthma patients) has shown the effectiveness of Molair in adults. Following a

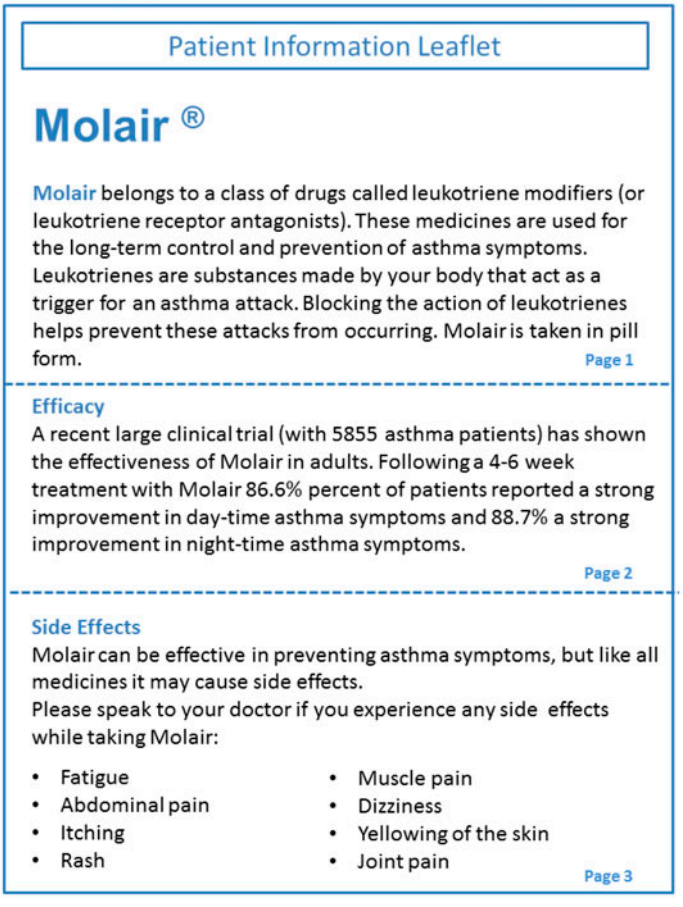

Figure 1. Molair patient information leaflet.
Note: Dotted lines represent page breaks. Efficacy information on (Page 2) was only presented in the 'Efficacy information' leaflet condition.

4–6 week treatment with Molair 86.6% percent of patients reported a strong improvement in day-time asthma symptoms and 88.7% a strong improvement in night-time asthma symptoms'.

Reading times for side effect information

The Qualtrics page timing function was used to measure how long participant spent on the side effect information page.

Efficacy and side effect expectation visual analogue scales

Three 100-point VAS were used to measure perceptions of efficacy (e.g. How effective do you think Molair is in general for the prevention of asthma symptoms? Rated from 0 = not effective at all to 100 = extremely effective). Four 100-point VAS assessed side effect expectations (e.g. How frequently do you think people in general develop side effects when taking Molair? Rated from 0 = never to 100 = always). Mean scores were computed for both sets of VAS. Internal consistency for both sets of VAS was high (Cronbach's α of .88 and .90, respectively).

Recall task

Participants were asked to type all the side effects they could remember from the leaflet. Responses were coded by MH as correct if they matched or were synonyms (e.g. tiredness for fatigue) of listed side effects and incorrect if they were not listed. Correct side effect recall and incorrect side effect recall scores were computed by counting correct and incorrect responses, respectively.

Recognition task

Participants saw a table with 16 symptoms in randomised order (see Figure 2): 8 side effects from the leaflet, 8 new symptoms. Listed side effects and new symptoms were matched in word length ($t(14) = .560$, $p = .586$). A post-test with $n = 33$ participants, recruited as per the main study, found no difference in perceived severity ($t(32) = .08$, $p = .941$). Participants were asked to indicate (yes/no) whether each symptom had been listed in the leaflet. Correct side effect recognition and incorrect side effect-recognition scores were computed by counting the number of correctly and incorrectly recognised side effects.

In addition, we computed more sophisticated recognition memory indices in line with Signal Detection Theory (SDT) (Green & Swets, 1966; McNicol, 2005). According to SDT, whether a participant responds that a symptom was listed in the leaflet will depend both on the memory strength of the symptom and the participant's general tendency to guess that a symptom was listed (response bias). Responses were coded as correct hits (responded listed, when listed), correct rejections (responded new, when new), misses (responded new, when listed) and False Alarms (responded listed, when new). False Alarm rates (number of false alarms/number of new symptoms) and correct hit rates (number of correct hits/number of listed side effects) were calculated. From these Response Bias (tendency to guess that a symptom was listed) and side effect

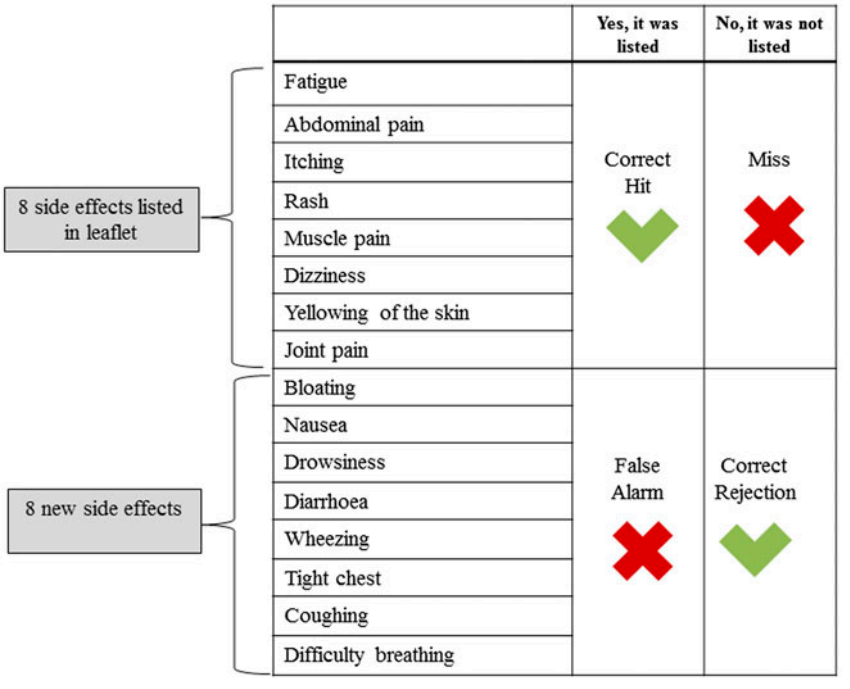

Figure 2. Side effect recognition task.

Recognition Sensitivity (ability to discriminate between listed side effects and new symptoms) were calculated[1]:

- side effect recognition sensitivity was operationalised as the difference between the *z*-scores of the correct hit and false alarm rates (Stanislaw & Todorov, 1999). Low recognition sensitivity could arise if a participant strategically responds all items were from the memorised list, resulting in a perfect correct hit rate and maximum false alarm rate. Higher side effect recognition sensitivity indicates better discrimination between previously listed side effects and new symptoms.
- Response Bias was computed by summing the *z*-score corresponding to the false alarm and the correct hit rate and multiplying the result by −1/2 (Macmillan, 1993). Higher response bias scores indicate more conservative responding i.e. decreased willingness to guess that an item was from the original list.

Symptom attribution vignette

Participants read the following vignette: 'Imagine you are suffering from asthma. You have been taking one 4 mg tablet of Molair every day for the last two weeks. At the beginning of the third week you get a headache'. Headache was not listed as one of Molair's side effects in the leaflet. Participants were then asked to indicate on 100-point visual analogue scales how likely they thought that six different factors (side effect of

Molair, eye strain, stress, beginning of a cold, lack of sleep, no particular reason; order randomised) caused the headache (from 0 = very unlikely to 100 = very likely).

Procedures

The study was categorised as exempt from ethical approval by the UCL Research Ethics Committee. Data was collected online with Qualtrics survey software (http://www.qualtrics.com). Participants gave informed consent, completed the PSM and the BMQ-General, read the asthma information and were randomised to leaflet conditions using the Qualtrics block randomisation function. Participants then completed the side effect and efficacy expectation VAS and the recall and recognition tasks (fixed order). Finally participants completed the symptom attribution vignette, demographics and self-reported asthma diagnosis questions and received a short written debriefing statement.

Statistical considerations

Sample size was calculated with GPower version 3.1. based on previously published data (Heller, Chapman & Horne, 2015), showing that 244 participants were required to predict side effect attribution in a multivariate linear regression model with four predictors. Pearson correlations were used to explore relationships between pharmaceutical schemas, side effect attribution and memory outcomes.

The frequency and distribution of memory outcomes (correct side effect recall, incorrect side effect recall, recognition sensitivity, criterion bias) was examined. Incorrect side effect recall was rare and outcomes were dichotomised (any incorrect recall yes/no). Associations between pharmaceutical schemas and dichotomised incorrect side effect recall were examined using logistic regression. Linear regression modelling was used to model associations between pharmaceutical schemas and side effect attribution and all other memory-related outcomes. Hierarchical linear regression modelling was used to explore the amount of variance explained by pharmaceutical schemas in these outcomes when controlling for leaflet condition, asthma diagnosis, gender and age.

Putative associations between pharmaceutical schemas and reading times for side effect information and between memory outcomes and side effect attribution were examined using correlational analysis and linear regression.

Correct recall and recognition sensitivity were examined as potential mediators in the relationship between pharmaceutical schemas and side effect attribution using bootstrapped confidence intervals (1000 bootstrap samples) of the estimated indirect effect using the PROCESS Macro for SPSS (Hayes, 2012).

Differences in expectations, side effect attribution and memory outcomes between participants randomized to the different leaflet conditions were examined with independent *t*-tests.

Results

Survey completion rates and data exclusions

Responses from the same IP address ($n = 29$), and responses with incomplete outcome data ($n = 33$) were excluded. Pharmaceutical schemas did not differ between completers and non-completers ($ps > .12$). Data from 260 participants was retained.

Demographic characteristics and reported asthma diagnosis

Participants were predominantly white (74.2%), female (58.8%), US residents (94.1%) without a reported asthma diagnosis (77.7%) (see Table 1).

Inter-correlations between pharmaceutical schemas

There were small to moderate correlations between individual measures assessing pharmaceutical schemas (see Table 2). Participants, who believed pharmaceutical medicines to be more harmful, perceived pharmaceuticals as less beneficial and overprescribed by doctors and perceived themselves as more sensitive to their effect.

Descriptive memory outcomes

Participants recalled on average only two of the eight listed PIL side effects (correct side effect recall, see Table 2). Around a fourth of participants (24.3%) recalled at least one unlisted side effect (Incorrect side effect recall). Correct and incorrect side effect recall were significantly negatively correlated ($r = -.134$, $p < .05$), indicating that participants who recalled more side effects correctly committed less recall errors.

Participants recognised on average five listed ($M = 5.45$, SD = 1.87) and two unlisted side effects ($M = 2.08$, SD = 2.00). Over three quarters of participants (75.4%) 'recognized' at least one unlisted side effect. Mean side effect Recognition Sensitivity was 1.24 (SD = 1.12). The mean Response Bias ($M = 0.09$, SD = 0.48) was above 0, indicating that participants were unwilling to guess that side effects were from the leaflet.

Pharmaceutical schemas and side effect attribution

Exploratory analyses showed that participants rated the headache symptom as more likely to be a side effect of Molair if they believed medicines to be more harmful,

Table 1. Sample characteristics.

Variable	$N = 260$
Age in years mean (SD)	34.7 (11.6)
Gender *n* (%)	
Female	153 (58.8)
Ethnicity *n* (%)	
White American	177 (68.1)
White British/Irish	16 (6.2)
Black	13 (5.0)
Indian/Pakistani/Bangladeshi	8 (3.1)
First Language *n* (%)	
English	242 (93.1)
Residence *n* (%)	
United States	241 (94.1)
Asthma *n* (%)	
Reported diagnosis	58 (22.3)
Taken asthma medication	52 (20.0)

Table 2. Correlations between pharmaceutical schemas, side effect attribution and memory outcomes.

		1	2	3	4	5	6	7	8	9	*M* (SD)
1	PSM	1	.34**	−.13*	.28**	.28**	−.07	.08	−.03	.06	2.6 (1.0)
2	General harm		1	−.32**	.57**	.38**	−.27**	−.01	−.27**	.13*	2.5 (0.8)
3	General benefit			1	−.16**	−.22**	.16**	−.04	.16*	.22**	3.8 (0.7)
4	General overuse				1	.22**	.03	−.02	.07	.22**	3.4 (0.8)
5	SE attribution					1	−.23**	−.02	−.20**	−.02	39.6 (26.2)
6	Correct SE recall;						1	−.13*	.72**	.03	2.2 (1.6)
7	Incorrect SE recall							1	−.21**	−.16**	0.3 (0.4)
8	Recognition sensitivity								1	.07	1.2 (1.1)
9	Criterion bias									1	0.10 (0.5)

*$p < .05$ (both two-tailed); **$p < .01$.

overused, and less beneficial and perceived themselves as more sensitive to medicines (see Table 2). Demographic factors, leaflet condition and self-reported asthma diagnosis showed no association with side effect attribution (all ps > .05). A multivariate linear regression model with BMQ-General scales and PSM entered jointly in the model explained 16.8% of variance in side effect attribution ($F(4) = 14.09$, $p < .001$). Both PSM ($\beta = .172$) and general harm ($\beta = .296$, ps < .01) remained significant predictors in the multivariate model, while general benefit was only marginally significant ($\beta = -.100$, $p = .096$).

Pharmaceutical schemas and memory for side effect information

Correct side effect recall

Exploratory analyses (see Table 2) showed that there were significant correlations between BMQ-general benefit and harm beliefs and correct side effect recall. Stronger beliefs in the harmfulness of pharmaceuticals were associated with reduced correct side effect recall ($r = -.273$), whereas stronger perceived benefits of pharmaceuticals were associated with increased correct side effect recall ($r = .164$, ps < .01). Perceived Sensitivity to Medicines (PSM) and beliefs that medicines are overprescribed by doctors (BMQ-General Overuse) were not associated with correct side effect recall. Figure 3 illustrates differences in correct side effect recall for participants scoring in the lower and upper 50th percentile (Median split) on the General Harm and General Benefit scales.

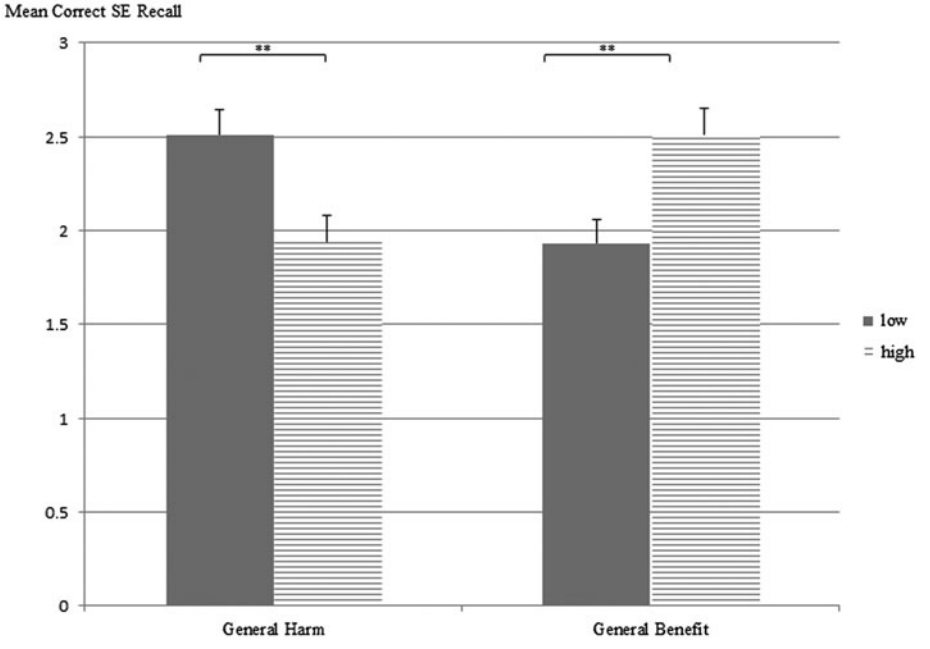

Figure 3. Mean correct side effect recall for participants with high and low general harm and benefit beliefs.
Note: **p < .01; SE = side effect; low/high general harm/benefit scores determined by median split; error bars represent standard errors.

A hierarchical regression model was then constructed to test for the amount of variance in correct side effect recall explained by pharmaceutical schemas, when controlling for age, gender, asthma diagnosis and leaflet condition (see Table 3, Model A). In this model both control variables (R^2 step 1 = .066, $p < .01$) and pharmaceutical schemas (R^2 change step 2 = .082, $p < .001$) significantly improved prediction. General Harm beliefs remained a significant predictor ($\beta = -.340$, $p < .001$) in the multivariate model. Probably owing to relatively high inter-correlations between beliefs (see Table 2), General benefit beliefs failed to reach significance in the full model.

Incorrect side effect recall

Exploratory analyses showed no associations between pharmaceutical schemas and the number of incorrectly recalled side effects (see Table 2). Univariate logistic regression models predicting dichotomised Incorrect Recall also found no associations with pharmaceutical schemas or control variables (all confidence intervals of ORs contained zero).

Recognition sensitivity

Exploratory correlational analyses showed that General Harm and General Benefit beliefs were also significantly associated with participants' ability to discriminate side effects from the leaflet from new unlisted symptoms (Recognition Sensitivity). Stronger General Harm beliefs were associated with reduced Recognition Sensitivity ($r = -.256$, $p < .01$), stronger beliefs in the benefits of medicines were associated with increased Recognition Sensitivity ($r = .160$, $p < .05$).

Table 3. Hierarchical regression models predicting correct and incorrect side effect recall.

	Model A		Model B		Model C	
	Correct side effect recall		Recognition sensitivity		Response bias	
	ΔR^2	β	ΔR^2	β	ΔR^2	β
Step 1	.066**		.101***		*.012*	
Leaflet Condition		−.028		.017		−.024
Asthma[a]		−.056		−.043		.069
Gender[b]		.183**		.187**		.030
Age		.146*		.226***		.061
Step 2	.082***		.087***		.089***	
General harm		−.340***		−.367***		.110
General benefit		.048		.038		.238***
General overuse		.202**		.238**		.191*
PSM		−.014		.013		.003
Total R^2	.147***		.188***		.102***	

Notes: PSM = Perceived sensitivity to medicines scale, [a,b]reference category = reported asthma diagnosis, male.
*$p < .05$; **$p < .01$; ***$p < .001$.

A hierarchical linear regression model, with all control variables entered in the first step and pharmaceutical schemas entered in the second step (see Table 3, Model B) showed that recognition sensitivity was better for women and older participants, with control variables accounting for around 10% of variance in Recognition Sensitivity. Adding pharmaceutical schemas to the model significantly improved prediction, accounting for an additional 8.7% of variance (see Table 3, Model B).

Response bias

Exploratory analysis (see Table 2) showed that General Harm ($r = .126$; $p < .05$), General Benefit ($r = .215$, $p < .001$) and General Overuse beliefs ($r = .223$, $p < .001$), were associated with higher response bias, indicating that participants with this belief set were less likely to guess that a symptom was from the leaflet. A hierarchical linear regression model (again with control variables entered in Step 1 and pharmaceutical schemas entered in step 2) found that control variables were not associated with Response Bias ($R^2 = .012$, $p > .05$), whereas pharmaceutical schemas accounted for 10% of variance (see Table 3, Model C).

Memory for side effect information and side effect attribution

Univariate linear regression models tested whether more accurate memory for side effects from the leaflet reduced attribution of an unlisted symptom as a side effect. As predicted, correct side effect recall ($\beta = -.234$) and Recognition Sensitivity significantly reduced side effect attribution ($\beta = -.207$, $ps < .001$). Response Bias ($\beta = -.019$, $p = .762$) and incorrect side effect recall ($\beta = -.017$, $p = .789$) were not associated with side effect attribution (see also Table 2).

Mediation analysis

Mediation analysis was used to examine whether the effect of pharmaceutical schemas on side effect attribution was mediated by memory for side effect information. We only tested for mediation effects for general harm and benefit beliefs, as there were no direct effects of either PSM or overuse on correct side effect recall and recognition sensitivity (see Table 2). A mediation model with General Harm beliefs as predictor, correct side effect recall as mediating variable and side effect attribution as outcome (see Figure 4(a)), showed that correct side effect recall significantly mediated the effect of General Harm beliefs on side effect attribution (indirect effect $ab = 1.23$; 95% CI [0.20; 2.65]; R^2 mediation effect size = .03; 95% CI [.01, .07]). The direct effect of Harm beliefs on attribution remained significant ($c' = 10.76$; 95% CI [7.00, 14.51], $p < .001$), suggesting partial mediation. An equivalent mediation model was constructed for General Benefit beliefs (see Figure 3(b)). In this model correct recall again significantly mediated the relationship with the bootstrapped confidence interval of the indirect effect again excluding zero (indirect effect $ab = -1.36$; 95% CI [−2.98; −0.38]; R^2 mediation effect size = .01; 95% CI [.002, .032]). As in the previous model, the direct effect of Benefit beliefs on attribution was significant ($c' = -7.53$ 95% CI [−12.37, −2.69], $p < .01$). Findings were similar when using recognition sensitivity as a mediator in models 4a and 4b, with both confidence intervals of the indirect effect excluding zero.

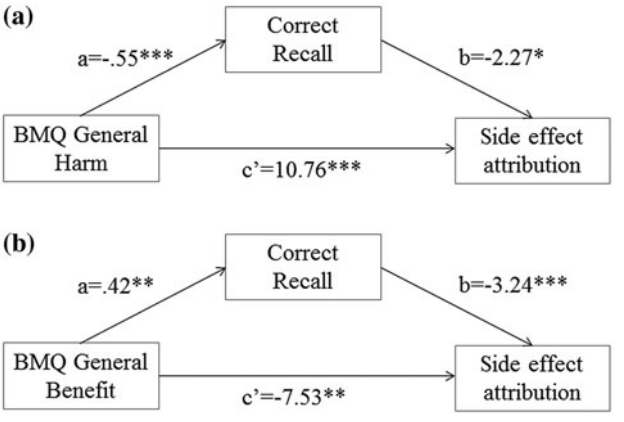

Figure 4. Correct recall mediates relationship between general harm and general benefit beliefs and side effect attribution.

Pharmaceutical schemas and reading times

Participants who believed medicines to be more harmful ($\beta = -.128$) and who perceived themselves as more sensitive to their effects ($\beta = -.138$, $ps < .05$) spent less time reading side effect information (all other BMQ-scales $ps > .05$). Older participants spent longer reading side effect information ($\beta = .292$, $p < .001$), but there was no difference between men and women ($\beta = .03$, $p = .61$) and participants with or without self-reported asthma ($\beta = .03$, $p = .66$) or any of the other control variables.

Testing for differences between leaflet conditions

Demographic characteristics were similar in both leaflet conditions ($ps > .05$). Participants in the efficacy information leaflet condition rated Molair as significantly more

Table 4. Expectations and memory outcomes by leaflet condition.

Variable	Efficacy information ($n = 133$)	No Efficacy information ($n = 127$)	Total ($N = 260$)	p-value
Expectations				
Side effect VAS; *M* (SD)	44.19 (23.25)	41.81 (22.71)	43.03 (22.98)	.405
Efficacy VAS; *M* (SD)	70.79 (18.08)	66.27 (15.40)	68.58 (16.94)	<.05
Memory outcomes				
Correct SE recall *M* (SD)	2.24 (1.68)	2.18 (1.60)	2.21 (1.63)	.764
Correct SE recognition *M* (SD)	5.44 (2.00)	5.45 (1.74)	5.45 (1.87)	.931
Incorrect SE recall *M* (SD)	0.27 (0.52)	0.35 (0.67)	0.31 (0.36)	.411[a]
Incorrect SE Recognition *M* (SD)	2.10 (2.00)	2.07 (1.92)	2.08 (2.00)	.820
Side effect attribution *M* (SD)	39.23 (27.54)	39.98 (24.89)	39.60 (26.23)	.816

Note: SE = Side effect; VAS = Visual analogue scale; [a]Pearson χ^2-test; all other tests independent samples *t*-test (all two-sided).

effective than participants in the no efficacy information condition ($t(258) = 2.17$, $p < .05$; see Table 4 for means). As shown by previous regression analyses, there was no significant difference in side effect expectations, memory outcomes or side effect attribution between the two groups (all ts < 1, ps > .05, see Table 4).

Discussion

In line with previous findings (Heller, Chapman & Horne, 2015), we found that more negative pharmaceutical schemas (beliefs that pharmaceutical medicines are harmful, less beneficial and high perceived sensitivity to medicines) were associated with increased attribution of an unrelated symptom (not listed in the patient leaflet) as a side effect. But this was the first study to show the role of pharmaceutical schemas in memory for side effect information: Participants who perceived pharmaceuticals as more harmful recalled fewer listed side effects and were less able to discriminate between listed and new side effects in the recognition memory task (recognition sensitivity). Pharmaceutical schemas accounted for around 8% of variance in both Recognition Sensitivity and in the number of correctly recalled side effects, when controlling for previous asthma diagnosis, age, gender and leaflet condition.

As predicted, better memory for listed side effects decreased the likelihood that an unlisted symptom was attributed as a side effect. The relationship between pharmaceutical schemas and side effect attribution was partially mediated by memory for side effect information. While including efficacy information in one version of the patient leaflet increased individuals' expectations of the drug's efficacy, it did not affect side effect expectations, memory for side effect information or side effect attribution.

Previous studies have shown poor memory for medical information (Barsky, 2002; Ley, 1979), but few have examined potentially modifiable psychological factors related to memory (Watson & McKinstry, 2009) and linked memory for side effects to symptom attribution decisions. There is evidence that illness schemas influence recall of illness symptoms (Baumann et al., 1989), but few other studies have examined the role of schemas in memory for side effects. Previous studies have for example shown that older adults, who may have more detailed side effect schemas, correctly recalled more severe than mild side effects, but had problems in recognising important side effects that required actions ('contact your doctor if you experience this') relative to younger participants (Friedman, McGillivray, Murayama, & Castel, 2015).

Perhaps contrary to clinical intuition, participants who worried more about the potential harmfulness of pharmaceuticals showed poorer memory for side effect information (reduced correct side effect recall and recognition sensitivity).

Possible reasons for this unexpected finding include avoidance of information and gist-based encoding. Participants with stronger harm beliefs spent less time on the page containing the side effect information, suggesting they may have paid less attention, resulting in poorer memory for side effects. This is in line with studies that show that anxious people may avoid anxiety inducing stimuli (Cisler, Bacon, & Williams, 2009; Onnis, Dadds, & Bryant, 2011) and qualitative studies where patients report actively avoiding information about side effects, to prevent becoming frightened and demotivated to take their treatment (Hayden, Neame, & Tarrant, 2015). Information about side effects may also have confirmed participants' negative preconceptions about medicines, leading them to scrutinise information less, encode only the general gist

(Brainerd & Reyna, 2002; Reyna & Brainerd, 1995) or to rely on existing schema when performing the memory tasks. Harm beliefs were associated with reduced recognition sensitivity (indicating more false alarms) supporting the use of gist-based memory strategies (Roediger & McDermott, 1995).

Some participants were randomised to receive information efficacy in the patient leaflet, after completing the belief measures. According to the affect heuristic (Slovic, Finucane, Peters, & MacGregor, 2007), higher efficacy perceptions should lead to more positive feelings about the treatment and reduced risk perceptions. The inclusion of efficacy information in the leaflet significantly increased efficacy expectations, but did not affect risk perceptions or side effect attribution or memory outcomes. Possibly the manipulation (adding one paragraph to an online patient leaflet) was too weak to raise efficacy expectations enough as to impact risk perception.

The study also clearly highlights the role of side effect memory in symptom attribution. People are more likely to make appropriate symptom attribution decisions if they correctly remember side effect information. Better memory for factual side effect information may reduce the likelihood that noisy common background symptoms (Reidenberg & Lowenthal, 1968) or symptoms of the disease (Thiwan et al., 2009) are reported as side effects. The misattribution of unrelated symptoms as side effects is problematic as it may increase non-adherence intentions (Heller, Chapman & Horne, 2015) and could reinforce pre-existing negative pharmaceutical schemas.

The study has several strengths and limitations. The analogue study approach, using a fictitious (but realistic) medication allowed us to control for previous experience with the medication and to unambiguously operationalise what constitutes an unrelated side effect. Recall and recognition memory was similar for participants with and without self-reported past asthma diagnosis, speaking to the potential generalisability of findings.

It was beyond the scope of this preliminary online study to assess other potentially important variables (e.g. health anxiety, somatisation, illness representations and previous side effect experience). Recall and recognition memory were measured within subjects, raising the possibility that recognition was influenced by previous recall. A replication of the findings, varying recall and recognition between subjects, is needed. Future studies should also explore whether pharmaceutical schemas are only associated with reduced memory for side effect information and not memory in general (e.g. by including a standardised memory test (e.g. Wechsler Digit Span Test (Wechsler, 2008)). Participants with more negative pharmaceutical schemas may have differed systematically on memory-relevant attributes such as educational background and need for cognition from participants with more positive schemas. Further studies could test whether there was a specific effect of schemas on memory rather than these factors, by attempting to modify pharmaceutical schemas and examining whether this affects memory for side effects. However, changing peoples' ingrained beliefs about pharmaceuticals may not be straightforward, particular in an online setting. Even relatively intensive interventions (e.g. individual sessions with a nurse (Chapman et al., 2015)) to change beliefs about prescribed medications and improve adherence have had mixed success (Chapman et al., 2015; Petrie, Perry, Broadbent, & Weinman, 2012; Zwikker et al., 2014).

The role of attentional processes in the association between medication beliefs and memory for treatment information also merits further investigation. Our finding that participants with negative medication beliefs spent less time reading side effect information

rests on online data, where a range of uncontrolled variables may have affected reading time. We also recognise that analogue studies have only limited external validity and that involvement of participants was probably low (e.g. participants recalled on average only two of eight listed side effects). However patient information leaflets are also often poorly read (Grime, Blenkinsopp, Raynor, Pollock, & Knapp, 2007) and recalled (Kessels, 2003) in clinical practice. A replication of the findings in clinical samples, prescribed real medication, with a range of mild to severe side effects is nevertheless highly warranted.

If replicated in clinical samples, our findings suggest that discussions and information about potential side effects could be individualised to take account of pre-existing pharmaceutical schemas to improve memory for side effect information. Despite the limitations inherent in an analogue study, our findings provide new knowledge about the psychological processes linking medicines information to the attribution of symptoms as medication side effects by showing that pre-existing pharmaceutical schemas affect both the quantity and accuracy of memory for side effect information.

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No potential conflict of interest was reported by the authors.

Note

1. Extreme correct hit and false alarm rates of 0 and 1, which would result in infinite parameter estimates were adjusted. Rates of 0 were replaced with $0.5/n$ and rates of 1 with $(n - 0.5)/n$, where n is the number of listed and new symptoms, respectively (Macmillan & Kaplan, 1985).

ORCID

Monika K. Heller http://orcid.org/0000-0001-8480-0037

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