Predictors of loss to follow-up in hip fracture trials: a secondary analysis of the FAITH and HEALTH trials

Sivaratnam, S.; Comeau-Gauthier, M.; Sprague, S.; Schemitsch, E.H.; Poolman, R.W.; Frihagen, F.; ... ; FAITH & HEALTH Investigators

Predictors of Loss to Follow-up in Hip Fracture Trials: A Secondary Analysis of the FAITH and HEALTH Trials

Surabhi Sivaratnam, BHSc, MD (Cand),[a] Marianne Comeau-Gauthier, MD, MSc,[a] Sheila Sprague, PhD,[a,b] Emil H. Schemitsch, MD, FRCSC,[c] Rudolf W. Poolman, MD, PhD,[d] Frede Frihagen, MD, PhD, FRCSC,[e] Mohit Bhandari, MD, PhD, FRCSC,[a,b] Marc Swiontkowski, MD,[f] and Sofia Bzovsky, MSc[b] on behalf of the FAITH and HEALTH Investigators

Background: Hip fracture trials often suffer substantial loss to follow-up due to difficulties locating and communicating with participants or when participants, or their family members, withdraw their consent. We aimed to determine which factors were associated with being unable to contact FAITH and HEALTH participants for their 24-month follow-up and to also determine which factors were associated with their withdrawal of consent.

Methods: We conducted 2 multivariable logistic regression analyses to determine which factors were predictive of being unable to contact participants at 24 months postfracture and withdrawal of consent within 24 months of their fracture. Results were reported as odds ratios, 95% confidence intervals, and associated *P*-values. All tests were 2-tailed with alpha = 0.05.

Results: We were unable to contact 123 of 2520 participants (4.9%) for their 24-month follow-up visits and 124 (4.9%) withdrew their consent from the trial. Being non-White ($P = 0.003$), enrolled from a non-European hospital ($P < 0.001$), and treated with arthroplasty ($P < 0.001$) were associated with an increased odds of not completing the 24-month follow-up visit. Being enrolled from a hospital in the United States ($P = 0.02$), from a hospital in Oceania, India, or South Africa ($P < 0.001$) as compared to a European hospital, and treated with arthroplasty ($P < 0.001$) were associated with an increased odds of consent withdrawal.

Accepted for publication August 11, 2020.

From the [a]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada; [b]Division of Orthopaedic Surgery, Department of Surgery, McMaster University, Hamilton, ON, Canada; [c]Department of Surgery, University of Western Ontario, London, ON, Canada; [d]Department of Orthopedic and Trauma Surgery, OLVG, Amsterdam and Leiden University Medical Center, Leiden, the Netherlands; [e]Division of Orthopaedic Surgery, Oslo University Hospital, Oslo, Norway; and [f]Department of Orthopaedic Surgery, University of Minnesota, Minneapolis, MN.

The HEALTH trial was supported by research grants from the Canadian Institutes of Health Research (CIHR) (MCT-90168), National Institutes of Health (NIH) (1UM1AR063386-01), ZorgOnderzoek Nederland-medische wetensehappen (ZonMw) (17088.2503), Sophies Minde Foundation for Orthopaedic Research, McMaster Surgical Associates, and Stryker Orthopaedics. The funding sources had no role in design or conduct of the study; the collection, management, analysis, or interpretation of the data; or the preparation, review, or approval of the manuscript. The FAITH trial was supported by research grants from the Canadian Institutes of Health Research (MOP-106630 and MCT-87771), National Institutes of Health (1R01AR055267-01A1), Stichting NutsOhra (SNO-T-0602-43), the Netherlands Organisation for Health Research and Development (80-82310-97-11032), and Physicians' Services Incorporated. M. Bhandari was also funded, in part, through the Early Research Award Program, which provided funding for this study as well as by a Canada Research Chair in Musculoskeletal Trauma, which is unrelated to this study (McMaster University, Hamilton, ON, Canada). The FAITH trial was also supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under Award Number R01AR055267-01A1. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Research reported in this publication was also supported by The County Durham & Tees Valley Comprehensive Local Research Network, which operates as part of the National Institute for Health Research Comprehensive Clinical Research Network in England. The funding sources had no role in design or conduct of the study; the collection, management, analysis, or interpretation of the data; or the preparation, review, or approval of the manuscript.

E. H. Schemitsch reports personal fees from Acumed, LLC, personal fees from Amgen Co, research support from Biocomposites, board or committee member for the Canadian Orthopaedic Association, personal fees from DePuy, board or committee member for the Hip Society, board or committee member for the International Society for Fracture Repair, personal fees from ITS, editorial or governing board for the Journal of Orthopaedic Trauma, board or committee member for the Orthopaedic Trauma Association, editorial or governing board for the Orthopaedic Trauma Association International, board or committee member for the Osteosynthesis and Trauma Care Foundation, personal fees from Pentopharm, personal fees from Sanofi-Aventis, personal fees from Saunders/Mosby-Elsevier, personal fees from Smith & Nephew, personal fees from Springer, personal fees from Stryker, personal fees from Swemac, and personal fees from Zimmer, outside the submitted work. S. Sprague reports editorial or governing board for BMS Women's Health, employment from Global Research Solutions Inc, and employment from McMaster University, outside the submitted work. R. W. Poolman reports board or committee member for the Dutch Orthopaedic Association, research support from Lima, and research support from Link Orthopaedics, outside the submitted work. F. Frihagen reports personal fees from Amgen Co, personal fees from Smith & Nephew, personal fees from Synthes, and personal fees from Zimmer, outside the submitted work. M. Bhandari reports research support from Acumed, LLC, research support from Aphria, research support from Ferring Pharmaceuticals, research support and personal fees from Pendopharma, and research support and personal fees from Sanofi-Aventis, outside the submitted work. M. Swiontkowski reports board or committee member for the American Orthopaedic Association, consultant to the Minnesota Board of Medical Practice, editorial or governing board and publishing royalties, financial or material support for the Journal of Bone and Joint Surgery—American, publishing royalties, financial or material support from Saunders/Mosby-Elsevier, publishing royalties, financial or material support from Wolters Kluwer Health—Lippincott Williams & Wilkins, outside the submitted work. The remaining authors report no conflict of interest.

Reprints: Sofia Bzovsky, MSc, Division of Orthopaedic Surgery, Department of Surgery, McMaster University, 293 Wellington St. N, Suite 110, Hamilton, ON L8L 8E7, Canada (e-mail: bzovskys@mcmaster.ca).

DOI: 10.1097/BOT.0000000000001928

Discussion: Certain factors may be predictive of loss to follow-up in hip fracture trials. We suggest that the identification of such factors may be used to inform and improve retention strategies in future orthopaedic hip fracture trials.

Key Words: loss to follow-up, withdrawal of consent, hip fractures

Level of Evidence: Prognostic Level II. See Instructions for Authors for a complete description of levels of evidence.

(*J Orthop Trauma* 2020;34:S22–S28)

INTRODUCTION

A difficulty frequently faced in hip fracture trials is loss to follow-up (LTFU), which includes participants not returning for their follow-up appointments or being unable to reach participants by telephone for data collection, as well as participants, or their family members, withdrawing their consent to participate in the trial.[1–3] Even the most rigorously designed orthopaedic hip fracture randomized controlled trials (RCTs) incur the problem of participant noncompliance with follow-up.[1–4] High LTFU rates may lower the statistical power of a study's sample size and can substantially bias the study's results if the outcomes of participants remaining in the study differ from those who were LTFU.[3,5] Moreover, high LTFU may result in a study's findings no longer reflecting the sample of patients who were recruited. Therefore, the minimization of LTFU is an important methodological consideration.[4]

The LTFU rates within trials can be quite high, with previous orthopaedic trauma RCTs reporting up to 28% LTFU.[1] Although hip fracture trials in older adults seem to have lower rates of LTFU, ranging typically from 2% to 12%,[6–8] including the FAITH (6.9%) and HEALTH (12.0%) trials,[9,10] it has been reported that approximately 20% of orthopaedic RCTs fail to report their LTFU.[3] Therefore, these rates may actually be higher and remain an important source of potential bias.[3] In other areas of orthopaedics, LTFU rates exceed the commonly accepted 20% LTFU threshold.[11,12] Recent research suggests that this 20% threshold may not be strict enough to mitigate the risk of bias incurred due to LTFU in orthopaedic trials.[13] Zelle et al[13] made this suggestion based on their findings that numerous statistically significant orthopaedic trials' results became nonsignificant when simulated with an LTFU rate of 20%. Therefore, Zelle et al[13] instead recommend that researchers aim for a follow-up rate that exceeds 80%.

Although the HEALTH and FAITH trials both achieved greater than 80% follow-up, the trial data can offer insights for both clinicians and researchers on participant characteristics that may be associated with being unable to contact participants. The objective of this preplanned analysis was to investigate and identify which baseline characteristics were predictive of being unable to contact participants within 24 months of femoral neck fracture in patients aged 50 years or older participating in the HEALTH and FAITH trials.[9,10] Although both of these large, international studies were rigorously designed and implemented extensive retention strategies, not all participants were compliant with follow-up. Using the data from these trials to identify factors that may be predictive of being unable to contact participants may allow future researchers to develop more targeted strategies that mitigate the risk of LTFU and ensure that the patients retained represent the sample that was recruited.

METHODS

Definition of Loss to Follow-up in HEALTH and FAITH Trials

Participants in the HEALTH and FAITH trials were deemed LTFU after their failure to complete the trial 24-month visit due to difficulties locating participants or with participants, or their family members, withdrawing their consent. Exhaustive measures had been taken by the trial personnel to contact patients before marking them as lost to follow-up. These measures included contacting the patient, their primary care physician, as well as 3 alternative contacts. Strategies used in the trials to minimize LTFU included aligning the follow-up schedule with that of their normal surgical fracture clinic visits, numerous attempts to contact participants or individuals affiliated with participants, routine verification of contact, and the selection of outcomes for which data could be collected through telephone rather than an in-person visit.

Statistical Methods

Demographics

We examined the demographic and injury characteristics of participants who study personnel were unable to contact at 24 months, those who withdrew their consent from the trials, and those who completed their 24-month follow-up visit. Mean values and SDs were presented for continuous variables, whereas frequencies and percentages were presented for categorical variables.

Analyses

We conducted 2 multivariable logistic regression analyses to investigate the association between selected factors and not completing the 24-month follow-up and withdrawing consent, respectively. In the first analysis, the dependent variable was not completing their 24-month follow-up visit for the reason that they could not be contacted in the HEALTH and FAITH studies during the 24-month follow-up period. It should be noted that participants who died during the 24-month follow-up period were not included as being LTFU. The number of independent variables and corresponding levels included in the 2 analyses were based on the recommendations of Peduzzi et al.[14] Notably, a low number of events per variable (EPV) (ie, EPV values less than 10) can lead to major problems involving model bias, precision, and significance. In this analysis, the number of events was the number of patients who were lost to follow-up, which was 123. To avoid overfitting and ensure that our EPV was greater than 10, we included 10 variables, with a total of 12 levels. The

selection of these independent variables was based on previous literature and expert opinions. The factors included age, sex, ethnicity [White vs. other (Indigenous, South Asian, East Asian, Black, or Hispanic/Latino)], body mass index (underweight [body mass index <18.5] versus other (body mass index ≥18.5), prefracture living setting (institutionalized vs. not institutionalized), prefracture functional status (use of an aid vs. independent ambulation), American Society for Anesthesiologists (ASA) physical status (Class I/II vs. Class III/IV/V), hospital location [Canada vs. the United States vs. Europe vs. Other (Oceania, India, and South Africa)], comorbidities (present vs. not present), and type of surgical treatment (arthroplasty vs. internal fixation). We also conducted a multivariable logistic regression analysis to investigate the association between the same selected factors and withdrawal of consent. The dependent variable was withdrawal of consent in the HEALTH and FAITH studies during the 24-month follow-up period. The statistical output of these analyses was reported as odds ratios (ORs) with corresponding 95% confidence intervals (CIs) and associated *P*-values. All analyses were conducted using R software (version 3.6.1, R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Participant Characteristics

There were 247 of 2520 (9.8%) participants in HEALTH and FAITH who were LTFU. Specifically, 123 of 2520 (4.9%) participants from the HEALTH (77/1441 participants, 5.3%) and FAITH (46/1079 participants, 4.3%) trials did not complete their 24-month visit. In addition, 124 of 2520 (4.9%) participants withdrew their consent to participate in the HEALTH (96/1441, 6.7%) and FAITH (28/1079 participants, 2.6%) trials.

Table 1 presents the demographic and injury characteristics of participants who did not complete their 24-month follow-up visit, withdrew consent, and those who were not LTFU. For those 123 participants who did not complete the 24-month visit (excluding those who withdrew consent), the mean age was 74.1 (SD 12.0), most were female (57.7%), White (75.2%), enrolled from a hospital in North America (39.0%), and were not living in an institutionalized setting prefracture (95.1%). For those 124 participants who withdrew their consent from the trial, the mean age was 78.4 (SD 9.8), most were female (71.0%), White (92.7%), enrolled from a hospital in North America (40.3%), and were not living in an institutionalized setting prefracture (91.9%). Among those 2397 participants who were not lost to follow-up, the mean age was 75.9 years (SD 10.7), most were female (66.4%), White (90.4%), enrolled from a hospital in Europe (43.7%), and were not living in an institutionalized setting prefracture (95.0%). It should be noted that in general, the majority of participants enrolled in both the FAITH and HEALTH trials were White (82.4% and 95.1%, respectively).

Factors Associated with LTFU

Participants of Indigenous, South Asian, East Asian, Black, or Hispanic/Latino ethnicity (OR vs. White 2.17, 95% CI: 1.30–3.61; $P = 0.003$) were at an increased odds of not completing the 24 month follow-up in the FAITH and HEALTH trials. Participants who were enrolled from a hospital in Canada (OR vs. Europe 2.51, 95% CI: 1.42–4.44; $P < 0.001$), from a hospital in the United States (OR vs. Europe 4.72, 95% CI: 2.73–8.17; $P < 0.001$), from a hospital in Oceania, India, or South Africa (OR vs. Europe 3.91, 95% CI: 1.96–7.82; $P < 0.001$), and treated with arthroplasty (OR vs. internal fixation 2.67, 95% CI: 1.71–4.17; $P < 0.001$) were also at an increased odds. Age, sex, body mass index, prefracture living setting, prefracture functional status, ASA physical status, and presence of a comorbidity were not found to be associated with not completing the 24-month visit (Table 2).

Similar to the first analysis, participants who were enrolled from a hospital in the United States (OR vs. Europe 1.77, 95% CI: 1.10–2.86; $P = 0.02$), from a hospital in Oceania, India, or South Africa (OR vs. Europe 2.75, 95% CI: 1.53–4.95; $P < 0.001$), and treated with arthroplasty (OR vs. internal fixation 3.10, 95% CI: 1.92–5.01; $P < 0.001$) were at an increased odds of withdrawing consent in the FAITH and HEALTH trials. In contrast to the prior analysis, we found that not having a comorbidity approached statistical significance (OR 1.79, 95% CI 0.99–3.23; $P = 0.053$) for being associated with an increased odds of withdrawing consent. Age, ethnicity, body mass index, prefracture living setting, prefracture functional status, and ASA physical status were also not found to be associated with withdrawing consent (Table 2).

DISCUSSION

The results of this analysis show that certain participant characteristics and clinical variables, including ethnicity, country of the participating hospital, and type of surgical treatment, have an impact on LTFU in femoral neck fracture patients aged 50 years or older. Specifically, participants with an ethnicity other than White, enrolled from a hospital not located in Europe, and treated with arthroplasty were at an increased odds of being lost to follow-up. Surprisingly, other factors, including sex, age, body mass index, prefracture living setting, prefracture functional status, and ASA class, were found to not be associated with LTFU in this population. Our results as well as other orthopaedic studies on predicting factors of LTFU have highlighted significant health care disparities that need to be addressed in terms of ethnicity, disability, unemployment, and social support, to name a few.[1,15–18] Identifying predictors of LTFU will help future trials in targeting their "retention efforts" in the participants associated with higher risk of LTFU.

Previous literature supports our finding that the country of the participating hospital is associated with LTFU. A systematic review investigating LTFU rates in 559 orthopaedic studies of 131,836 participants identified that treatment in the United States as compared to other countries was a predictive factor of LTFU ($P = 0.01$).[3] Somerson et al[3]

TABLE 1. Patient Demographics

Variable	Not LTFU*, N = 2273	Did Not Complete the 24-Month Visit, N = 123	Withdrew Consent, N = 124
Age, mean (SD) (y)	75.7 (10.7)	74.1 (12.0)	78.4 (9.8)
Sex, n (%)			
Male	770 (33.9)	52 (42.3)	36 (29.0)
Female	1503 (66.1)	71 (57.7)	88 (71.0)
Ethnic origin, n (%)			
Indigenous	5 (0.2)	2 (1.6)	0 (0.0)
South Asian	125 (5.5)	12 (9.8)	2 (1.6)
East Asian	20 (0.9)	4 (3.3)	1 (0.8)
Black	57 (2.5)	9 (7.3)	5 (4.0)
Hispanic or Latino	14 (0.6)	3 (2.4)	0 (0.0)
White	2041 (89.8)	91 (74.0)	115 (92.7)
Current drugs, n (%)†			
None	532 (23.4)	34 (27.6)	24 (19.4)
NSAIDs	299 (13.2)	20 (16.3)	12 (9.7)
General cardiac	824 (36.3)	39 (31.7)	45 (36.3)
Opioid analgesics	188 (8.3)	15 (12.2)	14 (11.3)
Pulmonary drugs	271 (11.9)	12 (9.8)	12 (9.7)
Antihypertension drugs	1189 (52.3)	56 (45.5)	60 (48.4)
Osteoporosis drugs	253 (11.1)	10 (8.1)	14 (11.3)
BMI, n (%)	N = 2232	N = 112	N = 115
Underweight (<18.5)	123 (5.4)	10 (8.1)	10 (8.1)
Normal Weight (18.5–24.9)	1152 (50.7)	62 (50.4)	50 (40.3)
Overweight (25.0–29.9)	701 (30.8)	33 (26.8)	37 (29.8)
Obese (>30.0)	256 (11.3)	7 (5.7)	18 (14.5)
Prefracture living setting, n (%)			
Institutionalized	110 (4.8)	6 (4.9)	10 (8.1)
Not institutionalized	2163 (95.2)	117 (95.1)	114 (91.9)
Prefracture functional status, n (%)			
Use of aid	539 (23.7)	28 (22.8)	33 (26.6)
Independent ambulator	1734 (76.3)	95 (77.2)	91 (73.4)
ASA physical status, n (%)			
Class I/II	1213 (53.4)	67 (54.5)	56 (45.2)
Class III/IV/V	1060 (46.6)	56 (45.5)	68 (54.8)
Centre, n (%)			
Canada	518 (22.8)	28 (22.8)	15 (12.1)
United States	546 (24.0)	48 (39.0)	35 (28.2)
Europe	994 (43.7)	23 (18.7)	54 (43.5)
Oceania	101 (4.4)	8 (6.5)	19 (15.3)
Africa	5 (0.2)	1 (0.8)	0 (0.0)
India	109 (4.8)	15 (12.2)	1 (0.8)
Comorbidity, n (%)			
Yes	2007 (88.3)	102 (82.9)	107 (86.3)
No	266 (11.7)	21 (17.1)	17 (13.7)
Surgical treatment, n (%)			
Arthroplasty	1268 (55.8)	77 (62.6)	96 (77.4)
Internal fixation	1005 (44.2)	46 (37.4)	28 (22.6)

*Participants who died during the 24-month follow-up period were captured under the "Not LTFU" group.
†More than one drug could be selected.
ASA, American Society of Anesthesiologists; BMI, body mass index; LTFU, lost to follow-up; SD, standard deviation.

indicated that the reasons for this difference remain unclear and are likely multifactorial. Similarly, in an RCT of 2381 adults with an open fracture, participants who received treatment in the United States (which has a predominantly privately funded health care system) were more likely to be LTFU than those who received treatment in Canada, Europe, or Australia (which have publicly funded health care systems) (OR 3.56, 95% CI 2.46–5.17; $P < 0.001$).[4] Although we also

TABLE 2. Prognostic Variables Associated With LTFU (n = 2520)

	Did Not Complete the 24-Month Visit (123 Events)		Withdrawal of Consent (124 Events)	
Variable	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Ethnicity				
Other vs. White	2.17 (1.30–3.61)	0.003	1.79 (0.83–3.89)	0.14
Hospital location		Overall: <0.001		Overall: <0.001
Canada vs. Europe	2.51 (1.42–4.44)	<0.001	0.58 (0.32–1.05)	0.07
United States vs. Europe	4.72 (2.73–8.17)	<0.001	1.77 (1.10–2.86)	0.02
Other vs. Europe	3.91 (1.96–7.82)	<0.001	2.75 (1.53–4.95)	<0.001
Surgical treatment				
arthroplasty vs. internal fixation	2.67 (1.71–4.17)	<0.001	3.10 (1.92–5.01)	<0.001
Age (10-y increase)	0.93 (0.77–1.13)	0.51	1.14 (0.92–1.41)	0.22
Sex				
Male vs. female	1.34 (0.91–1.98)	0.20	0.85 (0.56–1.28)	0.45
BMI				
Underweight (BMI <18.5) vs. other (BMI ≥18.5)	1.58 (0.79–3.17)	0.18	1.51 (0.76–3.02)	0.24
Prefracture living setting				
Institutionalized vs. not institutionalized	0.87 (0.36–2.07)	0.63	1.71 (0.85–3.45)	0.13
Prefracture functional status				
Use of aid vs. independent ambulator	1.08 (0.67–1.75)	0.57	1.00 (0.64–1.57)	0.99
ASA physical status				
Class III/IV/V vs. Class I/II	0.77 (0.50–1.18)	0.40	1.12 (0.74–1.69)	0.59
Comorbidity				
No vs. Yes	1.27 (0.71–2.22)	0.78	1.79 (0.99–3.23)	0.053

ASA, American Society of Anesthesiologists; BMI, body mass index; LTFU, loss to follow-up; OR, odds ratio.

identified that participants enrolled in hospitals located in Canada and other counties (Oceania, India, and South Africa) were at a higher risk of LTFU as compared to those enrolled in Europe, we are unaware of any studies that have made comparisons between these locations. Similar to our primary analysis, our secondary analysis demonstrated that participants enrolled in hospitals located in the United States and other countries (Oceania, India, and South Africa) were at an increased odds of withdrawing consent as compared to those enrolled in Europe, but to the best of our knowledge, there have not been previously conducted studies evaluating predictors of consent withdrawal in orthopaedics. Our results suggest that there may be geographic differences that may have enhanced follow-up and compliance. In Norway and several other European countries, where nearly all hospitals are government-run, patients "belong" to a hospital, which is determined by their proximity to the hospital. This European model of "belonging" to a certain hospital may prove to be more successful in participant retention because for most health issues, patients will have to go to that particular hospital. In addition, these patients may also feel more responsible toward their assigned hospital because they know there is a long-term relationship. To expand on this further, there have been some studies that have found decreased participant retention with increased living distance from their hospital.[16,19,20]

Similar to our findings, a cohort study of 3202 patients undergoing anterior cruciate ligament reconstruction found that those of non-White ethnicity (black: OR 3.64; other non-White: OR 1.81) were at a high risk for 2-year LTFU.[15] Ramkumar et al[15] suggested that the most pragmatic denominator among the described patients at risk for LTFU was possibly socioeconomic status, but they were unable to directly address it in their study other than controlling for level of education and marital status in their analyses, which still showed an increased LTFU associated with non-White ethnicities. Other orthopaedic studies have shown that when controlling for factors, including age, sex, insurance, income, and education, those of non-White ethnicity were less likely to receive operative fixation for a clavicle fracture,[21] and benefits from total knee arthroplasty or total hip arthroplasty.[22] In addition, other studies have suggested better compliance with follow-up when patients and their physician share the same ethnic identity.[23,24] Similar to Ramkumar et al, we were unable to address socioeconomic status in our analyses. At this time, there is limited research on what factors contribute to multicultural participants' recruitment and retention in studies. It is highly complex, and as the studies above suggested, there are other reasons why those of non-White ethnicity access health care differently and this probably has an impact on follow-up visit compliance. Collection of information on

level of education, working status, marital status, social support, and income would allow for researchers to assess the effect of socioeconomic status independently. An improved understanding of these factors would help ensure that patients recruited and retained in studies would be representative of the diverse populations that they are drawn from. Ensuring diversity would also assist in making study findings more generalizable to the whole population.

Our findings indicated that participants whose femoral neck fracture was treated with arthroplasty (OR vs. internal fixation 2.67, 95% CI: 1.71–4.17; $P < 0.001$) were associated with an increased odds of LTFU, as well as an increased odds of withdrawal of consent (OR vs. internal fixation 3.10, 95% CI: 1.92–5.01; $P < 0.001$) within 24 months of femoral neck fracture. To the best of our knowledge, no other orthopaedic trauma studies have evaluated the impact of surgical treatment for femoral neck fracture patients on LTFU, nor on withdrawal of consent. However, a systematic review and meta-analysis of 8 RCTs comparing arthroplasty to internal fixation in 2206 elderly patients with a displaced intracapsular femoral neck fracture found that those in the arthroplasty group reported significantly lower complications (risk ratio: 0.56, 95% CI: 0.38–0.80; $P < 0.01$), reoperations (risk ratio: 0.17, 95% CI: 0.13–0.22; $P < 0.00001$), revision rates (risk ratio: 0.11, 95% CI: 0.08–0.16; $P < 0.00001$), and better function compared to those treated with internal fixation, and they were less likely to suffer postoperative pain.[25] These findings lead us to suggest that those experiencing more complications postsurgery may be more likely to return to clinic for a follow-up visit and, therefore, not be lost to follow-up. In addition, the increased odds of LTFU in arthroplasty patients may be related to arthroplasty being a more definitive treatment, whereas internal fixation patients require monitoring to ensure fracture healing, which takes time and may translate to a greater attendance at follow-up visits.

Another study investigating hip fractures among elderly patients found that LTFU was highest among patients living in institutionalized settings, such as nursing homes, as well as patients who were not independent ambulators, which differed from our findings of no statistically significant differences between these groups of patients.[26]

It should also be noted that there is conflicting evidence regarding the association of certain factors with LTFU.[1,15,27,28] Although not focusing on the elderly hip fracture population, for example, previous orthopaedic trauma studies of younger adults investigating LTFU found that male sex is predictive of LTFU.[1,15] These findings were supported by other literature indicating that women are more inclined to visit their doctors than men, which in turn might imply that they would be more likely to attend follow-up appointments.[27] By contrast, a study investigating hip fractures among elderly people found that sex was not associated with LTFU.[28] Age may not be an important factor in predicting LTFU in the elderly population for the reason that older participants are less transient and may be easier to be contacted by study personnel, but other studies have demonstrated that younger adults may be at a higher risk of LTFU compared to older adults.[4,29] Specifically, in an RCT of 2381 adults with an open fracture, an age of <30 years (OR 2.16, 95% CI: 1.19–3.95; $P = 0.012$) significantly increased the odds of a patient being LTFU.[4] Another study found that each additional year in age reduced the odds of a participant changing some of their contact information by 2.2% (OR 0.98, 95% CI: 0.97–0.99), which would allow for study personnel to more easily contact study participants who are older.

Overall, the literature investigating LTFU in orthopaedic trials remains scarce and has not reached consensus on which factors are predictive of LTFU. Previous literature has also identified strategies that may be implemented to prevent LTFU in orthopaedic settings.[4] For example, a Cochrane review suggested that "incentives, communication strategies, new questionnaire strategies, behavioural or motivational strategies, case management, and methodological strategies" could be used to improve retention rates.[30] Some of these strategies were implemented in the FAITH and HEALTH studies. For example, telephone follow-ups were conducted when in-clinic visits were not possible.[5,13] However, these strategies may have been more effective if they were focused on participants who were at higher risk of being lost to follow-up. We hypothesized that the results of the present analysis would allow research personnel to be more cognizant of which participants are more likely to be lost to follow-up, allowing for targeted implementation of retention strategies. However, given our findings, a future area of study may entail evaluating these targeted strategies to help increase retention.

This analysis has both strengths and limitations. The strengths of this analysis include the use of data from 2 RCTs that were rigorously designed by the same principal investigators, followed similar follow-up regimens, and had large sample sizes. In addition, these RCTs enrolled patients from numerous countries, and thus both of these studies had high external validity. To the best of our knowledge, determining predictors of withdrawal of consent has not previously been evaluated in the field of orthopaedics and therefore, adds novel findings to the literature. Some of the limitations of the present analysis are as follows. Given that our data were retrospectively obtained from 2 completed RCTs, we were only able to include previously collected variables in the model. Socioeconomic factors such as alcohol consumption, smoking habits, and insurance status may have been important predictors of LTFU, but such data were not collected in the HEALTH and FAITH studies and, therefore, we were unable to analyze these factors. Because the FAITH and HEALTH trials included older patients, most individuals were already retired and for that reason, we were unable to include employment status before injury as a factor in the model. This factor may have been predictive of LTFU in a younger population, as has been suggested in previous literature.[1,18,31] Moreover, given that 123 patients were lost to follow-up, we were limited in the number of factors and corresponding levels that could be included in our model.

Overall, we conclude that certain characteristics and clinical variables may be predictive of LTFU in orthopaedic trials; however, further research must be done. In our study of elderly hip fracture patients with a 9.8% LTFU rate, participants with an ethnicity other than White, enrolled from a hospital not located in Europe, and treated with arthroplasty were at an increased odds of being lost to follow-up. Predicting factors for LTFU have previously

been mainly described for the trauma population so it is highly likely that the elderly hip fracture population does not share the same predictors. Additional research is necessary, given that current literature on this frequently encountered problem remains scarce, especially in the older hip fracture population. We suggest that the identification of such factors may be used to inform and improve retention strategies in future orthopaedic hip fracture trials.

ACKNOWLEDGMENTS

The authors thank the HEALTH Investigators and the FAITH Investigators (http://links.lww.com/JOT/B250).

REFERENCES

1. Zelle BA, Buttacavoli FA, Shroff JB, et al. Loss of followup in orthopaedic trauma: who is getting lost to follow-up? *J Orthop Trauma.* 2015; 29:510–515.
2. Sprague S, Leece P, Bhandari M, et al. Limiting loss to follow-up in a multicenter randomized trial in orthopedic surgery. *Control Clin Trials.* 2003;24:719–725.
3. Somerson JS, Bartush KC, Shroff JB, et al. Loss to follow-up in orthopaedic clinical trials: a systematic review. *Int Orthop.* 2016;40:2213–2219.
4. Madden K, Scott T, McKay P, et al. Predicting and preventing loss to follow-up of adult trauma patients in randomized controlled trials: an example from the FLOW trial. *J Bone Joint Surg.* 2017;99:1086–1092.
5. Murray DW, Britton AR, Bulstrode CJ. Loss to follow-up matters. *J Bone Joint Surg.* 1997;79:254–257.
6. Frihagen F, Nordsletten L, Madsen JE. Hemiarthroplasty or internal fixation for intracapsular displaced femoral neck fractures: randomised controlled trial. *BMJ.* 2007;335:1251–1254.
7. Parker MJ, Pryor G, Gurusamy K. Hemiarthroplasty versus internal fixation for displaced intracapsular hip fractures: a long-term follow-up of a randomised trial. *Injury.* 2010;41:370–373.
8. Chammout GK, Mukka SS, Carlsson T, et al. Total hip replacement versus open reduction and internal fixation of displaced femoral neck fractures: a randomized long-term follow-up study. *J Bone Joint Surg.* 2012;94:1921–1928.
9. HEALTH Investigators, Bhandari M, Einhorn TA, Guyatt G, et al. Total hip arthroplasty or hemiarthroplasty for hip fracture. *N Engl J Med.* 2019; 381:2199–2208.
10. Collaborators. Fixation using alternative implants for the treatment of hip fractures (FAITH) investigators. fracture fixation in the operative management of hip fractures (FAITH): an international, multicentre, randomised controlled trial. *Lancet.* 2017;389:1519–1527.
11. Sackett DL, Straus SE, Richardson WS, et al. *Evidence-based Medicine—How to Practice and Teach EBM.* New York, NY: Churchill Livingstone; 1997.
12. Kristman V, Manno M, Côté P. Loss to follow-up in cohort studies: how much is too much? *Eur J Epidemiol.* 2003;19:751–760.
13. Zelle BA, Bhandari M, Sanchez AI, et al. Loss of follow-up in orthopaedic trauma: is 80% follow-up still acceptable? *J Orthop Trauma.* 2013;27:177–181.
14. Peduzzi P, Concato J, Kemper E, et al. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol.* 1996;49:1373–1379.
15. Ramkumar PN, Tariq MB, Amendola A, et al. Risk factors for loss to follow-up in 3202 patients at 2 years after anterior cruciate ligament reconstruction: implications for identifying health disparities in the MOON prospective cohort study. *Am J Sports Med.* 2019;47:3173–3180.
16. Patterson JT, Albright PD, Jackson JH, et al. Travel barriers, unemployment, and external fixation predict loss to follow-up after surgical management of lower extremity fractures in Dar es Salaam, Tanzania. *OTA Int.* 2020;3:e061–e067.
17. Sleat GKJ, Lefaivre KA, Broekhuyse HM, et al. Predicting completion of follow-up in prospective orthopaedic trauma research. *OTA Int.* 2019;2: e047–e052.
18. ten Berg PWL, Ring D. Patients lost to follow-up after metacarpal fractures. *J Hand Surg Am.* 2012;37:42–46.
19. Wharton MG, Shultz CL, Packard BD, et al. Patient compliance with follow-up after open reduction and internal fixation for treating malleolar ankle fractures: a retrospective review. *UNM Orthop Res J.* 2019;8:82–84.
20. Badenhorst D, Van der Westhuizen C, Britz E, et al. Lost to follow-up: challenges to conducting orthopaedic research in South Africa. *South Afr Med J.* 2018;108:917–921.
21. Schairer W, Nwachukwu B, Warren R, et al. Operative fixation for clavicle fractures-socioeconomic differences persist despite overall population increases in utilization. *J Orthop Trauma.* 2017;31: e167–e172.
22. Irgit K, Nelson C. Defining racial and ethnic disparities in THA and TKA. *Clin Orthop Relat Res.* 2011;469:1817–1823.
23. Saha S, Arbelaez J, Cooper L. Patient-physician relationships and racial disparities in the quality of health care. *Am J Public Health.* 2003;93: 1713–1719.
24. Laveist T, Nuru-Jeter A. Is Doctor-patient race concordance associated with greater satisfaction with care? *J Heal Soc Behav.* 2002;43:296–306.
25. Ye CY, Liu A, Xu MY, et al. Arthroplasty versus internal fixation for displaced intracapsular femoral neck fracture in the elderly: systematic review and meta-analysis of short- and long-term effectiveness. *Chin Med J Engl.* 2016;129:2630–2638.
26. Nygard H, Matre K, Fevang JM. Evaluation of timed up and go test as a tool to measure postoperative function and prediction of one year walking ability for patients with hip fracture. *Clin Rehabil.* 2016;30:472–480.
27. Bertakis K, Azari R, Helms L, et al. Gender differences in the utilization of health care services. *J Fam Pr.* 2000;49:147–152.
28. Wilson RT, Chase GA, Chrischilles EA, et al. Hip fracture risk among community-dwelling elderly people in the United States: a prospective study of physical, cognitive, and socioeconomic indicators. *Am J Public Health.* 2006;96:1210–1218.
29. London D, Stepan J, Goldfarb C, et al. The (In)stability of 21st century orthopedic patient contact information and its implications on clinical research: a cross-sectional study. *Clin Trials.* 2017;14: 187–191.
30. Brueton VC, Tierney J, Stenning S, et al. Strategies to improve retention in randomised trials. *Cochrane Database Syst Rev.* 2013;12:MR000032.
31. Norquist BM, Goldberg BA, Matsen FA. Challenges in evaluating patients lost to follow-up in clinical studies of rotator cuff tears. *J Bone Joint Surg Am.* 2000;82:838–842.