The effects of message framing on patients' perceptions and willingness to change to a biosimilar in a hypothetical drug switch

Chiara Gasteiger, BA/BHSc[1], Annie S. K. Jones, MHP[1], Maria Kleinstäuber[1,2] PhD, Maria Lobo RN PhD[3], Rob Horne[4] PhD, Nicola Dalbeth MD FRACP[3,5] & Keith J. Petrie, PhD[1]

1. Department of Psychological Medicine, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand
2. Department of Psychological Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand
3. Department of Rheumatology, Auckland District Health Board, Auckland, New Zealand
4. Centre for Behavioural Medicine, UCL School of Pharmacy, University College London, United Kingdom
5. Department of Medicine, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

Corresponding author: Keith J. Petrie, Department of Psychological Medicine, Faculty of Medical and Health Sciences, University of Auckland, Private Bag 92019, Auckland, New Zealand.

E-mail: kj.petrie@auckland.ac.nz

Word count: 3094

Running head: MESSAGE FRAMING AND BIOSIMILAR SWITCHING

ABSTRACT

Objective. Patients may hold negative perceptions towards biosimilars which can create barriers to their uptake. Physicians also report uncertainty in how best to explain biosimilars. The aim of this study was to measure the effect of differently framed explanations on patients' perceptions of and willingness to change to a biosimilar in a hypothetical drug switch.

Methods. Ninety-six patients with rheumatic diseases taking an originator biologic were randomised to receive one of four biosimilar explanations - positive framing with and without an analogy, and negative framing with and without an analogy. Willingness to switch to a biosimilar, perceptions about biosimilars, and the effectiveness of the explanation were measured after the information delivery.

Results. Positive framing led to more participants being willing to switch (67%) than negative framing (46%). Framing significantly predicted willingness to switch to a biosimilar, with participants in the positive framing group being 2.36 times more willing to switch ($P = 0.041$). The positive framing group also reported significantly greater perceived efficacy of biosimilars ($P = 0.046$), and thought the explanation was more convincing ($P = 0.030$). The analogy did not enhance willingness to switch or understanding ($P > 0.05$).

Conclusion. Positive framing can improve perceptions of and willingness to switch to a biosimilar in patients currently taking biologic treatments.

SIGNIFICANCE AND INNOVATIONS

- Little is known about the best way to explain switching to biosimilars from biologics to ensure patient acceptance and positive perceptions.
- A brief positively framed explanation significantly improved participants' willingness to switch and the perception that a biosimilar would be as effective as a biologic.
- Patients hold concerns about biosimilars, particularly relating to safety, efficacy, manufacturing and clinical trials that need to be addressed to improve acceptability.

Biosimilars are the highly similar, but not identical, versions of a reference biologic medicine manufactured by a different company (1). Biosimilars have the same clinical therapeutic equivalence, purity and potency as their reference biologic, and can provide the same health benefits at a significantly reduced cost (2, 3). Biosimilars have been successfully incorporated into routine care for patients with rheumatic diseases in many countries (4, 5). Estimates demonstrate that $100 billion worth of biologic medicines are coming off patent by 2020, which will create significant opportunities to integrate biosimilars into pharmaceutical markets and widen the opportunity for patients to benefit from such treatments (6). This process has already begun with patients being switched to biosimilars in large scale clinical trials (7,8)

Patient and healthcare provider acceptance is vital to ensure the benefits from biosimilar use can be gained. Previous research suggests that both patients and providers hold negative perceptions towards biosimilar safety and efficacy (9-12). Physicians also report being unsure how to go about explaining biosimilars to patients, which further restricts their use (13, 14). A lack of acceptance and negative perceptions towards biosimilars may enhance the nocebo following a switch and increase non-adherence (15-16). Although studies highlight physicians' lack of confidence in explaining biosimilars and the importance of patient acceptance to ensure uptake (17-20), limited research has addressed these areas.

Framing has been used in medical explanations to highlight certain attributes of medicines, present medicine risk information, and to present health outcomes in losses or gains (21, 22). Differences in information framing has been found to change patient expectations and perceptions about medical treatments. Positively framed (e.g. 90% chance of not getting any side effects) compared to negatively framed explanations (e.g. 10% chance of obtaining side effects) have been found to enhance patients' perceptions towards vaccine efficacy and decrease both side effect expectations and reported side effects (23). Recently,

positive framing of side effect information has been found to significantly decrease symptoms attributed to a medicine (24). Additional linguistic tools, such as analogies, can also be effective for communicating medical information, and may be particularly helpful for improving patient understanding and retention of medical information, decreasing patient anxiety and building rapport (25-28). An analogy may help a patient understand a concept by putting it in terms of objects or processes that the patient is already familiar with. To our knowledge, no studies have compared the use of analogy and framing, or examined how these methods can be used to explain information pertaining to a biosimilar switch.

This study investigated how framing and analogy could be used to explain switching to biosimilars to patients with rheumatic diseases currently taking biologics. The aim of the study was to measure the effect of different explanations on patient perceptions of and hypothetical willingness to switch to a biosimilar treatment. The hypotheses tested were: 1) that positive framing would engender more positive views of biosimilars and increase patients' willingness to switch compared to a negatively framed explanation, 2) that using an analogy would further improve understanding and willingness to switch compared to the explanations with framing only.

MATERIALS AND METHODS

Study design and participants

This study was a parallel, four-arm randomized controlled trial with two assessment points (baseline and post-explanation). The trial was approved by the Health and Disability Ethics Committee (17/NTB/245) and Auckland District Health Board (A+7961). The study was also registered with the Australian New Zealand Clinical Trials Registry (52ACTRN12618000009213p).

Based on a previous study that aimed to modify perceptions of generic medicines (29), 96 participants (24 participants per arm) were required for the trial to have 90% power, a

significance level of 0.05 (2-tailed) and an effect size of f = 0.40. Participants were patients currently receiving a biologic treatment from the rheumatology department of an outpatient clinic in Auckland, New Zealand from April to July 2018. Of 247 patients who were sent recruitment letters, a total of 41 participants were enrolled directly into the study. Participants were also recruited through Facebook groups (n = 3), and flyers distributed by nurses and rheumatologists at appointments (n = 52), which gave a total sample of 96 participants (see Figure 1). Participants were included if they over 18 years of age, fluent in English and were taking an originator biologic at the time of data collection.

New Zealand has a single payer healthcare system, and all patients must meet predetermined eligibility criteria to access publicly funded biologic medicines. At the time of the study, no biosimilars were funded for rheumatic disease indications in New Zealand.

Procedure

Eligible patients were sent a recruitment letter and participant information sheet in advance of their next appointment. Interested participants contacted the researcher to arrange a time for their study session, either before or after their next appointment at the clinic, or at the Clinical Research Centre of the University of Auckland Clinical Campus. During the study session, participants provided written consent then completed the baseline questionnaire assessing demographic and clinical information, and illness perceptions. After completion, the researcher revealed the participant's group allocation. Randomisation was completed by an independent researcher not involved in the study using a random number generator, and contained in sequentially numbered opaque envelopes.

Participants were randomised (n = 24 in each study arm) to receive one of four video explanations about switching to a biosimilar. Each explanation was delivered using a computer tablet. For each arm, the video featured a clinician providing basic information about biosimilars, followed by one of four possible explanations - positive framing, negative

framing, positive framing plus an analogy, or negative framing plus an analogy (see Supplementary Material for script). The positive explanation employed a positive valence attribute frame, whereby the *similarities* between the biologic and biosimilar were emphasised. The physician featured in the video used positive body language and verbal cues (e.g. nodding and smiling) to promote a positive interaction. Comparatively, the negatively framed explanation focused on the *differences* between biologics and biosimilars, and the physician used negative body language and verbal cues (e.g. less confident vocal tone) to imply uncertainty regarding efficacy and safety. The analogy used focused on the concept of baking bread, using a cheaper yeast from a different brand. The analogy used the concept of two brands of yeast that would provide the same outcome and work in a similar biological way to produce bread, despite having differences in cost and manufacturing. The same physician (MB) was featured in each video explanation to ensure consistency. Each explanation video was approximately two minutes in length, with the analogy conditions lasting closer to two and a half minutes.

Immediately after viewing the explanation, participants completed the post–presentation questionnaire, which assessed beliefs about willingness to switch, as well as perceptions and concerns about biosimilars. All participants were offered a $20 shopping voucher for participation.

<INSERT FIGURE 1 ABOUT HERE>

Measures

Demographic and clinical information. In the baseline questionnaire, participants reported their age, ethnicity, gender, and education level. Participants also provided the name of their current biological treatment, length of treatment, and the condition being treated.

Illness perceptions. At baseline, illness perceptions were assessed using the nine-item Brief Illness Perception Questionnaire (Brief IPQ) (30). The Brief IPQ is a 9-item scale where each

item assesses the presence of an illness perception construct, on an 11-point numerical rating scale from 0 (not at all) to 10 (extremely). All items except the casual beliefs opened-ended question were included in the current study. The Brief IPQ has demonstrated appropriate discriminant validity and test-retest reliability (31).

Effectiveness of explanations. To assess how effective the explanations were, four items asked how reassuring and convincing the explanation was, how easy it was to understand, and how important participants believed a conversation about biosimilars is important and easy to understand the information was. Participants were also asked their willingness to switch from their current medication to a biosimilar in this hypothetical situation (yes/no).

Perceptions of biosimilars. Perceptions towards biosimilars were assessed using five items. Participants rated how much they expected side effects from a biosimilar, how effective and safe they believed them to be, as well as how anxious and concerned they were about switching to a biosimilar, on an 11-point numerical rating scale from 0 (not at all) to 10 (extremely). Higher scores indicated stronger perceptions of each item (e.g. more safe or more anxious).

Open-ended items. Three open-ended questions asked participants to describe concerns they had about switching to a biosimilar, what they found most worrying about the explanation, and what information would be important for patients to know about switching. One item also asked participants to state how much time they would want to discuss the change with their doctor and whether they would like to be referred to relevant websites.

Statistical analyses

Analyses were performed using SPSS version 22. Chi-square tests of independence and one-way analyses of variance (ANOVAs) were used to assess differences between groups at baseline in demographic and clinical characteristics. Two logistic regressions were employed to test the effect of framing on willingness to switch (coded as negative framing (0) versus

positive framing (1)), and to test the effect of the analogy on willingness to switch (analogy (0) versus framing (1)). In both regressions, willingness to switch was a binary outcome variable coded as willing (0) or not willing to switch (1).

Independent samples t-tests were used to assess the effect of positive and negative framing on perceptions of biosimilars. A two-way ANOVA was conducted to ascertain the effects of positive and negative framing (factor 1: positive versus negative framing), and an analogy (factor 2: analogy versus no analogy), on participants' understanding of the explanation.

Exploratory analyses were conducted whereby responses to each of the open-ended concern items were categorised and frequencies are reported. Each concern reported by a given patient were classified (total percentages may exceed 100%). Correlations were used to assess the association between the amount of time patients wanted to discuss switching with their physician and preference for biosimilars, perceptions towards biosimilars (safety, side effects and efficacy) and concern and anxiety about switching.

RESULTS

Characteristics of the sample are presented in Table 1. The mean age of the sample was 54.09 years (SD = 15.9), and the majority of participants were female (69%), identified as NZ European (67%), and had received a tertiary level education (53%). The most common biologic participants were currently taking was rituximab (35%), and more than half of the sample were taking their biologic treatment for rheumatoid arthritis (65%). There were no differences in any clinical and demographic characteristics, or medicine and illness related beliefs at baseline between trial arms.

<INSERT TABLE 1 ABOUT HERE>

Willingness to switch

Framing. When comparing the participants who received positive framing (with or without an analogy) with those who received negative framing (with or without an analogy), there was a statistically significant association between group and willingness to switch ($\chi^2_{(1)} = 4.27$, P = 0.039; see Figure 2). Over half of the positive framing group (67%, 32/48) reported they were willing to switch to a biosimilar, compared to only 46% (22/48) of those who received a negatively framed explanation. The logistic regression model was statistically significant ($\chi^2_{(1,96)} = 4.27$, P = 0.039). Framing significantly predicted willingness to switch to a biosimilar (Wald χ^2= 4.17, P =. 0.041, B = 0.86, Exp(B) = 2.36; see Table 2). The model explained 5.8% (Nagelkerke R^2) of the variance of being willing to switch to a biosimilar and correctly classified 60% of cases. Participants in the positive framing group were 2.36 times more likely to be willing to switch to the biosimilar (95% CI: 1.04-5.40).

<INSERT FIGURE 2 ABOUT HERE>

<INSERT TABLE 2 ABOUT HERE>

Analogy. A logistic regression was also conducted to examine the effects of the analogy on participants' willingness to switch to a biosimilar. This regression model was not statistically significant, showing that adding an analogy did not predict willingness to switch (See Table 2).

Perceptions of biosimilars

Participants who received a positively framed explanation thought the biosimilar would be significantly more effective (mean (SD) 6.40 (2.25)), than those who received a negatively framed explanation (mean (SD) 5.54 (1.83); P = 0.049). There were no significant differences between the positive and negative framing groups in perceived safety, expected side effects, concerns or anxiety about switching (P for all > 0.05).

Efficacy of the explanation

The positively framed explanation was rated significantly more convincing (mean (SD) 6.58 (2.87)) than the negatively framed explanation (mean (SD) 5.27 (2.99); P = 0.030). There were no differences between the framed explanations in reassurance, understanding and their perceived importance of a conversation about biosimilars (P for all > 0.05). A two-way ANOVA investigating differences between framing (positive or negative) and analogy (analogy or no analogy) on understanding of biosimilars found no significant interaction or main effects between groups (P > 0.05).

Consultation time

Participants reported that if they were to switch to a biosimilar in the future, they would want a mean initial discussion time with their physician of 38.7 minutes (SD = 25.4, range = 118). Length of consultation time was positively correlated with concerns about biosimilars (*r*'s = 0.30, P = 0.004), with patients who had greater concerns about taking a biosimilar wanting longer consultation times. Consultation times were not related to preferences for biosimilars, anxiety about switching, or the safety, side effects or efficacy of biosimilars (P > 0.05). Most patients (76%, n = 73) also wanted to be referred to a website with more information about switching.

Concerns

Table 3 provides example responses, frequencies and categories for each of the three open-ended items. When asked about their concerns regarding biosimilars, most participants were concerned about reduced efficacy (50%) and safety (46%) after switching. The manufacturing processes (9%), lack of clinical evidence (5%) were also reported concerns about biosimilars, with 13% of responses classified as "other". Participants reported that what was most worrying about the explanation were concerns regarding reduced efficacy (34%), cost and quality (28%), and safety (25%). Finally, participants reported that information that would be important for patients to know before switching included information around safety

(including possible side effects, 38%), efficacy (37%), evidence from clinical trials (19%), manufacturing information (10%), and whether it is possible to switch back to a biologic (7%). See Table 3 for example responses.

<INSERT TABLE 3 ABOUT HERE>

DISCUSSION

This study found that a positively framed explanation about switching to biosimilars encouraged 21% more participants to be willing to switch, compared to a negatively framed explanation. Positive framing was also more convincing and increased the perception that a biosimilar would be effective. The use of an analogy did not significantly improve willingness to switch or patient understanding of the explanation. Participants were predominantly concerned about efficacy and safety in regards to biosimilars, but also perceived evidence from clinical trials, and information about manufacturing processes to be important. Participants who were more concerned about switching wanted longer consultation times to discuss this process.

The findings from the current study are consistent with previous literature which suggests that framing can influence patients' treatment-related decisions and perceptions towards new medicines (23, 32). The findings also accentuate the importance of considering how biosimilars are explained to patients to ensure acceptance and enable informed choices (16, 18, 33). Previous research would suggest that positive framing can improve perceptions about safety and the side effects of medicines (32), although this was not found in the current study. It may be that the content of the explanation, particularly the uncertainty regarding the development of side effects, was too tentative to modify these concerns or perhaps too brief to impact perceptions. Alternatively, it may be more difficult to modify these perceptions in

relation to biosimilars rather than other medicines, as biosimilars are still largely unfamiliar to the lay public.

In contrast to the hypothesis and previous literature (26, 28), the addition of the analogy in two treatment arms did not improve understanding compared to the framed explanations. Participants may not have correctly understood the analogy or may have perceived it as irrelevant to their current medical treatment (34). Analogies unrelated to health care can lead to patients misbelieving that a problem or decision is trivial (35). The study findings highlight the importance for physicians to carefully formulate and explain analogies that can be tailored to the patient's level of health literacy, or to consider using analogies that have a medical focus. It is likely that analogies can increase patient understanding and inform treatment-related decisions if patients are able to establish a clear connection between the information and their specific situation.

Another important finding in the current study is that many patients have concerns about switching that need to be addressed when biosimilars become available. Importantly, those participants who were more concerned about switching indicated that they would want longer consultation times. Healthcare systems are already burdened by time constraints, and it is evident that patient dissatisfaction occurs when consultation times do not match expectations (36). Patients may turn to alternate and possibly inaccurate sources of information-seeking, such as the internet (37). Interestingly there is quite a mismatch between the average time patients say they require for explanation (over thirty minutes) and the time doctors indicate is sufficient for an explanation of a switch to a biosimilar (around ten minutes) (14). Thus there is a need for further research into the most effective methods for describing biosimilars to patients in a method which addresses concerns such as safety and efficacy.

There are limitations of the current study which need to be considered. Firstly, the assessment of willingness to switch measured behavioural intention in a hypothetical situation, which may not necessarily reflect the behavioural outcomes in a real-life switching scenario. Outcomes were only measured immediately following the explanation, so how these perceptions towards biosimilars may change over time is unknown. All explanation were delivered by a male physician. Patients often prefer same-sex physicians (38, 39), meaning the use of a male physician only for the video explanations in a majority female sample may have influenced results. It should also be noted that the explanations were relatively brief and much shorter than the ideal time indicated by patients. The recruitment of the study may influence the generalizability of the results, as a large number of patients approached about the study were not interested in participation. Finally, the researcher collecting the patient assessments was not blind to participant group allocation. Strengths of the study include the relevance of the sample included, as these patients are likely to be similar to those affected by the introduction of biosimilars. The explanations and study sessions were also conducted in a clinical setting, which further increases ecological validity. Additionally, the use of a video explanation by the same clinician ensured standardisation of information within each experimental condition.

In terms of clinical implications, the results suggest that a similar video explanation could be developed into an intervention to improve perceptions and willingness to switch to biosimilars. Patients could view such an intervention video prior to their consultation, to receive initial information about biosimilars. This could help to prevent lengthened consultation times, while still ensuring that patients have sufficient information to make informed treatment decisions.

Future research should investigate the efficacy of medically relevant analogies and consider tailoring the explanation to different levels of health literacy. Future explanations

should also incorporate information around efficacy, safety, and side effects to attempt to alleviate these concerns within patients. Once biosimilars are available, research could also investigate how positive framing might affect nocebo responses and non-adherence after switching.

In summary, this study suggests that positive framing can improve patients' perceptions of biosimilars and increase their hypothetical willingness to switch to a biosimilar from a biologic treatment. The study also revealed that patients with rheumatic diseases currently taking biologics have various concerns about switching to biosimilars, particularly regarding efficacy and safety. The findings emphasise the importance of carefully 1constructing and delivering information to patients about biosimilars, and highlights important areas of concerns that physicians should aim to address as biosimilars become readily available as treatment options.

REFERENCES

1. Eleryan MG, Akhiyat S, Rengifo-Pardo M, Ehrlich A. Biosimilars: Potential implications for clinicians. Clin Cosmet Investig Dermatol 2016;9:135-42.

2. Patel D, Park KT. Path of interchangeability of biosimilars in pediatric inflammatory bowel disease: Quality before cost savings. J Pediatr Gastroenterol Nutr 2017;65:134-36.

3. Escasany AA, Cumplido DR. Biosimilars: Current reality, promising future? Medicina Clínica 2015;145:18-20.

4. Moots R, Azevedo V, Coindreau JL, Dörner T, Mahgoub E, Mysler E, et al. Switching between reference biologics and biosimilars for the treatment of rheumatology, gastroenterology, and dermatology inflammatory conditions: Considerations for the clinician. Curr Rheumatol Rep 2017;19:1-16.

5. Rischin A, Östör AJK. Update on biosimilars in rheumatology. Inflammopharmacology 2017;25:177-84.

6. Blackstone EA, Fuhr JP. The economics of biosimilars. Am Health Drug Benefits 2013;6:469-79.

7. Jørgensen KK, Olsen IC, Goll G, Lorentzen M, Bolstad N, Haavardsholm EA, et al. Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial. Lancet 2017;389:2304–16.

8. Glintborg B, Sorensen IJ, Loft AG, Lindegaard H, Linauskas A, Hendricks O, et al. A nationwide non-medical switch from originator infliximab to biosimilar CT-P13 in 802 patients with inflammatory arthritis: 1-year clinical outcomes from the DANBIO registry. Ann Rheum Dis 2017;76:1426–31

9. Attara G, Bressler B, Bailey R, Marshall JK, Panaccione R, Aumais G. Canadian patient and caregiver perspectives on subsequent entry biologics/biosimilars for inflammatory bowel disease. Gastroenterology 2016;150:443-44.

10. Chapman SR, Fitzpatrick RW, Aladul MI. Knowledge, attitude and practice of healthcare professionals towards infliximab and insulin glargine biosimilars: Result of a UK web-based survey. BMJ Open 2017;7:1-8.

11. Cohen H, Beydoun D, Chien D, Lessor T, McCabe D, Muenzberg M, et al. Awareness, knowledge, and perceptions of biosimilars among specialty physicians. Adv Ther 2017;33:2160-72.

12. Sullivan E, Piercy J, Waller J, Black CM, Kachroo S. Assessing gastroenterologist and patient acceptance of biosimilars in ulcerative colitis and Crohn's disease across Germany. PLoS One 2017;12:1-14.

13. Danese S, Fiorino G, Michetti P. Viewpoint: Knowledge and viewpoints on biosimilar monoclonal antibodies among members of the European Crohn's and Colitis Organization. J Crohns Colitis 2014;8:1548-50.

14. Hemmington A, Dalbeth N, Jarrett P, Fraser AG, Broom R, Browett P, et al. Medical specialists' attitudes to prescribing biosimilars. Pharmacoepidemiol Drug Saf 2017;26:570-77.

15. Rezk MF, Pieper B. Treatment outcomes with biosimilars: Be aware of the nocebo effect. Rheumatol Ther 2017;4:209-18.

16. Rezk MF, Pieper B. To see or NOsee: The debate on the nocebo effect and optimizing the use of biosimilars. Adv Ther 2018;35:749-53.

17. Michetti P, Weinman J, Mrowietz U, Smolen J, Peyrin-Biroulet L, Louis E, Schremmer D, Tundia N, Nurwakagari P, Selenko-Gebauer N. Impact of treatment-related beliefs on medication adherence in immune-mediated inflammatory diseases: results of the global ALIGN study. Adv Ther 2017;34:91-108.

18. Inotai A, Csanadi M, Petrova G, Dimitrova M, Bochenek T, Tesar T, et al. Patient access, unmet medical need, expected benefits, and concerns related to the utilisation of biosimilars in Eastern European Countries: A survey of experts. BioMed Res Int 2018:1-9.

19. Minghetti P, Rocco P, Cilurzo F, Vecchio LD, Locatelli F. The regulatory framework of biosimilars in the European Union. Drug Discovery Today 2012;17:63-70.

20. Weise M, Bielsky MC, De Smet K, Ehmann F, Ekman N, Giezen TJ, et al. Biosimilars: What clinicians should know. Blood 2012;120:5111-17.

21. Levin IP, Schneider SL, Gaeth GL. All frames are not created equal: A typology and critical analysis of framing effects. Organ Behav Hum Decis Process 1998;76:149-88.

22. Tversky A, Kahneman D. The framing of decisions and the psychology of choice. Science 1981;30:453-58.

23. O'Connor AM, Pennie RA, Dales RE. Framing effects on expectations, decisions, and side effects experienced: The case of influenza immunization. J Clin Epidemiol 1996;49:1271-76.

24. Webster RK, Weinman J, Rubin GJ. Explaining all without causing unnecessary harm: Is there scope for positively framing medical risk information? Patient Educ Couns 2018:Advance online publication.

25. Casarett D, Pickard A, Fishman JM, Alexander SC, Arnold RM, Pollak KI, et al. Can metaphors and analogies improve communication with seriously ill patients? J Palliat Med 2010;13:255-60.

26. Donnelly CM, McDaniel MA. Use of analogy in learning scientific concepts. J Exp Psychol Learn Mem Cogn 1993;19:975-87.

27. Jankovic M, Loiacono NB, Spinetta JJ, Riva L, Conter V, Masera C. Telling young children with leukemia their diagnosis: The flower garden as analogy. J Pediatr Hematol Oncol 1994;11:75-81.

28. Pena GP, Andrade-Filho JS. Analogies in medicine: Valuable for learning, reasoning, remembering and naming. Adv Health Sci Educ Theory Pract 2010;15:609-19.

29. Colgan SL, Faasse K, Pereira JA, Grey A, Petrie KJ. Changing perceptions and efficacy of generic medicines: An intervention study. Health Psychol 2016;35:1246-53.

30. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. J Psychom Res 2006;60:631-37.

31. Broadbent E, Wilkes C, Koschwanez H, Weinman, J, & Petrie KJ. (2015). A systematic review and meta-analysis of the Brief Illness Perception Questionnaire. Psychol Health 2015; 11:1361-1385.

32. Moxey A, O'Connell D, McGettigan P, Henry D. Describing treatment effects to patients: How they are expressed makes a difference. J Gen Intern Med 2003;18:948-59.

33. Jacobs I, Singh E, Sewell KL, Al-Sabbagh A, Shane LG. Patient attitudes and understanding about biosimilars: An international cross-sectional survey. Patient Prefer Adherence 2016;10:937-48.

34. Penţa MA, Băban A. Message framing in vaccine communication: A systematic review of published literature. Health Commun 2018;33:299-314.

33. Frieden IJ, Dolev JC. Medical analogies: Their role in teaching dermatology to medical professionals and patients. J Am Acad Dermatol 2005;53:863-66.

34. Ley P. Satisfaction, compliance and communication. Brit J Clin Psychol 1982;21:241-54.

35. Barilli E, Savadori L, Pighin S, Bonalumi S, Ferrari A, Ferrari M, et al. From chance to choice: The use of a verbal analogy in the communication of risk. Health Risk Soc 2010;12:546-59.

36. Ogden J, Bavalia K, Bull M, Frankum S, Goldie C, Gosslau M, et al. “I want more time with my doctor”: A quantitative study of time and the consultation. Fam Pract 2004;21:479-83.

37. Lee K, Hoti K, Hughes JD, Emmerton L. Dr Google and the consumer: A qualitative study exploring the navigational needs and online health information-seeking behaviors of consumers with chronic health conditions. J Med Internet Res 2014;16:1-43.

38. Bertakis KD, Helms LJ, Callahan EJ, Azari R, Robbins JA. The influence of gender on physician practice style. Med Care 1995;33:407-16.

39. Varia AK, Osowo AT, Kim HN, Arora G, Machicao VI, Fallon MB, et al. Gender preference for endoscopists in the adult Hispanic patient: The results of a prospective study. Gastrointest Endosc 2010;71:217.

Table 1. Demographic, clinical and baseline psychological measures in experimental groups

	Total Sample N=96 Mean (SD) [%]	**Positive Framing n=24**	**Positive Framing with Analogy n=24**	**Negative Framing n=24**	**Negative Framing with Analogy n=24**
Age (years)	54.09 (15.9)	51.9(17.6)	56(15.7)	55(13.5)	53.5(17)
Gender					
Female	66 [69%]	20 [83%]	13[54%]	15[63%]	18[75%]
Male	30 [31%]	4 [17%]	11[46%]	9[38%]	6[25%]
Ethnicity					
NZ European/European	64 [67%]	14[58%]	17[71%]	10[42%]	15[63%]
Asian	15 [16%]	3[13%]	-	5[21%]	1[4%]
Pacific	7 [7%]	1[4%]	1[4%]	2[8%]	1[4%]
Māori	6 [6%]	1[4%]	-	1[4%]	1[4%]
Other	4 [4%]	5[21%]	6[25%]	6[25%]	6[25%]
Education					
Primary	5 [5%]	-	3[13%]	1[4%]	1[4%]
Secondary	30 [31%]	6[25%]	11[46%]	6[25%]	7[29%]
Tertiary	51 [53%]	17[71%]	9[38%]	14[58%]	11[46%]
Post-graduate	10 [10%]	1[4%]	1[4%]	3[13%]	5[21%]
Current biologic					
Rituximab	34 [35%]	5[21%]	10[42%]	11[46%]	8[33%]
Adalimumab	21 [22%]	8[33%]	5[21%]	3[13%]	5[21%]
Tocilizumab	17 [18%]	3[13%]	5[21%]	5[21%]	4[17%]
Infliximab	16 [17%]	5[21%]	1[4%]	4[17%]	6[25%]
Etanercept	8 [8%]	3[13%]	3[13%]	1[4%]	1[4%]
Time on biologic (weeks)	29.95 (29.1)	33.1(30.6)	22.9(22.8)	21.7(16.4)	42.2(38.4)
Rheumatic disease					
Rheumatoid arthritis	62 [65%]	15[63%]	16[67%]	17[71%]	14[58%]
Ankylosing spondylitis	16 [17%]	3[13%]	5[21%]	2[8%]	6[25%]
Psoriatic arthritis	13 [14%]	3[13%]	3[13%]	4[17%]	3[13%]
Granulomatosis with polyangiitis	2 [2%]	-	-	1[4%]	1[4%]
Juvenile idiopathic arthritis	2 [2%]	2[8%]	-	-	-
Adult onset Stills disease	1 [1%]	1[4%]	-	-	-
Perceived Sensitivity to Medicines	14.5(4.2)	14.8(5.3)	13.8(3.6)	15.3(3.9)	14.2(4.0)
General Beliefs about Medicines	27.4(5.5)	28.2(4.6)	26.3(6.1)	26.5(5.1)	28.7(6.1)
Illness Beliefs					
Consequence	5.8(2.8)	5.9(2.6)	6.3(2.2)	5.8(3.2)	5.2(3.1)
Timeline	9.4(1.5)	9.7(0.9)	9.5(1.4)	9(1.9)	9.5(1.6)
Personal control	5.7(2.6)	5.8(2.0)	5.5(2.6)	6.1(2.6)	5.3(3.1)
Treatment control	8.0(2.0)	8.0(1.6)	7.8(2.4)	8.6(1.4)	7.7(2.3)
Identity	6.0(2.6)	6.1(2.5)	6.5(2.3)	6.2(2.9)	5.0(2.7)
Concern	6.4(3.1)	7.3(2.6)	6.0(3.3)	6.8(2.9)	5.5(3.3)
Understanding	7.9(2.2)	8.5(1.8)	7.1(2.3)	8.3(2.3)	7.6(2.4)
Emotional response	5.0(2.8)	5.5(2.3)	5.4(2.6)	5.0(3.2)	4.1(3.1)

Table 2. Effect of Framing and an Analogy on Willingness to Switch

Variable	B	SE	Wald χ^2	OR Exp(B)	Sig.	95% CIs for OR	
Framing[a]	0.86	0.42	4.17	2.36	.041	1.04	5.40
Model χ^2 Nagelkerke	= 4.27, p = .039; R^2 = .058						
Explanation[b]	0.34	0.41	0.68	1.40	.411	0.63	3.16
Model χ^2 Nagelkerke	=.68, p = .410; R^2 = .009						

Note. The dependent variable is being willing to switch to a biosimilar, coded 0 = yes, 1 = no. OR= odds ratio.

[a]0 = negative framing, 1 = positive framing

[b]0 = analogy, 1 = framing

Table 3. Representative responses and frequencies from open-ended items.

Open-ended item	Categories	N (%)	Example responses
Concerns about biosimilars	*Reduced Efficacy*	52 (50%)	"…might not work as well… in comparison with the current biologic." "no guarantee that it would be effective as the branded version."
	Reduced Safety (side effects)	48 (46%)	"Same concerns as for biologics- the side effects, especially cancer." "Safety- is it safe for human consumption?"
	Manufacturing	9 (9%)	"Made in other country without Pharmac control over quality and process." "…why they need to use a different process."
	Lack of Clinical Trials	5 (5%)	"Not enough history…how many people tested it, where it's made." "Lack of studies to determine long term effects on patients."
Concerning information from explanations	*Reduced Efficacy*	21 (34%)	"It has taken almost 20 years to find a medication combo that works reasonably well- I worry that a biosimilar would be going backwards. "No guarantee that it would be as effective."

	Cost and Quality	17 (27%)	"…the outstanding message in the video for me, was cost savings." "…seems like a slightly inferior product."
	Reduced Safety (side effects)	15 (25%)	"More side effects could be possible."
	Lack of clinical trial evidence	7 (12%)	"Not much research as to how successful the switch will be, are we guinea pigs."
	Lack of Similarity	4 (5%)	"Change of ingredients- that they're not identical."
Information patients should know before switch	*Reduced Safety (side effects)*	40 (38%)	"What side effects are different between original and biosimilar."
	Efficacy	39 (37%)	How efficacy may differ (especially for drugs with high immunogenicity)." "That it would work the same or would be more effective."
	Clinical Trial Evidence	20 (19%)	"Rigorous trials to understand treatment success with branded/current biologic."
	Manufacturing	10 (10%)	"Where it is made. By whom." "How it is made + how it works."
	Switching Back	7 (7%)	"Can you go back if it is a choice (& it doesn't work as well)."

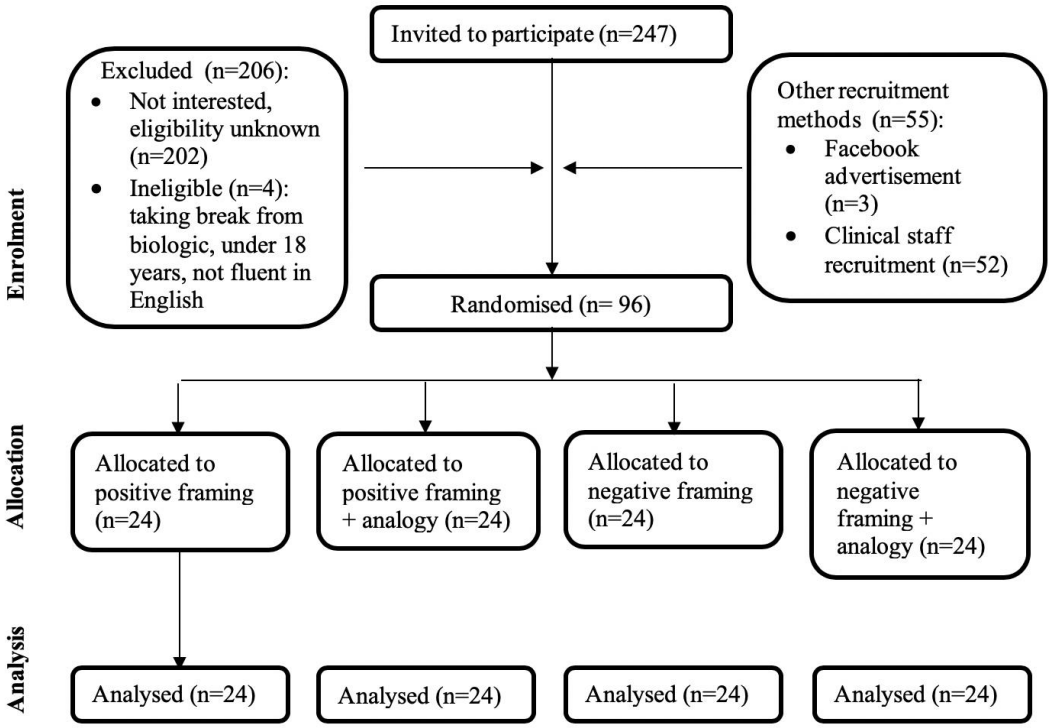

Figure 1. Study enrolment and retention.

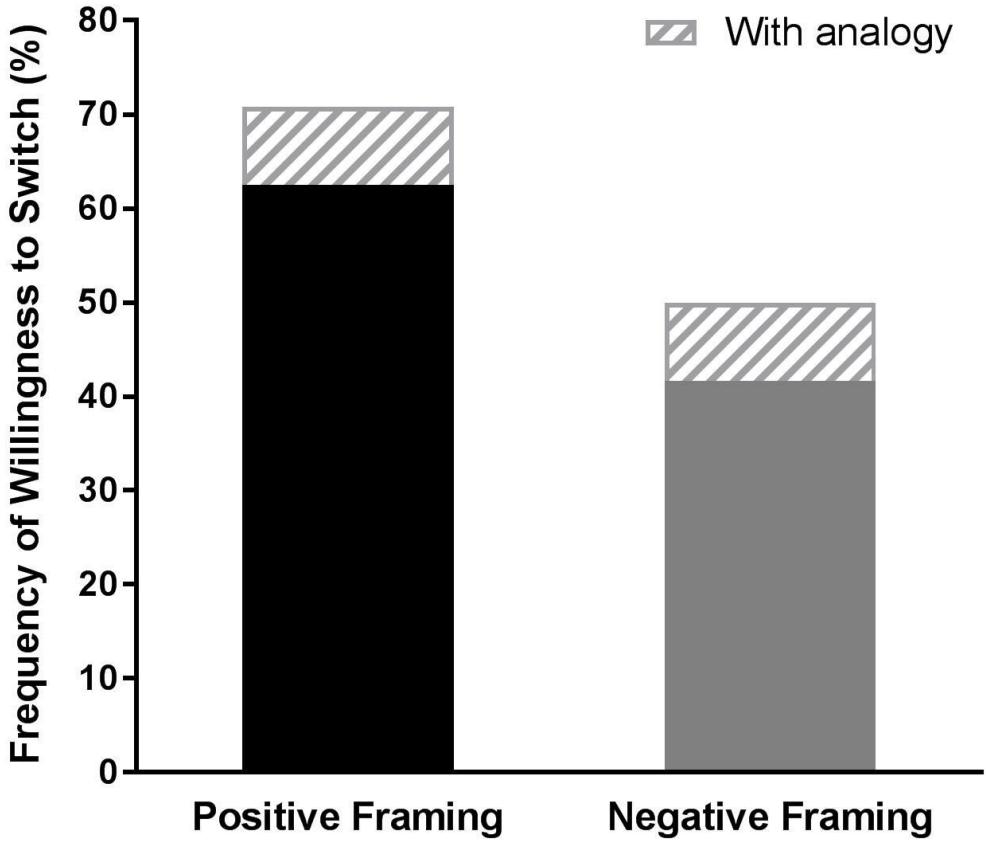

Figure 2. Bar graph demonstrating frequencies between groups in willingness to switch to a biosimilar.

SUPPLEMENTARY MATERIAL

Study Session Script

Preamble (all groups)

"Biosimilar medications are increasingly used in rheumatology and dermatology clinics worldwide. At present these medicines are not used in New Zealand, but it is possible that they will be used in future. You have been invited to participate in the study because you are taking a biologic medicine and we want to get the thoughts of patients currently on this type of medicine. It is important to say that the situation we describe is hypothetical and is not related to you or your current medicine. There are no plans at the moment to switch New Zealand patients to biosimilars. As biosimilars are likely to be prescribed for some patients in the future, this is an important study where we are interested in getting patients reactions to different ways of explaining a switch from the biologic drug that they are currently using to a biosimilar drug.

In this study, we want you to imagine that a doctor is explaining the switch from your current biologic X to a biosimilar, and we want to gather your reaction to this explanation. In this study patients are randomised (assigned by chance) to get different versions of this explanation. We want to find out if one of the explanations is better than the others. You will not be told which type of description you have been given. After you hear the explanation we will ask you to complete some questions and rating scales about your willingness to switch in this imaginary situation. Please be as honest as you can about your reaction to the explanation.

I want you to imagine that you are in a clinic with your rheumatologist. After your doctor has completed a clinical assessment, he discusses a change in your medication. This is a video of Dr YY explaining the change."

Video Script

"So now that we have reviewed your clinical progress and assessed how you are doing, I would like to talk to you about a change in your medication. I want to talk to you about switching to another biologic drug called a biosimilar. Switching to a biosimilar helps by saving health care costs. PHARMAC in New Zealand has a limited budget for buying medicines. As you know the biologic you are taking is a fairly expensive drug that costs about $15 to $20 thousand per year. A biosimilar will reduce this cost, possibly by about as much as a half and will help to save money to allow more people with arthritis and dermatology to get access to these expensive treatments."

Positive framing

"Let me tell you about the biosimilar. It's called a biosimilar because it is manufactured to be as similar as possible to the biologic that you are taking, and it is made using a pretty similar but not absolutely identical manufacturing process. It's been designed to work the same way though and it will work on the same biologic target as the drug that you are taking. It's pretty likely that the biosimilar will work the same way for you as your current biologic. It's a very similar medicine to the biologic that you have been taking and it's been manufactured to work in much the same way as the original biologic. But, as with any new drug, it is not possible to be absolutely certain that you will get the same beneficial effects or whether there might be some new small side effects. But I think that for you the benefits and risks are really similar for taking the biosimilar as to when you take the biologic."

Negative framing

"The biosimilar is called a biosimilar because it is manufactured to be as similar as possible to the biologic you are taking, but it is made through a different manufacturing process by a different company. The biosimilar has been designed to work the same way and to work on

the same biologic target as the drug you are on. But it is a different drug. I can't say for certain whether the biosimilar will work the same way as the current medicine for you, and whether the beneficial effects will occur to the same degree, or whether some new side effects might occur. Hopefully the benefits and risks are similar but there aren't any guarantees."

Analogy

"The process of making a biosimilar is a little bit like the process involved in making bread. The biological process involved in making bread may differ because different strains of yeast produce different flavours but they still produce a loaf of bread at the end of the process. So let's imagine that you are going to bake some bread and choose the cheaper Tasti Active Dried yeast over the Edmonds Surebake yeast, because it is on sale this week. Although the companies may have slightly different ways of producing the yeast, both yeasts will work in a similar biologic way to make the chemical process that will make the bread rise. We will keep monitoring you in the same way as you have been while you have been taking the biologic."