Effects of public trust on behavioural intentions in the pharmaceutical sector

Data from six European countries

Effects of Public Trust on Behavioural Intentions in the Pharmaceutical Sector: Data from Six European Countries

Dominic Balog-Way[a, *], Darrick Evensen[b], Ragnar Löfstedt[c], and Frederic Bouder[c]

[a]Department of Communication, Cornell University, Ithaca, NY, United States of America.

[b]Politics and International Relations Department, University of Edinburgh, Scotland, United Kingdom.

[c]King's Centre for Risk Management, Department of Geography, King's College London, Strand, London, United Kingdom.

[d]Centre for Risk Management and Societal Safety (SEROS), Department of Safety, Economics and Planning, University of Stavanger, Norway.

*Corresponding author. *E-mail address*: dominic.way@kcl.ac.uk (Dominic Balog-Way)

Abstract

Few studies have empirically examined the relationship between trust and its consequences in the pharmaceutical context (e.g. the consequences of trust in medicines advice for patient behaviour). This study empirically examined the European public's perceived trustworthiness of medical, societal, and industry sources of medicines advice, and its consequences for their behavioural intentions including their medicine-taking and information-seeking behaviour. A representative survey (N=6,001) was conducted with adults from six European countries: Great Britain, France, Germany, Denmark, Italy, and Poland. As expected, respondents consistently rated advice from medical sources (GPs, pharmacists, local hospitals, emergency services) as significantly more trustworthy than advice from societal sources (the Internet, friends/relatives,

and the mass media) and, especially, industry (pharmaceutical companies and brand specific websites). A structural equation model then revealed strong associations between the public's perceived trustworthiness of these medical, societal, and industry sources and their medicine-taking and information seeking intentions. Important national variations were found including in the public's opinions on when authorities should convey new safety information. Implications for communicating benefit-risk information in a more transparent regulatory environment are discussed, including the importance of maintaining and strengthening trust in medical actors and committing more resources to supporting national risk communication.

Keywords: trust, risk perception, medicines, behaviour, European Medicines Agency

(1.) Introduction

A raft of risk communication research has examined the strength of the relationship between public trust and its consequences for risk perception, risk acceptance, and behavioural intentions (*see* Earle, 2010: 565-567 for a discussion; Slovic, 1993, 2000; Earle and Cvetkovich, 1995; Sjöberg, 1999, 2001; Siegrist et al. 2007; Eiser et al. 2015; Poortvliet and Lokhorst, 2016). The trust-consequence relationship is influenced by contextual factors with strong correlations being found between trust and, for instance, an individual's knowledge of a hazard and agreement on hazard-related values (Siegrist et al. 2007; Earle, 2010).

Research on the trust-consequence relationship has particularly focused on environmental/ technological and food safety risk management contexts such as nuclear power, nuclear waste, and genetically modified organisms (GMOs). In contrast, few empirical studies on trust and its consequences have been conducted in the European pharmaceutical context (Bouder *et al*. 2015). A systematic review of 129 academic articles on health information seeking published from 1978 to 2010 revealed that only 8.5% of the sample included any measure of information or source credibility (of which trust was considered a sub-category) (Anker *et al.* 2011).

Despite this dearth of research, pharmaceutical regulators on both sides of the Atlantic have made (re)gaining trust a top priority over the past ten years or so (Hamburg and Sharfstein 2009, EMA 2015). There is a pressing policy need to examine empirically the trust-consequence relationship in this understudied context. For instance, Tustin (2010) reveals that trust in different sources for medical information can affect the extent to which patients comply with treatment plans. Furthermore, the EU's pharmaceutical regulator, the European Medicines

Agency (EMA), needs more rigorous empirical evidence to inform its strategy of building public trust (Eichler et al. 2009, 2012; Löfstedt and Bouder, 2014; Way, 2017).

(1.1) Trust and its consequences

Although there are competing definitions and types of trust (e.g. general, interpersonal, institutional), Siegrist and Cvetkovich (2000: 354) define social trust as "the willingness to rely on those who have the responsibility for making decisions and taking actions related to the management of technology, the environment, medicine, or other realms of public health and safety". Two comprehensive literature reviews have shown the complexity and diversity of the relationship between behaviour and trust including papers dedicated solely to definition as well as on dimensions, forms, heuristics, and models (Siegrist et al. 2008; Earle, 2010; Tuler and Kasperson, 2014). In multi-actor environments, such as the pharmaceutical context, this includes various individuals (e.g. medical doctors and pharmacists), institutions (e.g. pharmaceutical companies, and regulatory bodies), and groups (e.g. patient representatives) that are intimately involved in directly and indirectly communicating benefit-risk medicines information to the public (Way *et al*. 2016).

One notable research puzzle centres on the relationship between trust in individuals, institutions, and groups and its consequences for benefit perception, risk acceptance, affective responses, behavioural intentions, and others (Earle, 2010). In a seminal article, Paul Slovic (1993) emphasised the importance of trust, noting that high public concern about a risk is associated with high perceptions of risk, low benefits, and are viewed as unacceptable (e.g. nuclear power, pesticides or industrial chemicals). Vice versa, low public concern about a risk is associated with low perceptions of risk, high benefits, and are viewed as acceptable (e.g. X-

rays) (Slovic, 1993: 676). In light of these observations, a wave of empirical studies have since examined the relationship between trust and its consequences for various risks including nuclear waste (Mushkatel and Pijawka 1992; Tuler and Kasperson, 2014), gene technology (Siegrist, 1999, 2000), carbon capture and storage (Midden and Huijts, 2009), the 2010 ash cloud crisis (Eiser *et al*. 2015), genetically modified products (Gaskell et al. 1999; Frewer et al. 2003), and electro-magnetic fields such as from mobile phones and base stations (Siegrist et al. 2003, 2005). For example, after conducting four empirical case studies on trust in different risk management contexts, Löfstedt (2005) concluded that if there were high levels of public trust toward authorities, there would be low levels of public perceived risk; inversely, if there were high levels of public distrust toward authorities there would be higher levels of public perceived risk (also *see* Löfstedt, 1995).

One of the main conclusions from this research has been the importance of context in determining the strength of the relationship between trust and its consequences (Earle et al. 2007; Poortvliet and Lokhorst, 2016). Although there has been heated debate (e.g. Sjöberg, 1999, 2001; Slovic, 2000), a comprehensive review of the literature (Earle et al. 2007) found that "the relation between trust and risk perception […] is contingent upon certain contextual factors". Factors such as hazard knowledge and agreement on hazard-related values are known to be critically important in contributing to whether high/ low trust will strongly, moderately, or weakly influence public perceptions of risk (Earle et al. 2007; Earle, 2010).

Despite risk scholars acknowledging the importance of context, trust research has been dominated by studies examining environmental/ technological and food safety risks (Siegrist et al. 2007; Löfstedt and 6: 2008). In contrast, research on trust in the medical area has evolved separately with scholars, until recently (Holt et al. 2016), focusing on individual patients and

their trust in physicians and their advice (Löfstedt and Perri 6, 2008; Edwards and Elwyn, 2009). In a separate study on trust in online sources of medical information, Tustin (2010) found that patient compliance with physicians' treatment plans was lower if they trusted Internet sources of medical information; patients were found to turn to Internet sources due to dissatisfaction with their healthcare providers. Aside from these few isolated studies, trust in the medical/ pharmaceutical context has been largely overlooked by risk scholars and conceptualised narrowly by medical scholars and practitioners. Yet, there are many reasons why the European pharmaceutical context is likely to influence the relationship between trust and its consequences beyond the doctor's office. This includes the public having particularly low levels of trust in pharmaceutical companies and low knowledge of the organisations that monitor and evaluate medicines such as EMA (Bouder *et al*. 2015).

While specific research on trust and behaviour in the pharmaceutical sector has been scarce, a number of conceptions have flourished, which neglect non-pharmaceutical research outcomes. A crucial assumption among pharmaceutical researchers, observers and opinion leaders is that making vast quantities of information available to all under the concept of "transparency" would (re)build public trust in the scientific pharmaceutical evaluation system (Gøtzsche and Jørgensen, 2011; Passarani, 2010; Rodwin and Ambramson, 2012; Goldacre, 2012; Doshi et al. 2012; O'Reilly, 2015; Willmott, 2014, 2016). Research in non-pharmaceutical sectors, however, does not indicate an automatic link between greater transparency and trust/credibility building. Research from the Netherlands, for example, indicates that the reverse may actually be the case. The more transparent regulators and authorities become, the more the public actually see how policy makers apparently muddle through and bicker throughout the decision-making process (Lindbloom 1959; Stone, 2012), the more disenchanted they become with it (Bovens and Wille 2008; Grimmelikhuijsen 2010). In other words, the perceived

trustworthiness of regulators and policy makers are more or less based on pre-existing views of the government as a whole (Van De Walle 2004), and as the public receive more information, they are able to change their judgments based on increasingly accurate knowledge, which in many cases becomes rather more critical of the policy makers themselves (Mandak et al. 2007).

In the context of risk communication science, evaluating the evidence behind these claims is important in two related ways. As Fischhoff et al. (2011) note:

> *"One is that communications should be consistent with the science- and not do things known not to work nor ignore known problems. The second is communications should be evaluated-because even the best science cannot guarantee results. Rather, the best science produces the best-informed best guesses about how well communications will work. However, even these best guesses can miss the mark, meaning that they must be evaluated to determine how good they are and how they can be improved."* [23:2].

At the time of writing, there is no sign that key players in the sector, and chiefly the EMA have taken stock of possible negative impacts of untested measures introduced with the aim of increasing public trust. The EMA, for instance has neither undertaken nor announced plans to undertake a systematic review of its "landmark" transparency policies and/or trust in the pharmaceutical evaluation system (EMA 2014, 2016, 2018a)[1]. Rather, the vast majority of studies conducted by 'outsiders' such as medical scholars, data-miners, industry, and non-governmental organisations have focused on anecdotal evidence or provided some empirical

[1] While the agency has introduced a biennial survey of its closest stakeholders (EMA, 2017), EMA has not conducted research on its transparency policies or public trust.

evidence from the perspectives of external researchers wanting to re-use medicines data, such as on the accessibility and assessability of documents (Gøtzsche and Jørgensen, 2011; Chan et al. 2014; Goldacre, 2012; Doshi et al. 2013; Doshi et al. 2016). Recently, a handful of empirical studies have also explored the implications of the regulator's policies for communicating about the benefits and risks of medicines with the public, patients, and medical doctors in experiments (Lofstedt and Way, 2016a, 2016b) and surveys (Way *et al*. 2016; Bouder et al. 2015). Yet, few empirical studies on public trust in the European pharmaceutical system have been conducted. Therefore, this study provides empirical evidence that seeks to support EMA's transparency-driven trust-building strategy.

(1.3) Hypotheses

The study set-out to measure the public's perceived trustworthiness of ten medical, societal and industry 'sources'[2] of medicines advice (i.e. medicines communication channels) (*see* Box 1). In turn, the relationship between these measures of perceived trustworthiness and its consequences for the public's behavioural intentions[3] were examined.

The 10 medical, societal and industry sources were selected because past studies have identified these non-regulatory communication channels as important 'go-betweens' between key information sources and audiences such as EMA and patients, respectively (Dunwoody and Griffin, 2014; Bouder *et al*. 2015). The 10 sources or 'communication channels' act as key "conveyance devices that collect information from [another] source or sources, repackage it

[2] Some scholars make an important distinction between sources and channels (see Dunwoody and Griffin, 2014). From the public's perspective, however; information channels are more commonly referred to as sources. Therefore, communication channels and sources are referred to interchangeably in this study. For example, a doctor or pharmacist might be a source of medicines advice from the public's perspective even though they can be categorised, from a system's level perspective, as communication channels.
[3] The public's perceived likelihood of engaging in a given behavior.

and then disseminate it" (Dunwoody and Griffin, 2014). For example, doctors receive information from sources such as the regulators, medical journals and colleagues and, in turn, provide medicines advice to patients.

An alternative approach might have been to examine public trust in EMA and/or the public's domestic regulatory authorities. However, this would have been less meaningful, as past research has consistently shown that most Europeans have not heard of the concrete entities that regulate medicines in Europe (Bouder et al. 2015). Indeed, it would not be useful to measure the public's trust in entities that they are not even aware exists. The authors also wanted to advance understanding of the effects of trust beyond trust in large institutions, to trust in the full range of actors, including medical, societal and industry sources.

Box 1: Public sources of medicines advice grouped into three main categories

Category	Source of Medicines Advice
Medical	General Practitioners (GPs); Pharmacists; Local Hospitals; Emergency Services; Medical Journals
Societal	The Internet (in general); Mass Media (newspapers, television, radio, etc.); Friends or relatives
Industry	Pharmaceutical Companies (including websites); Brand-Specific Websites (of specific medicines)

Before conducting empirical investigations (Section 2), three hypotheses were developed based on the foregoing literature and the authors' previous empirical research on risk communication and transparency in the sector (Bouder *et al.* 2015; Löfstedt *et al.* 2015; Löfstedt and Way 2016a, 2016b; Way *et al.* 2016). The main dependent variable in our analysis is our survey respondents' answers to what action they would take if confronted with information about a potential problem with a medicine they are taking. We examine whether or not survey respondents indicate a behavioural intention to continue taking their medicine as usual *whilst* seeking additional information. The two actions brought together in this variable are important;

best medical advice would be for patients to not discontinue taking a prescribed medicine, unless told to do so explicitly by a relevant medical authority. Nevertheless, actively seeking additional information would be the best way to clarify whether a problem does or does not exist. Most healthcare professionals and regulatory agencies would recommend that patients continue taking their medicine (as prescribed by their doctor) and seek additional advice if they receive uncertain adverse medicines information (i.e. after receiving information pointing to a safety problem via letter, telephone, e-mail etc.) (e.g. NHS Choices). For this study, the authors chose to examine the behaviour that would be recommended by medical experts rather than making a subjective value judgement (e.g. NHS Choices, 2019).

We sought to associate *trust* specifically with *information seeking* and *compliance behaviour* because of tentative links that have been suggested, but not verified, between these three variables in literature on health information seeking. Although notable amounts of health information seeking occurs via both online and offline sources across European nations (Reifegerste *et al.* 2017), a large majority of research on health information seeking examines information specifically from online sources (e.g., Ayers and Kronenfeld 2007; Cline and Hayes 2001; Fergie *et al.* 2016; Gray *et al.* 2005; Lee *et al.* 2015; Percheski and Hargittai 2011; Powell and Clarke 2006). Some of this work on Internet information seeking reveals higher trust in traditional (offline) sources (Khoo *et al.* 2008). It also contends that seeking information online can improve or harm patient-physician relationships, depending on whether the patients then discuss the new online information with their physicians and on the strength of the patients' prior relationship with physicians (Broom 2005; Hay *et al.* 2008; Stevenson *et al.* 2007; Tan *et al.* 2017). Further, research suggests that information seeking online can lead to non-compliance in following recommended treatment, particularly in individuals with high

anxiety, diminishing health, and who perceive Internet health information to be important (Weaver *et al.* 2009).

The dynamics between physicians and the Internet as information sources suggests that evaluations of these two sources of information could shape both information seeking and compliance with prescribed treatment. Although there is nuance to the relationships in the aforementioned research, use of and perceived value in Internet information seems it could diminish compliance, whilst use of and perceived value in doctors would increase compliance. When presented with adverse information about a medicine, patients who trust primarily in physicians would follow physician advice and seek more information from medical sources to further their understanding of the issue, whilst patients who trust primarily non-medical Internet sources would have more cause to reject the treatment and seek information from Internet sources that could further increase scepticism (Tan *et al.* 2017, Tustin 2010). The literature in this area, however, does not extend much beyond looking at doctors and the 'Internet'. There are many forms of online information and many types of medical advice beyond one's primary care physician. Therefore, in our study, we include a wider range of sources of medical and societal information, and we add pharmaceutical industry sources due to our focus on behaviour related to specific medicines.

Our three hypotheses centre on the direct effects of the public's trustworthiness of medical, societal and industry sources and their behavioural intentions (Box 2, and see Figure 1 for the hypothesised pathways). We offer these hypotheses due to the expectation that medical sources would support the aforementioned best medical practice, that societal sources would raise concerns and scepticism, and that industry sources would defend the medicines they market.

Box 2: Hypotheses on the direct effects of trustworthiness in a safety scenario.

H_1	Higher trustworthiness of *medical* sources will directly predict *greater propensity* for the public to continue to take their medicine as usual and seek additional information.
H_2	Higher trustworthiness of *societal* sources will directly predict *diminished propensity* for the public to continue to take their medicine and to seek additional information.
H_3	Higher trustworthiness of *industry* sources will directly predict *greater propensity* for the public to continue to take their medicine and to seek additional information.

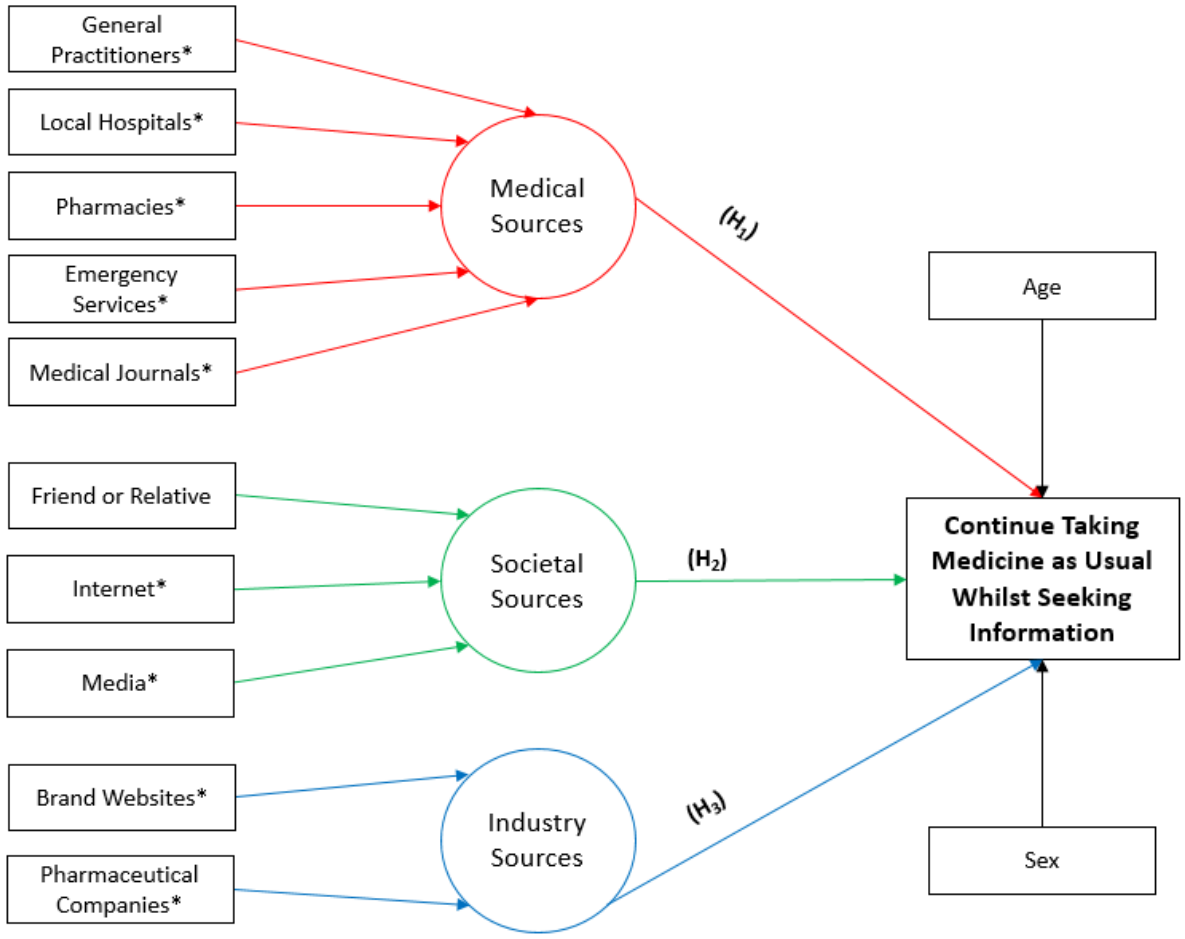

Figure 1: Model displaying the study's hypotheses about the relationship between public trust in medical, societal and industry sources of advice and the public's behavioural intentions.

(2.) Methods

(2.1) Sample

The data for this study originates from a survey conducted by the authors in November 2015. A random quota sample was obtained with 6,001 respondents aged 18-64 from Great Britain (N=1,000), France (N=1,000), Germany (N=1,000), Denmark, (N=1,001), Italy (N=1,000), and Poland (N=1,000). The sample was nationally representative for gender by age, where respondents live by region, and whether they are in work or not based on 2013 figures from Eurostat (Appendix A). Further demographic information was also collected for income, educational qualifications, and ethnicity/parents nationality (Appendix A). In addition, data from three countries surveyed in November 2013 by Bouder *et al.* (2015) was used to enable cross-sectional comparisons over time[4]. In 2012, a random quota sample was obtained with 3,083 respondents aged 18-64 from 3 repeated countries: Great Britain (N=1,014), France (N=1,061), and Germany (N=1,008). The 2012 sample was nationally representative for gender by age, where respondents live by region, and whether they are in work or not, based on 2012 figures from Eurostat, the official statistics office of the European Commission (*see* Bouder *et al*. (2015) for further 2012 sample information). All investigations were carried out in accordance with Maastricht University rules on ethical approval, where Bouder was based when the survey was conducted.

Both 2012 and 2015 respondents were recruited by Ipsos, a UK polling agency, through online panels and quota sampling. Large and varied sets of panel participants were first obtained

[4] Bouder *et al*.'s (2015) original study included 6 rather than 3 EU countries with a total of 5,648 respondents. However, only three countries are relevant to this paper.

through email lists, banners, websites, text ads, search engine methods, and other techniques. The agency then invited prospective respondents from these panels. Incentive points were offered to respondents – a common form of incentive for participants in online panel surveys – which helped reduce potential for response bias (Dillman, 2007). Notably, Ipsos has strict procedures and industry standard checks to preserve panel quality such as mechanisms to discourage professional responders and continually refresh respondents between surveys[5].

In the 2015 survey, response rates were calculated based on the number of invites sent, the number of incomplete interviews due to having a full quota and respondents screening out, and the number of completed interviews (*see* Bouder *et al*. (2015) for rates in 2012). They were 10.8% (GB), 13.3% (France), 14.6% (Germany), 8.5% (Denmark), 26.1% (Italy), and 10.4% (Poland) (*see* Appendix C for more details). These response rates can be considered as conservative estimates due to the nature of the recruitment process. Ipsos sent out a large number of invitations to its panels, but then established a quota for the number of respondents it accepted to ensure representativeness. Up to 100% of panellists could therefore have tried to respond, but once the quota was met, all future respondents were ineligible to participate.

(2.2) Questionnaire

The survey instrument was created in 2012 (Bouder et al. 2015) and only minor alterations were made for 2015 (Appendix B). First, additional follow-up questions were added to the 2015 questionnaire for 3 questions that produced the most interesting/important results in 2012. Second, a few questions were removed from the 2012 questionnaire to ensure the average

[5] For more information on Ipsos's procedures please visit www.ipsos-mori.com or Ipsos MORI (2018). Alternatively, the corresponding author would be more than happy to send over a more detailed document.

length of time for responding did not exceed 15 minutes. Limiting the number of changes allowed for more reliable cross-sectional comparisons between the 2012 and 2015 data. All questionnaires were translated into relevant sample languages by professional translators provided by Ipsos and double checked by the authors' native language colleagues from academia and regulation.

This paper reports on four sets of questions: (1) self-reported awareness and familiarity of national pharmaceutical regulatory authorities, (2) measures of trustworthiness, (3) behavioural intentions after personally receiving (e.g. via letter, telephone, e-mail etc.) information that points to potential safety problems with a medicine (i.e. 'adverse information'), and (4) opinions on receiving medicines information (e.g. when the public should receive unverified potentially adverse information in the first place).

Self-reported awareness and familiarity. Respondents were asked two self-reported knowledge questions about their relevant national-level regulatory body (although knowledge was not directly tested). First, "Have you heard of [relevant national-level regulator[6]]? (Yes/No)". In 2012, an additional 'don't know' response option was included for this question but was removed in 2015. Second, respondents that said 'Yes' were asked: "How familiar or unfamiliar are you with [relevant national-level regulator]? (Very familiar, Fairly familiar, Not very familiar, Not at all familiar, Don't know). 2015 respondents from Denmark were not asked either question because the agency changed its name less than one month before the survey was launched. To be clear, measures of respondents' trust or perceived trustworthiness of these concrete pharmaceutical regulatory entities – such as the UK MHRA – were not made. This is

[6] UK: MHRA (Medicines & Healthcare products Regulatory Agency); France: ANSM (L'Agence nationale de sécurité du médicament et des produits de santé); Germany: BfArM (Bundesinstitut für Arzneimittel und Medizinprodukte); Italy: AIFA (L'Agenzia Italiana del Farmaco); Poland: URPL (Urzad Rejestracji Produktow Leczniczych).

because previous surveys show that the vast majority of European citizens have not heard of either their supranational or national-level pharmaceutical regulators (although national variations have been found) (Bouder *et al*. 2015).

Trustworthiness of medicines advice. Trustworthiness of multiple abstract entities was measured by asking respondents to rate 10 different sources of information that provide advice on medicine-related risks (i.e. side effects): "How trustworthy or untrustworthy do you believe the following **sources** are in providing you with advice on the side effects associated with specific medicines?" (Very trustworthy, Fairly trustworthy, Neither trustworthy nor untrustworthy, Not very trustworthy, Not at all trustworthy, Don't know) [emphasis in original]. The sources of advice measured were: (1) General Practitioner (GP); (2) Local hospital; (3) Internet in general; (4) Brand specific websites (of specific medicines you may consider); (5) Media (e.g. newspapers, television, radio, etc.); (6) A friend or relative; (7) Pharmaceutical companies (including their websites); (8) Pharmacy, (9) Emergency services (e.g. 999)[7]; and (10) Medical journal. The ordering of sources was randomised between respondents.

Behavioural intentions. A set of questions measured respondents' medicine-taking and information seeking behavioural intentions after receiving potentially adverse information about a medicine they are taking. In both 2012 and 2015, respondents were asked: "If the information you personally receive (via letter, telephone, e-mail, etc.) points to potential safety problems with the medicine you are currently taking, do you think you are most likely to…" (1) Stop taking your medicine, (2) Reduce your dose of the medicine, (3) Continue taking your medicine as usual, (4) Seek additional advice about the medicine, or (5) Don't know. Two

[7] The telephone number for 'Emergency services' varied between sample countries.

follow-up questions – that were not included in the 2012 survey – were also asked in 2015. Respondents that indicated option 1, 2, and 3 above were asked to clarify their medicine seeking intentions: "You say you are most likely to [stop/reduce/continue]. After/Whilst doing so, would you also seek additional advice about the medicine?" (Yes/No/Don't Know). Alternatively, respondents that indicated option 4, were asked to clarify their medicine-taking intentions: "You say you are most likely to seek additional advice about the medicine. Whilst seeking advice, which of the following would you most likely do?" (1) Stop taking your medicine, (2) Reduce your dose of the medicine, (3) Continue taking you medicine as usual, or (4) Don't know. The 2015 survey therefore enabled respondents to indicate a combination of medicine taking (i.e., 'compliance') and information seeking behavioural intentions.

Opinions on receiving medicines information. Three constructs measured respondents' opinions on receiving medicines information. One question asked about general opinions on receiving more medicines information: "Do you think that receiving more information about the safety of a medicine would increase your confidence in taking medicines?" (Yes/No/Don't Know). Two questions asked about more specific opinions on when respondents would like to or think they should receive potentially adverse information on medicines. First, "Overall, do you think it is a good or bad idea to inform the general public about a potential medical safety problem with a medicine, **before** a scientific analysis has been undertaken? (By scientific analysis, we mean a full review of the available data by the regulators and pharmaceutical industry)" (Good idea, Bad idea, or Don't know) [emphasis in original]. Second, "At what stage would you like information to be conveyed to you about a possible safety issue of a medicine that you use or may use?" (1) When there is a possible sign of a safety problem; (2) When the problem has been investigated and it is not clear if it is related to the medicine; (3) When the problem has been investigated and a pharmaceutical company believes it is related

to the medicine; (4) When the problem has been investigated and regulators believe it is related to the medicine; or (5) Don't know.

(2.3) Data analysis

The 2012 and 2015 datasets were analysed using IBM SPSS Statistics in three stages. First, cross-sectional comparisons between the datasets were made to analyse changes over time in GB, France, and Germany. Second, cross-national comparisons were made between nations in the 2015 dataset (GB, France, Germany, Denmark, Italy, and Poland) (for 2012 cross-national comparisons *see* Bouder *et al*. 2015). Third, multivariate relationships between several variables – including trustworthiness and individuals' behavioural intentions – were analysed in a structural equation model (using Mplus software).

The first set of analyses compared variables across time between the 2012 and 2015 datasets. As this represents repeated cross-sectional data rather than longitudinal data from the same population (*see* Siegrist, 2014), we made comparisons: (1) via analysis of variance tests (ANOVAs) with post-hoc tests for pairwise comparisons and Bonferroni corrections for multiple comparisons, with nation as the factor variable – when the variable of interest is an interval variable, and (2) via chi-square significance in cross-tab tests when the variable of interest is categorical.

The second set of analyses compared the 6 nations included in the 2015 survey. Again, this included comparing (1) knowledge of concrete pharmaceutical regulatory entities, (2) trustworthiness of medicines advice, (3) opinions on receiving medicines information, and (4) behavioral intentions (section 2.2). Where the variable of interest was an interval variable,

ANOVA tests were used. For variables of interest with multiple categorical response options, dummy variables representing each response option were generated, which were used as the dependent variable in a binary logistic generalised linear model with pairwise comparisons across nations and Bonferroni corrections.

The third set of analyses sought to identify variables that predict behavioural intentions after personally receiving (e.g. via letter, telephone, e-mail etc.) information that points to potential safety problems with a medicine they are taking. Specifically, our dependent variable was propensity to continue taking the medicine whilst seeking additional information. The structural equation model allowed for simultaneous confirmatory factor analyses and regression pathways between the three latent variables (representing clusters of information sources) and the behavioural intention. The confirmatory factor analyses examined latent variables representing perceived trustworthiness in three groups of actors (specifically, medical, societal, and industry sources). Structural regression pathways were then included in the model that revealed direct effects of perceived trustworthiness in these actors on propensity to 'continue and seek'. The model used a weighted least square mean and variance adjusted (WLSMV) estimator and is stratified by nation to account for non-independence of responses *inter*nationally.

(3.) Results

(3.1) Self-reported awareness and familiarity

In 2015, the vast majority of respondents *said* 'No' they had not heard of their (relevant) national pharmaceutical regulatory authority in GB (78%), France (76%), Germany (85%), and

Poland (88%). Fewer respondents in Italy (61%) said 'No' they had not heard of theirs. Of those that said 'Yes' they had heard of their authority (N=1,117), over 50% in all five nations said they were 'not very familiar' or 'not at all familiar' with them: GB (71%), France, (61%), Germany (53%), Italy (52%), and Poland (56%). When combining awareness and familiarity questions, fewer than 8% of all respondents said they were either 'very familiar' or 'fairly familiar' with their authority in GB (6%), France (8%), Germany (7%), and Poland (6%), with marginally more indicating the same in Italy (18%).

(3.2) Trustworthiness of advice

Public trustworthiness of sources of advice on side effects (associated with specific medicines) was measured with a battery of 9-10 questions (Section 2.2). An initial exploratory factor analysis (principal axis factoring, promax [oblique] rotation) pooled the 9 common sources of advice in the 2012 data into three factors that represented respondents' trustworthiness of the following entities:

1. *Medical sources:* general practitioner (GP), local hospital, pharmacy, and emergency services (e.g. 999);
2. *Societal sources:* internet in general, mass media (e.g. newspapers, television, radio etc.), a friend or relative;
3. *Industry sources:* pharmaceutical companies (and their websites), and brand specific websites (of specific medicine you may consider).

Reliability scaling alpha values were: medical trust = 0.79, societal trust = 0.67 and industry trust = 0.81. The 2015 data included one additional source of advice not present in the 2012. We expected trustworthiness of 'medical journals' to pool with medical actors.

Medical sources were the most trusted sources of advice in GB, France, and Germany in both 2012 (mean of 3.93 on the five-point scale) and 2015 (mean of 3.95). Between 2012 and 2015, there were no significant differences for trustworthiness of medical sources within any nation (measured by an ANOVA with Bonferroni corrections; $p < 0.05$). Trustworthiness of societal sources increased significantly in France (+0.28) and Germany (+0.20) over time. Trustworthiness of industry sources increased in all nations, although industry trustworthiness was, notably, substantially lower on average than all other sources in both 2012 (2.44) and 2015 (2.85).

In 2015, trustworthiness of medical sources of advice was significantly higher in GB (3.98), France (3.89), and Denmark (3.94) than in Germany (3.78), Italy (3.75), and Poland (3.74) (measured by an ANOVA with Bonferroni corrections; $p < 0.05$.) (Figure 2). Trustworthiness of societal sources was the lowest in France (3.02) and GB (3.01) with France differing from all nations except GB, and GB having significantly less perceived trustworthiness of societal sources than Germany (3.19) and Poland (3.26). In 2015, trustworthiness of industry sources was significantly lower in France (2.68) and Germany (2.85) than all other nations, and significantly higher in Poland (3.2) than any other nation.

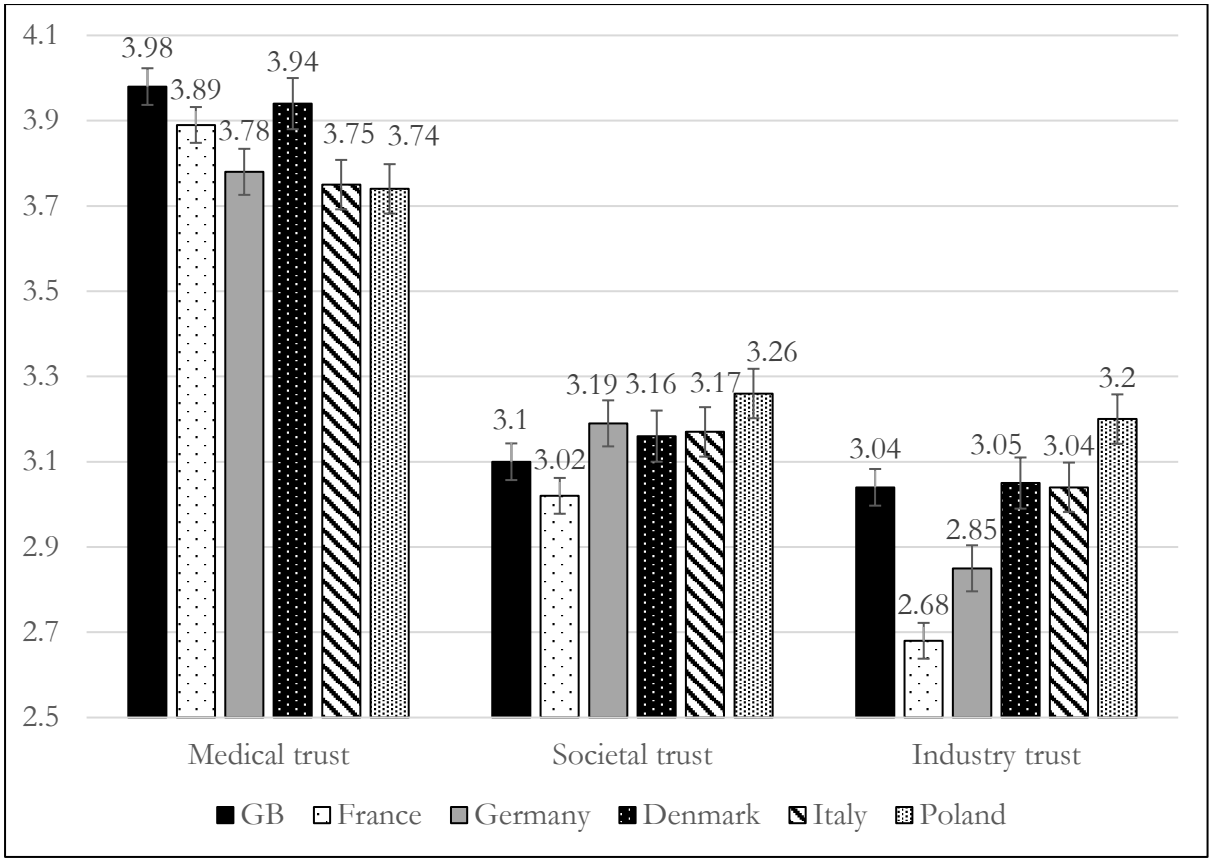

Figure 2: Public trustworthiness of sources of medicines advice in 2015.

(3.3) Behavioral intentions

One question in 2012 and 2015 measured respondents' behavioral intentions to receiving adverse information about a hypothetical medicine they are currently taking. Behavioral intentions includes behavior related to medicine-taking (i.e. continue to take the medicine as usual, reduce the dose of the medicine, or stop taking the medicine) and desire to seek information (or not) (section 2.2). After personally receiving adverse information (e.g. via letter, telephone, e-mail etc.) that points to potential safety problems with a medicine they are taking, the most popular behavioral intentions in both 2012 and 2015 were to either 'seek additional advice about the medicine' or 'stop taking the medicine' (Figure 3). Between 2012 and 2015, the percentage of respondents intending to 'seek additional advice about the

medicine' changed significantly in all nations. While seeking intentions increased in the case of Germany (+10%) – reflecting a concomitant decrease in respondents indicting they would stop taking their medicine (-15%) –, they decreased in GB (-4%) and France (-13%) (significant differences measured by a chi-square significance for a cross-tab test; $p < 0.05$). Respondents from GB were also found to be significantly more likely to seek additional advice about the medicine than respondents from Germany and France in both 2012 and 2015, while respondents from Germany and France were significantly more likely to stop taking their medicine (Figure 3).

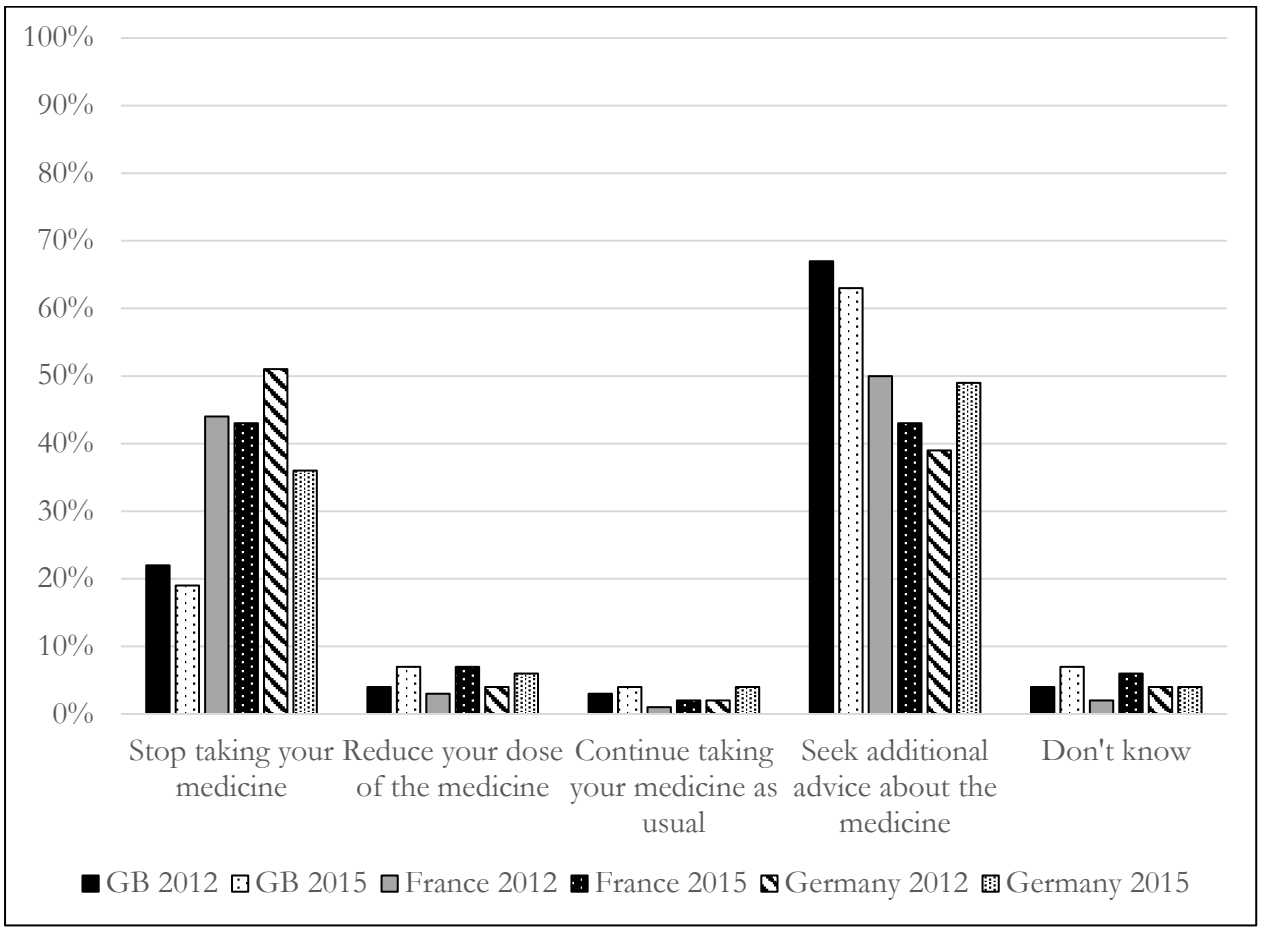

Figure 3: The public's behavioral intentions after receiving potentially adverse medicines information.

In 2015, two follow-up questions were asked that enabled respondents to indicate both their medicine-taking intentions (i.e. continue, reduce or stop) and desire to seek information (or not) (section 2.3). By combining all three questions, the percentages in Figure 4 were created. The plurality of respondents from each nation indicated that if respondents received information pointing to potential safety problems with their medicine they are currently taking, they would either (1) stop taking their medicine and seek more information (i.e. "stoppers") or (2) continue taking their medicine as usual whilst seeking more information (i.e. "continuers"). Stark differences between 2015 nations were identified. Respondents from GB and Denmark were far more likely to continue taking their medicine as usual whilst seeking additional advice than any other option (continuers). In contrast, respondents from France, Germany, Italy, and Poland were all inclined to stop taking their medicine whilst seeking information (stoppers) (significant differences measured by binary logistic generalised linear models with Bonferroni corrections).

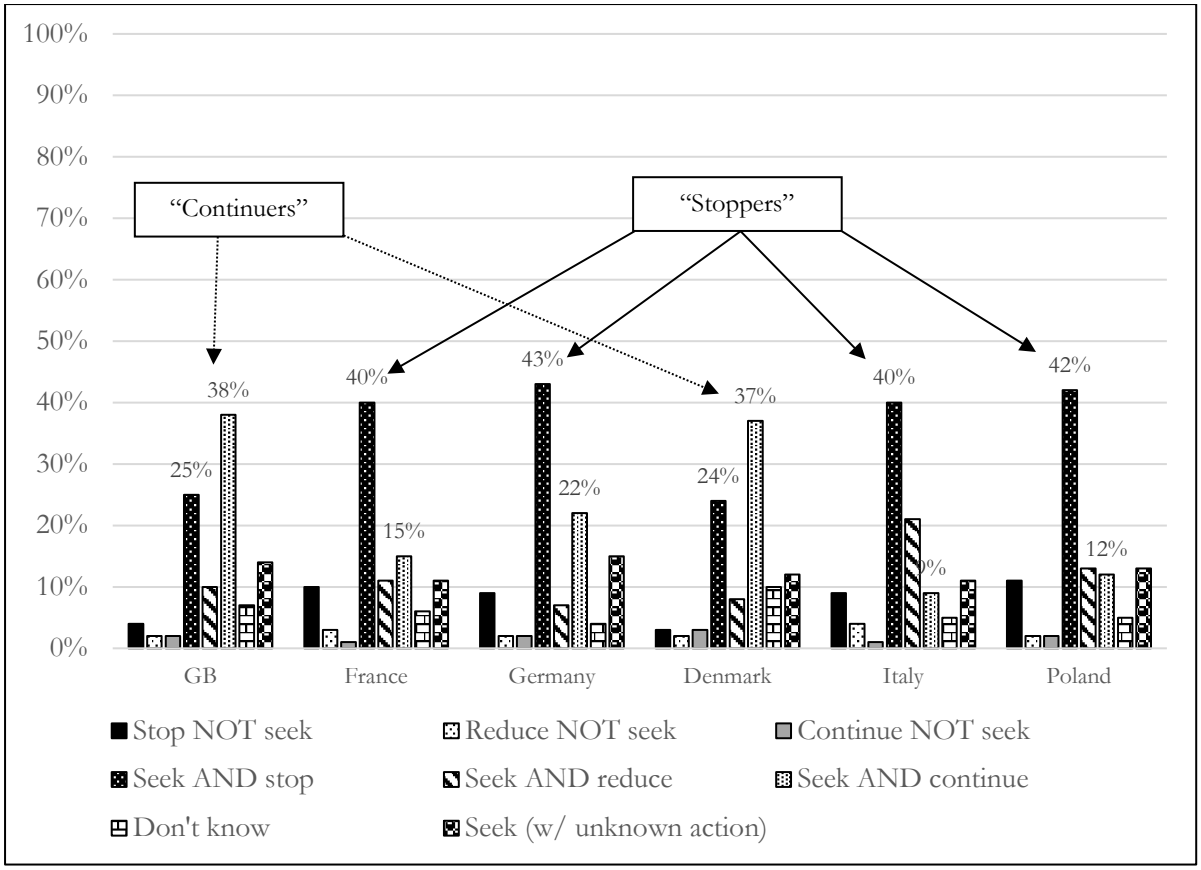

Figure 4: Combined data on the public's medicine-taking and information seeking behavioral intentions after receiving potentially adverse medicines information.

(3.4) Opinions on receiving information.

Two questions measured opinions on receiving medicines information ranging from general to more specific constructs. First, the vast majority of respondents in 2012 (71%) and 2015 (76%) indicated that receiving more information (in general) about the safety of a medicine would increase their confidence in taking medicines (Table I). In 2015, Demark (65%) had the fewest answering 'Yes' more information would increase their confidence in taking medicines, while Italy (85%) and Poland (81%) had the most (significant differences measured by binary logistic generalised linear models with Bonferroni corrections). Second, 59% of respondents in 2015 indicated that they think it is a good idea to inform the general public about a potential medical

safety problem with a medicine before a scientific analysis has been undertaken by the regulators and the pharmaceutical industry (Table II). National variations ranged from 52% in GB and Denmark to 69% in Poland indicating it is a good idea.

Table I: Do you think that receiving more information about the safety of a medicine would increase your confidence in taking medicines? Numbers in cells represent percentages; superscript letters that vary within a question denote statistically significant differences ($p < 0.05$, with Bonferroni corrections); statistical differences only presented for the first option in each question

	GB	France	Germany	Denmark	Italy	Poland
Yes	73[a]	78[a,b]	75[a]	65[c]	85[d]	81[b,d]
No	12	12	11	15	6	8
Don't know	15	10	13	19	9	11

Table II: Overall, do you think it is a good or bad idea to inform the general public about a potential medical safety problem with a medicine, **before** a scientific analysis has been undertaken?

	GB	France	Germany	Denmark	Italy	Poland
Good idea	52[a]	58[a,b]	59[b]	52[a]	63[b]	69[c]
Bad idea	28	25	23	27	23	17
Don't know	20	17	18	21	15	13

Complementing results from these three general questions, a fourth, more specific, question measuring opinions on receiving uncertain adverse medicines information asked at what stage respondents would like information to be conveyed to them about a possible safety issue with a medicine they use or may use (section 2.2). In all nations, respondents in both 2012 (58%) and 2015 (55%) indicated they would like this information 'when there is a possible sign of a safety problem' rather than 'when the problem has been investigated and it is not clear if it is related to the medicine', 'when the problem has been investigated and a pharmaceutical

company believes it is related to the medicine', or 'when the problem has been investigated and regulators believe it is related to the medicine' as well as those that indicated 'don't know' (Figure 3). This most popular response reduced over time in Germany (-7%) (Figure 5) with significantly more respondents indicating 'when the problem has been investigated and it is not clear if it is related to the medicine' (measured by a chi-square significance for a cross-tab test, $p < 0.05$). In 2015, few major differences emerged between nations (Figure 5).

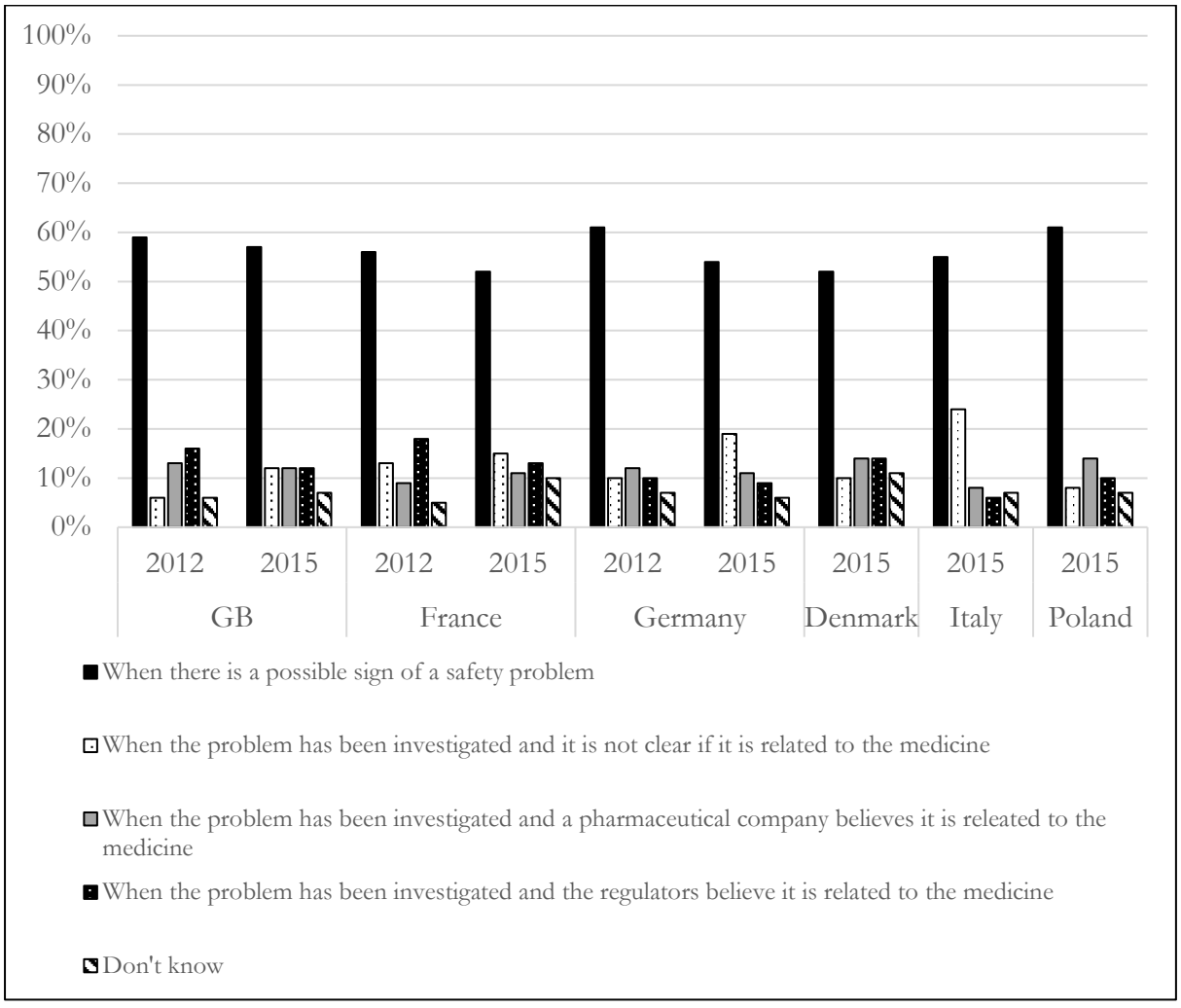

Figure 5: Opinions on when information on a potential safety issue should be given to the public

(3.5) Explaining behavioral intentions and opinions

A structural equation model examined the capacity for trust in information sources to predict respondents' behavioral intentions (Figure 7) (section 3.4).[8] Specifically, the model examined trust's relation to intentions to 'continue to take their medicine whilst seeking additional information' (hereafter, 'continue and seek' behaviour), that is, in a scenario where they received (e.g. via letter, telephone, e-mail etc.) information that points to potential safety problems with the medicine they are currently taking (*see* section 3.3). Confirmatory factor analyses were conducted whilst regressing the latent and measured variables on each other. The dependent variable of interest was a dichotomous variable: whether a respondent selected the behaviour of continue and seek or not. The confirmatory factor analysis was specified to generate the three latent factors identified in section 3.2: trustworthiness of medical, societal, and industry sources of advice about the side effects associated with specific medicines. All coefficients on pathways in Figure 7 represent either factor loadings (on arrows from measures of trustworthiness to the latent factors) or unstandardised regression coefficients (on all other arrows). The model explored the effect of the following on the dependent variable:

(1) direct effects from the latent variables representing trustworthiness (i.e. medical, societal, and industry sources of advice; $H_1 - H_3$), and
(2) age (measured linearly in years) and sex (with 'male' as the reference category).

The model had adequate to good fit (RMSEA = 0.048 [90% confidence interval of 0.045-0.050], CFI = 0.94, Chi-Square = 845 with 58 d.f.). Trustworthiness of *medical* sources of advice strongly (0.50) directly predicted 'continue and seek' behaviour (H_1 supported). Meanwhile, trustworthiness of *societal* (-0.48) sources directly reduced the likelihood of

[8] We used the default setting in *Mplus* for structural equation models with binary outcome variables, which utilises multivariate probit regressions and a robust weighted least squares estimator.

continue and seek behaviour (H_2 supported). There was no statistically significant relationship between *industry* sources and the behavioural intention (H_3 not supported). Age and sex both exerted an additional direct effect on continue and seek behaviour ('seek and continue' more likely for females and older respondents).

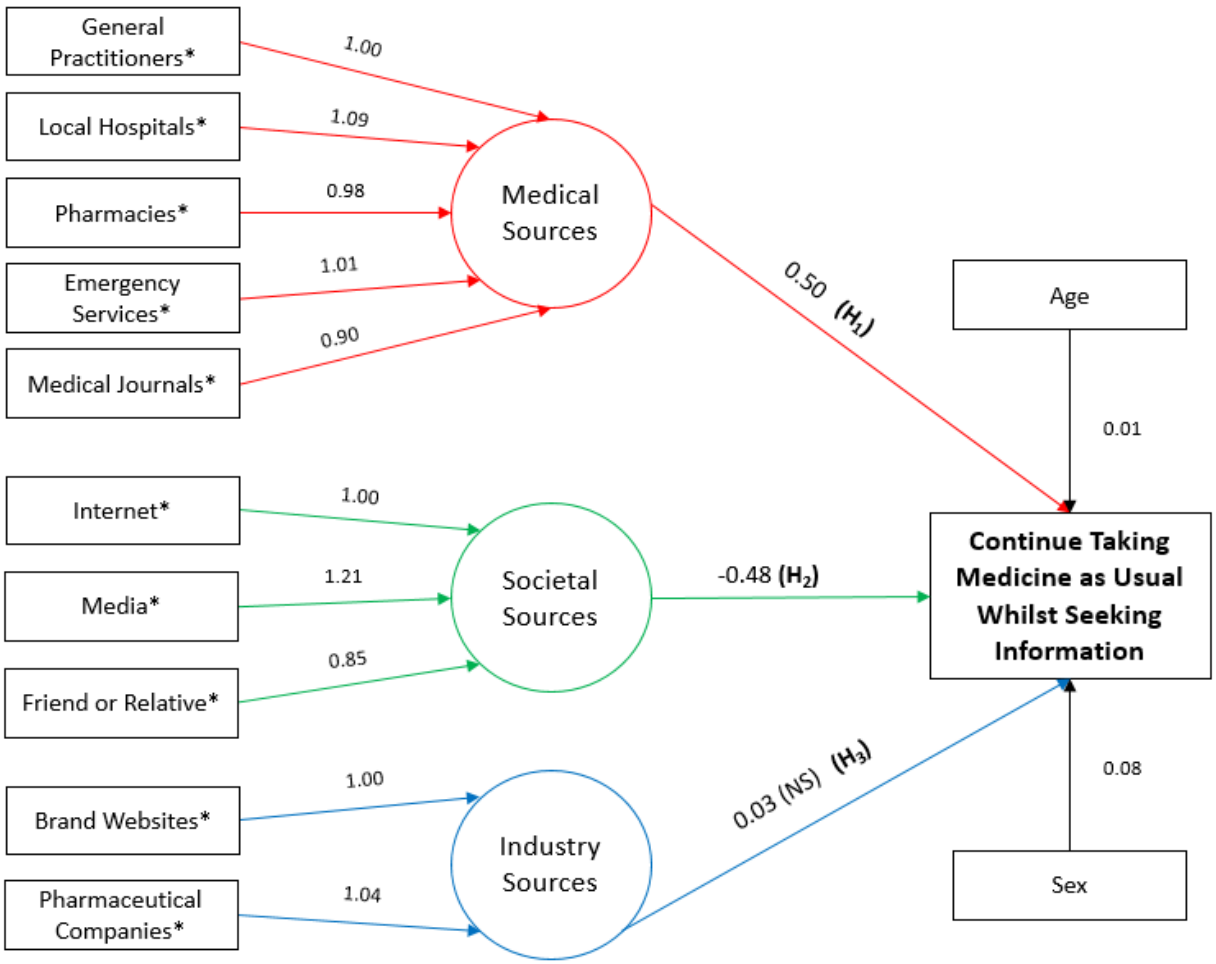

Figure 7: Structural equation model predicting respondents' behavioural intentions to 'continue to take their medicine as usual whilst seeking additional information' (i.e. 'continue and seek'), if they received information that points to potential safety problems with the medicine they are currently taking. *variables with an asterisk measure perceived trustworthiness of the entity listed. N.B. All factor loading and parameter estimates are significant at $p<0.001$, save sex to 'continue and seek' ($p<0.05$) and H_3 (non-significant). . The R^2 (effect size) for the dependent variable is 0.14.

(4.) Discussion

In the 'New Transparency Era' a strong emphasis has been placed on building public trust in medicines and the pharmaceutical evaluation system (Way, 2017). This study examined the relationship between the public's perceived trustworthiness of various medical, societal, and industry sources of advice on side effects and its consequences for behavioural intentions and public opinion, specifically, in a scenario where the public were to receive information pointing to potential safety problems with their medicine(s).

(4.1) Trustworthiness and its consequences

The study had four main findings. First, medical sources of advice (GPs, local hospitals, pharmacies, emergency services, and medical journals) were perceived as more trustworthy than societal and especially industry sources in all countries surveyed. In conjunction, all of these medical sources pooled together on factors analyses of the 2012 and 2015 data. This is consistent with past studies showing that the European public have high levels of trust in healthcare professionals and relatively low trust in pharmaceutical companies. For example, annual nationally representative polls conducted by Ipsos MORI between 1993 and 2015 show that, compared with a total of 24 professions, medical doctors have consistently been perceived as the most trusted professionals in Europe followed by teachers, judges, and scientists (Ipsos, 2016). Results from the present study are also consistent with findings that the pharmaceutical industry have relatively low levels of trust in Europe (albeit not as low as in the US) (Löfstedt, 2007; Löfstedt *et al*. 2011). For example, a survey by YouGov (2016), a UK polling agency, found that only 19% of the British public think that the pharmaceutical industry is trustworthy.

Second, a structural equation model revealed a particularly strong positive relationship (0.50) between the public's perceived trustworthiness of *medical sources* (GPs, local hospitals, pharmacies, emergency services, and medical journals) and intentions to continue taking their medicines as usual whilst seeking additional advice, if they received information pointing to potential safety problems with a medicine they are currently taking. This behaviour is what would be recommended by the regulators and healthcare professionals in such a scenario with NHS Choices (2019), the official health website of the UK National Health Service, making clear that patients should "…only ever stop taking prescribed medication if your GP specifically advises you to". Trust in *societal sources* had an equally strong effect, but in the opposite direction – higher societal trust made compliance less likely (-0.48).

Third, stark national variations were found in the type of behaviour the public intend to engage in after receiving potentially adverse medicines information. Respondents from GB and Denmark were far more likely than all other sample countries to indicate that they would *continue taking* their medicine as usual whilst seeking additional advice than any other option ('the continuers'). In contrast, respondents from France, Germany, Italy, and Poland were far more inclined to *stop taking* their medicine whilst seeking additional advice ('the stoppers') (40-43%). Continuer countries also rated medical sources as more trustworthy than stopper countries reflecting the strong medical source trust-behaviour relation. The divide between two distinct groups of continuers and seekers is also consistent with findings from Bouder *et al*. (2015), which identified clear national variations between "stoppers" (Germany, France, and Spain) and "seekers" (GB, Sweden, the Netherlands).

Fourth, the public self-reported low levels of knowledge of the regulators. The large majority of European citizens living in GB, France, Germany, Poland, and, to a lesser extent, Italy *said*

they had not heard of the concrete entities that regulate pharmaceuticals in their respective nations. Furthermore, the majority who said they had heard of them also indicated that they were 'not very' or 'not at all' familiar with the regulators. Considering respondents were asked *self-reported* knowledge questions that are vulnerable to social desirability bias (Fisher, 1993), the public's knowledge of relevant national authorities is also likely to be lower than these findings suggest.

The results have at least three main limitations. First, only one quantitative examination on trustworthiness and its consequences was examined. Risk communication scholars have emphasised the importance of measuring trust in a variety of ways by using a mix of both qualitative and quantitative methods (Pidgeon et al. 2007; Siegrist, 2010). This includes asking respondents to make different judgements of trust (or trustworthiness) that vary depending on the target, tangibility, type, and referent of judgement (Earle et al. 2007: 22). Findings from the present study therefore need to be compared with future studies using other measures of trust/trustworthiness in the understudied European pharmaceutical context. Second, respondents were asked questions about their intentions to engage in behaviour and opinions relating to medicines *in general*. The benefits and risks of medicines vary significantly depending on what they seek to treat (e.g. headaches, HIV/AIDS, multiple sclerosis, acne, etc.). Individuals may therefore have different behavioural intentions after receiving potentially adverse information depending on (a) what that information specifically says, and (b) what medicine it refers to. With that said, a survey (Way *et al*. 2016) of individuals diagnosed with various specific medical conditions found very similar results to those reported in the present study. Third, two cross-sectional datasets were analysed. A longitudinal study design would be required to test causal relationships over time (Siegrist, 2010).

(4.2) Implications for trust research

The first main implication of this study is that risk perception and communication researchers need to pay careful attention to the specific real-world risk context they are investigating when conducting trust research. The study identified a range of contextual factors that distinguish the (European) pharmaceutical context from other risk domains. One feature that distinguishes pharmaceuticals is that there is a remarkable lack of public knowledge about the concrete entities that regulate medicines and the underlying pharmaceutical regulatory system in Europe. In turn, this has important implications for who the public trust and seek information from to inform their medical decision-making. A second important feature is that, in lieu of knowing who regulates medicines, the public use a variety of information sources or 'communication channels' to inform their decision-making. This includes various medical, societal and industry sources of information. A third important feature is that there are clear differences between how the public are likely to react to new information on medicines between European countries. For example, while patients in some countries are more likely to continue taking their medicine if they receive adverse information, such as GB and Denmark, patients in other countries are more likely to stop taking their medicines, such as Germany and Poland. This has important implications for how benefits and risks are communicated in different national contexts. This study therefore furthers the conclusion from the trust literature that there are critical differences between risk management domains and countries (Löfstedt, 2005) and that the pharmaceutical domain is no exception.

A second main implication of this study for trust research is that concerted efforts need to be made to reduce fragmentation between the various fields risk perception and risk communication research (*see* Löfstedt and 6, 2008). The trust literature has historically been

dominated by investigations into environmental/ technological risks and, more recently, food safety issues (Way, 2017). In contrast, trust research in the pharmaceutical domain, has been largely disconnected from the environmental/ technological and food safety fields (Löfstedt and Perri 6, 2008). While this study highlighted key distinguishing features about the pharmaceutical domain, many of the challenges facing pharmaceutical risk regulators and communicators identified in this study are shared by risk regulators and communicators in other areas. Although there are some benefits of fragmentation, there is much more that can be done to cross-fertilise methods, findings and tools between different fields of trust research.

On the one hand, the medical/ pharmaceutical field could learn a great deal from over fifty years of experience from the environmental/ technological fields. While research on patient-doctor decision-making remains important in the medical context, the pharmaceutical information and communication environment has changed dramatically over the past twenty-five years (Way, 2017: 18). As this study showed, patients now obtain information from a wide variety of information sources beyond the doctor's office, some of which are more trusted than others. This is creating new challenges for pharmaceutical risk regulators and communicators many of which are well-known by environmental/ technological researchers and practitioners. For example, Kasperson and Stallen (1991) illustrate how the environmental/ technological fields of risk perception and communication have had a long history, with the nuclear power field emanating from 1950s public perceptions of nuclear power risk. The wealth of findings, methods and approaches from other fields could therefore be tested in the new pharmaceutical information environment.

On the other hand, the environmental/ technological and food safety fields could learn from the medical/ pharmaceutical field (Way et al. 2017). A key area of medical risk perception and

communication research has centred on the role of trust in patient-doctor decision-making (Mallia, 2013; Holt et al. 2016). An abundance of cutting-edge research has emanated from this research programme including on interpersonal relations between doctors, patients and other healthcare professionals. Indeed, doctors play a central role in communicating benefits and risks directly to patients and so are typically intimately involved in decision-making (Holt et al. 2016). Much research has also investigated how patients make medical judgements and decisions in a context where the benefits and risks affect them directly. A great deal of research from the pharmaceutical/ medical domain could therefore be tested in other fields in order to tackle some of the biggest challenges facing risk regulators and communicators.

(4.3) Implications for pharmaceutical regulation

What do these contextually-relevant results on trust imply for European pharmaceutical regulators? It is not yet clear what the full extent of EMA's transparency policies and the broader trend towards more data transparency will be for the public, as well as their trust in the pharmaceutical evaluation system. What is clear though is that the medicines information environment has changed with evidence that the public have begun to receive more disputed and conflicting information pointing to potential safety problems with their medicines through various information channels (Section 3.1). There is also clear evidence that this is not a hypothetical scenario (e.g. Butler, 2014; Burki, 2018). On the one hand, this trend may be short-lived. Future negative re-analyses may not be as widely publicised as they have over the past few years. While Ebrahim *et al*. (2014) found that there have been surprisingly few re-analyses conducted compared to those that could have been, EMA expect that the 'real' risk with issues around data transparency is low (personal communication, 2014). The agency also announced that due to its Brexit preparations it will temporary suspend the publication of

clinical data on its web-portal (EMA, 2018b), showing that there are important resource constraints to transparency (Way, 2017).

On the other hand, the number of re-analyses that point to potential safety problems may continue and, indeed, even increase over time (*see* O'Neill, 2006 for a theoretical discussion; Manson and O'Neill, 2007: 90). This latter scenario seems much more likely after (1) researchers become more aware of the data that is increasingly available and more sophisticated in analysing such large datasets (Doshi et al. 2013; Ebrahim et al. 2014), (2) the EMA's policies come into full effect and (3) the new clinical trial regulation comes fully into force providing outsides with even greater and unprecedented access to previously unavailable datasets (Clinical Trial Regulation [CTR] EU No. 536/2014). Indeed, a central trust-related goal of EMA's policies is to enable external re-analysis (Chan et al. 2014; Bonini, 2014), which means that the goal is precisely to encourage more re-analyses of regulatory data, something which pharmaceutical regulators themselves have been encouraging (Eichler et al. 2013). In this context, the result of this study has several important implications for the future of pharmaceutical regulation.

(4.3.1) Maintain and strengthen trust in medical actors

The first implication is that the regulators need to make concerted efforts to maintain and strengthen public trust in *medical sources* of advice in the new transparency era (i.e. GPs, pharmacists, local hospitals, medical journals, and emergency services) (Löfstedt, 2005, 2007). The study found that if the public receive more information pointing to safety problems with their medicine (e.g. originating or mediated from 'independent' re-analyses) then the level of trust they have in medical actors will strongly influence their compliance intentions – to

continue taking their medicine as usual whilst seeking additional advice about the problem. If the goal is to persuade the public to adopt this recommended advice (NHS Choices, 2019), then it is critically important to maintain the public's currently high levels of trust in medical sources. Vice versa, if this trust is not maintained in a more transparent environment, then the trust-consequence relationship found in this study would strongly suggest that there will be a downfall in prescription compliance (also *see* Bouder *et al*. 2015). In particular, in "stopper" countries (i.e. Germany, France, Poland, and Italy) compared to "continuer" countries (Denmark and GB), there is a need to maintain but, moreover, *strengthen* public trust in medical sources to avoid poor prescription compliance. Indeed, public trustworthiness of medical sources was rated as significantly higher in this 2015 study in GB and Denmark (the continuers) than in France, Germany, Italy, and Poland (the stoppers) (Figure 4). Furthermore, the fact that a variety of medical sources pooled together on the factor analyses of the 2012 and 2015 data (i.e. GPs, pharmacists, local hospitals, medical journals, and emergency services) means that there are a variety of medical actor avenues that the regulators can target for building trust and communicating benefit-risk with the public.

(4.3.2) Commit more resources to supporting national risk communication

The second implication is that, if public trust is to be maintained and strengthened, then EMA will have to commit more resources to supporting national authorities in a more transparent environment. Echoing previous studies, this study found that the large majority of European citizens have not heard of the regulators and, those that say they have, are unfamiliar with them. The European public also do not *directly* receive – or knowingly receive (e.g. patient leaflets) – benefit-risk information from pharmaceutical regulators. Rather, benefit-risk information is received by patients in a multi-actor environment that is made up of a complex web of relations

and information channels between various institutions, groups, and individuals (Pidgeon et al. 2003; Van Asselt and Renn, 2011). Along with identifying clear national variations, it is therefore apparent that EMA will have to work closely with national authorities that have intimate localised knowledge of national healthcare systems. This includes an in-depth understanding of the actors that are at the coal-face of communicating benefit-risk information with the public and, as this study shows, who are critical for maintaining public trust in the pharmaceutical system. In so doing, one goal will be to improve doctors' understanding of the benefit-risk evaluation system. Past studies show that medical doctors are ill-equipped, especially in terms of time and resources, to deal with complicated questions from patients about the intricacies of the medicines evaluation system (British Medical Association, 2016; Löfstedt *et al*. 2016). This is therefore one notable issue that needs to be addressed if the regulators' transparency and trust-building goals are to be achieved.

(4.3.3) Test for public trust across Europe

The third implication is that EMA and member state regulators need to test for trust not just in their institutions but, perhaps more importantly, in the various medical, societal, and industry actors from whom the public obtain mediated benefit-risk information. Testing for trust can help to guide the regulators' risk communication efforts and resources (Morgan et al. 2002; Löfstedt, 2005). In particular, it can provide a better understanding of what stakeholders and citizens need in terms of communication. Past studies have shown that if there are high levels of public trust then top down forms of communication may be acceptable (Löfstedt, 2005). However, if there is a lack of trust (because citizens see the regulators as incompetent) then the regulators will need to address that issue by hiring more competent civil servants and communicate to their citizens more carefully. The strong trust-consequence relationship in

those that are at the coal-face of communicating with the public (e.g. GPs, pharmacists, etc.) therefore means that the regulators need to closely examine public trust in them in order to be successful in the new transparency era. In so doing, this 2015 survey and that of Bouder *et al*. (2015) conducted in 2012 can provide a useful benchmark for the regulators. However, these studies examined a total of 9 EU countries and therefore do not reveal public perceived trustworthiness in all 28 member states as well as European Economic Area countries, Iceland, Lichtenstein, and Norway for whom the European regulators are responsible. Testing for trust across all EU nations therefore would be a critically important first step for communicating benefits and risk in the new transparency era (*see* Löfstedt, 2005; Earle, 2010 and Siegrist, 2010 on testing for trust).

(5.) Conclusion

This cross-sectional survey study of six EU nations measured the relationship between the public's trustworthiness of different sources of medicines advice and its consequences for their behavioural intentions and opinions in a scenario where they have received potentially adverse medicines information. Several strong, moderate and weak relationships were found and the most important implications of the study's findings for the regulators were discussed. This is particularly important since pharmaceutical regulators have sought to use information disclosure as a way to (re)gain public trust. The study provides a platform for future studies on trust and risk perception in the pharmaceutical context that can help to inform the regulator's future policies. The findings particularly emphasise the importance of testing for trust in a more transparent environment. It would be easy to underemphasise the need to conduct more quantitative and qualitative studies on trust to test these results and explore other trust issues in this understudied context. With that said, it is hoped that this study can trigger more research

in such an understudied context, especially considering there are important policy implications for the regulators who are operating in the new pharmaceutical transparency era.

REFERENCES

Anker, A. E., Reinhart, A. M., & Feeley, T. H. 2011. Health information seeking: a review of measures and methods. *Patient education and counseling*, *82*(3), 346-354.

Ayers, S. L., and J. J. Kronenfeld, J. J. 2007. Chronic illness and health-seeking information on the Internet. *Health: 11*(3), 327-347.

Bonini S., Eichler H-G., Wathion N., and G. Rasi. 2014. Transparency and the European Medicines Agency – Sharing of Clinical Trial Data. *New England Journal of Medicine*, 371:2452-2455.

Bouder F., Way D. H. P., Löfstedt R. and D. Evensen. 2015. Transparency in Europe: A Quantitative Study. *Journal of Risk Analysis*; 35(7):1210-1229.

Bovens M. A. P. and Wille A. 2008. Deciphering the Dutch drop: Ten explanations for decreasing public trust in the Netherlands. *International Review of Administrative Sciences* 74: 283-305.

Broom A. 2015. Virtually he@lthy: the impact of internet use on disease experience and the doctor-patient relationship. *Qual Health Res*,15(3):325-345.

Burki T. 2018. Cochrane review methods called into question. *The Lancet*, 392(10151), 906.

Butler D. 2014. Tamiflu report comes under fire. *Nature*, *508*(7497):439-440.

Chan A-W., Song F., Vickers A., Jefferson T., Dickersin K., Gøtzsche P. C., Krumholz H. M., *et al*. 2014. Increasing value and reducing waste: addressing inaccessible research. *The Lancet,* 383(9913):257-266.

Cline R. J., and K. M. Haynes (2001). Consumer health information seeking on the Internet: the state of the art. *Health education research*, *16*(6), 671-692.

Dillman, D. A. (2007) Mail and internet surveys: The tailored design method. John Wiley, Chichester, UK.

Doshi P., Goodman S. N. and J. P. Ioannidis. 2013. Raw data from clinical trials: within reach? *Trends in pharmacological sciences*, *34*(12):645-647.

Doshi P., Jefferson T., and C. Del Mar. 2012. The imperative to share clinical study reports. Recommendations from the Tamiflu Experience. *PLOS Medicine*, 9(4):E1001201.

Doshi P. and T. Jeffeson. 2016. Open data 5 years on: A case series of 12 freedom of information requests for regulatory data to the European Medicines Agency. *Trials*, 17(78):1-7.

Dunwoody S. and R. J. Griffin. 2014. The role of channel beliefs in risk information sharing. *In*: J. Árvai and L. Rivers III (eds.) *Effective Risk Communication*. Earthscan: Routledge, 220-233.

Earle T. C. and G. Cvetkovich. 1995. *Social trust: Toward a cosmopolitan society*. Greenwood Publishing Group.

Earle T. C., Siegrist M. and H. Gutscher. 2007. Trust, risk perception and the TCC model of cooperation. *In*: M. Siegrist, T. C. Earle, & H. Gutscher (eds.) *Trust in risk management: Uncertainty and scepticism in the public mind*. Oxon: Earthscan, 1-50.

Earle T. C. 2010. Trust in Risk Management: A Model-Based Review of Empirical Research. *Risk Analysis*, *30*(4):541-574.

Ebrahim S., Sohani Z. N., Montoya L., Agarwal A., Thorlund K., Mills E. J. and J. P. Ioannidis. 2014. Reanalyses of randomized clinical trial data. *JAMA*, *312*(10):1024-1032.

Edwards, A. and Elwyn, G. (2009) *Shared-decision-making in Healthcare: Achieving Evidence-Based Medicine* (2nd). Oxford: Oxford University Press

Eichler H-G., Abadie E., Breckenridge A., Leufkens, H. and G. Rasi. 2012. Open clinical trial data for all? A view from the regulators. *PLOS Medicine*, 9(4):e1001202.30.

Eichler H-G., Abadie E., Raine J. M. and T. Salmonson. 2009. Safe drugs and the cost of good intentions. *New England Journal of Medicine*, *360*(14): 1378-1380.

Eichler H-G., Pétavy F., Pignatti F. and G. Rasi. 2013. Access to patient-level trial data—a boon to drug developers. *New England Journal of Medicine*, 369(17):1577-1579.

Eiser J. R., Donovan A. and R. S. J. Sparks. 2015. Risk perceptions and trust following the 2010 and 2011 Icelandic Volcanic Ash Crises. *Risk Analysis*, *35*(2):332-343.

EMA. 2014. European Medicines Agency policy on publication of clinical data for medical products for human use. 2 October 2014. EMA/240810/2013.

EMA. 2016. Opening up clinical data on new medicines: EMA provides public access to clinical reports. 20 October 2016. EMA/650519/2016.

EMA. 2017. EMA Communication Perception Survey 2017. Accessed 07 October, 2019: https://www.ema.europa.eu/documents/report/ema-communication-perception-survey-report-2017_en.pdf

EMA. 2018a. Clinical data publication (Policy 0070) report Oct 2016-Oct 2017. 16 July 2018. EMA/630246/2017.

EMA. 2018b. Brexit preparedness: EMA to further temporarily scale back and suspend activities. 1 August 2018. EMA/483486/2018.

Fergie G., Hilton S. and K. Hunt. 2016. Young adults' experiences of seeking online information about diabetes and mental health in the age of social media. *Health Expectations*, *19*(6), 1324-1335.

Fischhoff B., Brewer N. and J. Downs. 2011. *Communicating Risks and Benefits: An evidence-based user's guide.* US FDA, White Oak, USA

Fisher R. J. 1993. Social desirability bias and the validity of indirect questioning. *Journal of consumer research*, 303-315.

Frewer L. J., Scholderer J. and L. Bredahl. 2003. Communicating about the risks and benefits of genetically modified foods: The mediating role of trust. *Risk analysis*, *23*(6):1117-1133.

Gaskell G., Bauer M. W., Durant J. and N. C. Allum. 1999. Worlds apart? The reception of genetically modified foods in Europe and the US. *Science*, *285*(5426):384-387.

Goldacre B. 2012. *Bad Pharma: How Drug Companies Mislead Doctors and Harm Patients*. London: Harper Collins.

Gøtzsche P. and Jørgensen A. Opening up data at the European Medicines Agency. *BMJ*, 2011; 342:d2686

Gray, N. J., Klein, J. D., Noyce, P. R., Sesselberg, T. S. and J. A. Cantrill. 2005. Health information-seeking behaviour in adolescence: the place of the internet. *Social science & medicine*, *60*(7), 1467-1478.

Grimmelikhuijsen S. 2010. Transparency of public decision-making: Toward trust in local government? *Policy and Internet*. 2(1), 5-35.

Hamburg M. and J. Sharfstein. 2009. The FDA as a public health agency. NEJM. 360:2493-2495.

Hay M. C., Cadigan R. J., Khanna D., Strathmann C., Lieber E., Altman R, McMahon M. *et al*. 2008. Prepared patients: internet information seeking by new rheumatology patients. *Arthritis and Rheumatism (Arthritis Care & Research)*, 15;59(4):575-582.

Holt D., Bouder F., Elemuwa C., Gaedicke G., Khamesipour A., Kisler B., Kochhar S., *et al*. 2016. The importance of the patient voice in vaccination and vaccine safety—are we listening? *Clinical Microbiology and Infection*, 22, S146-S153.

Ipsos MORI. 2016. Veracity Index 2015: Trust in professionals. Accessed 07 October, 2019: https://www.ipsos-mori.com/Assets/Docs/Polls/ipsos-mori-veracity-index-2015-topline.pdf

Ipsos MORI. 2018. Survey methods at Ipsos MORI. 2018. Accessed 07 October 2019: https://www.ipsos-mori.com/researchpublications/publications/235/Survey-Methods-At-

Kasperson R. E. and P. J. M. Stallen. 1991. *Communicating risks to the public: international perspectives*. The Netherlands: Kluwer Academic Publishers.

Khoo K., Bolt P., Babl F. E., Jury S. and R. D. Goldman. 2008. Health information seeking by parents in the Internet age. *Journal of paediatrics and child health*, *44*(7-8), 419-423.

Lee K., Hoti K., Hughes J. D. and L. M. Emmerton. 2015. Consumer use of "Dr Google": a survey on health information-seeking behaviors and navigational needs. *Journal of medical Internet research*, *17*(12), e288.

Lindbloom C. (1959) The science of "muddling through". PAR. 19: 79-88.

Löfstedt, R. E. Bouder, F. Wardman, J. and S. Chakraborty. 2011. The changing nature of communication and regulation of risk in Europe. *Journal of Risk Research*, 14(4): 409-429.

Löfstedt R. E., Way D. H. P, Bouder F. and D. Evensen. 2016. Transparency of medicines data and safety issues–a European/US study of doctors' opinions: what does the evidence show? *Journal of Risk Research*, 19(9):1172-11861-13.

Löfstedt R. 2005. *Risk management in post-trust societies*. New York: Palgrave Macmillan.

Löfstedt R. E. and F. Bouder. 2014. New Transparency Policies: Risk Communication's Doom? *In*: Árvai J and Rivers III L. (eds.) *Effective Risk Communication*. Oxon: Earthscan.

Löfstedt R. E. and P. 6. 2008. What environmental and technological risk communication research and health risk research can learn from each other. *Journal of risk research*, *11*(1-2):141-167.

Löfstedt R. E. 1995. The Barsebäck nuclear plant case. *Energy policy*, *24*(8):689-696.

Löfstedt R. E. 2007. The impact of the Cox-2 inhibitor issue on perceptions of the pharmaceutical industry: Content analysis and communication implications. *Journal of health communication 12*(5):471-491.

Löfstedt R. E. and D. H. P. Way. 2016a. Transparency and trust in the European pharmaceutical sector: outcomes from an experimental study. *Journal of Risk Research*, 19(9), 1082-1103.

Löfstedt R. E. and D. H. P. Way. 2016b. Transparency and trust in the European pharmaceutical sector: a commentary. *Journal of Risk Research*, 19(9), 1120-1128.

Mallia P. 2013. *The Nature of the Doctor-Patient Relationship: Health Care Principles Through the Phenomenology of Relationships with Patients*. London: Springer.

Mondak J. J., Carmines E. G., Huckfeldt R., Mitchell D. G. and S. Schraufnagel. 2007. Does familiarity breed contempt? The impact of information on mass attitudes toward Congress. *American Journal of Political Science*, *51*(1), 34-48.

Manson N. C. and O. O'Neill. 2007. *Rethinking informed consent in bioethics*. Cambridge and New York: Cambridge University Press.

Midden C. J. and N. Huijts. 2009. The role of trust in the affective evaluation of novel risks: The case of CO2 storage. *Risk analysis*, *29*(5):743-751.

Mushkatel A. H. and K. D, Pijawka. 1992. *Institutional trust, information, and risk perceptions; Report of findings of the Las Vegas metropolitan area survey* (No. NWPO-SE--055-92). Nevada Nuclear Waste Project Office, Carson City, NV (United States).

NHS Choices. 2019. Making sense of your medicines. Accessed 07 October, 2019: http://www.nhs.uk/Livewell/Pharmacy/Pages/Yourmedicinesquestions.aspx

O'Neill O. 2006. Transparency and the ethics of communication. In: C. Hood and D. Heald (eds.) *Transparency the key to better governance?* London: Proceedings of the British Academy.

O'Reilly E. 2015. European Ombudsman address at Edelman Trust Barometer Event – Trust in Government – Challenges. Accessed 07 October, 2019: http://www.ombudsman.europa.eu/en/activities/speech.faces/en/59066/html.bookmark

Passarani I. 2010. What do patients want of performance information? *BMJ*, 341:c6955.

Percheski C. and E. Hargittai. 2011. Health information-seeking in the digital age. *Journal of American College Health*, *59*(5), 379-386.

Pidgeon N., Kasperson R. E. and P. Slovic. 2003. *The social amplification of risk*. Cambridge: Cambridge University Press.

Pidgeon N., Poortinga W. and J. Walls. 2007. Scepticism, reliance and risk managing institutions: Towards a conceptual model of 'critical trust'. *In:* M. Siegrist, T. C. Earle, & H. Gutscher (eds.) *Trust in risk management: Uncertainty and scepticism in the public mind*. New York: Earthscan, 117-142.

Poortvliet M. P. and A. M. Lokhorst. 2016. The key role of experiential uncertainty when dealing with risks: its relationships with demand for regulation and institutional trust. *Risk Analysis,* 36(8):1615-1629.

Powell J. and A. Clarke (2006). Internet information-seeking in mental health: population survey. *The British Journal of Psychiatry*, *189*(3), 273-277.

Rodwin M. A. and J. D. Abramson. 2012. Clinical Trial Data as a Public Good. *The Journal of the American Medical Association*, 308(9):871-872.

Siegrist M. and G. Cvetkovich. 2000. Perception of hazards: The role of social trust and knowledge. *Risk analysis*, *20*(5),713-720.

Siegrist M., Earle T. C., Gutscher H. and C. Keller. 2005. Perception of mobile phone and base station risks. *Risk Analysis*, *25*(5):1253-1264.

Siegrist M., Earle T. C. and H. Gutscher. 2003. Test of a trust and confidence model in the applied context of electromagnetic field (EMF) risks. *Risk analysis*, *23*(4):705-716.

Siegrist M., Earle T. C. and H. Gutscher. 2007. *Trust in risk management: Uncertainty and scepticism in the public mind*. New York: Earthscan. .

Siegrist M. 1999. A causal model explaining the perception and acceptance of gene technology. *Journal of Applied Social Psychology*, *29*(10):2093-2106.

Siegrist M. 2014. Longitudinal studies on risk research. *Risk Analysis*, *34*(8):1376-1377.

Siegrist M. 2000. The influence of trust and perceptions of risks and benefits on the acceptance of gene technology. *Risk analysis*, *20*(2):195-204.

Siegrist M. 2010. Trust and confidence: The difficulties in distinguishing the two concepts in research. *Risk analysis*, *30*(7):1022-1024.

Sjöberg L. 2001. Limits of knowledge and the limited importance of trust. *Risk analysis*, *21*(1):189-198.

Sjöberg L. 1999. Perceived competence and motivation in industry and government as factors in risk perception. *Social trust and the management of risk*, 103-113.

Slovic P. E. 1993. Perceived risk, trust, and democracy. *Risk analysis*, *13*(6):675-682.

Slovic P. E. 2000. *The perception of risk*. New York: Earthscan publications.

Stevenson F. A., Kerr C., Murray E. and I. Nazareth. 2007. Information from the Internet and the doctor-patient relationship: the patient perspective--a qualitative study. *BMC Fam Pract*, 8:47.

Stone D. 2012 *Policy Paradox and the Art of Political Decision Making*. New York: WW Norton.

Tan S. S. L. and N. Goonawardene (2017). Internet health information seeking and the patient-physician relationship: a systematic review. *Journal of medical Internet research*, *19*(1), e9.

Tuler S. P. and R. Kasperson. 2014. Social distrust and its implications for risk communication: an example from high level radioactive waste management. In: J. Árvai and L. Rivers III (eds.) Effective Risk Communication. New York: Earthscan, 91-108.

Tustin, N. 2010. The role of patient satisfaction in online health information seeking. *Journal of health communication*, *15*(1), 3-17.

Van Asselt M. B. and Renn O. Risk governance. *Journal of Risk Research*, 2011; *14*(4):431-449.

Van de Walle S. 2004. Perceptions of administrative performance: the key to trust in government? (Doctoral dissertation, Katholieke Universiteit Leuven).

Way D. 2017. *Transparency in Risk Regulation: The Case of the European Medicines Agency*. PhD Thesis, King's College London.

Way D., Bouder F., Löfstedt R., and D. Evensen. 2016. Medicines transparency at the European Medicines Agency (EMA) in the new information age: the perspectives of patients. *Journal of Risk Research*, 19(9), 1185-1215.

Weaver III J. B., Thompson N. J., Weaver S. S. and G. L. Hopkins. 2009. Healthcare non-adherence decisions and internet health information. *Computers in Human Behavior*, *25*(6), 1373-1380.

Willmott G. 2014. Publish All Clinical Trials – Labour Call. 2014. Accessed 07 October 2019. http://www.gleniswillmott.eu/publish-all-clinical-trials-labour-call/

Willmott G. 2013. Labour MEP's campaign to open op clinical trials takes giant step forward. Accessed October 07 October, 2019: http://www.gleniswillmott.eu/labourmeps-campaign-to-open-up-clinical-trials-takes-giant-step-forward/

YouGov. 2013. British attitudes to the pharmaceutical industry. Accessed 07 October, 2019: https://yougov.co.uk/news/2013/08/30/report-british-attitudes-pharmaceutical-industry/

Appendix A: 2015 sample demographics (*see* Bouder *et al*. 2015 for data on the 2013 survey)

Table III: 2015 data: gender by age

		Male		**Female**	
		Eurostat (2013)	**2015 Survey**	**Eurostat (2013)**	**2015 Survey**
GB	18–24	7.60	7.64	7.50	7.45
	25–34	10.80	10.78	10.80	10.83

	35–44	11.00	10.94	11.10	11.13
	45–54	11.10	11.12	11.40	11.36
	55–64	9.20	9.22	9.50	9.52
Denmark	18–24	7.50	7.55	7.20	7.25
	25–34	9.60	9.60	9.50	9.46
	35–44	11.20	11.19	11.10	11.09
	45–54	11.90	11.85	11.70	11.64
	55–64	10.10	10.12	10.30	10.24
France	18–24	7.10	7.06	6.90	6.89
	25–34	10.00	10.07	10.30	10.31
	35–44	11.00	10.98	11.10	11.09
	45–54	11.10	11.07	11.40	11.44
	55–64	10.20	10.18	10.90	10.90
Germany	18–24	6.50	6.46	6.00	6.14

	25–34	9.90	9.93	9.60	9.55
	35–44	10.60	10.57	10.20	10.20
	45–54	13.60	13.47	13.00	13.02
	55–64	10.20	10.20	10.40	10.45
Italy	18–24	5.90	5.86	5.60	5.58
	25–34	9.40	9.42	9.40	9.37
	35–44	12.50	12.45	12.50	12.54
	45–54	12.10	12.13	12.50	12.52
	55–64	9.70	9.73	10.40	10.41
Poland	18–24	7.10	7.16	6.90	6.88
	25–34	12.40	12.38	12.00	12.02
	35–44	10.50	10.53	10.30	10.30
	45–54	9.70	9.72	9.90	9.87
	55–64	10.00	9.99	11.20	11.16

Table IV: 2015 data: region

Country	Region	Eurostat (2013)	2015 Survey
GB	North East	4.18	4.20
	North West	11.33	11.30
	Yorkshire and Humberside	8.53	8.50
	West Midlands	8.92	8.90
	East Midlands	7.31	7.20
	East of England	9.33	9.30
	South West	8.33	8.30
	South East	13.84	13.90
	Greater London	14.65	14.70
	Wales	4.84	4.80
	Scotland	8.74	8.90
Denmark	Hovedstaden (Capital Region of Denmark)	32.10	32.04
	Midtjylland (Central Denmark Region)	22.80	22.77
	Nordjylland (North Denmark Region)	10.20	10.22
	Sjaelland (Zeeland Region)	14.00	14.03
	Syddanmark (Region of Southern Denmark)	21.00	20.94
France	Region Parisienne	19.80	19.73
	Nord-Ouest	22.40	22.41
	Nord-Est	22.60	22.68
	Sud-Ouest	10.80	10.83
	Sud-Est	24.40	24.35
Germany	Nielsen I	16.00	15.95

	Nielsen II	21.70	21.67
	Nielsen IIIa	13.60	13.58
	Nielsen IIIb	13.40	13.27
	Nielsen IV	15.60	15.56
	Nielsen V (a&b)	4.50	4.54
	Nielsen VI	7.60	7.83
	Nielsen VII	7.60	7.60
Italy	Nord-ovest	26.10	26.23
	Nord-est	19.20	19.14
	Centro (I)	19.50	19.45
	Sud	23.90	23.86
	Isole	11.30	11.32
Poland	Region centralny (Central region)	20.40	20.05
	Region poludniowy (Southern region)	20.80	20.68
	Region wschodni (Eastern region)	17.40	17.38
	Region pólnocno-zachodni (North-western region)	16.30	16.28
	Region poludniowo-zachodni (South-western region)	10.50	10.39
	Region pólnocny (North region)	14.60	15.22

Table V: 2015 data: Working/not working for GB, Denmark, and France

	GB	**Denmark**	**France**

	Eurostat (2013)	2015 Survey	Eurostat (2013)	2015 Survey	Eurostat (2013)	2015 Survey
Working	73	73	74	74	67	67
Not working	27	27	26	26	33	33

Table VI: 2015 data: Working/not working for German, Italy, and Poland

	Germany		Italy		Poland	
	Eurostat (2013)	**2015 Survey**	**Eurostat (2013)**	**2015 Survey**	**Eurostat (2013)**	**2015 Survey**
Working	76	76	58	58	63	64
Not working	24	24	42	42	37	36

Appendix B: Final 2015 questionnaire

1. How easy or difficult is it for you to obtain information about medicines from each of the following sources?

Please choose one answer per row

ACROSS THE TOP

1. Very easy
2. Somewhat easy
3. Neither easy nor difficult
4. Somewhat difficult
5. Very difficult
6. Don't know

DOWN THE SIDE (RANDOMISE ORDER – CODES 7 AND 8 ALWAYS TOGETHER AND CONSECUTIVE)

1. General Practitioner (GP)
2.
3. Local hospital

4. Internet in general
5. Brand specific websites (of specific medicines you may consider)
6. Media (e.g. newspapers, television, radio, etc.)
7. A medically qualified friend or relative
8. Another friend or relative (not medically qualified)
9. Pharmaceutical companies (including their websites)
10. Pharmacy
11. Emergency services (e.g. **<DIFFERENT TEXT BASED ON NATION: GB**=999 **/ ALL OTHERS**=112**>**)
12. Medical journal
13. Groups representing patients

2. At what stage would you like information to be conveyed to you about a possible safety issue of a medicine that you use or may use?

Please choose one answer only

1. When there is a possible sign of a safety problem
2. When the problem has been investigated and it is not clear if it is related to the medicine
3. When the problem has been investigated and a pharmaceutical company believes it is related to the medicine
4. When the problem has been investigated and regulators believe it is related to the medicine
5. Don't know

3. Do you think that receiving more information about the safety of a medicine would increase your confidence in taking medicines?

Please choose one answer only

1. Yes
2. No
3. Don't know

4. If the information you personally receive (via letter, telephone, e-mail, etc.) points to potential safety problems with the medicine you are currently taking, do you think you are most likely to…

Please choose one answer only

1. Stop taking your medicine
2. Reduce your dose of the medicine
3. Continue taking your medicine as usual
4. Seek additional advice about the medicine
5. Don't know

4(a). You say you are most likely to **<INSERT ANSWER GIVEN AT Q5 IN LOWER CASE>**. **<INSERT "**After**" IF Q5=1 OR 2 / "**Whilst**" IF Q5=3 >** doing so, would you also seek additional advice about the medicine?

4(b). You say you are most likely to **<INSERT ANSWER GIVEN AT Q5 IN LOWER CASE>** . While seeking additional advice, which of the following are you most likely to do?

Please choose one answer only

1. Stop taking you medicine
2. Reduce your dose of the medicine
3. Continue taking your medicine as usual
4. Don't know

5. At what stage do you think that members of the general public should be informed about a potential medical safety problem with a medicine?

Please choose one answer only

1. As soon as a potential medical safety problem has been identified and before scientific analysis is complete to confirm whether or not there is a problem
2. After scientific analysis has been undertaken and the scientific analysis has confirmed there is a problem
3. Don't know

6. How trustworthy or untrustworthy do you believe the following **sources** are in providing you with advice on the side effects associated with specific medicines?

Please choose one answer per row

ACROSS THE TOP

1. Very trustworthy
2. Fairly trustworthy
3. Neither trustworthy nor untrustworthy
4. Not very trustworthy
5. Not at all trustworthy
6. Don't know

DOWN THE SIDE (RANDOMISE ORDER – CODES 7 AND 8 ALWAYS TOGETHER AND CONSECUTIVES)

1. General Practitioner (GP)
2.
3. Local hospital
4. Internet in general
5. Brand specific websites (of specific medicines you may consider)
6. Media (e.g. newspapers, television, radio, etc.)
7. A medically qualified friend or relative
8. Another friend or relative (not medically qualified)
9. Pharmaceutical companies (including their websites)
10. Pharmacy
11. Emergency services (e.g. **<DIFFERENT TEXT BASED ON MARKET: GB=**999 **/ ALL OTHERS=**112**>**)
12. Medical journal
13. Groups representing patients

7. Overall, do you think it is a good or bad idea to inform the general public about a potential medical safety problem with a medicine, **before** a scientific analysis has been undertaken? (By scientific analysis, we mean a full review of the available data by the regulators and pharmaceutical industry)

Please choose one answer only

1. Good idea
2. Bad idea
3. Don't know

8(a). Have you heard of **<INSERT TEXT BASED ON MARKET: GB=**MHRA / **DENMARK=**DKMA / **FRANCE=** l'ANSM / **GERMANY=**BfArM / **ITALY=**AIFA / **POLAND=**URPL**>**?

Please choose one answer only

1. Yes
2. No

8(b). In only a few words, what do you think **<INSERT TEXT BASED ON MARKET: GB=**MHRA/ **DENMARK=**DKMA / **FRANCE=** l'ANSM / **GERMANY=**BfArM / **ITALY=**AIFA / **POLAND=**URPL **>** do?

8(c). You said that you had heard of the below agency. How familiar or unfamiliar are you with each of those agencies?

Please choose one answer per row

ACROSS THE TOP
1. Very familiar
2. Fairly familiar
3. Not very familiar
4. Not at all familiar
5. Don't know

Appendix C: 2015 survey response rates

		GB	France	Germany	Denmark	Italy	Poland
Invites sent		9703	8228	7208	12114	4503	10477

Incompletes	*Quota full (age/ gender/ region/working status /overall)*	448	740	378	346	671	831
	Screened out for other reasons	11	21	20	14	7	9
	Terminated/ abandoned	78	88	63	97	51	100
Completed interview		1000	1000	1000	1001	1000	1000
Response rate		10.8%	13.3%	14.6%	8.5%	26.1%	10.4%