The Role of Simulated-Experience and Descriptive Formats on Perceiving Risks of Strong Opioids: A Randomized Controlled Trial With Chronic Noncancer Pain Patients

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Design: randomized controlled trial

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Highlights

- People learn about risk through description and/or experience
- These formats can have different effects on risk perception and behavior
- We investigated the effects of both formats on long-term strong opioid use
- Description was better at improving estimations of opioids' benefits and harms
- Simulated experience was better at motivating patients to relinquish opioids

Abstract

Objectives: Opioid prescription rates worldwide suggest miscalibrated risk perceptions among those who prescribe, dispense, and take opioids. Findings from cognitive science show that risk perceptions can differ systematically depending on whether people learn about risks by description or experience. We investigated the effects of descriptive and simulated experience risk formats on patients' risk perceptions and behavior regarding long-term strong opioid use.

Methods: 300 German patients with chronic noncancer pain were randomly assigned in an exploratory randomized controlled trial to either a descriptive format (fact box) or a simulated experience format (interactive simulation). Primary endpoints were subjective and objective risk perceptions and intended intake behavior.

Results: Both formats significantly improved patients' objective risk perception; patients who saw the fact box estimated some outcomes more accurately (p = .031). Formats were equally effective in improving patients' subjective risk perception in terms of opioids' harms; however, patients receiving the simulation showed a greater reduction and termination of their opioid intake (p = .030) and a higher uptake of alternative therapies.

Conclusions: Descriptive and simulated experience risk formats improve risk perceptions and behavior regarding potent but highly risky drugs.

Practice Implications: To eliminate risky behavior, simulated experience formats may be superior to descriptive formats.

Keywords: risk perception, drug safety, risk communication, description–experience gap, strong opioids, chronic noncancer pain

1. Introduction

Chronic pain, often defined as pain lasting longer than 3 months or past the normal time of tissue healing, affects about 20% of adults globally [1-3]. It is a major cause of decreased quality of life and disability [4]. Using strong opioids to treat chronic noncancer pain short-term can be reasonable, although evidence shows that even the short-term use of strong opioids is associated with small improvements in pain and function relative to placebo and no improvements relative to non-opioid medication, but also an increased risk of harms [5, 6]. Evidence for the long-term prescription of strong opioids to patients with chronic pain is scarce, as most opioid trials do not extend beyond 12 weeks. The few systematic reviews that summarize evidence in patients with chronic noncancer pain find that the benefit outcomes of long-term strong opioid use are even less favorable than for short-term use and that the risk of serious harms worsens over time [7-9]. Despite the lack of supporting evidence of their use, prescriptions of strong opioids—defined as step III opioids on the World Health Organization's pain ladder—have increased dramatically in Europe [10-13] and the United States [14, 15] over the last two decades. Since the early 2000s, opioids have increasingly been used to treat chronic pain in the United States. This change came in response to concerns about the undertreatment of pain, new clinical guidelines, and the declaration by the Joint Commission on the Accreditation of Healthcare Organizations of pain as the "fifth vital sign"[16]. Consequently, the average dose of prescribed opioids in the United States increased from approximately 100 to approximately 700 morphine milligram equivalents per person per year between 1997 and 2007 [17]. The connections between the increased medical use of opioids and increases in risks such as overdoses were not recognized until this surge [18]. National evidence- and consensus-based guidelines (e.g., in Germany [19] and the United States [20, 21]) now caution against the long-term use of strong opioids for chronic noncancer pain and recommend they be used only after thorough assessment of the benefits and harms in cases where close monitoring can be guaranteed. These guidelines have contributed to recent stagnations and declines in rates of opioid prescription in Europe and the United States. Nevertheless, in Germany

currently about 80% of long-term prescriptions (> 3 months) of strong opioids are for patients with chronic noncancer pain [22].

These prescription patterns suggest a miscalibration of risk perceptions and behavior among those who prescribe, dispense, and take opioids, which can be due to how risk information is framed and presented to patients and health care providers [23-29], as well as how people learn about risks—whether through personal experience (e.g., taking a medication and experiencing its consequences firsthand) and/or description (e.g., medical guidelines, patient information). Depending on whether an individual has experienced a rare or delayed risk, received a description thereof, or both, they may behave as if they overestimate, underestimate, or correctly estimate the risk. For instance, an individual who personally experiences a rare health-threatening risk may subsequently act as if that risk were significantly higher than is objectively the case [30, 31]. Conversely, an individual who experiences many episodes of potentially risky behavior (e.g., taking strong opioids on a daily basis) without the risk materializing—because the "experience samples" are often too small to include a rare and possibly cumulative risk (e.g., in substance use)—may subsequently behave as if they underestimate or underweight the risk [32-34]. This phenomenon is known as the description–experience gap [33]. When people learn about risks through both experience and description, experience seems to prevail over description. Yet it is unclear whether the description–experience gap also impacts the risk perceptions and behaviors of patients with chronic noncancer pain taking strong opioids for 3 months and longer.

To examine the effects of the two modes of learning about risks—through experience and through description—on risk perception and risk behavior within a health care practice that has become a serious drug safety concern, we set up an exploratory randomized controlled trial (RCT) with patients with chronic noncancer pain and investigated the effects of an intervention involving either a simulated-experience format or a descriptive format on their (i) objective risk perception, (ii) subjective risk perception, and (iii) risk behavior (continued intake of strong opioids).

2. Methods

The randomized controlled trial (RCT) we report here is part of the ERONA project (Experiencing the Risk of overutilizing Opioids among patients with chronic Noncancer pain in Ambulatory care), which investigates four groups involved in the long-term administration of strong opioids independently: family physicians, physicians specialized in pain therapy, patients with chronic (≥3 months) noncancer pain, and pharmacists who regularly dispense narcotic substances. The ERONA project is funded by a grant from the German Federal Ministry of Health (BMG). We described the methods in detail in a peer-reviewed study protocol [35] that has not since been amended, registered the trial at the German Clinical Trials Register (DRKS00020358), made trial information public on the Open Science Framework (OSF), and adhered to the CONSORT checklist.

2.1 Study oversight

The study is based on an exploratory independent RCT design with two parallel online intervention arms. Randomization to either intervention was achieved by simple randomization, which means that patients were assigned to either group by pure chance (i.e., like flipping a coin). Participants were blind to the type of intervention they received. Data were collected before intervention at baseline (T0), immediately after intervention (T1), and 9 months after intervention (T2). The Institutional Ethics Board of the Max Planck Institute for Human Development, Berlin, Germany approved the study (Ethic Approval ID: A 2020–05).

2.2 Sample frame and sample size

The sample frame comprised accredited offline panels of IPSOS Health (Nuremberg, Germany), consisting of general practitioners, physicians specialized in pain therapy, and patient support groups that declared willingness to support IPSOS's recruitments of patients for social science studies.

Power calculation showed that we required 150 participants per intervention arm, resulting in a total of 300 participants (for details, see [35]) in order to detect a 15% difference between intervention

groups, in a two-tailed test with a 5% level of significance and a power of 80%. The rationale for using a 15% difference as our benchmark was based on effects from survey studies [36-38] comparing currently available standard information to one or the other risk format we used in our trial. IPSOS started enrolment for the first wave (T0 and T1) in April 2020 and concluded the first wave in August 2020. Enrolment for the 9-month follow-up (T2) began in January 2021. We started with the participants who entered the study first at T0; the second wave was completed in April 2021. Eligibility was determined by a set of screener questions that ensured that only patients with chronic noncancer pain (≥ 3 months) who had been taking strong opioids for 3 months or longer were included in the study. Eligible candidates who expressed interest in participating via their physician or patient support group received an email with a link to the online RCT. After completing the pre-intervention survey questionnaire, participants were randomly assigned to one of the two intervention formats.

IPSOS recruited eligible participants until 150 participants were reached per intervention arm. Because IPSOS recruited eligible patients offline via practitioners or patient groups, the absolute number of patients who were initially invited to participate cannot be validly estimated. Altogether, the practitioners and patient groups report access to about 2,700 patients with chronic noncancer pain. Assuming that between 30% to 40% of these patients were approached via their practitioners or patient groups, between 810 and 1,080 patients may have been invited to participate in our trial. In total, 362 patients started the trial online, 18 were screened out due to ineligibility (e.g., pain < 3 months, treatment other than strong opioids) and 44 abandoned the survey before randomization to an intervention arm, leaving 300 patients who were randomized to either of the two intervention arms (150 per arm). Informed consent was acquired prior to the study. For the 9-month follow-up, IPSOS was able to re-recruit 123 of the participants (82.0%) in the descriptive group and 118 (78.7%) in the simulated experience group. Patients received €30 for participation in the study.

2.3 Interventions

A fact box format served as the descriptive intervention (see Figure 1a) and an interactive simulation as the simulated experience intervention (see Figure 1b).

[INSERT FIGURE 1 ABOUT HERE]

Both risk education interventions presented the same information on the benefit–harm ratio of long-term administration of strong opioids in patients with chronic noncancer pain as absolute risks, adjusted to the same denominator (per 100 patients), and compared with a control group (drug therapy with non-opioids such as paracetamol or placebo). The presented evidence is based on a peer-reviewed, published systematic rapid review—conducted for the ERONA project by the Cochrane Germany Foundation's Institute for Evidence in Medicine—on the benefits and harms of long-term use of strong opioids among patients with chronic noncancer pain [8, 39].

The interventions differed in several aspects: The interactive simulation (simulated experience intervention) presented information sequentially, and allowed participants to directly observe changes in outcomes over time after pressing the start button. In addition, participants could observe changes over time for any given point in time by moving a horizontal slider. They could also explore and sort specific risk information by activating/deactivating the respective buttons. In order to reduce differences in interactivity between the two formats that may trigger different cognitive mechanisms, the fact box (descriptive intervention)—typically a static tabular format that presents all information on benefits and harms for a given point in time at once—was implemented using MouselabWEB [40] (www.mouselabweb.org). In this format, participants accessed individual pieces of information about benefits and harms by moving the mouse pointer over boxes on the screen to reveal the numerical values. To prevent participants from abandoning the interventions prematurely, the "move on" button was deactivated for 3 minutes.

2.4 Survey questionnaire

The primary endpoints surveyed at baseline (T0) and immediately after interventions (T1) were (i) objective risk perception, (ii) subjective risk perception, and (iii) reported current (T0) and planned (T1)

opioid intake behavior. The primary endpoint investigated at the 9-month follow-up (T2) was (iv) reported actual opioid intake behavior. (i) Objective risk perception was operationalized by a series of six questions requiring participants to provide a specific numerical estimate for each of the outcomes (benefits/harms) presented in the intervention (see Figures 1 and 2). For example, for the benefit "reduction in pain" we asked: "How many people out of 100 taking strong opioids for 6 months or longer do you think will experience a reduction in pain of at least 30%?" Apart from the specific benefit (reduction in pain of at least 30%, increase in physical function of at least 30%) or harm (falls or fractures; dizziness; drug misuse or addiction; side effects such as obstipation, nausea, or vomiting) addressed, the wording of the questions was the same throughout. (ii) Subjective risk perception was measured using a 5-point Likert scale with five options: "The benefits of strong opioids clearly outweigh the harms," "The benefits of strong opioids somewhat outweigh the harms," "The benefits and the harms of strong opioids are balanced," "The harms of strong opioids somewhat outweigh the benefits," and "The harms of strong opioids clearly outweigh the benefits." (iii) To investigate patients' intended opioid intake behavior, we asked them before (T0) and after (T1) the intervention whether they were considering changing their use of strong opioids (yes/no). (iv) To investigate patients' actual opioid intake behavior (T2), we asked them at the 9-month follow-up to choose which of three options best described their opioid intake behavior since the intervention: "I have reduced my opioid intake," "I have terminated my opioid intake," or "I have not changed my opioid intake." Patients were also asked whether they had started an alternative therapy since their intervention (yes/no). If they had, they were shown nine alternative therapies (drug therapy with non-opioids [e.g., paracetamol]; physiotherapy, occupational therapy, manual therapy; endurance sports, rehabilitation sports, swimming; massages, cold/hot therapy; transcutaneous electrical nerve stimulation, acupuncture; relaxation techniques; mindfulness training; psychotherapy; multimodal therapy) and asked to specify which they had started since the last study contact.

Due to the known link between numeracy and medical risk literacy, we assessed participants' medical risk literacy using an adapted version of the validated Critical Risk Interpretation Test (CRIT)

[41]. We also collected data on the three items of Korff's disability index, for which people indicate the degree to which their pain disrupts their daily activities on a 10-point scale ranging from 1 [no impairment] to 10 [highest impairment].

The survey was first piloted with a total of 18 patients with chronic noncancer pain using strong opioids (> 3 months)—13 patients recruited from the Charité – Universitätsmedizin Berlin assessed the phrasing of the questionnaire and five patients from family medicine practices assessed the comprehensibility of the educational interventions.

2.5 Data analysis plan

To investigate the interventions' effects on (i) objective risk perception, we analyzed the change in the mean for each benefit and harm estimate as well as the change in the sum of correct estimates (maximum: six correct estimates) from T0 and T1 within and between intervention groups. We counted participants' risk estimates (e.g., 41 people out of 100 for reduction of pain) as correct if the numerical value fell within a $\pm$10% margin of the point estimate retrieved from systematic evidence synthesis (e.g., for pain, between 37 and 45). We allowed this $\pm$10% margin of error because point estimates retrieved from medical evidence [8] are not devoid of error variance. To analyze the interventions' effect on (ii) subjective risk perception, we investigated the change from T0 to T1 in patients' Likert-scale judgments within and between intervention groups. To evaluate the interventions' effect on patients' opioid intake behavior, we investigated the (iii) changes in patients' intended willingness to alter their opioid therapy (change: yes/no) within group from T0 to T1 and between groups at T1. To evaluate interventions' effect on (iv) patients' actual behavior, we investigated the proportion of patients reporting that they had changed their opioid therapy (i.e., reduced or terminated opioid intake) between intervention groups at T2. We also analyzed the difference between the proportion of people who indicated having taken up alternative therapies at T2 between intervention groups, as well as the consistency between patients'

intended uptake of any of these alternative therapies at T1 and their actual uptake at T2 within each intervention group.

The online questionnaire did not permit item nonresponse and was thus entirely complete. Differences between groups (e.g., between the two intervention groups per study population) were assessed using independent sample t-tests or Mann–Whitney U tests (for continuous variables), and X^2 tests (for categorical variables). Differences within each group (before–after comparisons) were tested using dependent sample t-tests (for continuous variables) or McNemar's test (for dichotomous data). Independent predictors (e.g., risk literacy, demographics) of risk perception and behavior were analyzed using regression analysis. For regression analysis, primary endpoints and moderator variables were categorized. Data were stored and analyzed with IBM SPSS Statistics 26 (New York City, United States). All percentages reported in the Results section are absolute percentage points.

To control for nonresponse bias [42], we collected information about the gender, age, and education of those who did not complete the survey and compared their characteristics with those of respondents [43, 44].

3. Results

3.1 Sample characteristics

A total of 300 patients with chronic noncancer pain (150 per intervention arm) participated in the RCT. Participants did not differ demographically per intervention arm. Table 1 reports the distribution of gender, age, education, and geographical location. Patients who finished the survey (respondents) and those who abandoned the survey prematurely (nonrespondents) differed on all four demographic aspects. Relative to respondents, nonrespondents were more likely to be male, older, less educated, and from the west and south of Germany.

[INSERT TABLE 1 ABOUT HERE]

3.2 Objective risk perception

At baseline, the intervention groups did not differ in their objective risk perception. Patients in both groups considerably overestimated the benefits of strong opioids and underestimated their harms (see Figure 2). Both interventions offered a significant improvement, reducing both over- and underestimations (see Figure 2). In the interactive simulation group, objective risk perception improved for all six benefits and harms; in the fact box group, objective risk perception improved for five of six benefits and harms (see Table 2). In the specific case of the outcome "increase in physical function," the change in mean estimates suggests at first glance that patients in both groups were more likely to underestimate the occurrence of the outcome after intervention. However, Table 2 shows that the absolute number of people arriving at a correct estimate within a $\pm$10% margin of error considerably increased after both interventions (fact box: increase of 64.7 absolute percentage points; simulation: increase of 52.7 absolute percentage points). Furthermore, the margin and amount of erroneous estimates considerably decreased (see Figure 2). Across all six benefit–harm outcomes, the proportion of correct estimates improved by 36.7 absolute percentage points to 59.4 absolute percentage points among patients who saw the fact box and by 20.1 absolute percentage points to 52.7 absolute percentage points among patients who encountered the simulation (see Figure 2). The likelihood of arriving at more realistic risk estimates was higher with the descriptive format than with the simulated experience format (U = 9652,50, z = –2.155, p = .031, r = 0.12) .

[INSERT FIGURE 2 ABOUT HERE]

3.3 Subjective risk perception

At baseline, within each intervention group 91.4% of patients believed that the benefits of strong opioids clearly or somewhat outweigh their harms. Both the fact box (T = 13.05, z = -7.94, p < .001, r = 0.45) and the simulation (T = 17.00, z = -8.89, p < .001, r = 0.52) proved effective in changing that perception towards an assessment that better reflected the potential harms of strong opioids (see Figure 3). The proportion of patients who thought the benefits clearly or somewhat outweigh the harms decreased by

39.4 absolute percentage points to 52.0 absolute percentage points within the fact box condition and by 46.7 absolute percentage points to 44.7 absolute percentage points within the simulation intervention. The proportion of patients who felt that the harms are on par with or outweigh the benefits increased in the fact box intervention by 39.0 absolute percentage points and in the simulated experience intervention by 46.6 absolute percentage points. Figure 3 provides additional details on the distribution per group.

[INSERT FIGURE 3 ABOUT HERE]

3.4 Reported intended and actual opioid intake behavior

At baseline (T0), 25.3% of patients in the fact box intervention and 22.0% in the simulation intervention indicated a desire to change their current intake of strong opioids (X^2 [1] = 0.46, p = .498). After intervention (T1), this number increased to 51.3% within the fact box group (increase: 26.0 absolute percentage points; *McNemar's* X^2 = 32.09, p < .001) and to 54.7% within the simulation group (increase: 32.7 absolute percentage points; *McNemar's* X^2 = 47.02, p < .001), with no difference in the extent of patients' intention to change their opioid therapy between intervention groups (X^2 [1] = 0.335, p = .564).

The self-reported actual intake of strong opioids measured at T2, however, differed between intervention groups (X^2 [2] = 7.02, p = .030). Of the 123 patients in the fact box group, 42 (34.1%) reported having reduced their intake of strong opioids, nine (7.3%) reported having terminated their intake, and 72 (58.5%) reported that they had not changed their intake. Among the 118 participants in the simulation group, 49 (41.5%) reported having reduced their intake of strong opioids, 18 (15.3%) reported having terminated their intake of strong opioids, and 51 (43.2%) reported no change (see Figure 4). Compared to patients in the descriptive intervention, more patients in the simulated experience intervention reported that they had started an alternative therapy after the intervention: 39.8% (n = 47 of 118) versus 26.8% (n = 33 of 123; X^2 [1] = 4.49, p = .032); this was also the case for starting an alternative drug therapy with non-opioids (t [73.43] = –2.21, p = .031, r^2 = 0.25) and

psychotherapy (t [67.32] = –2.46, p = .016, r^2 = 0.28). For the remaining seven alternative therapies, we found no difference in uptake between the groups (see Table 3 for details on all alternative therapies).

In the simulation group, patients' intention to change their opioid therapy immediately after intervention (T1) and their actual change in opioid therapy after 9 months (T2) did not differ (*McNemar's* X^2 = 0.114, p = .774). This was not the case for patients in the fact box group (*McNemar's* X^2 = 5.689, p = .017), where fewer patients who had initially intended to change their opioid therapy reported having actually done so.

[INSERT FIGURE 4 ABOUT HERE]

3.5 Influence of pain impairment, medical risk literacy, and demographic variables on primary endpoints

Independent of intervention format, patients' medical risk literacy was not associated with their objective risk perception (odds ratio [OR] =1.30, 95% CI: 0.77 – 2.21, p = .322), their subjective risk perception (OR = 1.07, 95% CI: 0.63 – 1.81, p = .789), their actual opioid intake behavior (OR = 1.15, 95% CI: 0.63 – 1.98, p = .626), or their uptake of an alternative therapy (OR = 0.87, 95% CI: 0.47 – 1.60, p = .650). The extent to which patients reported that their pain impairs their lives influenced findings on one primary endpoint: The more impairment patients reported, the less likely they were to change their subjective risk perception after intervention (OR = 0.22, 95% CI: 0.11 – 0.48, p = <.001). Neither the reported actual opioid intake behavior (OR = 0.95, 95% CI: 0.63 – 1.40, p = .780) nor the uptake of an alternative therapy (OR = 0.93, 95% CI: 0.58 – 1.49, p = .768) was affected by patients' reported impairment. Demographic variables (age, gender, education) did not influence the results on the primary outcomes.

4. Discussion and Conclusion

4.1 Discussion

In our RCT of 300 German patients with chronic noncancer pain we found that both risk education formats—descriptive and simulated experience—were effective in recalibrating patients' risk perceptions, leading to a more accurate evaluation of the benefits and harms of strong opioids. Both were also effective in improving patients' subjective risk evaluation of opioids' harms.

There were notable differences between the two education formats, with important implications for practice. First, more patients arrived at correct numerical estimates of opioids' benefits and harms after the descriptive intervention than after the simulated experience intervention. This finding is not in line with findings from other domains [e.g., 32, 45]. A possible explanation for this deviation is that to achieve some degree of comparable interactivity between the descriptive and the simulated experience format, the descriptive format in our study was not static, as is commonly the case, but interactive insofar that it required participants to move the mouse pointer to access each of the numerical values. While the simulated experience format offered comparable opportunities for active involvement (e.g., by interactive filter functions for exploring different information separately) the only necessary active behavior for participants to access the risk information was to press the "play" button in order to start the simulation; the use of all other features was optional. Only 15 of the 150 patients in the simulation group chose to restart the simulation or filter out specific benefit or harm outcomes. This means that only 10% harnessed the pedagogical and informative potential of the simulation. The rather inferior finding regarding patients' objective risk assessment documented in our trial suggest that the superiority of simulated experience formats over descriptive formats—documented in earlier research—might have partially been driven by a difference in the required active involvement between their used formats.

Second, although the simulated experience format was less effective than the descriptive format in improving patients' overestimations of the benefits and underestimations of the harms of long-term strong opioid use, it was equally effective in improving patients' subjective risk assessment: Patients in both groups were more likely to acknowledge the long-term harms of opioids after intervention. Both formats thus fostered meaningful gist knowledge [46, 47]—that is, both boosted patients' understanding of the bottom-line meaning of the benefit–harm ratio.

Third, patients in the simulated experience intervention reported significantly more often than patients in the fact box group that their actual opioid intake had changed. A greater proportion of patients in the simulated experience group indicated having started an alternative therapy; this was also the case for implementing intended behavior [48] after 9 months. Furthermore, patients in the simulated experience group reported more than twice as often as patients in the fact box group that they had terminated their opioid intake (15.3% of 118 vs. 7.4% of 123). One possible explanation for these results is that the sequential nature of the interactive simulation offers insight into the temporal dynamics behind the benefit–harm ratio—namely, that potent but risky drugs may initially offer benefits, but rare, serious, and increasingly more impactful harms emerge over time. This insight may have motivated people to consider alternative therapies. Indeed, we found that patients in the simulation group were more likely to start an alternative therapy with non-opioids than those in fact box group. Subsequent studies should examine the processes behind these differences in descriptive and simulated experience risk education in order to offer more detailed insight into how to further optimize descriptive and simulated experience interventions.

Medical risk literacy—known to affect numeracy—did not influence patients' objective or subjective risk perception, nor did it affect actual opioid intake behavior or uptake of alternative therapies at the 9-month follow-up. We assume that this was due to the fact that all educational material in our RCT was designed in accordance with guidelines for evidence-based health information [49], which requires a high degree of informational transparency in order to foster understanding of the numerical information. Patients who experienced a high degree of impairment due to their pain were less likely to change their positive subjective view on the benefits of strong opioids. This may be due to the fact that of those patients who reported an impairment of 6 or stronger (n = 205/300) on all three of the disability items listed in the Korff grading, 85.4% had already tried several other medical and nonmedical therapies. Some of these patients might have resisted pessimistic outlooks on strong opioids, given that they had few or no other options for effective pain treatment. Educating patients with chronic noncancer pain transparently and offering evidence-based information about opioids' benefits and harms before

prescribing any treatment might offer the best chance for keeping patients open to alternative pain management options.

Our study has limitations. First, our results are based on a convenience sample. Our analysis of people who prematurely left the survey shows some differences in age, gender, education, and region between respondents and nonrespondents, which limits the generalizability of findings. Second, our trial was conducted during the COVID-19 pandemic, which may have influenced the time and effort participants were able to invest in the material, particularly in the interactive simulation. Third, our study was powered to detect a difference of 15 percentage points or greater. If there were meaningful yet smaller differences between the intervention groups, our sample size would have been too small to sufficiently detect them. Fourth, the online questionnaire employed forced-choice items, which might have led a higher dropout rate. However, for online-based questionnaire surveys, dropout rates ranging from 20% to over 40% have been reported regardless of the presence of forced-choice items [50]. Of the 344 eligible participants who started our survey, 44 dropped out. The resulting 13% dropout rate is lower than what has been observed in other survey research, suggesting that the forced-choice items in our trial did not significantly alter people's response behavior.

4.2 Conclusion

The ERONA trial involving patients with chronic noncancer pain provides first evidence that descriptive and simulated experience educational tools can boost patients' understanding of the benefits and harms involved in long-term use of strong opioids. Furthermore, we found that simulated experience interventions in particular can foster patients' willingness to make informed choices about less risky therapy alternatives. Our results also suggest that there may be a description–experience gap in risk perception and risk behavior: While the descriptive format may be superior in boosting objective risk perception, the experiential format may be superior in boosting advantageous behavior and behavior change.

4.3 Practical implications

Our results suggest that health-related information should be conveyed differently depending on the goal of the educational intervention. If the goal is to improve patients' exact numerical knowledge about the benefits and harms of a risky drug, thereby fostering informed choice, a descriptive format with numerical transparency may be appropriate. If the goal is to boost patients' commitment to their intention to reduce or stop taking risky drugs and to promote a change in their consumption of the drug, simulated experience formats might be more suitable.

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Data availability: The data set from which the results were derived as well as details on the construction and content of the simulation can be made available to authorized individuals upon written request to the authors. Additional information will be made publicly available via the Open Science Framework under https://osf.io/swqpm/ when the ERONA project is concluded (anticipated: December 2021).

Declaration of interests: Claudia Spies reports interests from outside the submitted work. The other authors declare no competing interests.

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Figure 1: Descriptive and simulated experience risk education formats. Panel A: The descriptive risk education format used in the ERONA trial. Online, the numerical values were concealed and participants had to move the mouse pointer over the respective boxes on the screen to access the information. Panel B: In the interactive simulation used in the ERONA trial, participants could observe changes over time by moving a horizontal slider and explore specific risks by activating/deactivating the respective buttons.

Figure 2. Patients' risk estimates for each benefit and harm outcome before and after intervention per group (descriptive format [fact box] and simulated experience format [interactive simulation]). The red area within the dashed lines marks estimates within the ±10% margin of error of the correct number.

Figure 3. Patients' subjective risk perception before and after the intervention per group.

Figure 4. Actual opioid intake behavior per intervention group at 9-month follow-up.

Table 1. Demographic characteristics of the survey sample (per intervention group, in total) and nonrespondents (patients who abandoned the survey prematurely) (in total).

	Respondents Fact box (*n* = 150)	Respondents Simulation (*n* = 150)	*p**	Respondents (Total) (*N* = 300)	Non-respondents (*N* = 44)
	Percentage§			Percentage	
Female	52.7	44.7	*0.204*	48.7	45.0
Age (in years)			*0.298*		
<20	0	0		0	0
20–39	11.3	7.3		9.3	7.0
40–59	53.3	61.3		57.3	43.0
60–79	35.3	31.3		33.3	39.0
≥80	0	0		0	11.0
Education			*0.645*		
Lower secondary education	14.7	16.7		15.7	27.0
Secondary education	48.0	42.7		45.3	48.0
Upper Secondary education	37.3	40.7		39.0	25.0
Region of household			*0.303*		
North Germany	22.0	21.3		21.7	14.0
East Germany	29.3	21.3		25.0	20.0
South Germany	24.7	25.3		25.3	32.0
West Germany	24.0	32.0		28.0	34.0

* Based on chi-squared test, significance is two-tailed.
§ Percentages are rounded and may not total 100.

Table 2. Influence of descriptive versus simulated experience risk education format on patients' objective risk perception about the benefits and harms of long-term administration of strong opioids.

	Risk formats										
	Fact box (descriptive format) (n = 150)			Interactive simulation (simulated experience format) (n = 150)			Fact box vs. simulation				
								Before Intervention		After Intervention	
	Before intervention: Mean estimate (SD) Proportion of correct estimates (%)§	After intervention: Mean estimate (SD) Proportion of correct estimates (%)§	p* (r^2)&	Before intervention: Mean estimate (SD) Proportion of correct estimates (%)§	After intervention: Mean estimate (SD) Proportion of correct estimates (%)§	p* (r^2)&	Correct estimate	Mean difference	p** (r^2)&	Mean difference	p** (r^2)&
Reduction in pain	78.5 (22.2) 1.3%	44.5 (15.6) 46.7%	< 0.001* (0.84)	78.6 (20.8) 2.7%	48.7 (16.7) 35.3%	<0.001* (0.84)	41	0.1	.981	4.2	0.025* (0.13)
Increase in physical function	59.1 (19.1) 11.3%	56.4 (8.8) 70.7%	0.073	59.8 (18.0) 14.6%	57.1 (8.5) 67.3%	0.049* (0.16)	60	0.7	.718	0.7	0.468
Risk of falls/ fractures	13.7 (12.0) 1.3%	10.6 (5.7) 38.0%	0.001* (0.24)	15.2 (12.6) 2.6%	10.4 (4.7) 22.7%	<0.001* (0.39)	8	2.5	.292	0.2	0.834

Risk of misuse/ addiction	8.3 (8.0)	6.6 (3.8)	0.010* (0.20)	10.0 (9.5)	6.4 (3.6)	0.021* (0.39)	6	1.7	.095	0.2	0.619
	13.4%	64.7%		13.4%	58.7%						
Risk of dizziness	31.8 (15.2)	28.8 (8.6)	0018* (0.20)	32.1 (16.4)	29.1 (8.0)	<0.001* (0.19)	27	0.3	.887	0.3	0.759
	18.7%	67.3%		15.3%	62.7%						
Risk of nausea, obstipation, vomiting	36.6 (16.4)	58.8 (10.6)	<0.001* (0.76)	37.0 (18.1)	56.3 (10.5)	<0.001* (0.69)	65	0.4	.854	2.5	0.040* (0.12)
	6.0%	64.0%		7.4%	58.0%						

* Based on a dependent t-test, significance level is two-tailed.

** Based on an independent t-test, significance level is two-tailed.

§ Correct estimates, provided by the participants, within a ±10% margin of error.

& Effect size r^2 is only provided for significant p-values.

Table 3. Alternative therapies per intervention group—reported at 9-month follow-up (T2)—started by patients since they indicated (T1) an intention to take up an alternative therapy.

Alternative therapies among patients indicating having started an alternative therapy between study waves T1 and T2	Fact box intervention	Interactive simulation intervention	*p**
	n = 33 (of 123)	*n* = 47 (of 118)	*(r^2)*[&]
	n (%)	n (%)	
Drug therapy with non-opioids	9 (27.2)	24 (51.1)	*0.031** *(0.25)*
Physiotherapy, ergotherapy, manual therapy	15 (45.5)	24 (51.1)	*0.621*
Endurance/rehabilitation sports, swimming	12 (36.4)	11 (23.4)	*0.222*
Massages, cold/hot therapy	1 (3.0)	3 (6.4)	*0.639*
Transcutaneous electrical nerve stimulation (TENS), acupuncture	2 (6.1)	6 (12.8)	*0.459*
Relaxation techniques	15 (45.5)	16 (34.0)	*0.355*
Mindfulness training	3 (9.1)	5 (10.6)	*1.000*
Psychotherapy	1 (3.0)	9 (19.1)	*0.016** *(0.28)*
Multimodal therapy	6 (18.2)	8 (17.0)	*1.000*

*Based on an independent t-test, significance level is two-tailed.

[&] Effect size r^2 is only provided for significant p-values.