Comparing Total Hip Arthroplasty and Hemi-Arthroplasty on Secondary Procedures and Quality of Life in Adults With Displaced Hip Fractures

NCT00556842

Supplementary Appendix

Prepared on: September 12, 2019

SUPPLEMENTARY APPENDIX

Hip Fracture Evaluation with Alternatives of
Total Hip Arthroplasty Versus Hemi-Arthroplasty

Prepared on: September 12, 2019

Supplementary Appendix Table of Contents

1.0 HEALTH INVESTIGATORS

Steering Committee members vouch for the completeness and accuracy of the data, analyses reported, and for adherence of the trial to the protocol. The first author (Writing Committee Chair) wrote the first draft of the manuscript; all members of the Writing Committee made revisions and made the decision to submit the manuscript.

Writing Committee: Mohit Bhandari (Chair, McMaster University), Thomas A. Einhorn (New York University Langone Medical Center), Gordon H. Guyatt (McMaster University), Emil H. Schemitsch (University of Western Ontario), Robert D. Zura (Louisiana State University Health Sciences Center), Sheila Sprague (McMaster University), Frede Frihagen (Oslo University Hospital), Ernesto Guerra-Farfán (Hospital Vall d'Hebrón*)*, Ydo V. Kleinlugtenbelt (Deventer Ziekenhuis**)**, Rudolf W. Poolman (OLVG), Amar Rangan (The James Cook University Hospital), Sofia Bzovsky (McMaster University), Diane Heels-Ansdell (McMaster University), Lehana Thabane (McMaster University), Stephen D. Walter (McMaster University), P.J. Devereaux (Co-Chair, McMaster University).

Steering Committee: Mohit Bhandari (Chair, McMaster University), P.J. Devereaux (McMaster University), Thomas A. Einhorn (New York University Langone Medical Center), Frede Frihagen (Oslo University Hospital), Ernesto Guerra-Farfán (Hospital Vall d'Hebrón*)*, , Kenneth J. Koval (Orlando Regional Medical Centre), Rudolf W. Poolman (OLVG), Emil H. Schemitsch (University of Western Ontario), Kevin Tetsworth (University of Queensland), Lehana Thabane (McMaster University), Stephen D. Walter (McMaster University), Gordon H. Guyatt (McMaster University).

Global Methods Centre: Mohit Bhandari (Principal Investigator); Sheila Sprague (Research Director); Paula McKay (Manager); Kim Madden, Sofia Bzovsky, Kerry Tai, Taryn Scott, Marilyn Swinton (Research Coordination); Naveen Khan (Adjudication Coordination); Diane Heels-Ansdell (Statistical Analysis); Lisa Buckingham, Aravin Duraikannan (Data Management); (McMaster University).

United States Methods Centre: Thomas A. Einhorn (Principal Investigator); Heather Silva (Research Coordination) (Boston University Medical Center). Thomas A. Einhorn, David Novikov, Daniel P. Waren (New York University).

Netherlands Methods Centre: Ydo V. Kleinlugtenbelt, Ellie B.M. Landman (**Deventer Ziekenhuis; Definitive).** Martin J. Heetveld, Rudolf W. Poolman, Esther M.M. Van Lieshout, Paul T.P.W. Burgers (Erasmus MC, University Medical Center Rotterdam, Rotterdam; Pilot).

United Kingdom Methods Centre: Amar Rangan (The James Cook University Hospital, South Tees Hospitals NHS Foundation Trust, University of Oxford, University of York), Birgit Hanusch, Lucksy Kottam (The James Cook University Hospital, South Tees Hospitals NHS Foundation Trust).

Central Adjudication Committee: Robert D. Zura (Chair, Louisiana State University Health Sciences Center), Victoria Avram (McMaster University), Ajay Manjoo (McMaster University).

Data and Safety Monitoring Board (CIHR): John Antoniou (Chair), Tim Ramsay, Earl R. Bogoch, Andrew Trenholm.

Data and Safety Monitoring Board (NIH): Stephen Lyman (Chair), Madhu Mazumdar, Kevin J. Bozic, Mark Luborsky, Stuart Goodman, Susan Muray, Benjamin K. Potter.

Statistical Support: Diane Heels-Ansdell, Lehana Thabane, Nathan N. O'Hara, Gerard P. Slobogean, Quazi Ibrahim.

Participating Clinical Sites:

Canada:
University of Calgary - Richard Buckley, Robert Korley, Paul Duffy, Shannon Puloski, Eldridge Batuyong, Christopher Martin, James MacKenzie, Jason Werle, Kelly Johnston, Neil White, Marcia Clark, Gregory Abelseth, Stephen Hunt, Justin LeBlanc, Prism Schneider, Kimberly Carcary, Ross McKercher, Lisa Murphy, Melissa Lorenzo, Tanja Harrison, Leah Schultz, Aftab Akbari, Stephanie Yee, Tina Samuel, Saboura Mahdavi

University of British Columbia/Fraser Health Authority/Royal Columbian Hospital - Trevor B. Stone, Bertrand Perey, Farhad Moola, Darius Viskontas, Kelly Apostle, Dory Boyer, H. Michael Lemke, Robert McCormack, Mauri Zomar, Bindu Mohan, Karyn Moon, Raely Pritchard, Brenda Chen Fan, Kyrsten Payne.

St. Michael's Hospital - Aaron Nauth, Emil H. Schemitsch, Michael D. McKee, Jeremy A. Hall, Daniel Whelan, Sarah Ward, David Walmsley, Earl R. Bogoch, James P Waddell, Henry Ahn, Timothy R. Daniels, Milena R. Vicente, Jennifer T. Hidy, Melanie T. MacNevin, Paril Suthar.

Sunnybrook Health Sciences Centre - Hans Kreder, David Stephen, Richard Jenkinson, Markku Nousiainen, Terry Axelrod, Veronica Wadey, Sebastian Tomescu, Monica Kunz, Katrine Milner, Melanie MacNevin, Ria De Gorter (Cagaanan), Wesley Ghent, Fathima Adamsahib, Araby Sivananthan, Aimee Theriault, Michelle Arakgi, Phumeena Balasuberamaniam, Ravi Tuazon.

Vancouver General Hospital - Peter J. O'Brien, Piotr A. Blachut, Henry M. Broekhuyse, Pierre Guy, Kelly A. Lefaivre, Gerard P. Slobogean, Dean G. Malish, Raman Johal, Jessica Peattie, Abdullah Mamun, Benita Okocha, Irene Leung.

Hôpital de l'Enfant-Jésus – Étienne Belzile, Luc Bedard, Martin Bédard, Bernard Laliberté, Jean Lamontagne, Martin Lesieur, Luc Petitclerc, Marie-ève Roger, Stéphane Pelet, Luc Lemire, Hélène Côté.

Queen Elizabeth II Health Sciences Centre - Chad Coles, Ross Leighton, C. Glen Richardson, Michael Biddulph, Michael Gross, Michael Dunbar, J. David Amirault, David Alexander, Catherine Coady, Mark Glazebrook, David Johnston, William Oxner, Gerald Reardon, Ivan Wong, Kelly Trask, Shelley MacDonald.

Memorial University of Newfoundland - Andrew Furey, Craig Stone, Keegan Au, William Moores, Peter Rockwood, Carl Moores, Daniel Squire, Sarah Anthony, Minnie Parsons, Valisha Keough, Erin Baker.

Lakeridge Health – Samir Chhabra, Osama Gharsaa, Abdulmajid Ibrahim, Esmat Dessouki, Omar Dessouki, Aileen Manganaro, Kelly Fusco.

Hôpital Saint-François d'Assise – François Marquis, Annie Arteau, Marc Bouchard, Alexandre Leclerc, Michèle Angers, Sylvain Belzile, Sylvie Turmel

Hôpital du Sacré-Coeur de Montréal – G-Yves Laflamme, Benoit Benoit, Pierre Ranger, Michel Malo, Julio Fernandes, Julie Fournier, Karine Tardif.

Ottawa Hospital Research Institute, The Ottawa Hospital – Robert J. Feibel, Hesham Abdelbary, Christopher Kennedy, Paul Kim, Paul Beaule, Joel Werier, Alberto Carli, Peter Lapner, Geoff Dervin, Katie McIlquham, Sara A. Ruggiero, Carly St. Germain, Heather Cosgrove, Johanna Dobransky, Cheryl Kreviazuk

Humber River Hospital – Sebastian Rodriguez-Elizalde, Anna Rose Soliman, Sagar Desai, John Townley, Iriss Mariano, Theresa B. Pedutem, Mary June Francisco.

***United States**:*

Lahey Hospital and Medical Center - Andrew Marcantonio, Michael Kain, Lawrence Specht, John Tilzey, John Garfi.

Mayo Clinic – Andrew Sems, Tab Mabry, Joseph Cass, Michael Torchia, William Cross, Michael Taunton, Joaquin Sanchez-Sotelo, Rafael Sierra, Barbara Foreman.

Marshall University - Franklin D. Shuler, James Day, Tigran Garabekyan, Felix Cheung, Ali Oliashirazi, Jonathon Salava, Linda Morgan, Timothy Wilson-Byrne, Grant Buchanan, Milad Modarresi, Mary Beth Cordle.

Indiana University – Brian Mullis, Karl Shively, Andrew Parr, Janos Ertl, Ripley Worman, Mark Webster, Judd Cummings, Valda Frizzell, Molly Moore.

New York University – Thomas A. Einhorn, Kenneth A. Egol, Nirmal C. Tejwani, Roy I. Davidovitch, Ran Schwarzkopf, Jonathan M. Vigdorchik, James D. Slover, Sanjit R. Konda, Toni M. McLaurin, David Novikov, Pankajkumar Patel, Daniel P. Waren.

Orthopaedic Associates of Michigan – Clifford B. Jones, James R. Ringler, Debra L. Sietsema.

University Orthopaedic Associates – Carlos Sagebien, David Harwood, Stephen Kayiaros, Patricia Seuffert.

The CORE Institute – Clifford B. Jones, Russell Meldrum, Sarim S. Ahmed, Debra L. Sietsema.

Texas Tech University – Enes Kanlic, Amr Abdelgawad, Juan Shunia.

University of Pennsylvania – Samir Mehta, John L. Esterhai Jr, Jaimo Ahn, Derek Donegan, Atul Kamath, Neil Sheth, Annamarie Horan, Patrick Hesketh, Thomas Rose.

Duke University Medical Center – Rachel Reilly, Robert D. Zura, Steven Olson, Kendra Marr, Maria Manson, Cameron Howes.

University of Mississippi Medical Center – Benjamin M. Stronach, Patrick F. Bergin, Jennifer S. Barr, Clay A. Spitler, Josie M. Hydrick, Leslie N. Johnson.

Boston University Medical Center – Thomas A. Einhorn, Paul Tornetta III, William R. Creevy, Heather Silva, Michelle J. Lespasio, Hope Carlisle.

Colorado Orthopedic Consultants – Craig Davis, Philip Stull, Stewart Weinerman, Peter Weingarten, Steven Lindenbaum, Michael Hewitt, Rebecca Danielwicz, Janell Baker.

Mission Hospital Research Institute – Charles DePaolo, Christina Riggsbee, Tracey Nanney.

Park Nicollet Institute – Gregg Strathy, Kathleen Peter, Paul Johnson, and Meaghan Morton.

Rubin Institute for Advanced Orthopaedics – Michael Mont, Donald E. Delanois, Bhaveen Kapadia, Kimona Issa, and Marylou Mullen.

SUNY Buffalo – Mark Anders, Christopher Mutty, Matthew Phillips, Sridhar Rachala, Mary Bayers-Thering.

Allegheny – Timothy J. Sauber, Edward Westrick, Joseph Guth, Michael H. Maher.

University of Utah - Thomas F. Higgins, Erik N. Kubiak, Jeremy Gililland, David Rothberg, Christopher Peters, Christopher Pelt, Ami R. Stuart, Kirby Corbey, Ashley Neese, Mark T. Russell, Victor Solis, Andrea Gurule.

University of California Irvine - David Zamorano, John A Scolaro, Douglas Kiester, Deeba Pourmand.

St. Elizabeth Youngstown Hospital - Tyson T. Schrickel, John V. Gentile, Barbara M. Hileman, Elisha A. Chance.

Rothman Institute – Javad Parvizi, Tiffany Morrison.

Emory University School of Medicine – James Roberson, Thomas Bradbury, Greg Erens, Kyle Webb.

University of Arizona – Michael Dohm, Cindy Fastje, José Luis Camarena, Maria Gordon.

The Netherlands:
Deventer Ziekenhuis – Ydo V. Kleinlugtenbelt, Hans-Peter W. van Jonbergen, Willem H. Roerdink, Joost M. Reuver, Alexander F.W. Barnaart, Elvira R. Flikweert, Danielle D. Langeloo, Rinco C.T. Koorevaar, Hannie H.F. Elskamp-Meijerman, Ellie B.M. Landman.

Amphia Ziekenhuis - Leon H.G.J. Elmans, Joost A.A.M. van den Hout, Adrianus J.P. Joosten, Ad F.A. van Beurden, Stefan B.T. Bolder, Denise Eygendaal, Adrianus F.C.M. Moonen, Rutger C.I. van Geenen, Eric A. Hoebink, Robert Wagenmakers, Wouter van Helden.

Tergooiziekenhuizen - Harm M. van der Vis, Lijkele Beimers, Jasper de Vries, Arthur W. Zurcher, G.H. Rob Albers, Maarten Rademakers, Stefan Breugem, Ibo van der Haven, Pieter Jan Damen, Gythe H. Bulstra, Martin M. Campo, Mathijs P. Somford, Daniël Haverkamp.

OLVG - Rudolf W. Poolman, Bauke W. Kooistra, Willem Jan Kleyn Molekamp, Frank R.A.J. de Meulemeester, Arthur E.B. Kleipool, Robert Haverlag, Maarten P. Simons, Eduard L.A.R. Mutsaerts, Diederik H.R. Kempen, Mark C. Altena, Dirk Jan F. Moojen, John (S.J.) Ham, Arnard van der Zwan, Derek F.P. van Deurzen, Michel P.J. van den Bekerom, Vanessa A.B. Scholtes, Mariëlla E.M. Volkers, Amanda D. Klaassen, Loes W.A.H. van Beers, Nienke W. Willigenburg, Joint Research Group.

Isala Clinic – Sven H. van Helden, R.G. Zuurmond, Adriaan Mostert, P. Houben, G. Solinge, W.R. Spanjersberg, R. Nijveldt, K. van Egmond, Lonneke Buitenhuis.

Gelre Ziekenhuizen - Hugo W. Bolhuis, Pieter H.J. Bullens, Mike Hogervorst, Karin E . de Kroon, Rob H . Jansen, Ferry Steenstra, Eric E.J. Raven.

Spaarne Ziekenhuis - Peter A. Nolte, Michel P.J. van den Bekerom, Tjitte de Jong, Arthur van Noort, Diederik A. Vergroesen, Bernard G. Schutte.

Diaconessenhuis Leiden - Rover Krips, J. Bernard Mullers, Hans Schüller.

Medisch Centrum Haaglanden - Stefan B. Keizer, Jan-Willem A. Swen, Peter H.C. den Hollander, Bregje J.W. Thomassen.

IJsselland Ziekenhuis - W. Peter J. Fontijne, Saskia C. Wiersma, Bastiaan Boetes, Edgar J.T. ten Holder.

Ruwaard van Putten Ziekenhuis - Rob Kooijman, Roelf R. Postema, René J.T.M. Bleker, Harald I.H. Lampe.

Slotervaartziekenhuis - Lein Schuman, John Cheung, Frank van Bommel, W. Paul C.A. Winia, Daniel Haverkamp, Harm van der Vis.

Leids Universitair Medisch Centrum - Huub J.L. van der Heide, Jochem Nagels, Enrike H.M.J. van der Linden-van der Zwaag.

Gelderse Vallei - Jan P. van Dijk, Wouter H. van Helden.

Flevoziekenhuis - Mark L.M. Falke, Frans J. Kurek, Adrianus C.H. Slingerland.

Spain:

Hospital Vall d'Hebrón - Ernesto Guerra Farfán, Jordi Teixidor Serra, Jordi Tomás Hernández, Vicente Molero García, Jordi Selga Marsà, Juan Antonio Porcel Vázquez, Joan Minguell Monyart, Maria Villar Casares, Jaume Mestre Torres, Sandra Ponce Ruiz, Teresa Sanclemente Boli, Judith Sánchez-Raya, José Andrés Peiró, Diego Collado Gastalver, Víctor Barro Ojeda, Iñaki Mimendia Sancho, Maria Jurado Ruiz, Carla Carbonell Rosell, M. Cristina García Martínez, Luken Zubizarreta Barrutia, Martí Plomer Sánchez, Felipe Moreira Borim, Jorge Nuñez Camarena and Antoni Fraguas Castany, Yaiza García Sánchez, Míriam Garrido Clua.

Hospital Universitari Mútua de Terrassa – Pablo Castillón, Martí Bernaus, Francesc Anglés, Agustí Bartra.

Hospital Dr. Josep Trueta - Miguel Angel Froufe Siota, Diana Noriego, Samer Al-dirra, Xavier Madirolas, Cristina Martinez Merchan.

Hospital Universitario Costa del Sol - Enrique Guerado, Encarnación Cruz Ocaña, Juan Ramon Cano Manuel Godino, Miguel Hirschfeld, Laura Ramos, Antonio Royo, Adolfo Galán, Paqui Fontalba, Pilar Gavira.

University Hospital 12 de Octubre – José A. Moreno-Beamud, Emilio Delgado-Diaz, Arantxa Capel-Agundez, Pedro Caba-Dousseaux, Rafael Navarro-Arribas.

Hospital Clinic de Barcelona – Oscar Ares, Jenaro A Fernandez-Valencia, Alonso Zumbado, Pilar Camacho-Carrasco, Marta Gutierrez.

Norway:

Oslo University Hospital – Frede Frihagen, Lars Nordsletten, John Clarke-Jenssen, Geir Hjorthaug, Kaare Midtgaard, Lene B. Solberg, Carl Erik Alm, Jonas Rydinge, Marianne Westberg, Stephan Röhrl, Torben Ianssen, Knut Erik Mjaaland, Ole Christian Brun, Finnur Snorrason, Bernhard Flatøy Stian Svenøy, Elise Berg Vesterhus, Anne Christine Brekke, Sissel Knuts.

Ringerike Hospital – Ingunn Skaugrud, Engelke Randers.

Australia:

Royal Cornwall Hospital – Manish Divekar, Palakkad Easwaran, Daniel Williams, Robin Kincaid, Shaun Sexton, Shyam Maimen, Rory Middleton, Gavin Bartlett, Fiona Hammonds, Benita Adams, Anna Fouracres, Jackie Dingle, Jessica Summers, Nicki Devooght-Johnson, Alyson Andrew, Abigail Weeks.

East Sussex Healthcare – Adrian Butler-Manuel, Oliver Keast-Butler, Guy Selmon, Andrew Armitage, Simon Pearce, Simon Hoskinson, Miranda Champion, Satish Ganesan, Manjunathan Sivaprakasam, Zaid Al-Wattar, Paul Cameron, Kate Weatherly, Kim Miles, Janet Sinclair.

Leicester Royal Infirmary – John Davison, Jonathon White, Andrew Brown, S. Subramanian, Jenny Nichols, Aujlia Randeep, Christina Haines, Manjit Attwal, Dileep Kumar, Debbie Lee, Mona Mohamed, Sharon Siddons.
Northumbria Healthcare – Dominic Inman, Mike Reed, Ajay Malviya, An Murty, Paul Partington, Ian Carluke, Derek Kramer, Kevin Emmerson, Scott Muller, David Townshend, Juhu Joseph, Jonathon Coorsh, Sameer Khan, Rajesh Kakwani, Helen Shirley, Kerry Third, Christine Dobb, Deborah Bunn, Chris Herriott, Elizabeth Corbishley, Gail Waddell.

Barts Health NHS Trust – Joshua Lee, Steve Millington, Stephen Key, Daud Chou, Alex Vris, Sammy Hanna, Anna Berridge, Jamila Kassam, Catherine Hilton, Shanaz Ahmad.

Cambridge University Hospital – Christopher Gooding, Wasim Khan, Stephen McDonnell, Peter Hull, Joseph Queally, Frances New, Simone Hargreaves, Debbie Read.

University Hospital of North Tees – Rajesh Nanda, Christopher Tullock, Rajnikanth Logishetty, Antoni Nargol, Richard Jeavons, Angela Bradbury, Carol Bowler, Janet Austin.

The James Cook University Hospital – Birgit Hanusch, Amar Rangan, Paul Baker, Anthony Hui, Craig White, Ian Wallace, Simon Jameson, James Webb, William Eardley, Lucksy Kottam, Alanna Milne, Juliet James.

Yeovil District Hospital – Matthew Hall, Roshan Raghavan, Benedict Lankester, Paul Latimer, Paul Porter, Istvan Batta, Alison Lewis, Lucy Pippard.

South Devon Healthcare – Gordon Higgins, Veronica Conboy, Yousef El-Houdiri, Steve Blake, David Isaac, Pauline Mercer.

Sherwood Forest Hospital – Sreebala C.M. Srinivasan, Sachin P. Badhe, Amit W. Bidwai, Rebecca Boulton, Sarah Shelton.

Finland:
Turku University Hospital – Matti Seppänen, Mika Junnila, Jari Mokka, Kari Isotalo, Niko Strandberg, Jani Knifsund, Keijo Mäkelä, Keemu Hannes, Mikko Karvonen, Saara Meronen.

New Zealand:

North Shore Hospital – William Farrington, Rob Sharp, Otis Shirley, Luke Brunton, Marla Ross, Sherina Holland.

South Africa:

University of KwaZulu-Natal/Grey's Hospital - Rian Smit, Leonard Marais, Simphiwe Gumede, Reitze Rodseth.

2.0 SUPPLEMENTAL APPENDICES

2.1 Eligibility Criteria

Inclusion Criteria	
1)	Adult men or women aged 50 years and older (with no upper age limit).
2)	Fracture of the femoral neck confirmed with either anteroposterior or lateral hip radiographs, computed tomography, or magnetic resonance imaging (MRI).
3)	Displaced fracture that is not, in the judgment of the attending surgeon, optimally managed by reduction and internal fixation.
4)	Operative treatment within 3 days (i.e. 72 hours) of the patient being medically cleared for surgery.
5)	Patient was ambulatory prior to fracture, though they may have used an aid such as a cane or a walker.
6)	Anticipated medical optimization for arthroplasty of the hip.
7)	Provision of informed consent by patient or proxy.
8)	Low energy fracture (defined as a fall from standing height).
9)	No other major trauma (defined as an Injury Severity Score <17*).
10)	Assurance that surgeons with expertise in both total hip arthroplasty and hemi-arthroplasty were available to perform surgery. Note: Surgeons do not need to be experts in both techniques.

*The Injury Severity Score (ISS) is an anatomical scoring system that provides an overall score for patients with multiple injuries. Each injury is assigned an Abbreviated Injury Scale (AIS) score and is allocated to one of six body regions (Head, Face, Chest, Abdomen, Extremities (including Pelvis), and External). Only the highest AIS score in each body region is used. The 3 most severely injured body regions have their score squared and added together to produce the ISS score.

Exclusion Criteria	
1)	Patient not suitable for hemi-arthroplasty (e.g. inflammatory arthritis, rheumatoid arthritis, pathologic fracture (secondary to cancer), or severe osteoarthritis of the hip).
2)	Associated major injuries of the lower extremity (i.e., ipsilateral or contralateral fractures of the foot, ankle, tibia, fibula, knee, or femur; dislocations of the ankle, knee, or hip; or femoral head defects or fracture).
3)	Retained hardware around the affected hip that will interfere with arthroplasty.
4)	Infection around the hip (soft tissue or bone).
5)	Patients with a disorder of bone metabolism other than osteoporosis (i.e., Paget's disease, renal osteodystrophy, osteomalacia).

6)	Patients with a previous history of frank dementia that would interfere with assessment of the primary outcome (i.e., secondary procedures at 2 years).
7)	Likely problems, in the judgment of the investigators, with maintaining follow-up (i.e., patients with no fixed address, report a plan to move out of town, or intellectually challenged patients without adequate family support).
8)	Patients whose fracture occurred as a result of an act of violence.

* For Item 6 above, patients with a history of frank dementia were unlikely to survive to 2 years, which would cause problems with assessment of the primary outcome.

* Exclusion of a patient because of enrolment in another ongoing drug or surgical intervention trial was left to the discretion of the attending surgeon, on a case-by-case basis.

2.2 American Society of Anesthesiologists Physical Status Classification

Last approved by the ASA House of Delegates on October 15, 2014[1]

ASA Classification	**Definition**
ASA I	A normal healthy patient
ASA II	A patient with mild systemic disease
ASA III	A patient with severe systemic disease
ASA IV	A patient with severe systemic disease that is a constant threat to life
ASA V	A moribund patient who is not expected to survive without the operation
ASA V1	A declared brain-dead patient whose organs are being removed for donor purposes

2.3 Threshold Performance for Expertise in Total Hip Arthroplasty and Hemi-Arthroplasty

Surgeons participating in the HEALTH trial were required to meet both of the following two criteria for expertise for either THA or HA:

1. Surgeons must have performed at least 50 procedures (either THA or HA) in their career (including residency experience in which they assumed responsibility for the procedure).
2. Surgeons must have continued to perform at least five procedures (either THA or HA) in the year prior to trial start date, as well as each year for the duration of the study.

Surgeons who met the threshold for both THA and HA could perform either procedure based on randomization if no overwhelming bias in favour of one procedure was evident. A surgeon was considered biased for an approach if he/she had performed less than five cases of either procedure in his/her last 50 procedures for a displaced femoral neck fracture. One question on the surgical forms asked surgeons to indicate whether they met the expertise threshold for the procedure the patient received. No other methods were implemented to ensure that surgeons met the expertise criteria listed above.

Residents and fellows were able to perform the procedures under the supervision of a participating attending surgeon. The surgeon most responsible for the case must have met threshold expertise criteria and must have been present in the operating room for the critical aspects of the procedure.

The critical aspects of THA procedures that required the presence of an expert surgeon were:

- Trial component insertion and verification of hip stability
- Implant insertion to ensure correct alignment of femoral and acetabular components
- Cement procedure, if used
- Final assessment of hip stability after implant insertion

The critical aspects of HA procedures that required the presence of an expert surgeon were:

- Trial component insertion and verification of hip stability
- Implant insertion to ensure correct version)
- Cement procedure, if used
- Final assessment of hip stability after implant insertion

2.4 Trial Interventions and Standardization of Peri-Operative Care

A. Total Hip Arthroplasty (THA)

To optimize feasibility and applicability of results, this study did not standardize the surgical approach, the use of cemented components, the implant manufacturer, or femoral head size. Surgeons used the manufacturer specific implant guides and jigs for insertion of the total joint arthroplasty. Proscribed approaches did not include minimally invasive total hip arthroplasty (i.e., 2 incision approaches) and hinged prostheses or capture cups.

Surgeons documented the following:

1. Augmentation of the acetabular liner
2. Type of acetabulum implant used
3. Fixation of the acetabular component to the acetabulum with screw fixation
4. Acetabular component modularity
5. Material of acetabular liner
6. Manufacturer

B. Hemi-Arthroplasty (HA)

Surgeons used modern implants for HA excluding non-modular, non-canal filling unipolar implants such as Moore's and Thompson's prostheses. The choice of modular unipolar versus bipolar HA were not standardized. This study did not standardize whether implants were inserted with cement or with a press-fit design. Surgeons used the manufacturer specific implant guides and jigs for insertion of the total joint arthroplasty.

Surgeons documented the following:

- Type of HA performed
- Manufacturer
- Implant material
- Bearing surface of the implant

C. Standardization of Procedures and Peri-Operative Care

Given the inherent variability in practice patterns among orthopaedic surgeons, it was important to ensure that surgeons adhered as closely as possible to the surgical management protocol and to current accepted practice.

Peri-Operative and Post-Operative Treatment Common to Both Groups

To ensure similar peri-operative regimens, it was recommended that participating centers standardize key aspects of pre- and post-operative care.

Pre-Operative Care

1. Pre-operative antibiotic prophylaxis (i.e., cephalosporin, Ancef, or equivalent coverage).
2. Thromboprophylaxis (i.e., Thromboembolic Disease Stockings (TEDS), pneumatic compression boots, or medical prophylaxis to be discontinued in sufficient time to allow surgery as guided by International Normalized Ratio (INR) / Partial Thromboplasty Time (PTT)).
3. Medical consultation to optimize condition prior to surgery.

Post-Operative Care

1. Antibiotic prophylaxis (i.e., cephalosporin or equivalent) for 24 hours.
2. Thromboprophylaxis with unfractionated heparin, Low Molecular Weight Heparin (LMWH), warfarin, anti-platelet agents, or intermittent pneumatic compression boots.
1. Weightbearing as tolerated was allowed as patients autoprotect the affected hip during rehabilitation. Post-surgery, patients were weightbearing as tolerated, and then advanced according to the attending surgeon's best judgment (i.e., touch weightbearing was permitted, and then advanced according to the surgeon's best judgment).
2. Calcium 600 mg by mouth (PO) daily and vitamin D 1,000 International Units (IU) per day (provided there were no contraindications) and further investigation and treatment of osteoporosis as recommended by a local osteoporosis expert/consultant.
3. Appropriate nutritional assessment with administration of oral micronutrient feeds as needed.

Other Care

Due to a lack of evidence favouring a particular approach, the following was recorded, but not standardized:

1. Use of pre-operative traction.
2. Surgical delay.
3. Type of anesthetic (i.e., general or regional).
4. Physiotherapy and rehabilitation programs.

2.5 Follow-up Processes

Time-point	Assessment Procedures	Data Collection
1 week (Up to 3 months)	In Person/Hospital/Clinic (if prior to discharge)	•Follow-up Form •Secondary Procedures, AE Forms •SF-12, WOMAC, EQ-5D (self-administered*) (asking about patient function prior to surgery)

1 week (Up to 5 weeks)	In Person/Hospital/Clinic (if prior to discharge)	•TUG Test
10 weeks (5 weeks to 4 months)	In Person/Hospital/Clinic (if prior to discharge) or Telephone	•Follow-up Form and TUG Test •Secondary Procedures, AE Forms •SF-12, WOMAC, EQ-5D (self-administered*) •Radiographs
6 months (4 to 7.5 months)	In Person/Hospital/Clinic or Telephone	•Follow-up Form and TUG Test •Secondary Procedures, AE Forms •SF-12, WOMAC, EQ-5D (self-administered*)
9 months (7.5 to 10.5 months)	In Person/Hospital/Clinic or Telephone	•Follow-up Form •Secondary Procedures, AE Forms •SF-12, WOMAC, EQ-5D (interview-administered)
12 months (10.5 to 15 months)	In Person/Hospital/Clinic or Telephone	•Follow-up Form and TUG Test •Secondary Procedures, AE Forms •SF-12, WOMAC, EQ-5D (self-administered*) •Radiographs
18 months (15 to 21 months)	In Person/Hospital/Clinic or Telephone	•Follow-up Form •Secondary Procedures, AE Forms •SF-12, WOMAC, EQ-5D (interview-administered)
24 months (21 to 30 months)	In Person/Hospital/Clinic or Telephone	•Follow-up Form and TUG Test •Secondary Procedures, AE Forms •SF-12, WOMAC, EQ-5D (self-administered*) •Radiographs •Planned revision surgery after 24 months

* Interview-administered data collection done if patient was unable to complete self-administered forms.
AE = Adverse Event, EQ-5D = EuroQol-5D, SF-12 = Short Form-12, TUG = Timed Up and Go, WOMAC = Western Ontario McMaster Osteoarthritis Index.

2.6 Outcome Definitions

Primary Outcome

Outcome	**Definition**
Unplanned Secondary Hip Procedure (study event)	Unplanned secondary procedures that were classified as study events included: o Closed reduction of hip dislocation o Open reduction of hip dislocation o Open reduction of fracture o Soft tissue procedure o Insertion of antibiotic spacer o Full implant exchange o Partial implant exchange – stem only o Partial implant exchange - head only o Partial implant exchange - liner only

Outcome	Definition
	o Partial implant exchange - head and liner o Partial implant exchange – acetabular component only o Partial implant exchange – acetabular component and head o Implant adjustment – re-orientation of the stem o Implant adjustment – re-orientation of the acetabulum component o Implant removal with no replacement o Excision heterotopic ossification o Supplementary fixation o Other
Reason for Unplanned Secondary Procedure	Classification of the reason for unplanned secondary procedures included: o Treat a peri-prosthetic fracture o Treat hip instability or dislocation o Treat infection – superficial o Treat infection – deep o Treat wound necrosis o Treat another wound healing problem o Remove heterotopic ossification o Manage abductor failure o Manage another soft tissue problem (i.e. pseudotumor) o Correct implant failure –loosening or subsidence o Correct implant failure - breakage o Treat implant wear o Treat osteolysis o Treat implant corrosion o Improve function o Relieve pain

Secondary Outcomes

Outcome	Definition
Mortality	Mortality was adjudicated by the Central Adjudication Committee and it was considered to be an event if it occurred within 24-months of the initial hip fracture surgery.
Serious Adverse Events	Serious adverse events, as diagnosed by physicians at the clinical sites, were documented. A serious adverse event was defined as any adverse event that is fatal, life threatening, requires or prolongs hospital stay, results in persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an important medical event, symptom, sign, illness, or experience that develops or worsens in severity during the study.
Hip-Related Complication	The Central Adjudication Committee reviewed hip-related complications including peri-prosthetic fracture, hip instability or dislocation, implant failure (loosening/subsidence and breakage), wound healing problems (including superficial/deep infection, wound necrosis), soft tissue problems (i.e. pseudotumor), heterotopic ossification, abductor failure, implant wear

Outcome	Definition
	and corrosion, osteolysis, neurovascular injury, decreased function, and pain.
Functional Outcomes and Quality of Life	Functional outcome and quality of life were measured using self-administered and interview-administered questionnaires. Functional outcome questionnaires included a generic health status measurement instrument (SF-12), a hip function and pain questionnaire (WOMAC), a health outcome measure (EQ-5D), and a functional mobility test (TUG). The SF-12 Health Survey is a standardized instrument to measure health-related quality of life. This self-administered, 12-item questionnaire covers eight main health domains that make up the Physical and Mental Health Composite Scores (PCS & MCS). Each domain consists of one or two questions and is scored separately from 0 (lowest level) to 100 (highest level). The WOMAC is a self-administered questionnaire that assesses the three dimensions of pain, disability and joint stiffness in knee and hip osteoarthritis, and consists of 24 questions. This questionnaire uses a Likert scale, consisting of responses including: none, mild, moderate, severe, and extreme. Specifically, for the WOMAC questionnaire, the Likert scale is in reverse order. Therefore, a higher score indicates worse pain, stiffness, and functional limitations. The ranges for each dimension are: 0-20 for pain, 0-8 for stiffness, and 0-68 for physical function.[2] The EQ-5D is a standardized instrument that measures quality of life in five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). Each dimension has three response options: 1=no problems, 2=some problems, and 3=extreme problems. Each response corresponds with a one-digit number that can then be combined into a 5-digit number to describe the participant's state of health. The participant's state of health is then translated into a corresponding utility score.[2] The EQ-5D also includes a visual analogue scale (VAS) that assesses the individual's health today on a scale from 0-100, with the endpoints being 'worst imaginable state of health' and 'best imaginable state of health'.[3,4] The TUG test is a standardized, physical test to assess balance and mobility in the participants. The participant is timed while they perform simple physical movements, such as rising from an arm chair, walking 10 feet, walking back to the chair, and sitting down. A faster time indicates that the participant has greater functional performance, while a lower score may identify participants who are at risk for increased falls in the community.[5] The SF-12, WOMAC, and EQ-5D were asked at 10 weeks, 6, 9, 12, 18, and 24-month visits. The TUG was performed at 1 and 10-week 6, 12, and 24-month visits.

2.7 Overview of Adjudication

Adjudication Processes

The following information was excerpted from the HEALTH Adjudication Charter, which documents the responsibilities of the Central Adjudication Committee and the adjudication processes for the HEALTH trial.

1) Fracture Eligibility

The Central Adjudication Committee adjudicated fracture eligibility for all patients based on available pre-surgery and post-surgery x-rays, and completed case report forms. If the fracture did not meet all inclusion criteria or met one of the exclusion criteria, the fracture was deemed ineligible.

2) Technical Placement of Prostheses

The Central Adjudication Committee adjudicated the technical placement of the prosthesis based on available pre-surgery and post-surgery x-rays to determine if the quality of the implant placement was acceptable or unacceptable. This was unrelated to fracture eligibility.

3) Additional Surgical Procedures

The Central Adjudication Committee adjudicated additional surgical procedures that occurred within two years of initial surgery after the participant had completed their 24-month visit (or following early withdrawal) to determine if they were study events. Planned surgeries were not considered study events. If a participant had multiple unplanned surgeries for one indication, each unplanned surgery was considered a study event in addition to the first. Any unplanned surgery after the initial fixation that satisfied the criteria below was considered to be a study event:

- Treat a peri-prosthetic fracture
- Treat hip instability or dislocation
- Treat infection – superficial
- Treat infection – deep
- Treat another wound healing problem
- Treat another soft tissue problem
- Remove heterotopic ossification
- Manage abductor failure
- Correct implant failure – loosening or subsidence
- Correct implant failure – breakage
- Treat implant wear and corrosion
- Treat osteolysis
- Treat neurovascular injury
- Improve function
- Relieve pain

The Central Adjudication Committee reviewed all available x-rays, and data from the patient's completed case report forms.

4) Hip-Related Complications

The Central Adjudication Committee adjudicated adverse events related to the patient's randomized hip as reported by the clinical site after each participant had completed their 24-month follow-up (or following early withdrawal). The Central Adjudication Committee also reviewed all available x-rays (scheduled visits and unscheduled visits) to look for radiographic evidence of hip-related complications that were not reported by the clinical site. The Central Adjudication Committee was responsible for determining when the hip-related adverse event was first diagnosed/evident on participant x-rays. Hip-related complications that were considered study events included:

f) Peri-prosthetic fracture
g) Hip instability or dislocation
h) Implant failure (loosening/subsidence and breakage)
i) Wound healing problems (including superficial/deep infection, wound necrosis)
j) Soft tissue problems (i.e. pseudotumor)
k) Heterotopic ossification
l) Abductor failure
m) Implant wear and corrosion
n) Osteolysis
o) Neurovascular injury
p) Decreased function
q) Pain

The Chair of the Central Adjudication Committee independently reviewed all cases of heterotopic ossification that were identified by the Central Adjudication Committee. For each participant that was identified as having radiographic evidence of heterotopic ossification, the Chair independently reviewed the x-rays from each post-operative assessment and determined the severity of heterotopic ossification using the classification system developed by Brooker and colleagues:

- Stage I: Islands of bone within soft tissues of any size of the hip
- Stage II: Bone spurs from pelvis or femur, leaving at least 1 cm between opposing bone surfaces
- Stage III: Bone spurs from pelvis or femur reducing the space between opposing bone surfaces to less than 1 cm
- Stage IV: Ankylosis of the hip

The Central Adjudication Committee reviewed all available x-rays, and data from the patient's completed case report forms.

5) Mortality

The Central Adjudication Committee adjudicated mortality as required following a patient's early withdrawal. The Central Adjudication Committee reviewed all data from the patient's completed case report forms, available clinical notes, and/or x-rays to confirm the cause of death. They also commented on the relation to the treatment arm.

2.8 Statistical Analyses for Primary and Secondary Outcomes

Analyses included patients in the groups to which they were assigned. Patients were censored at 24 months of follow-up or at the time of their last follow-up for patients lost to follow-up. The primary analysis was a proportional hazards model using a competing risk analysis (death as the competing risk) with time to the HEALTH primary study endpoint as the outcome. The independent variable was THA versus HA, and the following covariates were used: age (50-80 years or >80 years), pre-fracture living setting (institutionalized or not institutionalized), pre-fracture functional status (using aid or independent ambulator), and ASA Class (Class I/II or III/IV/V). For these covariates, we used values that were entered into the minimization system at time of enrollment. For our competing risk analyses, we used the method described by Zhou et al. to account for clustering within surgeons.[6] The estimates from the competing risk analysis for clustered data analyses were marginal estimates. We report the treatment effects as hazard ratios (HRs) with 95% confidence intervals (CIs). No adjustment for multiplicity was made and the 95% CIs do not adjust for multiplicity. Kaplan-Meier curves were constructed for the primary outcome.

Cox proportional hazards modeling was used to estimate the relative effect of THA versus HA on time to mortality, serious adverse events, and hip-related complications, separately, and included the same independent variables as listed for the primary analysis as well as including surgeon as a random effect. The hip-related complications analysis was a competing risk analysis with death as the competing risk. The estimates from the competing risk analysis for clustered data analyses were marginal estimates. We report the HRs and 99% CIs for the proportional hazards models. We performed proportional hazards regressions only for hip-related complications in which there were at least 50 events. Using multi-level models, the effect of THA versus HA on quality of life (SF-12, EQ-5D), function (WOMAC), and mobility (TUG) were estimated separately. Randomized treatment, visit (entered as a categorical variable) were also included as independent variables. Because we believed that the effect of THA versus HA may change over time, we also included an interaction term between treatment and visit. When the interaction term between treatment and visit was not statistically significant at alpha=0.05, we removed it from the model. When the interaction term was significant, we reported the treatment effect at each visit. We accounted for death via joint modelling, using the method described by Rizopoulos.[7] The SF-12, WOMAC, and EQ-5D were summarized using mean difference (MD) and 99% CIs. We analyzed the TUG as a dichotomous outcome with the following categories: a) patients who complete the test in ≤12 seconds, and b) those who require >12 seconds to complete the test or were unable to complete the test. We selected 12 seconds as the cut-off because this was the threshold used by the Centers for Disease Control and Prevention.[8] The TUG was summarized using odds ratios and 99% CIs. For our multi-level analyses of quality of life, function, and mobility, all available data were used with no imputation performed. The models do not require that a patient have valid scores at all follow-up visits. We chose alpha levels of 0.05 and 0.01 for the primary and secondary outcomes, respectively. When scoring the WOMAC domains, we used the mean of the items that were answered in our calculation if at least 4 of the 5 pain items were answered, at least 1 of the 2 stiffness items were answered, and if at least 14 of the 17 function items were answered. If there were less items answered, the domain was set to missing. To calculate the WOMAC total score, we required non-missing scores for all 3 domains.

When scoring the SF-12, we required at least half of each of the items in each domain to be answered to use the mean of the non-missing items as the domain score. The physical component summary score and the mental component summary score were only calculated if all 8 domains were non-missing.

All 5 questions of the EQ-5D were required to calculate the utility score.

2.9 Subgroup Analyses and Hypothesized Effects

At the trial onset, we specified in the trial protocol that no subgroup analyses would be conducted. However, towards the end of the trial, prior to unblinding, the following subgroup analyses were decided upon and were conducted to investigate the following prognostic factors as possible effect modifiers. The HEALTH primary endpoint was the dependent variable for these analyses. For these subgroup analyses, we used the data from our database. What was captured in the database reflects the true values for these factors, which may be different than what was originally entered into the minimization system at time of enrollment.

1. Age (i.e., 50-80 years or >80 years): Hypothesized that THA will be better relative to HA in the younger subgroup than in the older patients.
2. Pre-fracture living setting (i.e., institutionalized or not institutionalized): Hypothesized that THA will be better relative to HA in those not institutionalized than those institutionalized.
3. Pre-fracture functional status (i.e., using aid or independent ambulator): Hypothesized that THA will be better relative to HA in independent ambulators than in those using an aid.
4. American Society for Anesthesiologists (ASA) Class (i.e., Class I/II or III/IV/V): Hypothesized that THA will be better relative to HA in Class I/II than in Class III/IV/V.

These subgroup analyses were performed (separately) by including the subgroup factor as an independent variable in our proportional hazards regression model along with an interaction term between it and randomized treatment. We used the criteria suggested by Kasenda et al. to guide inferences about the credibility of our subgroup analyses.[9]

After unblinding, we identified three post hoc subgroup analyses and performed them as follows:

1. Added a three-category age (50 to 70 years or 71 to 80 year or ≥ 81 years) as an independent variable in our proportional hazards regression model along with an interaction term between it and randomized treatment. We hypothesized that THA will be better relative to HA in the youngest subgroup than in the older patient subgroups.
2. Added a three-category age (50 to 70 years or 71 to 80 year or ≥ 81 years) as an independent variable and interaction of age with treatment group into our final WOMAC total score model. We hypothesized that THA will be better relative to HA in the youngest subgroup than in the older patient subgroups.
3. Added country (Canada or Netherlands or USA or Australia or Norway or Spain or UK or Finland or New Zealand or South Africa) as an independent variable in our proportional hazards regression model along with an interaction term between it and randomized treatment. We hypothesized no difference across countries in treatment effects.

2.10 Sensitivity Analyses

At the trial onset, we did not specify in the trial protocol that any sensitivity analyses would be conducted. However, towards the end of the trial, prior to unblinding, we decided to conduct the following sensitivity analyses, with the HEALTH primary endpoint as the dependent variable:

a) The primary analysis without including surgeon as a random effect
b) The primary analysis with country included as an independent variable
c) A per-protocol analysis
d) An as-treated analysis
e) Unstratified proportions analyses where we made varying assumptions about risk of event in those who were lost to follow-up

2.11 Interpretation of Blinded Data

Hypothesis: We hypothesize that THA will have similar or lower rates of secondary procedures and higher functional outcome scores at 24 months compared with HA.

Here, we present alternative interpretations of blinded preliminary results. Blinded data interpretation may decrease the frequency of misleading data interpretation. Widespread adoption of blinded data interpretation with a minimum set of recommendations should be widely adopted.[10]

Secondary procedures over two years did not differ between treatment groups X and Y. The Kaplan Meier curve for the primary outcome suggests that the hazard ratios (HRs) remain constant up to 1 year (HR=1.30, 95% CI 0.86-1.95, p=0.217; non-significant estimates favoring treatment Y) and suggested estimates favouring treatment X after 1 year (up to 2 years) (HR=0.24, 95% CI 0.08-0.73; p=0.011).

Deaths did not differ between treatment groups X and Y over a 2-year period (p=0.493).

Serious adverse events (p=0.052) and hip-related complications (p=0.277) between treatment groups X and Y did not differ over a 2-year period.

Treatment X demonstrated significantly better overall WOMAC and EQ-5D utility scores ($p<0.05$) compared to Treatment Y (and trended towards better SF-12 PCS scores) over a 2-year period. TUG scores (cut-off 12 seconds) did not differ between treatment groups (0=0.181).

Subgroup analyses did not show any differences in the treatment effect between different subgroups ($p>0.05$).

Given the above preliminary findings, the more plausible hypothesis follows. Treatment X is THA and Treatment Y is HA. THA does not result in a statistically significant difference in secondary procedure rates over a 2-year period compared to HA; however, our findings suggest THA may have more secondary procedures earlier (less than 1 year, possibly driven by higher dislocations *results still blinded*) and HA may have more secondary procedures after 1-year post-fracture in those who did not have a secondary procedure during the first year. Functional outcome scores over 2 years favour THA compared to HA. These differences in function are small (although statistically significant). A lack of difference in secondary procedures, hip-related complications, and deaths, a lack of subgroup effects, and modest improvements in function render THA mildly superior to HA over 2 years. It's not unreasonable to consider the two treatments similar given

small differences in functional scores. The extra cost of THA to the modest benefits in function may not render it the primary implant of choice in this patient population.

If treatment X is HA and treatment Y is THA, then HA does not result in a statistically significant difference in secondary procedure rates over a 2-year period compared to THA. However, our findings suggest HA may have more secondary procedures earlier (less than 1 year) and THA may have more secondary procedures after 1-year post-fracture, in those who did not have a secondary procedure during the first year. Further, functional outcome scores over 2 years favour HA compared to THA. These differences in function are small (although statistically significant), and somewhat unexpected. A lack of difference in secondary procedures, hip-related complications, and deaths, a lack of subgroup effects, and modest improvements in function render HA mildly superior to THA over 2 years. It's not unreasonable to consider the two treatments similar given small differences in functional scores. However, the extra cost and added complexity of THA may not render it the primary implant of choice in this patient population.

REFERENCES

1. American Society of Anesthesiologists . ASA Physical Status Classification System. https://www.asahq.org/resources/clinical-information/asa-physicalstatus-classification-system. Published 2017. Accessed February 6, 2017.
2. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. *Arthritis Rheum*. 2001;45(5):453-461.
3. Van Reenen M, Janssen B, Oppe M, Kreimeier S, Greiner W. *EQ-5D-Y User Guide Basic Information on How to Use the EQ-5D-Y Instrument*.; 2014. https://euroqol.org/wp-content/uploads/2016/09/EQ-5D-Y_User_Guide_v1.0_2014.pdf. Accessed June 19, 2019.
4. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med*. 2001;33(5):337-343.
5. Zasadzka E, Borowicz AM, Pawlaczyk M, Roszak M. Assessment of the risk of falling with the use of timed up and go test in the elderly with lower extremity osteoarthritis. *Clin Interv Aging*. 2015;10:1289-1298.
6. Zhou B, Fine J, Latouche A, Labopin M. Competing risks regression for clustered data. *Biostatistics*. 2012;13(3):371-383.
7. Rizopoulos D. JM: An R Package for the Joint Modelling of Longitudinal and Time-to-Event Data. *J Stat Softw*. 2010;35(9):1-33.
8. Centers for Disease Control and Prevention . Assessment: Timed Up & Go (TUG). https://www.cdc.gov/steadi/pdf/TUG_Test-print.pdf. Published 2017. Accessed June 26, 2019.
9. Kasenda B, Schandelmaier S, Sun X, et al. Subgroup analyses in randomised controlled trials: cohort study on trial protocols and journal publications. *BMJ*. 2014;349:g4539-g4539.
10. Järvinen TLN, Sihvonen R, Bhandari M, et al. Blinded interpretation of study results can feasibly and effectively diminish interpretation bias. *J Clin Epidemiol*. 2014;67(7):769-772.
11. Fergusson D, Aaron SD, Guyatt G, Hébert P. Post-randomisation exclusions: the intention to treat principle and excluding patients from analysis. *BMJ*. 2002;325(7365):652-654.