



Changing understanding, perceptions, pain relief of and preference for generic medicines with patient education: An experimental intervention study

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ABSTRACT

Background: Generic medicines have been associated with less perceived efficacy and more side effects compared to brand name drugs. Educational interventions to improve individuals' negative perceptions of generic medicines show contradictory effects.

Objective: This study investigated whether an interventional video that informs about the approval process of releasing medicines has better effects on outcomes related to perceptions and effectiveness of generic medicines in participants with headaches, in comparison with another interventional video that addresses bioequivalence between brand name and generic drugs or a control video.

Methods: Participants with frequent tension headaches were randomized to one of three groups (one of two interventional videos or the control video). One of the interventional videos explained the process of approval of generic medicines ($n = 34$), the other one explained the bioequivalence between brand name and generic drugs ($n = 35$). The control video informed participants about the epidemiology and etiology of headaches ($n = 34$). After watching the video, participants treated their next two consecutive episodes of headache with a brand name and a generic analgesic in randomized order.

Main outcome measures: Self-report measures of understanding and perceptions of and preference for medicines, pain severity and side effects.

Results: Linear mixed models showed that both interventional videos improved participants' understanding of generic medicines. The generic drug approval process video enhanced the perceived effectiveness, safety and quality of generic drugs. The bioequivalence video positively influenced the preference for generic drugs. The brand name and generic drug were equally effective in relieving pain in participants who watched either the generic drug approval process or the bioequivalence video.

Conclusions: Information about both, approving a switch from brand name medicines to generic counterparts and bioequivalence, can be important and should be addressed in future educational interventions.

Introduction

The World Health Organization (WHO) defines a generic drug as a “pharmaceutical product, usually intended to be interchangeable with the innovator product, which is usually manufactured without a license from the innovator company and marketed after the expiry of patent or other exclusivity rights.”¹ This interchangeability can be ensured by the principle of bioequivalence. According to the Food and Drug Administration (FDA) of the USA, bioequivalence is given when a generic drug is identical in dosage, form, safety, strength, route of administration,

quality, performance characteristics and intended use to the innovator product.² In contrast to the generic drug that is usually labeled with the name of the active ingredient, innovator drugs are often marketed with a brand name. In the following we therefore use the term “brand name drug” whenever we refer to an innovator product. A recently published analysis of a database of US health insurance claims with more than 3.5 million patients showed that generics provided comparable clinical outcomes to those of the brand name drugs for different chronic somatic and mental health conditions.³

Prescribing generic instead of brand name drugs has become more

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and more common. Pressure on health expenditure has increased worldwide and health authorities have generally encouraged the use of generic medications as a way of containing drug costs, as generics typically offer cost savings of between 30% and 60% of the price of brand name medicines.^{4,5} Although the bioequivalence of generic drugs with brand name counterparts has to be ensured, there are occasional case reports of patients who showed deteriorating clinical outcomes, lowered adherence, and side effects after using generic medicines.^{6,7} However this seems to happen in definable groups of patients, e.g. patients who underwent generic substitution of psychotropic medication.^{6,7} A substantial proportion of the general population perceives generic medicines with skepticism. Around 20–30% of the population view generic drugs as less effective and of poorer quality than their branded counterparts.⁸

The label “generic” in itself has been associated with negative expectations and beliefs that can contribute to less efficacy and more side effects from the drug.⁹ For example, branding a well-known pain medication can make it significantly more effective at relieving headache compared to the same medication unbranded.¹⁰ An experimental study demonstrated that the change of a medication formulation, to a generic formulation in particular, reduced the effectiveness of the medication and increased side effects.¹¹ In New Zealand a new, generic formulation of a thyroid hormone replacement drug was introduced and after the formulation change received extensive media coverage, the number of adverse reaction reports increased dramatically.¹² In a recently published study, perceptions of and preferences for generic compared to brand name drugs were investigated in patients who switched from either a generic or a brand name antidepressant to a new generic medicine. A greater proportion of patients who originally took a brand name antidepressant, compared to those who previously took a generic one, perceived their new medication as less effective, less safe and as having more side effects. Patients’ report of side effects was the same in both groups.¹³

In summary, the results of these previous studies encourage research on interventions to change individuals’ perceptions of generic medicines and to establish more accurate views on generic drugs. In two previous studies, patients’ acceptance of a substitution of their brand name medicine for a generic was significantly increased by an educational video.^{14,15} The interventions in both studies focused on differences between both types of drugs in terms of advantages of the generic drug (e.g., lower costs). A recent study in a group of participants with frequent headaches examined the impact of an educational intervention on perceptions, efficacy and side effects of a generic analgesic compared to a branded equivalent.¹⁶ The intervention addressed common misperceptions of generic medicines and emphasized the bioequivalence of generic and brand name medication. In contrast to a control intervention, the experimental intervention was successful in increasing the reported preference for generic medicines and in improving the understanding of generic medication. However, despite the change in acceptance of generic medication, a paradoxical effect was demonstrated, showing that participants in the intervention group reported less pain relief and more symptoms after taking the generic analgesic compared to taking the brand name medication. A possible explanation for this effect was that the experimental intervention shifted participants’ attention to the value of branding (e.g., perceived higher quality of the brand name medicine) and thus paradoxically improved the response to the brand name drug relative to the generic drug.

Recent studies have demonstrated that trust in the pharmaceutical industry and medicines is an important predictor of patients’ perceived efficacy of a drug.^{13,17} It could be possible that just focusing on bioequivalence between brand name and generic drugs, as has been the approach in most of the educational interventions in earlier research, is not a sufficient strategy to increase patients’ trust. An earlier study in community pharmacies showed that around 30% of the customers had low trust in the bioequivalence between generic and brand name drugs.¹⁸ Amongst other factors in this study, participants’ lower trust

was associated with their disagreement that generic substitution saves money for the consumer or for the society.¹⁸ It could be possible that trust in medicines could be increased by informing patients about the approval process of medicines. For example, a recently published study demonstrated in patients with chronic diseases that, although 89% believed that the drug agency of their home country ensures safety and effectiveness of generic medicines, 74% expressed little familiarity with the approval process for generic drugs.¹⁹ The central aim of the current study was to examine the effect of an interventional video that focuses on improving knowledge about the approval process of generic drugs on the understanding and perceptions of and preference for generic drugs as well as pain relief and side effects.

Accordingly, a brief video intervention was developed specifically for use in this study that explained the process of how the release of generic medicines is approved, i.e., the pathway from the expiring patent of the brand name drug to the license to manufacture a generic drug through to the final switch from brand name to generic drug formulations. It was hypothesized that this “generic drug approval process” video would improve our participants’ understanding and perceptions of and preference for generic drugs significantly more than a video addressing drug bioequivalence and a control video, which have already been developed for use in an earlier study by Colgan et al.¹⁶ It was also predicted that the generic drug approval process video would help to reduce the negative effect of the label “generic” on the analgesic’s pain relief and side effects compared to the bioequivalence and the control video.

Methods

Participants

Participants were recruited between September and November 2018 from the University of Auckland via flyers, email-notices, pre-lecture presentations, and posts on social media. To participate in the study the following inclusion criteria had to be met: a) able to read and write in English; and b) experience approximately ≥ 1 headache in an average 2-week period. Participants were excluded if they a) had known allergies to ibuprofen or other non-steroidal anti-inflammatory medications, b) had medical conditions such as asthma, history of stomach ulcers or bleeding, high blood pressure, impaired kidney function or heart failure, cluster headaches or headaches with associated neurological symptoms (e.g., weakness, sensory change or visual disturbance), c) had known allergies to the inert components of the tablets (e.g., croscarmellose sodium), d) were women who were pregnant or breastfeeding, or e) had a postgraduate degree or PhD in psychology. Participants who reported to be diagnosed with migraines were included as long as they experienced both tension-type headache and migraine headache episodes and were able to distinguish between both. They were instructed to take the study medication only for episodes of tension-type headache. All health information in this study was gained from participants’ self-report only. Participants’ medical files were not accessed. The study was registered *a priori* at Open Science Framework and at [Aspredicted.org](https://aspredicted.org) (registration number: 14,786). The study was approved by the University of Auckland Human Participants Ethics Committee.

Study procedure

Individuals interested in participating in the study were emailed a participant information sheet and a checklist of eligibility criteria. Those who confirmed meeting all eligibility criteria were emailed an invitation to a lab appointment. Individuals who experienced both tension-type headache and migraine headache episodes were asked to describe the nature of their tension-type headache and migraine flares. We only included participants who described unique symptoms of their tension-type headaches (e.g., bilateral location, pressing or tightening [non-pulsating] quality, not aggravated by routine physical activity, no

nausea or vomiting, no photo- or phonophobia)²⁰ and of their migraines (e.g. unilateral location, pulsating quality, aggravation by routine physical activity, nausea, vomiting, photo- or phonophobia, eventually aura)²⁰ and who were able to distinguish between both forms of headaches. At the beginning of this appointment participants first completed a questionnaire (*pre-video*) and provided written informed consent. Participants were randomly assigned to one of the three video interventions (two interventional and one control video). The randomization was conducted by a research associate, not affiliated with the study, using a random number generator. Group allocation was provided in sealed opaque, sequentially numbered envelopes to the experimenter.

After watching their allocated video, participants filled in the post-video questionnaire (*post-video*). They were then given pain medication to take home and treat their next two consecutive headaches: one dose of 400 mg of each, a brand name and a generic ibuprofen. Participants were explicitly told which drug was generic and which was a brand name by the experimenters. Each drug bag had a sticker that clearly indicated the brand name and the generic drug. The order of taking the brand name product and the generic medicine was randomized. At both of the next two consecutive episodes of headache, participants were asked to complete a paper copy questionnaire before and 1 h after taking the ibuprofen (*pre-* and *post-medication* assessment at follow-

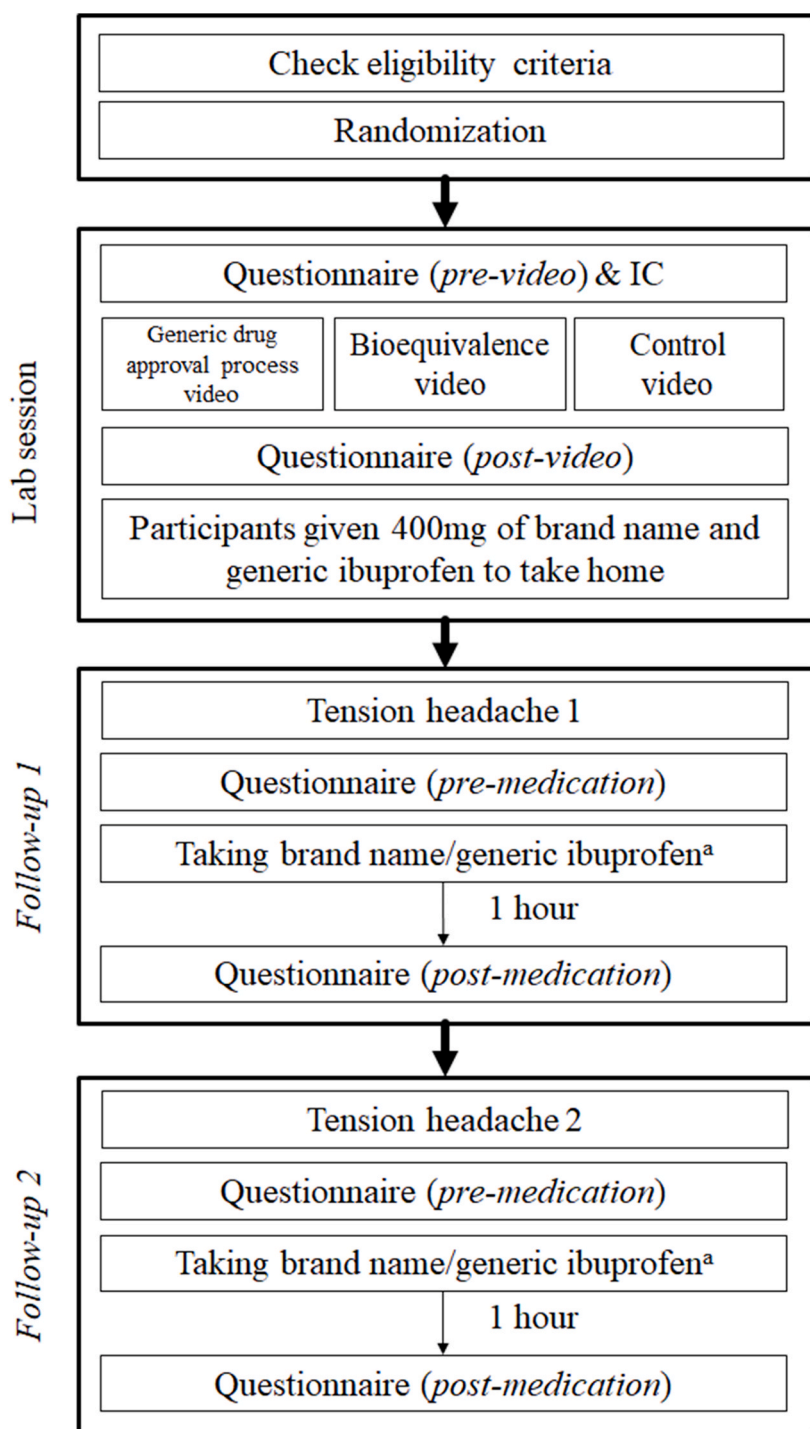


Fig. 1. Study procedure (IC = informed consent, ^athe order of taking the brand name and the generic ibuprofen was randomized).

up 1, i.e., the first episode of headache after the lab session] and follow-up 2 [i.e. the second, consecutive episode of headache after the lab session]). Participants were asked to record the dates of when the episodes of headaches happened and were provided with stamped and addressed envelopes to return the completed questionnaires. The study procedure is summarized in Fig. 1.

Interventional and control videos

The first intervention video was specifically developed for use in this study. We consulted a number of health specialists (physicians, a pharmacist, and experts involved in the approval and funding of generic medicines) who were interviewed and provided information about how generic medicines are approved. This video explained the process of how medicines and a switch from a brand name product to a generic drug formulation is approved in the participants' country of residence (*generic drug approval process* video). In addition, the video contained interviews with experts involved in the approval and funding process of generic drugs. The second interventional video had already been developed for use in the study by Colgan and colleagues.¹⁶ It explained the concept of bioequivalence between branded originator drugs and their generic counterparts (*bioequivalence* video). Health specialists were interviewed and provided accurate information addressing common misperceptions of generic medicines. The control video, which also had already been developed for use in the study by Colgan and colleagues,¹⁶ showed an interview with a consultant neurologist talking about different types of headaches, their epidemiology and factors that cause them (*control* video). All videos were between 7 min 50 s and 8 min long.

Measures

Outcomes

Understanding and perceptions of and preference for a generic medicine or a brand name equivalent were assessed with eight 10 cm visual analogue scales (VAS).¹⁶ Two VAS were administered to assess participants' *understanding* of medicines. Participants were asked about their understanding of what a generic medicine is and of what a brand name medicine is. We measured participants' *perceptions* of medicines regarding safety, quality, effectiveness and side effects with four VAS. We asked participants to rate the expected safety, quality, effectiveness, and side effects of a generic compared to a branded formulation of medicine. We used two VAS to assess participants' *preference* for a generic versus a brand name formulation of medicine in general, and in case of a serious illness. The complete eight VAS are provided in the Supplementary Online Material. Understanding and perceptions of and the preference for generics were assessed at *pre-video*, *post-video*, and *post-medication* at follow-up 2.

Participants were asked to indicate the *intensity of headache pain* on a 10 cm VAS before and 1 h after taking the ibuprofen medication (0 = no pain, 10 = worst possible pain) at the first and second follow-up (*pre- and post-medication* at follow-up 1 and 2). To assess *side effects* after taking the drug at the first and second follow-up (*post-medication* at follow-up 1 and 2), participants were asked to read a list of 52 symptoms and to indicate the symptom severity on a 4-point Likert scale (0 = not present to 3 = severe). Participants were instructed to indicate for each perceived symptom whether they thought it was a side effect caused by the ibuprofen (0 = no, 1 = yes, 2 = unsure). This list of symptoms included 46 items from the General Assessment of Side Effects Scale (GASE)²¹ and 16 other common symptoms frequently reported as side effects associated with ibuprofen use.

Control variables

Participants were asked about *sociodemographic variables* (sex, age, ethnicity, education, study subject), *pain characteristics* (frequency, duration of pain episodes during a typical day, previous treatments for headaches), *general health*, *health-care use* (GP visits during past 12

months) and about the *previous use of generic medicines* and *associated adverse events*. Participants' *general beliefs about medicines* were measured with the total score of the general subscale of the Beliefs About Medicines Questionnaire (BMQ)²² and *perceived sensitivity towards medicines* was assessed with the total score of the Perceived Sensitivity Towards Medicines Scale (PSMS)²³ before watching the video. High total scores on the BMQ-General indicated individuals' negative beliefs about medication (e.g., medicines are harmful and overused by doctors). High total scores on the PSMS indicated that individuals felt very sensitive towards the effects of medicines.

Participants also completed the Positive and Negative Affect Scales (PANAS)²⁴ to assess *positive and negative affect* before watching the video and the *emotional response* (state positive and negative affect) immediately after watching the video. Participants were asked at post-video to *evaluate the video* on three 11-point numerical rating scales (NRS), indicating how engaging (0 = not at all engaging, 10 = extremely engaging), how informative (0 = not at all informative, 10 = extremely informative), and how comprehensible the video was (0 = not at all easy to understand, 10 = extremely easy to understand).

Statistical analyses

With a power analysis for a study design including three groups we estimated that a minimum sample of 102 participants would be needed to examine a small group*ibuprofen formulation interaction effect on the change score of intensity of headache pain ($f = 0.18$), a power level of 0.90, an alpha level of 0.05, and an expected correlation among repeated measures of 0.5.

T-test, Chi²-tests and ANOVAs were used to examine differences in demographic, control and outcome variables between all three groups at baseline (pre-video). We considered several characteristics of the video (e.g., impact on participants' affective state, evaluation of video's informativity, comprehensibility and level of engagement) as important confounding variables because they can influence how individuals process the content of a video.^{25,26} These variables are related to both the dependent variable (i.e., understanding, perceptions, preference, pain relief and side effects) and the independent variable (i.e. type of video) and could represent an alternate reason to explain effects of our videos.²⁷ We have already tried to keep these confounders constant across our interventions (e.g., by using the same background music in all of our three videos). However, a well elaborated experimental study should include statistical methods to check whether potential confounding variables vary systematically between the study conditions. To investigate whether our intervention videos had a systematic effect on participants' affective state, two ANCOVAs with the post-video score of either the PANAS Positive Affect or Negative Affect subscale as dependent variable were conducted (independent variable: intervention, covariate: PANAS Positive Affect or Negative Affect subscale score at pre-video, respectively). Differences in participants' evaluation of certain characteristics of the interventional videos (perceived informativity, comprehensibility and level of engagement) were investigated with one-way ANOVAs.

Linear mixed models using a maximum likelihood estimation and an unstructured covariance matrix with the random effect of participant were used to investigate the effect of the intervention on the *understanding and perceptions of and preference for a brand name or a generic version of a medicine* over time (two predictors: intervention [generic drug approval process, bioequivalence and control video]; time [pre-video, post-video, post-medication at follow-up 2]). Linear mixed models were also used to investigate the effect of the intervention on *pain intensity* over time (three predictors: time [pre- and post-medication at follow-up 2]; version of medicine [brand name and generic drug]; intervention). Linear mixed models were finally used to investigate the effect of the intervention on the report of *side effects* after the use of ibuprofen (two predictors: version of medicine; intervention). Bonferroni-corrected, post hoc contrasts were used to break up

significant main and interaction effects and to examine differences between intervention groups and between the two versions of ibuprofen. Perceptions of the allocated video and affect-related variables (PANAS) that showed significant differences between the intervention groups at post-video were added to all linear mixed models as covariates. The data were analyzed using IBM SPSS (Version 25). For all analyses an overall alpha level of 0.05 was applied.

Results

Participant characteristics

A sample of 103 eligible participants was randomized to the three intervention groups (generic drug approval process video: $n = 34$; bioequivalence video: $n = 35$; control video: $n = 34$; see Fig. 2). Loss to follow-up rates were low, 1 to 2 participants per group. Table 1 summarizes all participant characteristics at baseline (pre-video). The sample of this study was 66% female and on average 27 (SD = 8.46) years old. More than half of the sample were NZ Europeans (52%). The second largest ethnic group were Asians (37%). The remaining participants were from Maori, Pacific Island or from other ethnic backgrounds.

There were no differences between the intervention groups on any demographic or pain characteristics, participants' general symptoms report, general beliefs about medicines, perceived sensitivity towards medicines, general health rating, health-care use, previous experiences with generic medicines and trait affect (p -values $\geq .051$). Participants did not differ in the pre-video values on their understanding of, their perceptions of or preference for brand name or generic medicines (see Table 2, p -values $\geq .227$) or usual pain intensity (see Table 1).

The amount of time that passed between the lab appointment and taking the brand name ibuprofen or taking the generic ibuprofen did not differ between the intervention groups (see Table 1). The time the first and the second episode of headache happened after the lab appointment did not differ between the intervention groups (see Table 1). We also did not find differences between the brand name analgesic ($M = 8.78$, $SD = 10.64$) and generic ibuprofen ($M = 8.69$, $SD = 8.41$) in the number of days passing between the lab session and the use of the medication ($p = .798$).

Pre-analyses: participants' affect and evaluation of the interventional and control videos

After controlling for participants' level of trait positive affect, individuals in the three intervention groups did not differ in their level of *positive affect* after watching the allocated educational video, $F(2,100) = 1.84$, $p = .165$. Results of an ANCOVA, controlling for participants' level of trait negative affect, showed a main effect of the video on the level of *negative affect*, $F(2,100) = 4.16$, $p = .018$. Bonferroni-corrected post hoc tests revealed that participants in the generic drug approval process video group ($M = 10.88$, $SD = 1.53$; Mean Diff = 1.29, $p = .038$) and in the bioequivalence video group ($M = 11.03$, $SD = 1.45$; Mean Diff = 1.34, $p = .045$) had significantly lower negative mood than participants in the control video group ($M = 12.59$, $SD = 3.72$). There was no difference between participants in the generic drug approval process video group compared to those in the bioequivalence video group (Mean Diff = -0.05 , $p = 1.000$).

Participants' evaluation of how *informative* they found the allocated educational video ($F[2,100] = 0.94$, $p = .395$) did not differ between the intervention groups. However, the evaluation of how *engaging* ($F[2,100] = 5.79$, $p = .004$) and how *comprehensible* participants experienced the allocated video ($F[2,100] = 4.65$, $p = .012$) significantly varied between the intervention groups. Post hoc tests showed that the bioequivalence video ($M = 8.37$, $SD = 1.37$) was rated as significantly more engaging compared to the generic drug approval process video ($M = 7.38$, $SD = 1.52$; Mean Diff = 0.99, $p = .020$) and compared to the control video ($M = 7.32$, $SD = 1.43$; Mean Diff = 1.05, $p = .013$). The control video group and generic drug approval process video group did not differ in their ratings (Mean Diff = -0.06 , $p = .986$). Post hoc tests demonstrated that the bioequivalence video ($M = 9.49$, $SD = 0.74$) was evaluated to be easier to understand compared to the generic drug approval process video ($M = 8.59$, $SD = 1.62$; Mean Diff = 0.90, $p = .013$). The remaining post hoc tests of the level of understanding did not result in significant group differences (p -values $\geq .163$). According to the results of these pre-analyses, the following linear mixed models were controlled for the level of negative affect and participants' evaluations of the allocated video (how engaging and easy to understand participants experienced the video) at post-video.

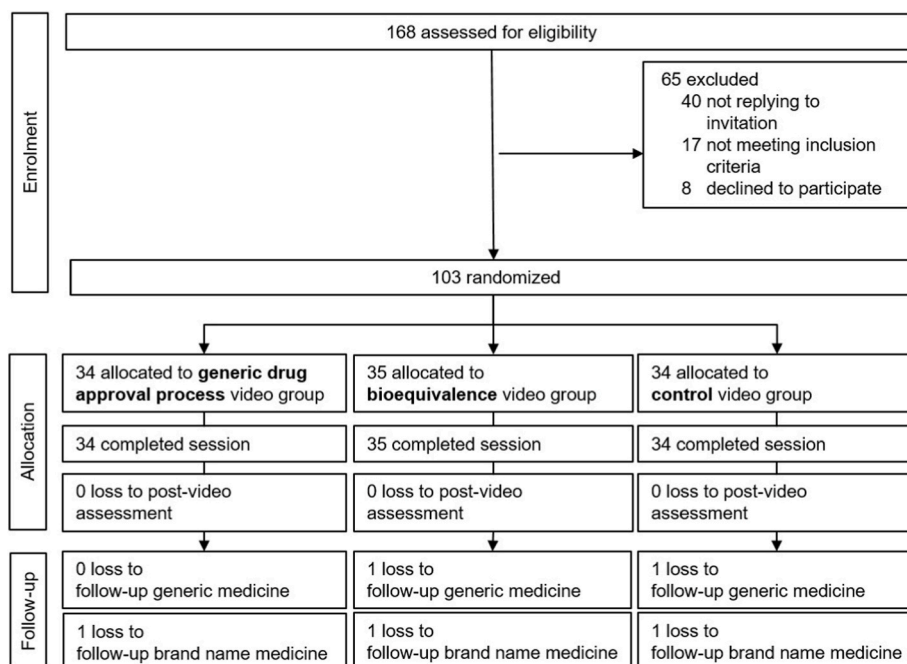


Fig. 2. CONSORT flow diagram.

Table 1

Differences in demographic, pain characteristics, perceived health status, symptom report, health-care use, beliefs about medicines, perceived sensitivity towards medicines, previous experiences with generic medicines, trait affect at baseline (pre-video).

	Total sample N = 103		Generic drug approval process video n = 34		Bioequivalence video n = 35		Control video n = 34		Test statistics
	n ^d /M ^e	% ^d /SD ^e	n/M	%/SD	n/M	%/SD	n/M	%/SD	
Sex (female)	68	66.0%	22	64.7%	20	57.1%	26	76.5%	$\chi^2(2, N = 103) = 2.91, p = .233$ F (2,100) = 0.39, p = .677 p = .750 ^a
Age (years)	26.65	8.46	25.76	7.79	26.60	7.93	27.59	9.69	
Ethnicity									
NZ European/European	53	51.5%	14	41.2%	19	54.3%	20	58.8%	p = .879 ^a
Maori/Pacific Islander	7	6.8%	3	8.8%	3	8.6%	1	2.9%	
Asian	38	36.9%	15	44.1%	12	34.3%	11	32.4%	
Other ^b	6	5.8%	3	8.8%	1	2.9%	2	5.9%	
Education & employment status									p = .207 ^a
Undergraduate	60	58.3%	22	64.7%	19	54.3%	19	55.9%	
Graduate/Postgraduate	31	30.1%	10	29.4%	11	31.4%	10	29.4%	
Faculty	4	3.9%	0	0.0%	2	5.7%	2	5.9%	
Staff	8	7.8%	2	5.9%	3	8.6%	3	8.8%	p = 1.000 ^a
Study subject									
Medicine	24	23.3%	11	32.4%	8	22.9%	5	14.7%	
Pharmacy	2	1.9%	2	5.9%	0	0.0%	0	0.0%	
Psychology	20	19.4%	8	23.5%	6	17.1%	6	17.6%	
Health Science	5	4.9%	2	5.9%	3	8.6%	0	0.0%	$\chi^2(4, N = 103) = 9.43, p = .051$
Other	32	31.1%	7	20.6%	11	31.4%	14	41.2%	
Headache frequency									
1–2 headaches/week	88	85.4%	30	88.2%	29	82.9%	29	85.3%	
3–4 headaches/week	11	10.7%	3	8.8%	4	11.4%	4	11.8%	$\chi^2(2, N = 103) = 1.05, p = .618$ $\chi^2(2, N = 103) = 0.69, p = .764$ $\chi^2(2, N = 103) = 0.73, p = .748$ p = .771 ^a p = .236 ^a $\chi^2(2, N = 103) = 0.42, p = .869$ $\chi^2(2, N = 103) = 0.69, p = .758$ $\chi^2(2, N = 103) = 1.18, p = .584$ $\chi^2(2, N = 103) = 0.62, p = .747$ $\chi^2(2, N = 103) = 1.58, p = .438$ $\chi^2(2, N = 103) = 2.90, p = .246$ p = .170 ^a p = .097 ^a F (2,100) = 1.74, p = .181 F (2,100) = 0.39, p = .679
≥5 headaches/week	4	3.9%	1	2.9%	2	5.7%	1	2.9%	
Headache duration									
<1 h	41	39.8%	17	50.0%	8	22.9%	16	47.1%	
≥1 h/<4 h	44	42.7%	10	29.4%	25	62.9%	12	35.3%	
≥4 h	18	17.5%	7	20.6%	5	14.3%	6	17.6%	
Previous treatments									F (2,100) = 1.74, p = .181 F (2,100) = 0.39, p = .679 F (2,100) = 11.55, p = .644 F (2,99) = 1.36, p = .262 F (2,100) = 2.78, p = .067 F (2,100) = 1.88, p = .158 F (2,100) = 280, p = .756 p = .694 ^a p = .844 ^a F (2,100) = 0.33, p = .720 F (2,100) = 0.53, p = .589 F (2,100) = 0.83, p = .440
No treatment	27	26.2%	9	26.5%	11	31.4%	7	20.6%	
Paracetamol	80	77.7%	28	82.4%	26	7.4%	26	76.5%	
Ibuprofen	70	68.0%	22	64.7%	23	65.7%	25	73.5%	
Aspirin	3	2.9%	0	0.0%	2	5.7%	1	2.9%	
Other medication	9	8.7%	1	2.9%	3	8.6%	5	14.7%	
Massage	22	21.4%	6	17.6%	8	22.9%	8	23.5%	
Relaxation	22	21.4%	7	20.6%	9	25.7%	6	17.6%	
Rest	52	50.5%	17	50.0%	20	57.1%	15	44.1%	
Sleep	71	68.9%	25	73.5%	24	68.6%	22	64.7%	
Avoiding activity	21	20.4%	7	20.6%	5	14.3%	9	26.5%	
Drinking water	74	71.8%	28	82.4%	24	68.6%	22	64.7%	
Heat/cold pack	12	11.7%	3	8.8%	2	5.7%	7	20.6%	
Other treatment	10	9.7%	3	8.8%	1	2.9%	6	17.6%	
Average GP visits (past 12 months)	3.94	3.85	3.53	3.22	4.91	5.16	3.35	2.53	
General health rating ^c	2.89	0.67	2.97	0.67	2.83	0.66	2.88	0.69	
Amount of time (days) that passed between the lab appointment and taking the brand name ibuprofen	8.78	10.64	8.27	7.18	6.79	5.93	11.33	15.85	
generic ibuprofen	8.61	8.41	8.44	6.35	8.29	9.65	9.12	9.10	
Amount of time (days) that passed between the lab appointment and the first episode of headache	5.44	5.08	5.79	5.64	4.76	4.89	5.76	4.76	F (2,100) = 11.55, p = .644 F (2,99) = 1.36, p = .262 F (2,100) = 2.78, p = .067 F (2,100) = 1.88, p = .158 F (2,100) = 280, p = .756 p = .694 ^a p = .844 ^a F (2,100) = 0.33, p = .720 F (2,100) = 0.53, p = .589 F (2,100) = 0.83, p = .440
second episode of headache	11.99	11.69	11.00	6.79	10.32	9.46	14.70	16.51	
Symptom report past week (GASE)	23.81	14.86	23.24	13.03	20.03	9.22	28.26	19.74	
Beliefs about medicines (BMQ)	19.28	5.09	19.85	5.32	17.94	3.96	20.09	5.73	
Perceived sensitivity medicines (PSM)	10.29	2.89	10.38	2.59	10.00	2.97	10.50	3.13	
Previous intake of generics	91	88.3%	30	88.2%	32	91.4%	29	85.3%	
Previous AE with generic medicine	4	3.9%	1	2.2%	1	2.9%	2	5.9%	
VAS usual pain intensity	5.25	1.72	5.14	1.79	5.17	1.80	5.45	1.57	
PANAS-Positive Affect	32.13	6.67	33.09	7.23	31.54	6.73	31.76	6.12	
PANAS-Negative Affect	18.23	5.80	17.47	5.25	18.00	5.62	19.24	6.49	

Note.

Cell values report either absolute value/percentage or mean/standard deviation.

AE = adverse effects; GP = general practitioner; BMQ = Beliefs About Medicines Questionnaire; PSM = Perceived Sensitivity Towards Medicines Scale; GASE = General Assessment of Side Effects Scale; PANAS = Positive Affect Negative Affect Scale; VAS = Visual Analogue Scale.

^a Fisher's exact test, exact significance (2-sided).

^b Middle East, South America, South Africa.

^c 4-point Likert scale (1 = poor, 2 = fair, 3 = good, 4 = excellent).

^d n and % are reported for categorical variables.

^e M and SD are reported for continuous variables.

Table 2

Raw mean values and standard deviations (before and after watching the video and after taking the medication after the second episode of headaches) and test statistics of the linear mixed models of the effect of the video interventions on understanding of, perceptions of and preference for generic compared to brand name drugs.

	Generic drug approval process video			Bioequivalence video			Control video			Main effect intervention	Main effect time	Intervention* time interaction
	Pre	Post	FU-2	Pre	Post	FU-2	Pre	Post	FU-2			
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)			
Understanding branded drugs	8.29 (1.75)	9.25 (1.22)	9.15 (1.09)	8.74 (1.68)	9.44 (1.30)	9.46 (0.73)	8.37 (1.89)	8.33 (1.97)	8.52 (1.81)	F (2,103) = 1.58 p = .210	F(2,102) = 8.10 p = .001	F (4,102) = 2.19 p = .075
Understanding generic drugs	7.94 (1.90)	9.17 (1.19)	8.87 (1.40)	8.65 (1.80)	9.66 (0.53)	9.37 (0.77)	8.14 (1.55)	8.31 (1.51)	8.28 (1.84)	F(2,103) = 4.48 p = .014	F(2,101) = 14.70 p < .001	F(4,102) = 4.24 p = .003
Quality	4.41 (1.43)	5.32 (1.14)	5.58 (1.76)	4.63 (1.41)	5.05 (0.82)	4.86 (0.67)	4.58 (1.97)	4.83 (1.84)	4.94 (1.87)	F (2,103) = 2.74, p = .070	F(2,103) = 4.21 p = .017	F (4,103) = 2.01 p = .099
Effectiveness	4.87 (1.43)	5.57 (1.34)	5.40 (1.50)	4.81 (1.43)	5.07 (0.82)	5.08 (0.74)	4.80 (1.76)	5.09 (1.72)	5.02 (1.76)	F(2,103) = 3.19 p = .045	F(2,103) = 4.18 p = .018	F(4,103) = 2.35 p = .059
Safety	4.86 (1.66)	5.76 (1.43)	5.28 (1.31)	5.28 (1.11)	5.29 (0.81)	5.24 (1.13)	5.27 (1.48)	5.06 (1.50)	5.34 (1.60)	F (2,103) = 2.07 p = .132	F (2,99) = 1.91 p = .308	F(4,99) = 6.33 p < .001
Side effects	5.17 (1.39)	5.29 (1.08)	5.49 (1.36)	5.10 (1.21)	5.06 (0.75)	4.99 (1.05)	5.04 (1.43)	4.95 (1.57)	5.42 (1.96)	F (2,104) = 3.09 p = .050	F (2,101) = 0.88 p = .417	F (4,101) = 1.00 p = .413
Preference (general)	5.36 (2.46)	5.56 (1.86)	5.14 (1.93)	5.23 (2.53)	7.57 (2.45)	6.15 (2.05)	5.11 (2.62)	4.69 (2.18)	4.67 (1.95)	F(2,102) = 14.03 p < .001	F(2,102) = 3.84 p = .025	F (4,102) = 2.30 p = .064
Preference (serious illness)	3.90 (2.24)	5.11 (1.67)	4.72 (2.21)	4.55 (2.67)	6.05 (2.32)	6.08 (2.06)	4.51 (2.90)	4.28 (2.52)	4.36 (2.63)	F (2,104) = 1.65, p = .197	F(2,102) = 9.77 p < .001	F(4,102) = 4.60 p = .002

Note.

Pre = pre-video, post = post-video, FU-2 = follow-up 2.

Bold font indicates significance.

Effects of intervention

Understanding of brand name or generic medicines

A better understanding of either brand name or generic medicines was indicated by high values on the VASs assessing understanding of each version of the medicine.

Understanding of brand name medicines. A linear mixed model showed a significant main effect of time ($p = .001$), but no effect of intervention ($p = .210$). The time*intervention interaction ($p = .075$) did not reach significance (see Table 2 and Supplemental Online Material). Post hoc contrasts showed no differences between the intervention groups at post-video ($p \geq .073$). After the second headache (post-medication at follow-up 2), participants in the bioequivalence video group showed a significantly better understanding of brand name drugs compared to the control group ($p = .047$). The remaining post hoc between-group contrasts at follow-up 2 (post-medication) were not significant ($p \geq .499$). None of the covariates was associated with the outcome ($p \geq .513$).

Understanding of generic medicines. A linear mixed effect model revealed a significant effect of time ($p < .001$) and of intervention ($p = .014$) and a significant time*intervention interaction ($p = .003$; see Table 2 and Fig. 3). After watching the allocated video, participants in the generic drug approval process video group ($p = .002$) and in the bioequivalence video group ($p < .001$) indicated that they better understood the meaning of generic medicines than individuals in the control video group. At follow-up 2 (post-medication) only participants in the bioequivalence video group had a significantly better understanding of generic medicines compared to the control group ($p = .013$). All remaining post hoc contrasts between the intervention groups at post-video ($p = .532$) and follow-up 2 (post-medication) (p -values $\geq .290$) did not reach significance. None of the covariates had an effect.

Perceptions of brand name or generic medicines

Low scores of VASs indicated strong positive perceptions of brand name drugs, while a score of 5 indicated no perceived difference and

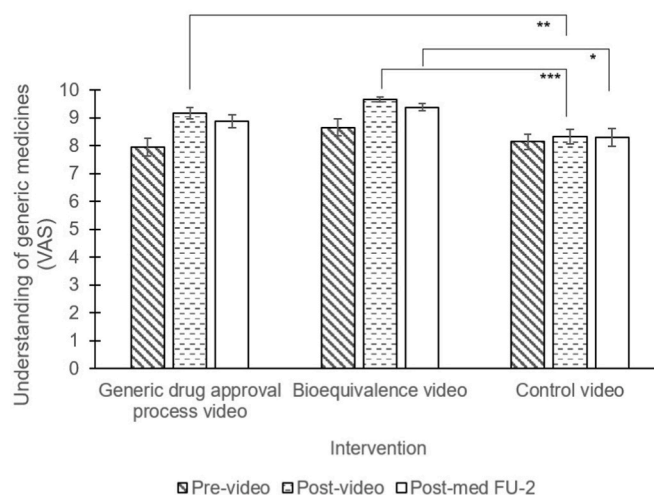


Fig. 3. Post hoc between-group contrasts at the assessment before and after watching the allocated video (pre- and post-video) and at the second follow-up (post-medication) regarding the understanding of a generic medicine (VAS = Visual Analogue Scale: high values indicate a better understanding, low values indicate less understanding; post-med FU-2 = post-medication at follow-up 2; * $p < .05$, ** $p < .01$, *** $p < .001$).

higher scores indicated strong positive perceptions of generic medicines. Before watching the allocated video, participants across all three intervention groups tended to perceive brand name medicines to be of higher quality and more effective than their generic counterparts (pre-video means: $4.41 \leq M \leq 4.87$). With regard to perceived safety and side effects of medicines, participants tended to perceive generic drugs slightly more positively than brand name drugs before watching the video (mean values at pre-video: $5.86 \leq M \leq 5.17$) (see Table 2).

Perceived quality. A linear mixed model resulted in a significant main effect of time ($p = .017$) and of intervention ($p = .070$). The time*intervention interaction did not reach significance ($p = .099$) (see Table 2 and Supplemental Online Material). Post hoc contrasts showed no between-group differences at post-video ($p \geq .065$). However, at the second follow-up (post-medication), participants who watched the generic drug approval process video rated the perceived quality of generic medicines significantly higher than participants in the bioequivalence video group ($p = .010$) and in the control group ($p = .011$). Bioequivalence and control video groups did not differ ($p = 1.000$). The covariates had no effect ($p \geq .153$).

Perceived effectiveness. The analysis showed a significant main effect of time ($p = .018$) and of intervention ($p = .045$). The time*group interaction ($p = .059$) slightly failed to gain significance (see Table 2 and Supplemental Online Material). Post hoc tests showed that participants who watched the generic drug approval process video had a significantly enhanced perception of the effectiveness of generic medicines at post-video compared to participants who watched the bioequivalence video ($p = .007$) or the control video ($p = .024$). Bioequivalence and control video groups did not differ ($p = 1.000$). The reported between-group differences at post-video diminished at follow-up 2 (post-medication) ($p \geq .056$). How engaging participants experienced their allocated video ($p = .036$), but none of the other covariates ($p \geq .318$), was associated with participants' perception of the effectiveness of generic medicines.

Perceived safety. A linear mixed model revealed neither an effect of the intervention ($p = .132$) nor of time ($p = .308$), but a significant time*intervention interaction ($p < .001$) (see Table 2 and Fig. 4). Post hoc tests showed that participants who watched the generic drug approval process video had a significantly enhanced perception of the safety of generic medicines at post-video compared to participants watching the bioequivalence video ($p = .005$) or the control video ($p < .001$). Bioequivalence and control video groups did not differ ($p = 1.000$). The reported group differences at post-video diminished at follow-up 2 (post-medication) ($p \geq .927$). Negative affect after watching the allocated video ($p = .017$) and how engaging participants experienced their allocated video ($p = .035$) were significantly associated with the perceived safety of medicines. How well participants understood the video did not have an effect as covariate ($p = .526$).

Perceived side effects. Results of the linear mixed model showed

neither main nor interaction effects (see Table 2). How engaging participants found the allocated video ($p = .020$), but none of the other covariates ($p \geq .105$), was significantly associated with perceived side effects of the analgesic.

Preference for brand name or generic medicines

Zero-values of the administered VASs indicated a preference for brand name drugs, a score of 5 indicated no preference and a score of 10 indicated a preference for generic medicines.

General preference for a generic or brand name drug. Before watching the video, participants across all groups had in general the tendency to prefer the generic over the brand name drugs ($5.23 \leq M \leq 5.36$, see Table 2). Mixed linear models revealed a significant effect of time ($p = .025$) and of intervention ($p < .001$). A group*intervention interaction ($p = .064$) did not reach significance (see Table 2 and Supplemental Online Material). Post hoc tests demonstrated that after watching the allocated video, the preference for generic medicines significantly increased in participants in the bioequivalence video group compared to individuals in the generic drug approval process video group ($p = .009$) and in the control group ($p < .001$). Participants in the generic drug approval process video and control video group did not differ ($p = .174$). After the second episode of headaches (post-medication at follow-up 2), individuals in the bioequivalence video group still preferred generic drugs significantly more than individuals in the control group ($p = .015$). All remaining post hoc contrasts at follow-up 2 ($p \geq .067$) indicated nonsignificance. How engaging participants found the video ($p = .027$), but none of the other covariates ($p \geq .382$), was related to the preference rating.

Preference for a generic or brand name drug when having a serious illness. In case of having a serious illness, participants across all intervention groups would have tententially preferred the brand name drug at baseline ($3.90 \leq M \leq 4.55$, see Table 2). A linear mixed model showed a significant main effect of time ($p < .001$), but not of intervention ($p = .197$). The time*group interaction effect became significant ($p = .002$, see Table 2 and Fig. 5). Post hoc contrasts showed that participants in the bioequivalence video group preferred generic medicines significantly more compared to participants in the control group at post-video ($p = .014$). This effect failed to reach significance at follow-up 2 (post-medication) ($p = .071$). No differences were found between individuals

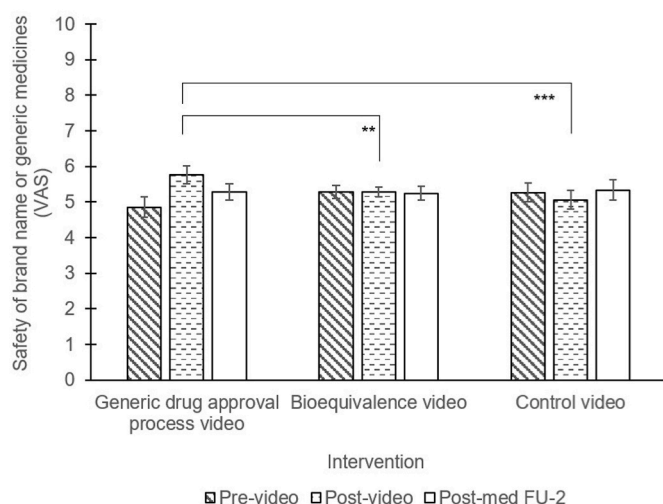


Fig. 4. Post hoc between-group contrasts at the assessment before and after watching the allocated video (pre- and post-video) and at the second follow-up (post-medication) regarding the perceived safety of generic compared to brand name drugs (VAS = Visual Analogue Scale: high values indicate strong positive perceptions of generic drugs, low values indicate strong positive perceptions of brand name drugs; post-med FU-2 = post-medication at follow-up 2; ** $p < .01$, *** $p < .001$).

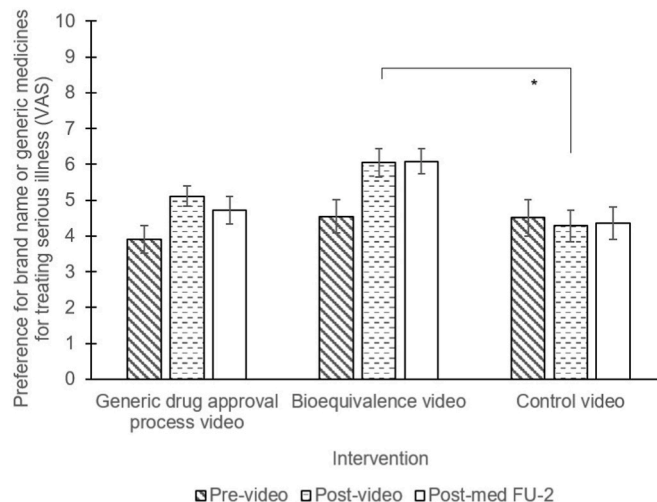


Fig. 5. Post hoc between-group contrasts at the assessment before and after watching the allocated video (pre- and post-video) and at the second follow-up (post-medication) regarding the preference for a generic or a brand name medicine for treating a serious illness (VAS = Visual Analogue Scale: high values indicate preference for generic medicines, low values indicate preference for brand name medicines; post-med FU-2 = post-medication at follow-up 2; * $p < .05$).

in the bioequivalence and generic drug approval process video group or between individuals in the generic drug approval process video group and the control group, either at post-video ($p \geq .234$) or at follow-up 2 (post-medication) ($p \geq .109$). None of the covariates had a significant effect ($p \geq .401$).

Headache intensity

A linear mixed model revealed a significant main effect of time ($F [1,96.07] = 332.52$, $p < .001$) and of the version of medicine ($F [1,99.55] = 4.67$, $p = .033$). The main effect of intervention ($F [2,102.29] = 2.73$, $p = .070$) was not significant. None of the interaction effects became significant (p -values $\geq .218$). The level of how engaging participants experienced the allocated video ($p = .013$), but none of the other covariates ($p \geq .214$), was associated with pain intensity. Post hoc contrasts comparing both versions of medicine showed that in participants in the control group pain intensity was significantly higher after taking the generic compared to the brand name drug ($p = .047$; see Fig. 6). No participants in the drug approval process video group ($p = .477$) or in the bioequivalence video group ($p = .547$) reported differences in the headache intensity after taking the generic compared to the brand name drug. In none of the groups were differences in pain intensity found before taking the brand name drug compared to taking the generic drug (p -values $\geq .314$). Mean and standard deviations of pain intensity are summarized in Table 3.

Side effects

The linear mixed model did not reveal a main effect of intervention ($F [2,103] = 1.55$, $p = .216$), but of the version of medicine ($F [1,103] = 4.43$, $p = .038$). The intervention*version of medicine interaction effect ($F [2,103] = 0.11$, $p = .896$) was not significant. None of the covariates was related to the report of side effects ($p \geq .428$). Post hoc tests did not reveal significant differences in the report of side effects after taking the generic compared to the brand name ibuprofen across all study groups ($p \geq .085$). Mean values and standard deviations are summarized in Table 3.

Discussion

The central aim of the current study was to examine the effect of a video intervention to improve knowledge about the process of approving generic drugs on different outcomes in headache patients. We hypothesized that the generic drug approval process video would have a better effect on all outcomes measured in our participants with headache compared to a video focusing on bioequivalence or a control video. The innovative aspect of our study was that the intervention video that was developed especially for use in this study explained the *process* of how generic medicines are released, i.e., the pathway from the expiring patent of the brand name drug to the license to manufacture a generic drug and finally to the switch from brand name to generic drug formulations. In contrast, educational interventions in previous studies mainly addressed the *bioequivalence* between generic and brand name drugs.

The first important finding was that, contrary to our hypothesis, the generic drug approval process video and the bioequivalence video had similarly positive effects on the understanding of generic drugs. Our findings from the bioequivalence video are partly consistent with the results of a previous study,¹⁶ which used the same bioequivalence video as we did. Colgan and colleagues¹⁶ demonstrated that the bioequivalence video improved both the understanding of brand name as well as generic medicines. The current study shows that it does not seem to matter whether an educational intervention focuses more on bioequivalence or more on the drug approval process. Both interventions, compared with a control group, equally improved the understanding of a generic drug specifically. Our participants evaluated both videos to be equally informative. Both videos provide important information about generic drugs, just from different perspectives. Colgan and colleagues¹⁶ showed an effect of the bioequivalence video on the understanding of brand name drugs. We could not demonstrate this effect in our study. It has to be considered that the participants of this study already had good knowledge about the different formulations of drugs before they watched the video compared with participants in the trial by Colgan and colleagues.¹⁶ This could probably explain why the effect of the interventional videos on the understanding of brand name medicines could not be demonstrated in our study.

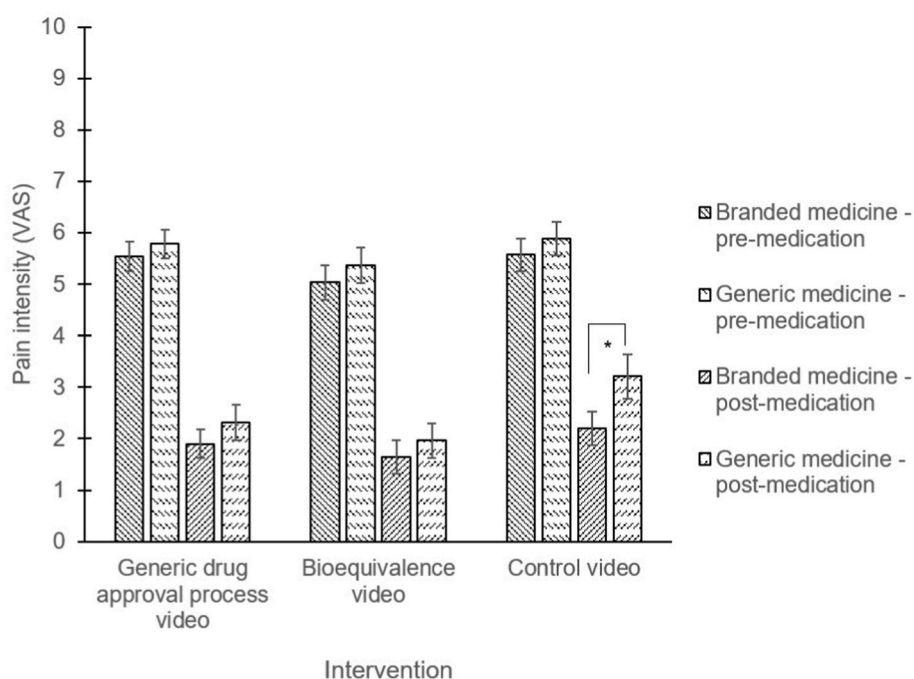


Fig. 6. Post hoc contrasts between the two versions of medicine after taking the medication (post-medication) regarding pain intensity (VAS = Visual Analogue Scale: high values indicate high pain intensity, low values indicate low intensity; * $p < .05$).

Table 3

Raw mean values and standard deviations of pain intensity (before and after taking the pain medication) and report of side effects (after taking the pain medication) at follow-up 2 (2nd episode of headaches).

	Generic drug approval process video				Bioequivalence video				Control video			
	Brand name drug		Generic drug		Brand name drug		Generic drug		Brand name drug		Generic drug	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
Pain intensity	5.54 (1.70)	1.90 (1.65)	5.78 (1.62)	2.31 (2.00)	5.03 (1.94)	1.64 (1.89)	5.36 (1.99)	1.96 (1.93)	5.57 (1.85)	2.20 (1.83)	5.89 (1.86)	3.21 (2.49)
Report of side effects		1.26 (2.11)		1.41 (1.94)		0.71 (1.25)		0.57 (1.09)		2.24 (4.43)		1.94 (4.07)

Note.

Pre = before taking the analgesic. Post = after taking the analgesic.

A second important finding was that the generic drug approval process video and bioequivalence video had differential effects on perceptions of and preferences for the different formulations of medicines. Aligned with our hypothesis, explaining how generics are approved was more successful in enhancing participants' perception of the quality, effectiveness and safety of generic medicines than explaining bioequivalence. These effects were only apparent immediately after watching the generic drug approval process video. Participants who received information about bioequivalence preferred generic medicines more often than participants in the control group or participants watching the generic drug approval process video.

The differential effects of our interventional video on perceptions of medicines and preferences for medicines is important to discuss. The preference for a generic medicine was increased after watching the video about bioequivalence, in particular. Colgan and colleagues¹⁶ showed a similar superior effect of the bioequivalence video compared with a control video on participants' preference for a generic drug. In contrast, the generic drug approval process video used in the current study was found to change perceptions rather than preferences. These results show that individuals' changes of perceptions of medicines are not necessarily associated with their drug preferences. Perceptions and preferences had already deviated at the pre-video assessment of our study. Participants showed a tendency to *prefer* generic over brand name drugs. At the same time, they perceived brand name medicines to be of higher quality and effectiveness. Different factors that could explain this conflicting difference between perceptions and preferences should be considered. One factor could be the impact of certain characteristics of the style of the interventional video. We showed significant differences between videos in participants' evaluation of the video's comprehensibility and level of engagement. Participants judged the bioequivalence video to be significantly more engaging and easier to understand than the generic drug approval process and the control video. The covariate analysis confirmed the confounding effect of the video's level of engagement. The more engaging participants perceived a video the more they preferred generic drugs after watching that video. A long history of research on multimedia presentations has repeatedly demonstrated that engaging the audience facilitates processing and learning of content.²⁸ Factors that influence audience engagement are various.²⁹ The level of engagement of a video intervention should be considered more carefully in future research on educational health videos. Another explanatory factor of deviations between perceptions of and preferences for generic drugs could be sociodemographic aspects. Our participants were young, mainly students, and mainly highly educated. Young age and high educational level has been demonstrated to be associated with a preference for generic medicines in previous research.^{30,31} Although our participants had more positive views on brand name drugs at baseline, it has to be considered that students are often short of money. This could explain why they showed tendentially a higher preference for cheaper generic medicines at baseline.

Contrary to our hypothesis, a third important finding of this study showed that the generic drug approval process video and the

bioequivalence video had a similar effect on the pain-relief experienced by the pain drug. A significantly increased pain-relieving effect of the brand name drug compared with the generic drug in the control group was neither present in the participants who watched the generic drug approval process video nor in the participants who watched the bioequivalence video. The generic and brand name ibuprofen in this trial were bioequivalent. Thus the difference in efficacy between the brand name and the generic drug in the control group has to be attributed to factors other than the active ingredient of the analgesic, such as perceptions of and expectations about generic medicines, for example.⁹ It seems that both interventional videos, educating individuals about the bioequivalence between brand name and generic drugs as well as about the approval process of generic drugs, were able to diminish the negative effect of labeling a painkiller as generic. A recently published study investigated the association between trust in medicines and pharmaceutical companies and interpreting symptoms as side effects of a medicine.¹⁷ The authors of this earlier study showed that trust in medicines and pharmaceutical companies decreased the likelihood of attributing symptoms to a medicine. It would be an interesting question for future research as to whether the drug approval process video and the bioequivalence video equally created trust and whether trust could be a mechanism that explains the diminished negative effect of the label "generic". In contrast to this trial, participants in the study by Colgan and colleagues¹⁶ who watched the bioequivalence video experienced significantly less pain relief and more side effects after taking the generic drug compared to the brand name analgesic. Compared to the study by Colgan and colleagues¹⁶ (M of VAS_{understanding generic drug} = 6.30), participants in the current trial already had a substantial better understanding of generic medicines (M of VAS_{understanding generic drug} = 8.47) before watching the video. Moreover, in our total sample 88.3% had already experienced using generic drugs, which allows the conclusion that our participants were already familiar with generic medicines. Currently taking a medication and familiarity with a medication are associated with attitudes towards medicines.^{30,32} It is possible that in a sample of individuals who are more experienced with taking generic medicines, an educational intervention acts differently than in a group of less experienced individuals.

Although this study has strengths, such as the randomized controlled design with two interventional and a control video, several critical aspects should be considered for the interpretation of the results of this trial. Firstly, the findings of this study are based on a very young and highly educated sample. Previous research has shown that especially educational level and age appear to be demographic factors that are strongly associated with a preference for generic drugs.^{30,31} Younger and higher educated people seem to have a higher acceptance of generic medication. Secondly, an over-the-counter analgesic was used in this study. Familiarity with over-the-counter drugs is higher than with prescribed medication and may limit the generalizability of the results. Thirdly, we examined the effect of our interventional videos on the pain-relieving effect only across two consecutive episodes of headaches. A lot of factors besides our video and the medication can have impact on

the pain-relieving effect and could bias our results. Increasing the number of follow-up assessments could help to increase the reliability of our findings. Finally, an essential criticism addresses the fact that we only involved health specialists in our decision on topics and content for our generic drug approval process videos, but not patients.

Conclusions

In conclusion, both the generic drug approval process and the bioequivalence video interventions helped to improve the understanding of generic medicines. The generic drug approval process video improved our participants' perceived effectiveness, safety and quality of generic drugs, while the bioequivalence video enhanced their preference for generic drugs. Both of the educational video interventions used in this study positively influenced the pain-relieving effect of the generic analgesic.

Switching from brand name to generic drugs can have substantial positive financial effects, for health-care systems as well as consumers. A recently published cost analysis of a switch to generic medicines showed in a large sample that genericization, i.e., the process of becoming a generic, especially of costly drugs, can change cost-effectiveness of a regimen significantly.³ At the same time, switching from a brand name drug to a generic formulation can be associated with a reduced effectiveness, more side effects and in turn with increased costs (e.g., because patients need follow-up appointments) and increased patients' distress.^{6,7} Therefore, it is important to provide patients both at pharmacies and elsewhere with appropriate information about generic substitution and interchangeable medicines, e.g., through educational campaigns. As the results of this study show, both the process of approving a switch from brand name medicines to generic counterparts and bioequivalence can be important and should be addressed in future educational interventions. For future studies, it will be important to better understand which factors mediate the effect of educational interventions on perceptions and the efficacy of generic drugs. Trust in pharmaceutical agencies was demonstrated to be an important predictor of patients' ratings of the efficacy of a new generic and should be investigated as a potential acting mechanism.¹³

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Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or decision to submit the paper for publication. The corresponding author had full access to all the data in the study and final responsibility for the decision to submit.

CRediT authorship contribution statement

Maria Kleinstäuber: Investigation, Conceptualization, Methodology, Formal analysis, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration. **Sarah Colgan:** Investigation, Conceptualization, Methodology, Writing - original draft, Writing - review & editing. **Keith J. Petrie:** Investigation, Conceptualization, Methodology, Resources, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.sapharm.2020.09.014>.

References

1. World Health Organization. *WHO Expert Committee on Specifications for Pharmaceutical Preparations – WHO Technical Report Series, No. 863 - Thirty-Fourth Report*. Geneva (Switzerland): World Health Organization; 1996.
2. Shah US. *Regulatory Strategies and Lessons in the Development of Biosimilars*. *Pharmaceutical Sciences Encyclopedia*. Hoboken, NJ: Wiley; 2013:1–42.
3. Desai RJ, Sarpatwari A, Dejene S, et al. Comparative effectiveness of generic and brand-name medication use: a database study of US health insurance claims. *PLoS Med*. 2019;16:20.
4. Haas JS, Phillips KA, Gerstenberger EP, Seger AC. Potential savings from substituting generic drugs for brand-name drugs: medical expenditure panel survey, 1997–2000. *Ann Intern Med*. 2005;142:891–897.
5. Zarowitz BJ. The generic imperative. *Geriatr Nurs*. 2008;29:223–226.
6. Desmarais JE, Beauclair L, Margolese HC. Switching from brand-name to generic psychotropic medications: a literature review. *CNS Neurosci Ther*. 2011;17:750–760.
7. Straka RJ, Keohane DJ, Liu LZ. Potential clinical and economic impact of switching branded medications to generics. *Am J Therapeut*. 2017;24:e278–e289.
8. Colgan S, Faasse K, Martin LR, Grey A, Petrie KJ. Perceptions of generic medication in the general population, doctors and pharmacists: a systematic review. *BMJ Open*. 2015;5, e008915.
9. Faasse K, Martin LR. The power of labeling in nocebo effects. In: Colloca L, ed. *Neurobiology of the Placebo Effect*. vol. 139. San Diego: Elsevier Academic Press Inc; 2018:379–406.
10. Branthwaite A, Cooper P. Analgesic effects of branding in treatment of headaches. *Br Med J*. 1981;282:1576–1578.
11. Faasse K, Cundy T, Gamble G, Petrie KJ. The effect of an apparent change to a branded or generic medication on drug effectiveness and side effects. *Psychosom Med*. 2013;75:90–96.
12. Faasse K, Cundy T, Petrie KJ. Medicine and the media. Thyroxine: anatomy of a health scare. *BMJ*. 2009;339:b5613.
13. MacKrell K, Petrie KJ. What is associated with increased side effects and lower perceived efficacy following switching to a generic medicine? A New Zealand cross-sectional patient survey. *BMJ Open*. 2018;8, e023667.
14. Valles JA, Barreiro M, Cereza G, et al. A prospective multicenter study of the effect of patient education on acceptability of generic prescribing in general practice. *Health Pol*. 2003;65:269–275.
15. Sedjo RL, Cox ER. The influence of targeted education on medication persistence and generic substitution among consumer-directed health care enrollees. *Health Serv Res*. 2009;44:2079–2092.
16. Colgan SLE, Faasse K, Pereira JA, Grey A, Petrie KJ. Changing perceptions and efficacy of generic medicines: an intervention study. *Health Psychol*. 2016;35:1246–1253.
17. Webster RK, Weinman J, Rubin GJ. Medicine-related beliefs predict attribution of symptoms to a sham medicine: a prospective study. *Br J Health Psychol*. 2018;23:436–454.
18. Olsson E, Svensberg K, Wallach-Kildemoes H, et al. Swedish patients' trust in the bioequivalence of interchangeable generics. What factors are important for low trust? *Pharm. Pract. Spain*. 2018;16:9.
19. Kesselheim AS, Gagne JJ, Franklin JM, Eddings W, Fulchino LA, Campbell EG. Do patients trust the FDA?: a survey assessing how patients view the generic drug approval process. *Pharmacoepidemiol Drug Saf*. 2017;26:694–701.
20. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition. *Cephalalgia*. 2018;38:1–211.
21. Rief W, Barsky AJ, Glombiewski JA, Nestoriuc Y, Glaesmer H, Braehler E. Assessing general side effects in clinical trials: reference data from the general population. *Pharmacoepidemiol Drug Saf*. 2011;20:405–415.
22. Horne R, Weinman J, Hankins M. The Beliefs about Medicines Questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health*. 1999;14:1–24.
23. Horne R, Faasse K, Cooper V, et al. The perceived sensitivity to medicines (PSM) scale: an evaluation of validity and reliability. *Br J Health Psychol*. 2013;18:18–30.
24. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect – the PANAS Scales. *J Pers Soc Psychol*. 1988;54:1063–1070.

25. Chen CM, Wu CH. Effects of different video lecture types on sustained attention, emotion, cognitive load, and learning performance. *Comput Educ.* 2015;80:108–121.
26. Craig S, Graesser A, Sullins J, Gholson B. Affect and learning: an exploratory look into the role of affect in learning with AutoTutor. *J Educ Media.* 2005;80:108–121.
27. Betrancourt M, Benetos K. Why and when does instructional video facilitate learning? A commentary to the special issue "developments and trends in learning with instructional video". *Comput Hum Behav.* 2018;89:471–475.
28. Chi MTH, Wylie R. The ICAP Framework: linking cognitive engagement to active learning outcomes. *Educ Psychol.* 2014;49:219–243.
29. Webster J, Ho H. Audience engagement in multimedia presentations. *Database Adv Inf Syst.* 1997;28:63–77.
30. Kleinstäuber M, MacKrell K, Petrie KJ. Characteristics of individuals who prefer branded innovator over generic medicines. *Drugs Ther Perspect.* 2018;34:478–483.
31. Mattioli F, Siri G, Castelli F, et al. Approval rating and opinion of outpatients and general practitioners toward generic drugs: a questionnaire-based real-world study. *Patient Prefer Adherence.* 2017;11:1423–1433.
32. Sundell Andersson K, Jönsson AK. Beliefs about medicines are strongly associated with medicine-use patterns among the general population. *Int J Clin Pract.* 2017;70:277–285.