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Original article

The effect of message framing and the nature of the targeted illness on individuals' intention to participate in clinical trials

L'effet du cadrage du message et du statut de la maladie concernée sur l'intention des individus de participer aux essais cliniques

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ABSTRACT

Introduction. – Clinical trials are considered as the most useful methods to evaluate the efficacy of new medical treatments, but the participation of healthy individuals is often too small, which limits the statistical power of the trial and hence its effectiveness.
Objective. – The goal of the present research is to assess, for the first time, the effects of message framing (gain versus loss) and of the nature of the illness targeted by a clinical trial (highly- versus mildly-contagious) on individuals' intention to enter it.
Methods. – The experimental manipulation is carried out within a scenario promoting a clinical trial, in a 2 (framing: gain vs loss) × 2 (nature of the illness: highly- vs mildly-contagious) between-participants design. After reading the scenario, participants were asked to rate their intention to enter the trial and their perception of its utility.
Results. – Statistical analyses validated a causal model explaining that a gain-framed message describing a highly-contagious illness increases the perception of the utility of the clinical trial, which in turn enhances the intention to participate.
Conclusion. – The discussion mainly focuses on the contributions of these findings at a theoretical level, considering the limits and potential of their possible application.

Mots clés :
Cadrage du message
Implication personnelle
Essai clinique
Perception du risque
Utilité

RÉSUMÉ

Introduction. – Les essais cliniques sont considérés comme étant les méthodes les plus utiles pour évaluer l'efficacité des nouveaux médicaments, mais la participation d'individus « sains » est souvent trop faible, ce qui diminue le pouvoir statistique de l'essai et donc son efficacité.
Objectif. – L'objectif de la présente recherche est de tester, pour la première fois, les effets du cadrage du message (en gain versus perte) ainsi que du type de maladie concernée par l'essai clinique (fortement versus faiblement contagieuse) sur l'intention d'individus sains d'y participer.
Méthode. – La manipulation expérimentale s'effectuait en inter-participants par l'intermédiaire de la version du scénario, à savoir 2 (cadrage : gain vs perte) × 2 (statut de la maladie : hautement vs faiblement contagieuse). Immédiatement après la lecture du message, les participants devaient estimer leur intention de participer à cet essai clinique ainsi que l'utilité des essais cliniques.
Résultats. – Les analyses statistiques valident un modèle causal selon lequel un message cadré en gain et décrivant une maladie fortement contagieuse augmente la perception de l'utilité de l'essai proposé, engendrant alors une hausse de l'intention d'y participer.
Conclusion. – La discussion porte principalement sur les contributions de ces résultats tant au niveau théorique qu'à celui de ses possibles applications.

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1. Introduction

Imagine you see at the television an advertisement promoting the participation of healthy adults in the first phase of a clinical trial aiming to find a cure for a relatively mild disease: would you be more willing to enter it when hearing about the benefits that your participation would bring to medical research, or the harm your refusal risk to cause to medical advancement? More importantly, would you be interested at all in this clinical trial? Imagine now that the same advertisement recommended your participation in a trial aiming to find a cure for a highly-contagious disease that you could easily develop: would this change your previous decision?

Clinical trials are one of the most powerful research methods to increase medical knowledge about health technologies and the treatment of diseases. They are scientific experiments, supervised by regulatory authorities, carried out to test the effectiveness of health care services (such as drugs) or health technologies. Clinical trials testing drugs usually begin with a first phase aiming to analyze their pharmacodynamics and pharmacokinetics in a population of healthy volunteers, with the exception of clinical trials testing poisoning drugs (e.g. chemotherapy). Unfortunately, problems with recruitment of healthy participants in this first phase have a great impact on this type of clinical trials' efficacy, preventing the advancement to the following phases, which are necessary to assess the effects and efficacy of the drug, and limiting the statistical power of the trial. For example, in France, the number of volunteers decreased by 40% between 2000 and 2009: these data led the Lilly Institute to carry out an inquiry between November 2009 and January 2010 with a representative sample of individuals aged more than 18 years, on their perception of clinical trials. Results demonstrated that 54% of the interviewed individuals would refuse to participate in a clinical trial, even if the majority perceive clinical trials as indispensable to clinical development (94%). One of the main challenge of public health concerning this topic is thus to develop effective informative and promotional campaigns to increase the recruitment of individuals who have never enrolled in a trial.

Considerable research has examined the role played by message framing in persuasion processes, especially when considering its influence on health decision-making (Gong et al., 2013). Social marketing advertisements often vary in terms of positive or negative framing, especially with regards to health-promotion appeals (Rothman & Salovey, 1997). Message framing is a concept referring to the way information is formulated in a message; it can be related to different aspects of persuasive communications (Levin, Schneider, & Gaeth, 1998), but the most well-known is certainly the distinction concerning the framing of the consequences of behavioral alternatives, meaning either gains or losses. In this context, message framing refers to the emphasis of the message on the positive or negative consequences of adopting or failing to adopt a particular behavior (Tversky & Kahneman, 1981; Rothman, Salovey, Antone, Keough, & Martin, 1993; Bartels, Kelly, & Rothman, 2010). For instance, a gain-framed message promoting physical activity would state "Engaging in daily physical activity will increase your body strength and strengthen your immune system, improving your health", whereas the same message with a frame on losses would state "Not engaging in daily physical activity will decrease your body strength, weakening your immune system, and worsening your health".

At first, research on framing effects demonstrated that loss-framed messages were the most effective promoting detection behaviors, such as HIV testing (Kalichman & Coley, 1995) and mammography (Cox & Cox, 2001). Gain-framed messages were instead the most persuasive promoting prevention behaviors, such as the use of condoms (Garcia-Retamero & Cokely, 2011) and sunscreen (Lee & Aaker, 2004). The persuasiveness of one type of framing over the other has been explained according to the degree of risks presented by the target behavior. Engaging in a detection behavior (such as mammography) is for instance a risky decision, possibly leading to the discovery of an issue (such as a lump; Lee, 2000; Lasser, Ayanian, Fletcher, & Good, 2008; Green et al., 2008). Consistent with the underlying tenets of prospect theory (Kahneman & Tversky, 1979) stating that individuals are risk-seeking when facing possible losses, loss-framed messages are considered to be the most effective to promote detection-oriented behaviors. On the opposite, engaging in prevention behaviors (such as sunscreen use) prevent diseases and improve personal health; the risks in these situations are linked to the decision not to perform such behaviors. As individuals are risk-adverse when facing possible benefits, gain-framed messages are considered to be the most effective promoting prevention behaviors (Rothman & Salovey, 1997).

However, the explanation of framing effects according to the risks of engaging or not in a behavior is not supported by more recent empirical results. Data concerning the effectiveness of loss-framed messages for detection behaviors are heterogeneous, as several studies reported little or no effects (e.g. Apanovitch, McCarthy, & Salovey, 2003; Rivers, Salovey, Pizarro, Pizarro, & Schneider, 2005). In a first review, O'Keefe and Jensen (2007) carried out a meta-analysis of 93 studies showing a small but significant advantage for gain-framed over loss-framed messages in encouraging disease prevention behaviors. Examining the data by behavior type, however, a significant gain-framed advantage was apparent only for dental hygiene behaviors, and not for other types of prevention behavior. In a second review, O'Keefe and Jensen (2009) conducted a meta-analysis on 53 different articles testing framing effects on detection behaviors. Their results demonstrated that loss-framed messages were slightly more persuasive than gain-framed ones only for appeals advocating breast cancer detection behavior, but not for other kinds of behavior (such as skin cancer, dental problems, and other types of cancer. . .). This heterogeneity could be interpreted as depending on the fact that framing effects on behavioral intention are moderated and mediated by other factors (Rothman, Wlaschin, Bartels, Latimer, & Salovey, 2013; Updegraff & Rothman, 2013), such as individuals' perception of the efficacy or utility of the behavior suggested in response to the health threat. Indeed, the choice of engaging in a health behavior is not uniquely based on the evaluation of its risks (i.e. its costs), but also and more importantly on the perception individuals have of its utility (i.e. its benefits; Conner & Norman, 2005). When an individual is threatened by a health issue, he is in fact willing to adopt any behavioral strategy that could effectively reduce or eliminate such threat (Witte, 1992; Maloney, Lapinski, & Witte, 2011; Redmond, Dong, & Frazier, 2015). Stephenson & Witte (1998) exposed participants to a message stressing the negative consequences of skin cancer, varying the description of prevention behaviors' efficacy as either high (describing the effectiveness and ease of sun block use in preventing skin cancer) or low (stressing the fact that it is anyway impossible to undo any past skin damage). Results demonstrated that individuals' intentions to engage in prevention behaviors were significantly higher when receiving the high-efficacy message. The perception of the behavior as effective is in fact a necessary condition for individuals to choose to engage in it: if the behavior is perceived to be ineffective in responding to a health issue, there is no reason for individuals to choose it.

The effectiveness of message framing is thus determined by the perception individuals have of the target behavior. When the perceived risks of a behavior is the strongest barrier to engage in it, a loss-framed message is expected to be the most effective, as in a loss-framed condition individuals will perceive the risky behavior as highly useful. On the opposite, a gain-framed message is expected to be the most persuasive for those behaviors that are perceived as not risky, but rather strongly beneficial. The

effectiveness of gain-framed information is in fact proportional to the degree that people perceive the behavior as an effective mean to maintain or improve health (Rothman & Salovey, 1997). What does happen then for those behaviors that are perceived as both risky and useful? How should a communication be framed in order to increase the perception of usefulness, and thus the intention to engage in the suggested behavior? To respond to this question, we decided to carry out a study analyzing the effects of message framing in a domain where it has never been tested before: the promotion of healthy volunteers' participation in clinical trials.

2. Conceptualization and hypotheses: utility and risk perception

2.1. The target: participating in a clinical trial

The decision to enter a trial is a complex and articulated choice involving a variety of factors (Ross, Grant, & Counsell, 1999; Ellis, 2000).

Several exploratory studies demonstrated for example that participation is mostly fostered by the consideration of altruistic and personal benefits (Llewellyn-Thomas, McGreal, Thiel, Fine, & Erlichman, 1991; Wright et al., 2004; McCann, Campbell, & Entwistle, 2010) and logistical factors such as timing, location, travel costs (Morse, Simon, Besch, & Walker, 1995; Aaronson et al., 1996). One of the main barriers to participation is individuals' perception of the dangers of clinical trials (Ross et al., 1999; Grunfeld, Zitzelsberger, Coristine, & Aspelund, 2002; Mills et al., 2006).

The purpose of our research being analyzing how message framing influences the decision to engage in a risky behavior by improving individuals' perception of its usefulness, clinical trials are an appropriate target behavior, as their public consideration appears to be organized around two crucial features: utility and risk perception. The survey we referred to in section 1, carried out in France by the Lilly Institute (2009–2010) which analyzed individuals' representation of clinical trials, showed that 61% of the entire sample perceived clinical trials as too risky for the participants, and just 46% stated they would enter one. At the same time, clinical trials were considered useful and indispensable to guarantee the reliability of medical treatments (by 94% of the sample). Even if individuals consciously evaluate clinical trials as useful and important, at a practical level they are afraid to enter one (similar results have been collected in the USA by Comis, Miller, Aldigé, Krebs, and Stoval, 2003). How could message framing be employed to foster a positive attitude towards participation?

3. What type of message framing is the most appropriate to promote a useful but risky health behavior?

Considering that clinical trials are perceived as risky and useful at the same time, both framings could be highly persuasive, depending on which feature most importantly characterizes participants' perception of the clinical trial. If the main feature of individuals' perception concerns the dangers of clinical trials, a loss-framed communication should be the most persuasive. Perceiving clinical trials as too risky, individuals should be the most willing to enroll when reading about the negative outcomes of non-participation, for example the failure to discover a new treatment against a disease.

However, as clinical trials aim to find a cure for an illness, individuals could consider the decision not to enter a trial as the riskiest one. In this case, a gain-framed communication, describing the positive outcomes of participation, should be more persuasive than a loss-framed one. It is thus possible to suppose that when a clinical trial is described as necessary to discover the treatment to a contagious illness, individuals will be more persuaded by a gain-framed message, as the clinical trial will be evaluated as highly useful and important.

Describing a highly-contagious illness is in fact supposed to strengthen individuals' involvement in the situation. The intensity of message framing effects on health-related decisions directly depends on individuals being involved in the situation and concerned by the specific health issue (Rothman et al., 1993; Meyers-Levy & Maheswaran, 2004). For instance, Rothman et al. (1993) analyzed framing effects on individuals' intentions to use sunscreen, measuring their involvement by assessing their perception of the risk of developing skin cancer. Gain-framed pamphlet resulted the most persuasive, but the difference between the effects of a positive versus negative framing was significant only for individuals highly concerned about skin cancer, who felt the most vulnerable to the threat. When participants were not involved in the issue, message framing did not have any significant effect on individuals' decision.

Hence, it is possible to suppose that by varying the contagiousness of the targeted illness, individuals will perceive the risks as associated with the decision not to enter the trial aiming to find a cure for it. The resulting clinical trial will in this case be important and useful, and in turn expected to increase the persuasive power of a gain-framed message, describing for example the clinical trial as profitable to the progress of medical research. Furthermore, it is possible to hypothesize that framing effects will not be significant when individuals are moderately involved, when receiving information about a mildly-contagious illness.

Taken together, we contend that a gain-framed message rather than a loss-framed one will be more effective in promoting participation in a clinical trial when combined with the description of a highly-contagious illness because such pairing will improve individuals' perception of the trial's utility, explaining the intention to engage in it. Therefore, we posit:

- H1: a gain-framed (versus loss-framed) message promoting participation in a clinical trial aiming to find a cure against a highly-contagious (versus mildly-contagious) disease will be the most persuasive, increasing individuals' intention to enter it;
- H2: this effect will be mediated by the perception of the clinical trial's utility.

4. Method

4.1. Design and procedure

Two hundred French university undergraduates accepted to participate in our study in a university classroom environment. Participation was voluntary, not required or rewarded with either money or course credits. As the interest of the present research is to assess how to increase the participation of individuals who have never enrolled in a trial before, we asked the respondents whether they ever entered one and whether they know someone who did. The 18 participants who reported to have some prior experience of clinical trials were excluded from the sample. The remaining 182 participants (106 women and 76 men; age range 18–27 years, M = 20.62, SD = 3.86) were randomly assigned to one of the four experimental conditions, in a 2 (nature of the illness: contagious versus non-contagious) × 2 (message framing: loss versus gain) between-subjects design. Participants were homogeneously distributed across experimental conditions, with no significant differences in regard to gender ($\chi^2(1, n = 182) = 2.29$, $p = .51$) or age ($F(3.178) = .51$, $p = .67$), which allowed us to collapse all the following analyses across these variables.

An A4-size folded paper booklet was handed to participants to complete, and collected later at an agreed-upon time. At first, participants read a message (approximately 350 words in length; Appendix A) promoting participation in a clinical trial aiming to find a cure for ophthalmic herpes. The choice of this illness depended on our intention to create messages about a real illness which has severe and possibly unchangeable consequences, but which is relatively uncommon, so that the majority of participants would be naïve with no previous preconception about its contagiousness. Indeed, the World Health Organization demonstrates that while oral and genital herpes are quite common (between 60% and 90% of the worldwide population has oral herpes, while 24% of the worldwide population has genital herpes), the incidence of ocular herpes is significantly lower (0.06% of the worldwide population). In order to test for the possible parasite effects of knowing already about ophthalmic herpes, we asked participants whether they knew about it: only 11.5% of the participants responded affirmatively. We controlled the influence of this variable in later regression analyses, as explained in section 5 of this paper.

Within the message, nature of the illness and message framing were manipulated. Participants were asked to respond to a series of questions concerning the manipulation check, demographic measures, and dependent measures. Finally, participants were thanked and fully debriefed.

4.1.1. Manipulation of the nature of the illness

In order to manipulate participants' perception of the threat, we described ophthalmic herpes as either highly- or mildly-contagious. In the "highly-contagious" experimental condition, the message described ophthalmic herpes as transmissible through saliva exchange (e.g. "Ophthalmic herpes is transmitted through saliva. For example, drinking from the same glass or bottle of an affected person can generate a contamination"). In the "mildly-contagious" experimental condition, ophthalmic herpes was described as transmissible through blood exchange (e.g. "Ophthalmic herpes is transmitted through blood. For example, the inaccurate sterilization of equipment for tattoo and piercing can generate a contamination").

4.1.2. Framing manipulation

In order to manipulate message framing, we described either the benefits of participation or the costs of non-participation. The gain-framed message began with the description of the positive consequences of participation, at a social and scientific level (e.g. "The participation in clinical trials is beneficial to science development: by entering a clinical trial, you will contribute to the progress of medical research"). The loss-framed message began with the description of the negative consequences of non-participation (e.g. "The non-participation in clinical trials is detrimental to science development: by not entering a clinical trial, you will contribute to the decline of medical research").

4.2. Dependent measures

Dependent measures were rated on a 7-point scale ranging from 1 ("not at all") to 7 ("extremely").

4.2.1. Manipulation check

Participants' perception of the threat was assessed through a three-item scale ($\alpha(n = 3) = .71$; e.g. "Ophthalmic herpes is a contagious illness").

4.2.2. Behavioral intentions

Participants rated their intentions on a three-item scale ($\alpha(n = 3) = .71$; e.g.: "I intend to participate in the clinical trial").

Table 1
Treatment means and standard deviations for all dependent measures.

		Highly-contagious		Mildly-contagious	
Measures	Frame	Gain	Loss	Gain	Loss
Manipulation check	M	5.29	5.18	4.21	4.08
	SD	1.03	1.18	1.23	1.13
Behavioral intentions	M	3.88	2.77	3.23	3.09
	SD	1.57	1.11	1.11	1.28
Perceived risks	M	3.65	3.98	4.01	3.53
	SD	1.52	1.64	1.71	1.68
Perceived utility	M	6.45	5.83	5.97	5.82
	SD	.67	1.08	1.17	1.38

4.2.3. Perceived risks

Participants' perception of the risks of the clinical trial was measured by a two-item scale ($r(n = 2) = .77$; e.g.: "The proposed clinical trial is dangerous").

4.2.4. Perceived utility

Participants rated their perception of the trial utility on a two-item scale ($r(n = 2) = .79$; e.g.: "The proposed clinical trial will be useful to the advancement of medical research").

5. Results

Treatment means for all measures are reported in Table 1. An ANOVA was conducted for the manipulation check, whereas a MANOVA was carried out on all the other dependent variables.

5.1. Manipulation check

The manipulation of the nature of the illness was effective in influencing participants' perception of the threat ($F(1, 180) = 41.73$, $p < .001$, $\eta^2 = .18$). In the "highly-contagious" condition, participants perceived the ophthalmic herpes as more frequent and contagious (M = 3.74, SD = .89), than in the "mildly-contagious" condition (M = 2.83, SD = .72).

5.2. Behavioral intentions

The nature of the illness did not influence individuals' intention to participate ($F(3, 178) = .72$, $p = .39$). Message framing had a significant main effect ($F(3, 178) = 10.75$, $p < .001$, $\eta^2 = .06$). Participants in the "gain-framed" condition had higher intentions (M = 3.55, SD = 1.38) than those in the "loss-framed" condition (M = 2.94, SD = 1.21). More importantly, the effect of illness × framing interaction was significant ($F(3,178) = 6.56$, $p < .01$, $\eta^2 = .04$).

Message framing significantly influenced behavioral intentions when participants perceived the illness as highly-contagious ($t(1,84) = 3.77$, $p < .001$, $d = .82$), whereas it had no effect when they perceived it as mildly-contagious ($t(1,94) = .65$, $p = .26$). More precisely, individuals perceiving a highly-contagious illness were more willing to enter the trial when in the "gain-framed" condition (M = 3.88, SD = 1.57) rather than in the "loss-framed" one (M = 2.77, SD = 1.11).

5.3. Perceived risks

The independent variables had neither simple nor interactive effects (all $F < 1$) on individuals' perception of the clinical trial's risks.

5.4. Perceived utility

Utility perception was not affected by the nature of the illness ($F(3, 178) = 2.16$, $p = .14$). Message framing had a significant

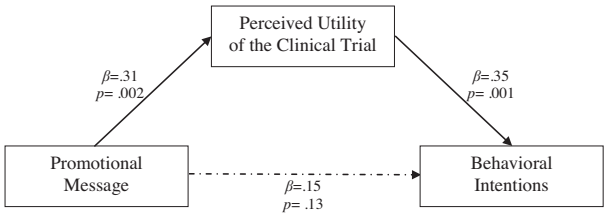

Fig. 1. Mediation model.

effect on individuals' perception of the utility of the trial ($F(3, 178) = 5.27$, $p < .05$, $\eta^2 = .03$). Participants in the "gain-framed" condition perceived the clinical trial as more useful (M = 6.21, SD = .99) than those in the "loss-framed" condition (M = 5.83, SD = 1.24). Even if the illness × framing interaction effect was not significant ($F(3, 178) = 2.02$, $p = .16$), we decided to go further in the analysis, to scrupulously test whether the effects of message framing change depends on the description of the illness. As expected, when in the "mildly-contagious" condition, utility perception was not influenced by message framing ($t(1,94) = .73$, $p = .23$), whereas it was the case in the "highly-contagious" condition ($t(1,84) = 3.19$, $p < .001$, $d = .69$). More precisely, participants perceiving a highly-contagious illness evaluated the clinical trial as more useful in the "gain-framed" condition (M = 6.45, SD = .67) rather than in the "loss-framed" one (M = 5.83, SD = 1.08) (Table 1).

5.5. Mediation hypothesis testing

To explain the persuasiveness of the combination of gain-framing and highly-contagious illness, we conducted a mediation analysis (Baron & Kenny, 1986) considering only participants receiving the messages proposing both or neither feature (i.e. the most versus the least persuasive). The measure of participants' knowledge about ophthalmic herpes, as well as participants' gender and age, were included in all regression analyses, and did not yield any significant result on either dimensions of behavioral intention or perceived utility. The first two regression analyses confirmed the significant effect of the message on behavioral intentions ($F(4,92) = 6.97$, $p = .01$, $r^2 = .06$; $\beta = .27$) and utility perception ($F(4,92) = 9.31$, $p = .003$, $r^2 = .08$; $\beta = 31$). When utility perception was included in the regression, it demonstrated to have a significant effect on behavioral intentions ($F(5,92) = 12.53$, $p = .001$, $r^2 = .16$; $\beta = .36$) and rendered insignificant the effect of the message ($F(5,92) = 2.46$, $p = .12$, $\beta = .16$). A separate Sobel test (Sobel, 1987) confirmed this mediation to be complete ($z = 2.28$, $p = .01$). These results validate a causal model (Fig. 1) explaining that a gain-framed message describing a highly-contagious illness increases the perception of the utility of the clinical trial, which in turn enhances the intention to participate.

6. Discussion

The current research demonstrates that the persuasiveness of message framing depends on receivers' perception of the target behavior, and more precisely on the subjective evaluation of its risks and usefulness, rather than on its function (Bartels et al., 2010). Our findings showed more precisely that participants highly concerned about the addressed health issue are the most persuaded by gain-framed information, as they perceive clinical trials to be useful, confirming the postulate that the persuasiveness of gain-framed communications depends on the perceived effectiveness of the target behavior as a useful response to the threat (Rothman & Salovey, 1997). Perceived utility is in fact a valid mediator of message's effects on the intention to participate in the advertised clinical trial. Present data also illustrates that when participants are moderately concerned about the addressed issue, their intentions are not influenced by message framing. Such result is in agreement with past research on the role of personal involvement as a predictor of framing effects (Maheswaran & Meyers-Levy, 1990; Schneider et al., 2001; Lee & Aaker, 2004; Meyers-Levy & Maheswaran, 2004): the more an individual is involved in the situation, that is to say, concerned about the health issue, the more he looks for contextual clues to help him choose the most satisfactory response, being in this way the most sensitive to message framing.

This research has surfaced some issues that merit further research. For example, it suggests that the key-factor of the persuasiveness of a message promoting the participation in a trial is utility perception, rather than risk perception, which is somehow in disagreement with past research on the barriers to entering clinical trials, demonstrating that one of the barriers to participation is individuals' perception of a trial as too risky with regards to possible adverse effects (Ross et al., 1999; Mills et al., 2006; Luebbert & Perez, 2015). It is thus possible to question the reason why utility perception was influenced by the features of the promotional message, whereas risk perception remained unaltered. This could possibly be due to the fact that the employed messages did not describe detailed dangers of the clinical trial, such as possible side effects. Further studies could thus address this issue describing more precisely the risks of participating, increasing in this manner the salience of this dimension in the decision-making process.

Another important question addresses the main limitations to the applicative potential of present results, depending on specific methodological choices. First, the study employed a paper-and-pencil strategy: individuals' perception and intentions could in fact be different when facing the possibility to enter a clinical trial in reality. In addition, one could question the fact that such a small sample, of such a young age, and entirely composed of university students is representative of the entire healthy population. The young age of our participants does not represent a limitation to ecological validity, as healthy youngsters are a population highly demanded for the first phase of most clinical trials dealing with drugs. However, a student sample is often not sufficiently representative of the general population targeted by specific prevention and promotion programs, also with regards to the recruitment strategy, which is not the same in a university context than in a real-world context (Rodgers & Franko, 2015). In addition, while the choice of ophthalmic herpes has an importance to reduce the influence of previous preconceptions regarding this illness (as it is relatively uncommon), the study did not measure the participants' possible representation of it and their feeling of concern about it, which could influence individuals' engagement in the situation and, thus, their decision to engage in the promoted behavior. While these methodological elements could limit the direct application of present results to promotional campaign, it is important to consider that this is the first study analyzing framing effects on the intention to participate in a trial. The aim being to test for the first time framing effects on the intention to enter a trial, the present study should lead to further research that could increase the external validity of our methodology. Indeed, the development of health-promotional programs is based on several research steps to determine its usefulness (Marchand, Stice, Rohde, & Becker, 2011). A first step concerns efficacy trials, designed to assess the effectiveness of such programs in controlled and optimal conditions. A second step concerns effectiveness studies, examining the program usefulness in real-world and pragmatic conditions, with a more heterogeneous sample. The present study is to be considered as a first step, an efficacy trial, which is very important to open the door to further effectiveness studies with higher ecological validity, aiming to determine the possibly effective application of present findings in actual programs to improve the participation of healthy volunteers to clinical trials.

This paper makes several important theoretical contributions. First, it endorses, for the first time in the research field of message framing, the persuasiveness of gain-framed communications over loss-framed ones, promoting participation in clinical trials among healthy individuals. Second, the present study contributes to past literature on framing effects, which examined the persuasiveness of framing taking into consideration the dimension of safety versus riskiness of different health behaviors (Rothman et al., 1993). The current research fosters past findings concerning the fact that framing effects depend on individuals' subjective perception of a behavior rather than on its function (Bartels et al., 2010), and underlines the importance of yet another dimension explaining framing effects: perceived utility. A risky behavior can in fact be effectively promoted by a gain-framed message if individuals perceive it as a useful response to a health threat (Witte, 1992). Third, this paper extends recent research on the effects of personal involvement, influenced by varying the contagiousness of a disease, as an explicatory factor of framing effects (Meyers-Levy & Maheswaran, 2004). This is not a suggestion to promote a behavior by deceiving individuals through the description of an illness as contagious even if it is not. In the present study, the description of the illness as contagious served to increase participants' involvement, which could be increased through other strategies such as stressing the severity of the illness rather than its contagiousness, or engaging in direct-to-consumer advertising (Herzenstein, Misra, & Posavac, 2004).

The present paper is just a first step towards the creation of effective communications promoting clinical trials among healthy individuals. Shedding light on the mechanisms underlying the persuasiveness of positively-framed communications in a controlled context, mainly based on individuals' involvement in the situation and on their perception of the usefulness of the trial, the experimental study we presented clears the way to further research on the potential practical application of present findings.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Appendix A. Persuasive Communication in {Highly Contagious/Mildly Contagious Illness} and [Gain/Loss] Formats

[Participation/Non-participation] in clinical trials is [beneficial/detrimental] to science development: by [entering/not entering] a clinical trial, you will contribute to the [progress/decline] of medical research. The discovery of new drugs and treatments will [advance/recede]. We will [win/lose] the war against serious diseases.

Collaborating with a pharmaceutical laboratory, we are currently organizing the promotion of a clinical trial in order to recruit participants. This trial aims to analyze the pharmacokinetic of a new drug (Gerilitin) against ophthalmic herpes. Analyzing the pharmacokinetic of a drug means testing:

- its absorption: the speed of the passage from oral solution to bloodstream
- its metabolism: the way the compound is transformed by the liver and other organs
- the distribution of the metabolized compound into muscles and organs
- the excretion (removal) of the metabolized compound from the body.

Medical research in France is accurately supervised. It is in France that in 1988, for the first time in Europe, the law Huriet-Sérusclat begins the protection of volunteers, guaranteeing the ethic development of clinical trials. The clinical trial we are proposing concerns a drug against ophthalmic herpes. Herpes is a viral disease, which causes the eruption of fever blisters on skin and mucus membranes. Ophthalmic herpes affects eyes, causing transparent blisters on the internal side of the eyelids, which rapidly become yellowish, scabby and tingling. These annoying and disturbing physical manifestations are not the only negative consequences of the disease. Ophthalmic Herpes can in fact infect optical nerves, affecting the cornea and causing serious and irreversible sight problems.

Ophthalmic herpes is transmitted through {saliva/blood}. For example, {drinking from the same bottle or glass of an affected person/the inaccurate sterilization of equipment for tattoos and piercings} can generate a contamination.

Before pharmaceutical companies start clinical trials with human participants, the compound must be tested in pre-clinical studies, involving cell culture and animal experiments. Gerilitin, treatment for ophthalmic herpes, already demonstrated to be effective during this preclinical phase. We are then proposing the participation to the following phase, analyzing the pharmacokinetic of the treatment in healthy volunteers. The volunteers will not have any contact with the disease: the drug is administrated with the only aim to analyze whether it is absorbed, metabolized and eliminated well by a healthy body. This phase is necessary and imperative in order to test afterwards the efficacy of the drug in treating actually affected patients.

By [participating/not participating] to this trial, you will contribute to the [progress/decline] of medical research concerning Ophthalmic Herpes. We will [win/lose] the battle against this serious disease which is transmitted through {frequent/rare} and {common/uncommon} behaviors.

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