mymobility® Clinical Study

A Prospective Multicenter Longitudinal Cohort Study of the mymobility Platform

CLU2018-13CH

Version 4.0

14 February 2022

Global

STUDY SPONSOR

Zimmer Biomet
Clinical Affairs Department
1800 West Center Street, MS #4020
Warsaw, IN 46580
800-613-6131

STATEMENT OF COMPLIANCE

Only the Principal Investigator is required to sign during initial site start-up process.

The study is conducted in accordance with ISO 14155 Standard for Clinical Investigation of Medical Devices For Human Subjects – Good Clinical Practice[(i)], the ICH Guideline on Good Clinical Practice[(ii)], the Declaration of Helsinki[(iv)], and is in accordance with US Code of Federal Regulations 21 CFR Parts 11, 50 and 56[(iii)], as well as any regional or national regulations, as appropriate. IRB or EC approval for each site will be obtained prior to conducting this study, as applicable.

The investigator agrees:

- To assume responsibility for the proper conduct of the study at this site and supervise all testing involving human subjects.
- To conduct the study in compliance with this protocol, any future amendments, and with any other study conduct procedures provided by the Sponsor.
- To ensure that the requirements for obtaining informed consent from each subject are met.
- Not to implement any changes to the protocol without written agreement from the Sponsor and prior review and written approval from my institutional review board except where necessary to eliminate an immediate hazard to subjects.
- That I am thoroughly familiar with the appropriate use of the investigational product, as described in this protocol and any other information provided by the Sponsor.
- That I am aware of, and will comply with, good clinical practice (GCP) and all applicable regulatory requirements.
- To ensure that all persons assisting me with the study are adequately informed about the investigational product and have been trained on their study-related duties and functions as described in the protocol.

Investigator Signature: _____ Date: _____

Printed Name: _____

Contents

I. Contact Information/List of Investigators

Title	mymobility® Clinical Study
Protocol Number	CLU2018-13CH
Study Sponsor Contact Information	Zimmer Biomet US, Inc. (or its subsidiary), referred to herein as "Zimmer Biomet" 1800 West Center Street, MS #4020 Warsaw, IN 46580 Phone: 800-613-6131 **Regional Sponsor Contact Information:** Toermalijnring 600 3316 LC Dordrecht Netherlands Zimmer Gmbh Sulzerallee 8 CH – 8404 Winterthur Zimmer Biomet Pty Ltd 12 Narabang Way Belrose, NSW 2085 02-9485-5611
Monitoring Contact Information	Zimmer Biomet or designee
Investigational Site Information	This study will include up to 36 sites. Details regarding the sites involved will be maintained in the Sponsor's Trial Master File.
Mymobility Technical Support Information	a. Technical Support Email support@zbmymobilitysolutions.com b. Technical support at 844.799.8208 *Responses will be provided within one business day.*

II. Abbreviations

App	Smartphone Application
ACF	Acute Care Facility
ASC	Ambulatory Surgery Center
CI	Confidence Interval
EC	Ethics Committee (also referred to as IRB in US)
eCRF	Electronic Case Report Form
ePro	Electronic Patient Reported Outcomes
EDC	Electronic Data Capture
EMEA	Europe, the Middle East and Africa
EQ-5D-5L	EuroQol-5 Dimensions-5 Levels (Health-Related Quality of Life Survey)
ER	Emergency Room
GDPR	General Data Protection Regulation
HIPAA	Health Insurance Portability and Accountability Act
HOOS, JR.	Hip Disability and Osteoarthritis Outcome Score (Short Form)
ICF	Informed Consent Form (US only: Informed Consent and Authorization)
IFU	Instructions for Use
IRB	Institutional Review Board (also referred to as EC OUS)
KOOS, JR.	Knee Injury and Osteoarthritis Outcome Score (Short Form)
MUA	Manipulation Under Anesthesia
PKA	Partial Knee Arthroplasty (Replacement)
POD	Post-Operative Day
PROM	Patient-Reported Outcome Measure
PT	Physical Therapy
RCT	Randomized Controlled Trial
ROC	Receiver Operating Characteristics
ROM	Range of Motion
SOC	Standard of Care
SIV	Site Initiation Visit
SLS	Single Leg Stance Test
SNF	Skilled Nursing Facility
SOC	Standard of Care
THA/THR	Total Hip Arthroplasty (Replacement)
TJA/TJR	Total Joint Arthroplasty (Replacement)
TKA/TKR	Total Knee Arthroplasty (Replacement)
TUG	Timed Up and Go Test

III. Study Synopsis

Title	mymobility® Clinical Study
Protocol Number	CLU2018-13CH
Sponsor	Zimmer Biomet US, Inc. (or its subsidiary), referred to herein as "Zimmer Biomet"
Manufacturer	Zimmer Biomet
Study Device(s)	mymobility App
Study Objectives/Endpoints (RCT)	To determine if mobile application-guided education and exercise paired with accurate and sensitive activity monitoring, captured from consumer wearables for the entire episode of care can provide a viable (and potentially improved) alternative to current standard of care (SOC) for hip and knee arthroplasty. **Primary Endpoint:** Non-inferior results between the current SOC and the mymobility platform for all-cause 30-day readmission rates. **Secondary endpoints** include KOOS, JR. (Knee); HOOS, JR. (Hip), manipulation under anesthesia (knee), single leg stance test, timed up and go (TUG), satisfaction for those subjects who complete the mymobility program compared to those who complete traditional, standard of care education and rehabilitation. **Economic Analysis:** Determine if subjects who complete the mymobility program incur less cost and fewer resources than subjects receiving traditional SOC. Potential data collection points include: number of PT visits, discharge disposition, ER visits, readmissions, reoperations, unscheduled surgeon visits, and time processing paperwork and approvals for the entire episode of care (30 days prior to surgery through 90 days post-op).
Indications/Target population	Inpatient and outpatient (including ASC) subjects indicated for unilateral, primary total or partial knee arthroplasty or total hip arthroplasty who meet the inclusion/exclusion criteria for study participation.
Inclusion/Exclusion criteria	<u>Inclusion Criteria</u> • Subject must be 18 years of age or older. • Subject qualifies for a primary, unilateral total or partial knee arthroplasty, based on a physical exam

	and medical history. • Investigator plans to treat subject with a commercially-available device, used on-label according to the manufacturer's instructions for use, as part of their clinical care. • Subject owns and maintains an iPhone capable of pairing to the Apple Watch, supporting iOS updates and is compatible with the mymobility App. • Subject is willing and able to complete the protocol required follow-up. • Subject is able to read and understand the language used in the mymobility App for their region. • Subject is willing and able to provide written Informed Consent and Authorization by signing and dating the IRB/EC approved Informed Consent Form and Authorization. Where applicable, subject must also be willing to provide authorization for use of protected health information in accordance with local privacy laws. • Subject is mobile with no more than a single cane/single crutch assist preoperatively. <u>Exclusion Criteria</u> • Subject is a current alcohol or drug abuser. • Subject has inflammatory arthropathies which would interfere or compromise the activity profiles within this study. • Subject is considered a member of a protected population (e.g., prisoner, mentally incompetent, etc.). • Subject is currently participating in any other surgical intervention, physical therapy or pain management study which would compromise the results of this study. • Subject requires simultaneous or staged bilateral replacements, staged <90 days apart. Subjects can be enrolled into the study for the second, staged arthroplasty if scheduled >89 days after their first, contralateral replacement. Additionally, subjects who complete the entire study (1 year) for one joint may be enrolled for a second joint.

Study Design	This is a post-market prospective, multi-center longitudinal study in subjects undergoing primary TKA, THA, or PKA. The study will contain three cohorts. The first cohort ("Pilot and Time Cohort") will consist of a pilot cohort of subjects and will primarily serve to determine site study staffing needs and time required for various elements of study execution. The second cohort ("RCT Cohort") will consist of a randomized controlled subject cohort and will compare outcomes of mobile application-guided exercises, education and activity with SOC pathways (including PT, if applicable). The third cohort ("Correlative Analytics Cohort") will seek to collect enough data to enable the creation of predictive algorithms for outcomes of joint replacement. All subjects will receive a TKA, THA, or PKA using SOC procedures and commercially-available devices used on-label according to the manufacturer's instructions for use. After the joint replacement procedure, subjects will then complete prescribed post-operative activities, such as in-person physical therapy according to SOC or performing exercises as scheduled through the mymobility App. Follow-up assessments will be conducted at approximately 30 days and 90 days post-op, and virtual assessments (including subject questionnaires and recording of medical events/adverse events) will occur at approximately 180 days and 365 days post-op.
Clinical Phase	Post-market
Sample Size	Up to 10,500 subjects, including 500 control subjects receiving SOC PT in the RCT Cohort, will be enrolled during all three cohorts.
Length of Study	The maximum duration of subject participation in the study will be approximately 17 months. Subject participation will start after obtaining informed consent, and will continue for up to 14 months (12 months +/- 60 days) after the index procedure. • Pre-op (up to 180 days prior to surgery) • Surgery • 30 days (+/- 14 days) – 1 Month / Early post-op • 90 days (+/- 21 days) – 3 Month • 180 days (+/- 42 days) virtual visit – 6 Month • 365 days (+/- 60 days) virtual visit – 12 Month / 1 Year Subject recruitment is expected to require approximately 24 months, for a total study duration of 40 months.

Materials and Methods	Inclusion of up to 10,500 subjects, including 500 control subjects. Prospective follow up visits until 1 year post-operative
Data Collection	• Electronic Data Capture system • mymobility App • Apple Health & Fitness Recorder
Statistical Reporting	Data collected will be summarized descriptively and will be the basis of study reports. Statistical analysis will be conducted by Zimmer Biomet or its designee.
Scores/Performance Assessments	• KOOS, JR. (for PKA or TKA subjects only) • HOOS, JR. (for THA subjects only) • Customized Questionnaire(s) • Range of Motion (ROM) • EQ-5D-5L • Resource utilization data (office visits, PT visits, ER visits, readmissions)
Standards	The study is compliant with the below: • ISO 14155: 2020 - Clinical investigation of medical devices for human subjects - Good clinical practice. • ICH Guideline on Good Clinical Practice • The Declaration of Helsinki (DoH) - Ethical principles for medical research involving human subjects. • US Code of Federal Regulations 21 CFR Parts 11, 50, and 56

IV. Data Collection Overview

Source document worksheets will be provided to the sites to assist with data collection. Sites will be encouraged to utilize these worksheets, however their use will not be required if other source documentation is available for the data points including direct entry into an electronic data capture (EDC) system. All data collected manually by the site (i.e. not collected via mymobility or directly into the EDC system) will be entered into an EDC system.

Data Collection Activities	Pre-op	Surgical & Discharge	1 Month Post-Op	3 Month Post-op	6 Month Virtual	12 Month Virtual
Informed Consent	X					
Inclusion/Exclusion Criteria	X					
Randomization (RCT only)	X					
Demographic & History Form*	X					
Physical Exam	X		X	X		
Procedure & Perioperative Information		X				
Other Device Documentation		♦				
Chart Review*				X		X
Patient Questionnaire #1 (EDC)*	●					
Patient Questionnaire #2 (EDC)*			●			
Patient Questionnaire #3 (EDC)*				●		
EQ-5D-5L (EDC)*	●		●	●	●	●
KOOS, JR, HOOS, JR (via mymobility App). Control patients will complete in the EDC*	●		●	●	●	●
Adverse Event Form		♦	♦	♦	♦	♦
Medical Event Log		♦	♦	♦	♦	♦
Protocol Deviations*	♦	♦	♦	♦	♦	♦
Study Completion*	♦	♦	♦	♦	♦	♦
Time Documentation (Pilot Only)	X	X	X	X		

X Completed by Investigator or Designee
● Completed by subject (required)
♦ Completed by Investigator or Designee as applicable
* Forms that can be directly entered into the EDC system

V. Introduction and Purpose

Postoperative rehabilitation after total joint arthroplasty (TJA) has traditionally been initiated via discharge to a rehabilitation facility or through formal outpatient physical therapy (PT).[1] This has resulted in the cost of approximately $648 million per year for PT after primary TJA, with up to 25% of these costs utilized on less common modalities.[2] As elective TJA patients have increased their mobility in the early postoperative period and hospital or ambulatory surgery center (ASC) length of stay has decreased over time, patient-initiated therapy has become an emerging alternative for postoperative recovery. Previous randomized controlled trials have demonstrated that monitored home exercises can have equivalent outcomes when compared to formal outpatient PT after TJA for both range of motion (ROM) and patient reported outcome measures (PROMs).[3-8] However, there remains a substantial subgroup of patients (up to 20%) who may crossover to formal PT following patient-initiated therapy, highlighting a potential opportunity to provide an optimized home program that provides more effective simulated physical therapy in the postoperative TJA period.

PROMs have previously provided subjective measurements of patient pain, function and satisfaction after TJA. Unfortunately, objective measurements (e.g. measurements of physical function) are often lacking after TJA. Previous studies demonstrate that early initiation of activity after TJA can improve functional outcomes, suggesting that activity level may serve as a quantifiable measurement of recovery during the postoperative period.[9] Accelerometers and pedometers have been utilized to characterize preoperative function prior to TJA,[10] postoperative function after total hip arthroplasty (THA),[11] postoperative function after total knee arthroplasty (TKA),[12-17] and postoperative function after TJA.[18] However, the resultant physical objective measurements (i.e. step count, stair climbing and chair rising) have not been found to correlate with more formal outcomes scores, including patient satisfaction, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Short Form Health Survey (SF-36).[19-20] In one study, these objective measurements were passively collected utilizing an activity monitor for 48 hour intervals at 6 weeks and 6 months postoperatively.[20] Active systems, such as mobile applications accessed through electronic smartphones or tablets, interface directly with patients and are able to provide pre- and postoperative instructions with the intent of improving guidance for performing daily therapeutic exercises.[21] To the best of our knowledge, no study has been conducted utilizing an active care management system monitoring physical function while providing daily feedback for pre- and postoperative care for TJA.

Active biometric monitoring systems, such as the Apple Watch, have the ability to monitor step count, stair climbing, standing duration, exercise calorimetry, number of exercise minutes, and patients' heart rate (i.e. average, variability) both at rest and when performing exercises.[22] When coupled with an episode of care management application on a mobile platform, TJA patients can be continuously monitored, given important reminders, and instructed to conduct daily rehabilitative exercises autonomously. The combination of a mobile platform coupled with a consumer wearable device (e.g., smartwatch) has the

potential to revolutionize perioperative care for TJA.

The randomized controlled arm of this study aims to demonstrate non-inferiority of the mymobility smartphone (mobile) application (App) with Apple Watch platform in a TJA episode of care, by comparing subjects who receive standard of care (SOC), formal outpatient PT to a study group of subjects who complete remotely guided education and exercise via a mobile application, along with a wearable device. The correlative signature arm will compile key mymobility data, which includes data collected from an Apple Watch, from across the episode of care in TJA to a larger dataset, which will be analyzed to better understand and predict rare events and complications within this population. The purposes of the study are to evaluate the following measures and, as applicable, compare them to the comparator group results:

1. Determine if physical measurements and PROMs are similar between groups
2. Determine if subject satisfaction is higher in the study group
3. Determine the economic benefits to practices, patients and payers
4. Determine if complication outcomes are similar in the study group
5. Determine if the combination of data collected through an episode of care management application on a mobile platform combined with objective physical measurements can be utilized to predict the probability of post-operative complications, discharge disposition, ROM, and other PROM scores. This data set will also be used for future product feature development such as risk stratification, correlative signature modeling, and algorithm development.

VI. Study Objectives

Primary Objectives: The study objectives are to evaluate clinical outcomes, economics, and satisfaction with mymobility and the Apple Watch while developing a correlative heuristic considering multiple endpoints within the THA, TKA and PKA populations. To accomplish the objectives of this multifaceted protocol, the study has been broken into three cohorts with varying objectives. All mymobility study subjects will ultimately be part of the Correlative Analytics cohort. Additional objectives for each cohort are listed below.

A. Pilot & Time Cohort (Cohort I)

Primary Objectives

1. Determine study and product onboarding requirements (time and staff)
2. Determine time required for instrumentation of mymobility App and Apple Watch
3. Determine study execution requirements (time and staff)
4. Verify enrollment assumptions and customized survey content
5. Determine time required to attain subject understanding of use of Apple Watch

features (steps, stand hours, active calories, exercise minutes, heart rate - resting, walking, variability, flights climbed)

B. Randomized Controlled Trial (RCT) Cohort (Cohort II)

Primary Objective

1. Demonstrate non-inferiority of the study group, when measuring 30-day all cause readmission rates, when compared to the control group who will undergo standard of care education and an outpatient PT regimen.

C. Correlative Analytics Cohort (Cohort III)

In addition to traditional data collection mechanisms, four passive outcome measures will be captured among all mymobility study subjects via the Apple Watch sensors in combination with the mymobility App, attempting to develop correlative measures to assist surgeons in understanding and managing risk in their patient populations. These correlative outcomes will be measured using steps, stand hours, active calories, exercise minutes, heart rate (average, resting, walking, and variability), and flights climbed that will be analyzed in statistical models (including multivariate regression models). Details and methodology are provided in **Section XVI.**

Primary Objectives

1. Assess the differences in episode of care data compiled, collected, and delivered in the mymobility platform to correlate the incidence of the seven most common post TJR medical complications (UTI, ileus, MI, pneumonia, DVT/PE, prolonged wound drainage, wound infection).
2. Assess the ability of preoperative and episode of care data compiled, collected, and delivered in the mymobility application (from, among other sources, the Apple Watch sensor platform) to correlate with discharge disposition (home vs. non-home - ACF or SNF)
3. Identify 90-day mymobility data points which correlate with 30-day post op ROM data (90 degrees of flexion) within the TKA and PKA populations.
4. Assess the ability of postoperative data compiled, collected, and delivered in the mymobility application (from, among other sources, the Apple Watch sensor platform) collected during postoperative days 0-90 to predict which subjects will have a “very satisfied” or “satisfied” score on the Patient Satisfaction component of Patient Questionnaire #3 at 90 days.

Secondary Objectives

1. Utilize the unique patient clinical data that is available with the mymobility application to correlate early post-operative outcomes of various implant groups (e.g. brand, type, manufacturer) to preoperative and postoperative activity profiles, surgical techniques, patient attributes, and other routine outcomes data collected.

2. To provide a real-world data set on the mymobility cohort, including physiologic monitoring data, that enables ongoing exploratory data analysis and retrospective cohort study that will inform future product feature development and research. An example of such analysis that would support surgeons to make patient-specific recommendations is: study subjects could be "binned" according to 5-year age grouping (age 30-34, 35-39, etc.) and BMI (20-24, 25-30, etc.), and regression analysis could be used to correlate watch sensor data with superior outcomes. Statistically valid correlations would enable product features that support a surgeon to more easily identify whether or not a given patient's activity is following a pattern associated with superior clinical outcome.

VII. Study Design and Endpoints

This is a multi-center, staged cohort study evaluating clinical outcomes, economics, and satisfaction with mymobility in the episode of care for the primary THA, TKA and PKA populations. Up to 10,000 subjects will be participating in the mymobility platform. Approximately 500 subjects will participate as a control group in the RCT cohort described in **Section XI.** Up to 36 sites globally will contribute to this study. Each investigator will be experienced in total knee arthroplasty (TKA), partial knee arthroplasty (PKA) or total hip arthroplasty (THA).

Each Principal Investigator will be responsible for obtaining Institutional Review Board (IRB) or Ethics Committee (EC) approval as required prior to conducting the study. In order to avoid potential selection bias, each Investigator will offer study participation to each eligible subject presenting as a candidate for partial or total knee replacement or total hip arthroplasty using approved, commercially-available devices used on-label according to the manufacturer's instructions for use. The device selection criteria are discussed in **Section VIII.**

Eligible candidates who express interest in study participation will be offered Informed Consent. All potential study subjects will be required to participate in the Informed Consent process and will not be considered enrolled in the study until the candidate has signed and dated the IRB/EC approved subject Informed Consent Form (ICF). Study data cannot be collected until the candidate has completed the informed consent process and signed and dated the IRB/EC approved ICF.

All study subjects will undergo preoperative and postoperative clinical evaluations as part of the standard of care at each institution. Post-operative clinical evaluations will be conducted after surgery (30 and 90 days). A virtual visit, utilizing the mymobility App or EDC system, will occur at 180 and 365 days post-op.

The target population is patients who have made the decision to undergo a total hip, total knee, or partial knee replacement. The target population is further defined in the inclusion/exclusion criteria in **Section VIII.**

RCT: Primary Endpoint

1. Demonstrate non-inferiority of the study group in the number of readmissions through 30 days post-op.

RCT: Secondary Endpoints

1. Non-inferiority of the mymobility cohort for PROMs (HOOS, JR., KOOS, JR.) and EQ-5D-5L.
2. Manipulation Rates (knee), Timed Up and Go (TUG) and single leg stance test (SLS).
3. Satisfaction/Engagement: Assess differences between the study groups in subject satisfaction from Custom Satisfaction Survey(s).
4. Resource Utilization: Assess differences in resource-utilization in the study group for the entire episode of care (90 days postoperative). Potential data collection points include number of PT visits, discharge disposition, emergency room visits, readmissions, reoperations, unscheduled surgeon visits, and reduction in time processing paperwork and approvals from PT.

VIII. Study Population

The study population for primary statistical analysis will be comprised of individuals who require primary, unilateral total or partial knee arthroplasty, or total hip arthroplasty and satisfy the inclusion/exclusion criteria outlined in this section of the protocol. In order to avoid potential selection bias, each Investigator will offer study participation to each eligible patient presenting as a candidate for primary, unilateral total or partial knee arthroplasty, or total hip arthroplasty using any approved, commercially-available PKA, TKA or THA device used on-label according to the manufacturer's instructions for use. Eligible candidates who express interest in study participation will be offered an Informed Consent Form.

The current Version 4 of the study protocol narrowed the eligibility to total knee and partial knee arthroplasty, removing total hip arthroplasty. Previously enrolled patients who received THA will continued to be followed as part of the study. Additionally, patients with planned THA surgery and approached for participation prior to implementation of this protocol will be allowed to enroll.

A. Inclusion Criteria

1. Subject must be 18 years of age or older.
2. Subject qualifies for a primary, unilateral total or partial knee arthroplasty, based on physical exam and medical history.
3. Investigator plans to treat subject with a commercially-available device, used on-label according to the manufacturer's instructions for use, as part of their clinical

care.

4. Subject owns and maintains an iPhone capable of pairing to the Apple Watch, supporting iOS updates, and is compatible with the mymobility App.
5. Subject is willing and able to complete the protocol required follow-up.
6. Subject is able to read and understand the language used in the mymobility App for their region
7. Subject is willing and able to provide written Informed Consent and Authorization by signing and dating the IRB/EC approved Informed Consent and Authorization Form . Where applicable, subject must also be willing to provide authorization for use of protected health information in accordance with local privacy laws.
8. Subject is mobile with no more than a single cane/single crutch preoperatively.

B. Exclusion Criteria

1. Subject is a current alcohol or drug abuser as defined by the investigator.
2. Subject is considered a member of a protected population (e.g., prisoner, mentally incompetent, etc.).
3. Subject has systemic inflammatory arthropathies which would interfere or compromise the activity profiles within this study.
4. Subject is currently participating in any other surgical intervention, physical therapy or pain management study which would compromise the results of this study.
5. Subject requires simultaneous or staged bilateral replacements, staged <90 days apart. Subjects can be enrolled into the study for the second, staged arthroplasty if scheduled >89 days after their first, contralateral replacement.

Additionally, subjects who complete the entire study (1 year) for one joint may be enrolled for a second joint as a new subject.

IX. Study Device Information

A. mymobility Product Description

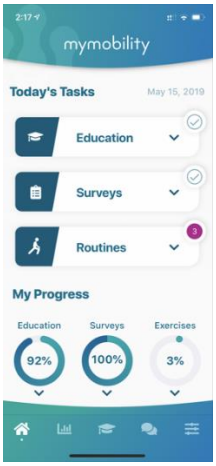
The mymobility App is a mobile software platform designed to facilitate remote episode of care management and asynchronous communication between the provider care team and their patient via provider-approved care plans and engagement communications. Current care pathways have been developed for: Total Hip Replacement, Total Knee Replacement and Partial Knee Replacement. Designed for the orthopedic population, mymobility also integrates wearable data from the Apple Watch into provider dashboards, providing enhanced understanding and monitoring of patients throughout the episode of care. This study will utilize version 1.01 of the mymobility App and all future versions as they are released. Version dates will be captured for the purpose of analysis.

Subjects will be provided an Apple Watch to pair with their iPhone for use in the study. If subjects already own a Series 3 or newer Apple Watch, they will be able to use their watch for the study purposes. Details of watch use and data safety are detailed in **Sections XI** and **XII.**

B. mymobility App Overview

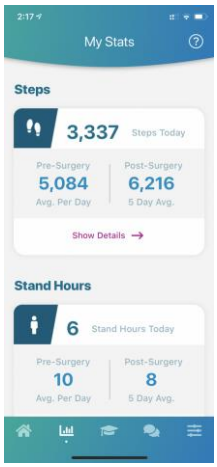
1. Patient To Do List

The login screen shows "To Do List", which identifies assigned activities to be completed during the patient's episode of care. Examples include: an education ePub (Preparing the Operative Site), a Patient Reported Outcomes Measure (KOOS, JR.), and an exercise routine (Week 1 Routine). Once the patient completes an activity, a check mark will appear next to the item signifying completion.



2. Patient Dashboard

By selecting "My Stats," patients will see a similar screen. Here certain items tracked by the mymobility application have shared visibility to the patient and care team. These stats include, but are not limited to: education, questionnaire, exercise completion, or steps collected by the Apple Watch over the last week with a line graph showing trends.



3. Patient Exercises

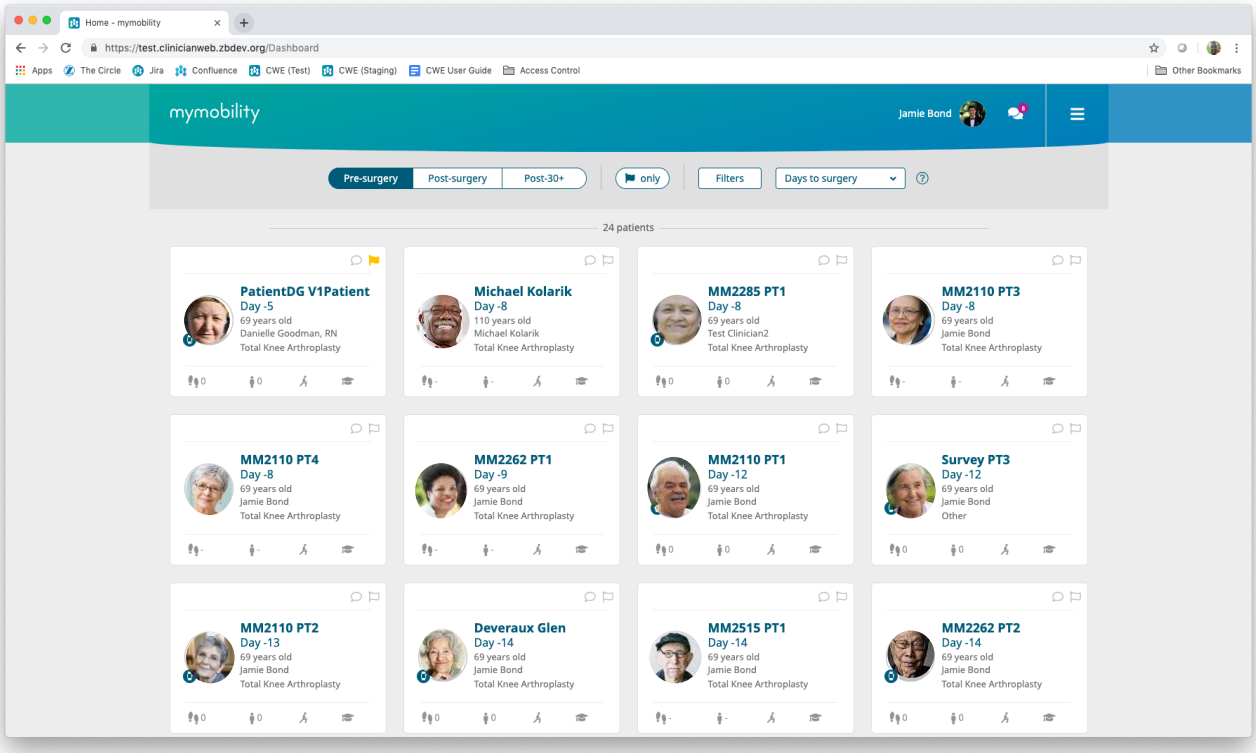
While completing assigned exercises, the patient will follow audio/video instructions as shown in the below example. The application provides a verbal description of the exercise and shows the movement from a variety of angles to communicate correct form to the patient. Patients self-report the number of repetitions performed for each exercise.

4. Apple Watch Integration

The essential application on the Apple Watch reminds the patient about activities on their To Do list as a convenient reminder without requiring the patient to open the application on the phone. The application also collects step counts and other HealthKit data (as described above), which is shared with the patient's care team at their consent and with their authorization. The mymobility application will sync directly with the Apple Watch once the application is installed on the iPhone. Progress updates are easily accessible on the Apple Watch as seen on the below images. Apple HealthKit data points of steps, stand hours, active calories, exercise minutes, heart rate (resting, walking, and variability), and stairs will be essential for creation of correlative statistical models of these biometric measurements with post-op complications and outcomes as described above.

5. Provider Dashboard

When the surgeon or a designated member of their team logs in to the clinician dashboard, a display of the care team's patients is immediately visible. Patients are sorted by metrics tracked through the mymobility application and a flagging system/message icons are displayed to alert care team members to important activities for each patient. Clinicians can perform a variety of tasks in the dashboard, including creating new patients and searching specific groups of patients.



X. Study Procedures

A. Screening

Potential subjects will be screened from each investigator's subject population. Subjects may be pre-screened for eligibility based on the inclusion and exclusion criteria. The site will maintain a Screening Log to track all screened subjects, including subjects who do not meet the study criteria and those who decline to participate. The log will document general demographic information for each screened patient as well as reasoning for patients who do not enroll.

B. Offer Study Participation

Study participation will be offered to each eligible patient presenting as a potential candidate. Eligible candidates who express interest in study participation will be offered Informed

Consent. Prior to patient involvement in the study, the patient must participate in the Informed Consent process and sign and date the IRB/EC-approved ICF.

C. Informed Consent Process

For candidates that express interest, the Investigator or Designee will describe relevant study information, including the purpose, procedures, alternative treatments, possible risks, and potential benefits associated with study participation. The Investigator or Designee will also describe the types of patient information that may be collected or analyzed during the study and with whom that information may be shared. The Investigator or Designee will also review, along with the candidates, the ICF approved by both the governing IRB/EC and the study Sponsor. Candidates shall have sufficient time to read and understand the IRB/EC approved ICF and discuss whether they wish to participate in the study. Candidates will be asked to acknowledge whether all of their questions and concerns have been addressed to their satisfaction. Any questions that candidates may have will be addressed appropriately by the Investigator or Designee. Candidates will be further instructed that they are free to obtain additional information from the Investigator or Designee at any time, that they are free to decline participation, and that they are free to withdraw their consent and authorization and discontinue their participation at any time without prejudice but for the requirement to return the watch if they withdraw prior to completing the final follow-up visit.

The Informed Consent process may be completed in-person or through an IRB/EC approved remote method. After completing the Informed Consent process, candidates who agree to enter the study must sign and date the IRB/EC approved ICF. The ICF must be signed and dated prior to onboarding. Study data will not be collected until the ICF has been signed and dated. If the candidate does not wish to participate (does not sign and date the ICF), data for that candidate will not be collected for this study.

A copy of the signed and dated ICF must be provided to the study subject. The original signed and dated ICF is to be filed in the subject's medical record, study subject binder, or regulatory binder.

D. Subject Enrollment

Once the ICF has been signed and dated by the subject, the subject will be considered enrolled in the study. A unique subject identification number (Subject ID) will be assigned to each participating subject.

This unique Subject ID number will be used throughout the study for identification. The subject will be considered an active study subject after receiving training in the appropriate use, participation and functionality of the mymobility platform and Apple Watch. In the event that the subject does not undergo knee or hip arthroplasty as outlined in the inclusion criteria, the subject will be considered a screen failure and a **Study Completion Form** will be used to document the subject's exit from the study.

E. Baseline/Preoperative Assessment

The following baseline/pre-operative data will be collected at the time of enrollment:

1. Inclusion/Exclusion Criteria
    a. Randomization (RCT cohort only, recorded in EDC)
2. Demographics & History Form
3. Pre-op Physical Exam
    a. Knee/Hip specific assessments including ROM
4. EQ-5D-5L
5. KOOS, JR. or HOOS, JR.
6. Patient Questionnaire #1
7. Protocol Deviations (as applicable)
8. Study Completion (as applicable)

Subjects may be consented up to 180 days prior to surgery. Preoperative forms, mymobility App registration, and Apple Watch distribution must be completed during the pre-op interval. The suggested visit window to allow best utilization of pre-operative mymobility App content is 14-30 days prior to the surgery.

Data from Standard of Care (SOC) assessments performed prior to enrollment may be used provided that data was obtained within 180 days of surgery and the patient consented to its use. In the event that surgery is rescheduled to a date greater than 180 days from enrollment, the site should reaffirm study participation with the subject prior to surgery and reobtain study assessments.

Physical exam assessments are intended to be completed at in-person visits. However, remote visits may be utilized to capture assessments if institutional restrictions prevent an in-person visit. Protocol deviations will document incomplete data.

F. Surgical Technique

Standard operative procedures will be followed and all surgical procedures will be performed under aseptic conditions. Investigators will implant all commercially-available partial or total knee components or total hip components in compliance with corresponding labeling requirements and in accordance with appropriate surgical technique(s).

G. Surgical and Discharge (Data Collection)

The following data will be collected about the surgery and immediate post-operative period, up to and including subject discharge:

1. Procedure & Perioperative Information
    a. Implants and instrumentation data
    b. Length of Stay and Discharge Disposition
2. Other Device Documentation (as applicable)

3. Adverse Event Form (as applicable)
4. Medical Event Log (as applicable)
5. Protocol Deviations (as applicable)
6. Study Completion (as applicable)

Previously enrolled patients who received a hip resurfacing procedure will be classified as total hip arthroplasty. Additionally, if the actual procedure differs from the procedure selected on the inclusion/exclusion form, then the inclusion/exclusion form should be updated to the actual procedure.

H. Postoperative Follow-up Procedures (Data Collection)

Postoperative clinical evaluations/assessments will be conducted at the following visit intervals:

Clinical Interval	Target Visit Timeframe (from Surgery)	Approximate Window in Days
1 month (30 days)	30 days	-/+ 14 days
3 month (90 days)	90 days	-/+ 21 days
6 month (180 days)	180 days	-/+ 42 days
1 year (365 days)	365 days	-/+ 60 days

The following clinical data will be collected postoperatively:

1. Post-op Physical Exam
    a. Single Leg Stance (SLS) and Timed Up and Go (TUG) test. (RCT Only)
    b. Knee/Hip specific assessments including ROM
2. EQ-5D-5L
3. KOOS, JR. or HOOS, JR.
4. Patient Questionnaire #2 (at 30 day visit)
5. Patient Questionnaire #3 (at 90 day visit)
6. Chart Review (at 90 and 365 day visits)
    a. Complications, readmissions, ER visits, non-SOC visits, physical therapy
7. Medical Event Log (as applicable)
8. Adverse Event Form (as applicable)
9. Protocol Deviation (as applicable)

10. Study Completion (as applicable)

Sites will be required to follow subjects postoperatively for 365 days +/- 60 days. Unless the study is otherwise closed, data will continue to be collected until the subject completes the study per the protocol, voluntarily withdraws from the study, is withdrawn from the study by the investigator, is lost to follow-up, undergoes revision to remove the implanted device, or expires. See Management of Incurrent Events (**Section XII**) for additional details. Reason(s) for study completion must be documented on the **Study Completion Form**.

Post-op physical exam assessments are intended to be completed at in-person visits. However, remote visits may be utilized to capture assessments if institutional restrictions prevent an in-person visit. Protocol deviations will document incomplete data.

XI. Pathway Specific Procedures

A. mymobility Procedures – Correlative Analytics Cohort (N=10,000)

These study procedures apply to all study subjects in all cohorts who have signed the ICF and are selected to receive the mymobility platform. The correlative analytics cohort includes all subjects in all three cohorts of the study who receive the mymobility platform. Procedures for control subjects in the RCT cohort are discussed in **Section XI.**

1. Preoperative Visit (up to 180 days before surgery)

i. If not previously completed, the subject will go through the full informed consent process and will sign and date the EC/IRB-approved ICF as outlined in **Section X**.

ii. Subject registration for the mymobility App includes the creation of a study Subject ID number via the study EDC system and placement into the master Zimmer Biomet electronic data collection (EDC) database.

iii. During the download of the mymobility App to the iPhone, the coordinator and subject will:

- Verify that the phone and Apple Watch operating systems (iOS and Watch OS) software are current.
    - Should an update of iOS or Watch OS be required, where possible, the update should be completed while the patient is at the site. In some situations, internet connectivity issues can cause significant delays with updating an OS. Under these circumstances the patient may complete the update at home. Additionally, Zimmer Biomet may approve a remote onboarding and watch pairing process for specific sites.
- Turn on measurements of correct HealthKit data types.

- Review instructions on pairing of the Apple Watch, daily charging instructions, how to look at activity rings, set alerts, and other functionalities.

iv. At this time, subjects with a compatible model of iPhone will also download the Apple Health and Fitness Recorder App to their iPhone. Following the download, the coordinator and subject will:

- Validate the correct data is being captured from the Apple Watch to the Apple Health and Fitness Recorder App.

v. Subjects who do not already own an Apple Watch Series 3 or newer will receive one for use in the study.

2. Preoperative Time period (approximately 30 days before surgery)

i. Subjects will begin to receive mymobility educational material through the App on their phones.

ii. Collection of mymobility data will begin. This will include within-App questions that are answered by the subject, care plan adherence data and full time HealthKit data collected by the Apple Watch (steps, flights climbed, HR, stand hours) - transferred to the mymobility platform, except for times when the Apple Watch is being charged. At this time, applicable subjects will also have data collected by the Apple Health and Fitness Recorder App.

iii. mymobility study subjects will follow the entire prescribed pathway of educational content, PROMs surveys, disposition questionnaires, and exercises until day of surgery in addition to their institution's standard of care preoperative procedures including education, classroom work and medical clearances.

iv. Research coordinators or clinical staff may call subjects to remind them to complete all tasks as directed by mymobility and to confirm that they are charging and wearing the Apple Watch daily, not having problems using mymobility or the Apple Watch, etc. Study subjects will also be provided a direct phone number to the office research coordinator if they have questions regarding the mymobility App or Apple Watch functions.

- Research coordinators should contact mymobility Technical Support to document any problems subjects are having with mymobility usage.
- Research coordinators can also review the clinical dashboard to assess if study subjects are using the mymobility care platform and, together with the clinical team, will contact study subjects at clinically appropriate timelines who do not appear to be adhering to their daily, assigned regimen.

3. Discharge Disposition and Prescribed Physical Therapy

i. It is intended that after surgery, study subjects will utilize the monitored home exercises within the mymobility platform to reduce the need for in person outpatient physical therapy. Physical therapy prescribed at time of discharge will be documented on the **Procedure & Perioperative Information Form** with the clinical reasoning.

ii. All subjects receiving physical therapy will remain in the analysis of the study group.

iii. If subjects are discharged to a postoperative nursing facility, they will continue using the mymobility with Apple Watch application(s) and continue to track all prescribed mymobility activities and passively-collected biometrics as described above.

4. Week 1 after surgery

i. Study subjects will begin their assigned, mymobility guided, home-based care pathway immediately upon discharge (these subjects will also have had the extensive preoperative teaching pathway from mymobility to prep them for their independent post-op therapeutic exercises).

ii. Study subjects are recommended not to have any scheduled home PT visits or home health visits, however, should subjects require these services they may be prescribed physical therapy and remain in the study.

iii. For those study subjects not receiving physical therapy, the surgeon's office may contact patients during the first post-op week to ensure they are comfortably using the mymobility App with Apple Watch platform in the place of standard physical therapy.

5. Postoperative Week 2 through Day 90

i. Study subjects will be encouraged not to participate in any formal outpatient post-operative physical therapy, however the surgeon has the opportunity to prescribe physical therapy at any time and for any duration during the course of recovery.

ii. Around the time of the 30-day and the 90-day time points, subjects will be asked to complete a PROM survey that they will receive through the mymobility App. In addition, an EQ-5D-5L and general satisfaction(s) question will be sent via email through the EDC system.

iii. Post-operative clinical evaluations will be conducted after surgery (30 and 90 days).

6. Postoperative Day 91 to 365

i. Subjects will continue wearing their Apple Watch and will keep the mymobility App active. They will continue to receive messages and recovery tips for 365 days following their surgery.

ii. 180 days after surgery, subjects will be asked to complete a PROM survey that they will receive through the mymobility App. In addition, an EQ-5D-5L questionnaire will be sent to them via email through the EDC system.

iii. 365 days after surgery, subjects will be asked to complete a final PROM survey that they will receive through the mymobility App. In addition, an EQ-5D-5L questionnaire will be sent to them via email through the EDC system.

7. End of Study

i. Subject participation will conclude after the final (365 day) PROM survey/satisfaction questionnaires are completed.

ii. Subjects may uninstall the mymobility App and/or Apple Health and Fitness Recorder from their iPhone.

B. Additional Cohort-Specific Procedures

1. Pilot & Time Study Cohort (N = up to 300, up to 6 centers)

This is an office workflow-focused cohort that will also evaluate study and product onboarding requirements (time and staff), time requirements for instrumentation of the mymobility App and Apple Watch, study execution requirements (time and staff), verifying enrollment assumptions and customized survey content, and time required to attain subject understanding of how to use Apple Watch features (steps, stand hours, active calories, exercise minutes, heart rate - resting, walking, variability, flights climbed)

i. All pilot study subjects will undergo all study procedures outlined in listed in **Section XI**.

ii. Additional time and resource data utilization regarding the instrumentation, onboarding and monitoring of subjects with the mymobility platform will be captured.

2. Randomized Controlled Trial (RCT) Cohort (N = 1,000)

For sites participating in both the Pilot and RCT cohorts, enrollment in the RCT cohort will begin once enrollment is complete at the site for the pilot cohort**.** Randomization will occur during the pre-operative visit after subjects have signed the ICF for participation in the study. A standard, stratified 1:1 randomization of total hips, total knees, and partial knees will be used to assign subjects to either the mymobility/Apple Watch study group or the standard of care control group. Stratification will ensure that within hips and knees, each procedure type will have a balanced allocation of control

and study patients.

a. Study Group (N=500)

Once randomization is completed, all subjects who were randomized to the mymobility group (mymobility/Apple Watch platform) will undergo all routine study procedures outlined in **Section XI**. In addition, each subject will:

i. At the preoperative, 30 day and 90 day visits, subjects will undergo a physical exam.

ii. At the 30 day and 90 day visits, subjects will undergo a Timed Up and Go (TUG) assessment and Single Leg Stance (SLS) assessment. A description of each assessment is listed below:

a. TUG assessment: the subject will be asked to rise from a sitting position, walk 3 meters as quickly as they feel safe and comfortable, turn around and walk back to take a seat in the chair. They will be timed from initiation of standing to a return to the sitting position. The subject will get one practice trial prior to scoring the assessment.

b. SLS assessment: Three, one-minute maximum, timed observations will be obtained. The average of the three timed observations will be calculated at the time of data analysis.

b. Control Group (N=500)

Subjects randomized to the control group will undergo traditional, standard of care procedures at their institution without the use of the mymobility platform

i. Control subjects will receive the standard of care (SOC) at the institution, including postoperative PT, and go through normal preoperative standard of care including joint camp classes, preoperative medical clearance, and traditional preoperative education.

ii. Control subjects will not be provided with the Apple Watch or mymobility App.

iii. Control subjects will go through each institution's standard of care (SOC) perioperative management pathway.

iv. Control subjects will complete the same PROM surveys and patient questionnaires as the mymobility group but they will be completed through the EDC system or on paper.

v. Control subjects will complete all Timed Up and Go, Single Leg Stance and ROM assessments, equivalent to the mymobility group above.

XII. Reporting

A. Activities Required Prior to Initiation of the Study

1. Institutional Review Board/Ethics Committee Informed Consent Approval

A Sponsor-approved Informed Consent Form (ICF) template (Appendix 3) will be provided for IRB or EC submission and approval. If the IRB or EC requires revisions to the provided ICF, the requested revisions must be submitted by the Investigator to the Sponsor for review and approval. Once the Sponsor has reviewed and approved the revision, the ICF will be re-submitted to the IRB or EC for final review and approval. A copy of the final IRB or EC approved ICF must be submitted to the Sponsor.

B. Clinical Data Collection/Submission

The Sponsor will collect all data in a central database (e.g. EDC, mymobility, HealthKit). The Sponsor will manage the collection of data into the Apple Health and Fitness Recorder App. The management of all study data received by the Sponsor will be the responsibility of the Sponsor or its designee. The use or disclosure of all protected health information will comply with all relevant data privacy and data security laws and requirements. All information will be treated with strict adherence to professional standards of confidentiality and will be held by the Sponsor under adequate security and restricted accessibility.

Data analysis will be conducted by the Sponsor or designee. All data will be encrypted and all personnel in the data management team will comply with relevant data privacy and data security laws and requirements. All electronic systems used to create, modify, maintain, or transmit study records will be validated according to 21 CFR Part 11[iii]. Title 21 CFR Part 11 of the Code of Federal Regulations deals with the FDA (U.S. Food and Drug Administration) regulatory guidelines on electronic records and electronic signatures in the United States. Appropriate audit trails exist on both the front and back end of the data management systems. The database will be subject to quality control checks and the resulting output will be used to generate data queries. Each participating Investigator will receive study reports on their own data and the collated data for the whole study group. Study metrics, e.g. summary tables, graphical output and descriptive statistics will be produced and may be available as hard copy. Strict confidentiality of individual hospital data will be maintained.

Reports and communications relating to study subjects will typically identify each subject only by the subject's initials (except in regions prohibited by regulations), assigned study Subject ID number, date of surgery, operative side, and date of birth (or year of birth depending on local regulations). This code must be clearly linked to the subject identity and can only be decoded by the study center. This does not include reports and communications transmitted via mymobility App, which are only able to be viewed by the subject and study center personnel.

Data collected by the Apple Watch will be transferred to the mymobility application from the

HealthKit application. HealthKit data is not transferred to Apple in connection with the study. Additional electronic clinical data collected by/entered into the mymobility App by the Investigator or subject will be transmitted directly to the Sponsor via the mymobility App. Apple may receive certain information from the Apple Health and Fitness Recorder App and the Sponsor, but Apple will never receive any data that directly identifies any participant of the study. Any data Apple receives as part of the study will not be combined with any data any participants separately choose to provide to Apple as part of their use of Apple products or services, such as iTunes. Apple will use any data received as part of this study in its health and fitness research and in its product development, design, and improvement activities.

For selected US sites, data elements such as subject co-morbidities, diagnosis, readmissions, ER visits and hospital visits may be obtained utilizing the OrthoVal program instead of manual chart reviews.

1. Summary of Case Report Form Data Collection

Study data will be collected on source documents, which may include study-specific worksheets provided by the Sponsor, or direct entry into the EDC system.

The following source document worksheet completion guidelines should be followed:

- Complete carefully and accurately.
- Complete header information consistently across all source document worksheets for each individual study subject (when study-specific forms are used).
- Be sure that data on the source documents match that which is entered through the electronic data capture (EDC) system.
- Use the study subject's unique Subject ID number assigned as instructed. Do not provide information that is not requested on the source document worksheet.
- Ensure that all fields are completed. For fields completed by the subject, efforts should be made to obtain any missing responses prior to the subject completing their visit.

2. Data Submission

Data captured on source document worksheets will be submitted directly to the Sponsor by electronic data capture and submission via a method approved by the Sponsor. Every effort must be made to ensure data submission to the Sponsor is made within 30 days of the visit completion.

3. Quality Assurance of Data

The Investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor in the source document worksheets and in all required reports. Data reported on the source document worksheets and clinic records should be consistent, or the discrepancies should be explained. All

electronic systems used to create, modify, maintain, or transmit electronic study records will be validated according to 21 CFR Part 11[iii]. The Sponsor will maintain quality control systems, in accordance with the Sponsor's policies and procedures. The Sponsor disclaims any responsibility for ensuring the accuracy of information collected by the Apple Watch or HealthKit application.

The standard procedures for handling and processing records will be followed per ISO 14155:2020[i] and Zimmer Biomet Standard Operating Procedures (SOPs) for this study.

4. Patient Surveys Date of Completion

Dates within the EDC may differ based on time zones factors. A similar thing occurs within mymobility where study reports from the Sponsor may show a different date than what the clinic user sees within the mymobility dashboard. The Sponsor will accept +/-2 days between audit trail dates and what is inputted into the EDC by the site or patient.

C. Reporting Requirements

1. Investigator Reporting Responsibilities

The Investigator should ensure the accuracy, completeness, legibility, and timeliness of data reported to the Sponsor in accordance with this protocol. The Investigator or Designee will provide periodic reports to their IRB/EC as required to maintain IRB or EC approval throughout the study and will provide any required final reporting to the IRB or EC upon study completion/termination. A copy of all IRB or EC re-approval letters must be submitted to the Sponsor. If the IRB or EC terminates or suspends its approval of the study, the Investigator or Designee will suspend study-related activities and will promptly notify the Sponsor. The Investigator should also promptly provide written reports to the Sponsor and the IRB or EC regarding any changes significantly affecting the conduct of the study and/or increasing risk to the subjects.

2. Retention of Records

Study records in the possession of the Investigator must be retained by the Investigator or Designee for a minimum of 2 years from the Investigator's study termination date, or per applicable local law, regulatory and/or IRB or EC requirements (whichever time period is greater). Measures shall be taken to prevent accidental or premature destruction of study records.

D. Management of Incurrent Events

1. Failure to Obtain Informed Consent and Authorization

Study data will not be collected until the Informed Consent has been signed and dated by the candidate. If a candidate does not wish to participate (does not sign and date the Informed Consent), data for that candidate will not be collected for this

study.

2. Medical Events / Adverse Events

See **Section C Safety Management** – Medical Events/Adverse Events Section of this protocol for additional information regarding adverse event classifications.

All new medical issues or problems reported by patients or found during chart review will be noted on the **Medical Event Log**, which will contain steps to determine whether the event should be considered a reportable adverse event.

Medical events include:

- New medical problems
- New resource utilization such as non-routine visits to a physician, hospital, emergency department, or urgent care center. Routine surgery follow-up visits, vaccinations, and wellness/standard of care visits should not be considered Medical Events.

All medical events determined to be reportable adverse events are required to be reported on the **Adverse Event Form**. The completed **Adverse Event Form** must be submitted to the Sponsor in a timely manner. The Investigator or Designee will also promptly provide the Sponsor with any additional requested information required for the Sponsor to comply with regulatory requirements (including requests for medical records). If applicable per their reporting requirements, the Investigator or Designee will also report applicable adverse event(s) to their IRB/EC.

Adverse events include:

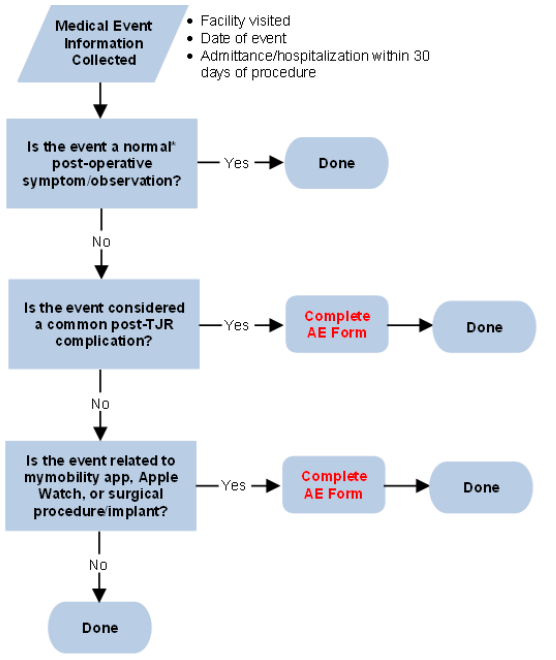
- Medical event that is one of the common post-TJR complications
- Medical event that has a relationship to the mymobility app, Apple Watch, procedure, or implant.
- Study joints that receive a treatment of manipulation under anesthesia

A medical event which is considered to be a normal post-operative symptomology or observation following any joint replacement surgery (e.g. joint pain, swelling, decreased range of motion, incisional pain) should not be classified as an adverse event unless it is considered to be more severe, of longer duration, is otherwise more pronounced than is typical, or is serious. Refer to **Section XIII** for the definition of a Serious Adverse Event.Events occurring after the index joint arthroplasty procedure discharge which are determined by the investigator to not be related to the joint arthroplasty procedure, device, use of the mymobility application or Apple Watch, should not be classified as adverse events, regardless of severity or seriousness.

Medical and adverse event collection will begin only after the patient has study surgery.

Specific instructions regarding Medical Events and Adverse Events:

- Readmission is defined as admittance to a hospital following discharge after the index joint surgery. This includes readmissions for observation as well as same day readmission/discharge. Prolonged hospitalization after the index joint surgery is not considered a readmission.
- If multiple medical events are all associated with the same medical issue, then it may be appropriate that only one adverse event is completed, rather than an adverse event for every medical event.
- Knee codes 30 to 60 are to be used for study joint knee events
- Hip codes 70 to 97 are to be used for study joint hip events
- Codes 01 to 29 are general or non-study joint events



*Normal: anticipated/expected in occurrence, severity, and seriousness. If the event does not meet all three criteria, this should be answered "No."

Reporting and Documentation of Adverse Events and Adverse Device Effects

Adverse Events and Adverse Device Effects will be documented on the Adverse Event Report form over the whole time of the investigation including information on the date of onset, treatment and resolution, as well as assessment of both the seriousness and the relationship to the study device. Further, the outcome of complications will be documented and any changes in outcome are to be updated during the course of the study. In case of early termination of the study, further follow-up of the patient shall proceed according to the hospital's standard procedure.

Reporting and Documentation of Serious Adverse Events, Serious Adverse Device Effects, and Device Deficiencies

Serious Adverse Events and Serious Adverse Device Effects will be reported to the Sponsor as soon as possible. The incidence will be documented on the Adverse Event Report form over the whole time of the investigation including information on the date of onset, treatment and resolution, as well as assessment of both the seriousness and the relationship to the study device based on the evaluation of the investigator. The outcome of such complications will be documented and any changes in outcome will be updated during the course of the study. In case of early termination of the study, further follow-up of the study subject shall proceed according to the hospital's standard procedure.

Device Deficiencies (including the device, mymobility App, and Apple Watch) that did not lead to an adverse event but could have led to a medical occurrence if suitable actions had not been taken, if intervention had not been made, or if circumstances had been less fortunate shall be reported to the Sponsor as soon as possible.

The Investigator is responsible for reporting all SAEs, SADEs and Device Deficiencies that could have led to a SADE to the Ethics Committee or Institutional Review Board if required by national regulations or by the EC/IRB.

The Sponsor is responsible for determining the final classification of adverse events.

3. Revision

In the event that removal of one or more of the implanted devices used in the joint arthroplasty procedure is necessary, the Investigator will determine the best treatment and/or revision method for the subject.

Once the revision surgery has been completed, the Investigator or qualified Designee must complete an **Adverse Event Form**. Subjects who have tibial articulating surface exchanges may remain enrolled in the study. All other revisions will result in the subject being terminated from the study and a **Study Completion Form** must be completed.

4. Investigator Withdrawal

The Investigator can choose to withdraw a subject from the study if it is deemed to be in the subject's best interest or the subject does not consent to continue in the study after being informed of changes in the research that might affect them. The reason for the Investigator's withdrawal of the subject must be documented on the **Study Completion Form**.

5. Subject Withdrawal

Study subjects may choose to withdraw from the study at any time, for any reason. If possible, a final evaluation will be completed for any subject who no longer wishes to participate in the study. The reason for the subject withdrawal must be documented on the **Study Completion Form**.

6. Lost to Follow-up

A study subject will be considered lost to follow-up after they have missed two consecutive visits and attempts to locate and evaluate the subject using the procedure outlined below have failed. All attempts to contact the subject are to be documented in the subject's study files and on the **Study Completion Form**. Missed visit(s) also must be documented using the **Protocol Deviations** form. The first three contact attempts should be made by telephone, email, or message through the mymobility app, with additional attempts as outlined in the following table:

If	Then
a response is not received after three (3) phone calls, emails, or messages through the mymobility app	The Investigator or Designee should send a certified letter to the subject requesting a response.
all attempts to contact the subject are unsuccessful or the subject is contacted and chooses to withdraw from the study	A **Study Completion Form** will be completed and will specify the reason the subject is no longer participating in this study. If the subject has already received an Apple Watch, the coordinator will have the subject unpair and return the Apple Watch as soon as possible and will track this on the Device Accountability Log. Return mailers will be provided for subjects who have moved or are unable to come into the clinic to return the Apple Watch. Subjects will be instructed that they may uninstall the mymobility and/or Apple Health and Fitness Recorder Apps if desired.

If attempts are made to contact a patient to schedule a visit and the patient is determined to be lost to follow-up, then additional attempts will not be required for watch retrieval.

7. Protocol Deviations

Investigators should not deviate from the study protocol unless it is to eliminate hazard to the patient. If a protocol deviation does occur, the deviation must be documented on the **Protocol Deviation Form** and submitted to the Sponsor. Each significant deviation will be reported to the IRB/EC, if applicable, within the appropriate deadlines stipulated by the appropriate regulatory authorities. Significant deviations are defined as those impacting or potentially impacting patient safety.

Site-facing forms that are partially or completely missed should be documented as protocol deviations. Protocol deviations will not be required for patient-facing surveys that are partially or completely missed. Partially or completely missed patient surveys for patients enrolled under a previous protocol version will also not require protocol deviations. Additionally, protocol deviations will not be required for out of window patient-facing surveys.

Chart reviews are required at the 3 month and 1 year intervals. The intention is that the review identifies potential medical and adverse events that have not been previously reported. A chart review will provide the same information whether it is completed in-window or late out-of-window. As such, protocol deviations will not be required for conducting late chart reviews.

8. Study Termination

Study subject participation is expected to end upon completion of the subject's last follow-up visit (365 days) unless the subject voluntarily withdraws from the study, is withdrawn from the study by the Investigator, is lost to follow-up, undergoes revision to remove the implanted device, or expires. Reason(s) for study completion must be documented on the **Study Completion Form**.

Some patients might not respond to 1 year surveys and can be considered Lost to Follow-up. Surveys completed beyond 18 months postop should not be collected or entered into the EDC.

If the Sponsor decides to terminate the study early, the Sponsor will inform the Investigators of the reason for early study termination. It is the responsibility of the Investigators to inform their IRB/EC as applicable according to local and national laws/regulations.

9. Modification of the Protocol

All amendments to this protocol shall be agreed to by the Sponsor and the Investigator(s) and be recorded with a justification for the amendment prior to

implementation. Approval of the applicable IRB/EC must be obtained prior to implementation, if required according to the local and/or national laws/regulations.

XIII. Safety Management

Adverse events are required to be reported on the Adverse Event Report case report form. The completed Adverse Event Report case report form must be submitted to the Sponsor in a timely manner. The Investigator or Designee will also promptly provide the Sponsor with any additional requested information required for the Sponsor to comply with regulatory requirements. If applicable per their reporting requirements, the Investigator or Designee will also report applicable adverse event(s) to their IRB or EC.

A. Medical Events/Adverse Events Definitions and Classifications

An adverse event is synonymous with complication or medical event. Adverse events will be classified by type, severity, and outcome and may be collected systematically or non-systematically.

The following definitions are from ISO 14155:2020[(i)].

Classification of the Event

Adverse Event (AE):
An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated.

Note 1: This definition includes events related to the investigational medical device or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.

Serious Adverse Event (SAE):
A Serious Adverse Event is any adverse event that led to any of the following:

a. death.
b. serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:
    1. a life-threatening illness or injury, or
    2. a permanent impairment of a body structure or a body function including chronic diseases, or
    3. in-patient or prolonged hospitalization, or

4. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
5. fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment.

Note: Planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered a serious adverse event.

Adverse Device Effect (ADE):
An Adverse Device Effect is an adverse event related to the use of an investigational medical device.

Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment implantation, installation, or operation, or any malfunction of the medical device.

Note 2: This definition includes any event resulting from use error or from intentional misuse of the medical device.

Note 3: This includes 'comparator' if the comparator is a medical device.

Serious Adverse Device Effect (SADE):
A Serious Adverse Device Effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Intensity of Symptoms

Mild:
The subject is aware of the sign or symptom, but finds it easily tolerated. The event is of little concern to the subject and/or little clinical significance. The event is not expected to have any effect on the subject's overall health or well-being.

Moderate:
The subject has discomfort enough to cause interference with or a change in usual activities. The event is of some concern to the subject's health or well-being and may require medical intervention and/or close follow-up.

Severe:
The event interferes considerable with the subject's usual activities. The event is of definite concern to the subject and/or poses substantial risk to the subject's health or well-being. The event is likely to require medical intervention and/or close follow-up and may be incapacitating or life threatening. Hospitalization and treatment may be required.

Note: The term "severe" refers to the intensity of the event and can be used with any event, without regard to whether or not it meets the criteria for being classified as "serious" or "unanticipated". For example, a subject can have a severe headache, but it is not a serious event.

Outcome Definitions

The outcome is in relationship to the Adverse Event, not the treatment rendered for the event (if any).

Resolved:
The adverse event has been resolved and/or no further treatment is required to treat the reported condition or illness.

Tolerated:
The adverse event will most likely never be resolved. The subject "tolerates" the illness or condition as a matter of life.

Pending:
Treatment or diagnostic studies were prescribed for the adverse event and the outcome of the adverse event is not yet known.

Study Withdrawal:
Due to the adverse event, the subject was withdrawn from the study.

Device Removal:
The adverse event resulted in the removal of an implanted device.

Reoperation of Affected Joint:
The adverse event resulted in reoperation of the study joint, but the reoperation did not include removal of an implanted device.

Death:
The outcome indicates the subject died as a direct result of the reported adverse event.

Collection Approach

The type of approach taken to collect adverse event information may be systematic or non-systematic.

Systematic:
Based on checklists, questionnaires, or tests.

Non-Systematic:

Based on spontaneous reporting and recording.

XIV. Monitoring

Prior to initiating the clinical study, the Sponsor, or its designee, will conduct a site initiation visit (SIV) to ensure the Investigator(s) and study staff understands the study protocol and requirements. Prior to study initiation, the Investigator must have a fully executed CTA and IRB or EC approval of the study protocol and the study Informed Consent Form (ICF).

During the course of the study, the Sponsor, or designee, will conduct periodic central or onsite monitoring and maintain contact with the study staff to monitor compliance and evidence of adverse events, in accordance with the Sponsor's policies and procedures. The Sponsor will address any identified non-compliance with the executed CTA, study protocol, and applicable regulatory requirements.

If onsite monitoring visit(s) are deemed appropriate by the Sponsor, the Investigator will permit representatives of the Sponsor's monitoring team to have direct access to inspect all source data/documents, study documents/binders, corresponding sections of study subject medical/hospital records, and any other documents relevant to the study. All Sponsor onsite visits (including site initiation) will be documented using the Site Monitoring Visit Log.

XV. Risk Analysis

The control group in this study receives the institutional standard of care, which may vary from no post-operative rehabilitation to inpatient rehabilitation. The study group is managed with one specific postoperative protocol: the utilization of computer-based perioperative care. Computer-based rehabilitation protocols have been previously described and are the standard of care at many institutions. The specific computer-based platform utilized in this study includes an Apple Watch and the mymobility application.

While this combination of new technologies provides the patient and surgeon with a more structured, efficient and informed perioperative experience, there is no specific intervention or postoperative recommendation involved in this study that is considered to be outside of the current standard of care. The study group is receiving one of the current standards of perioperative care, being delivered through a novel combination of technologies.

There are several categories of risk that may be relevant in this study.

A. Risks

1. Risk of Privacy Breach

The Sponsor has put in place physical, electronic, and administrative safeguards to help protect the privacy of health information. However, as is the case with all applications, the Sponsor unfortunately cannot guarantee security for data collected, leading to private health information becoming available to others without their

permission.

2. Intraoperative Risk

The study does not involve any alteration to the surgical procedure being performed. Therefore, there is no risk of any intraoperative complication due to this study.

3. Risk of Additional Rehabilitation with Apple Watch and mymobility Platform

There is negligible risk of intervention in the study group, considering that computer-guided postoperative rehabilitation programs are already considered within the standard of care after a joint arthroplasty. Many centers across the country have demonstrated the success and equivalency of a variety of postoperative rehabilitation programs, including a) no formal physical therapy, b) computer-guided therapy, c) home physical therapy, d) outpatient physical therapy, and e) inpatient rehabilitation. All of these postoperative rehabilitation strategies fall within the standard of care. The degree, frequency, or formality of postoperative therapy has never been demonstrated to have a detrimental effect on surgical recovery or impact the complication rate. To the contrary, the recent literature[3-8] has demonstrated that alternative programs to formal physical therapy are safe, increase patient satisfaction, and are cost-effective.

4. Risk of Failure to utilize the Apple Watch/mymobility combination

If a subject fails to properly utilize the study's technology platform, they would receive no specific guidance for rehabilitation after their joint arthroplasty. There is minimal physical risk of this failure, as having no formal guidance after surgery is one of the current standards of care.

5. Skin irritation

The Apple Watch may cause a rash on the wrist or pressure artifacts (sores).

B. Minimization of risk

All protected health information will be appropriately managed and protected in HIPAA-compliant systems with currently appropriate standards of data management. GDPR regulation is to be followed for EMEA subjects. All Australian participants are covered by the provisions relating to the European subjects.

All control and study subjects will have standard follow-up appointments with their care team, and either standard or augmented communication options to contact their care team. This allows for ample opportunity for the care team to intervene for any subject who appears to require additional rehabilitation services. These additional services are allowed in the control and study group when a subject is found to require additional rehabilitation.

C. Indemnity

If an injury is caused to a patient as a result of procedures undertaken in accordance with the Study, the Sponsor is liable for damages resulting from the study.

XVI. Statistical Methods

Subjects using the mymobility application will be evaluated for pain, function, quality of life, and early post-operative outcomes. Data collected in this study will be summarized descriptively and descriptive summaries will be the basis of any study reports issued. These summaries may be used for interim study reports and may also be used to support regulatory submissions, presentations, and/or publications. Additional surgical technique and instrumentation data may be collected and evaluated.

A. General Statistical Methods

Statistical methodology will consist of summarizing collected data descriptively. Categorical data (e.g., gender or race) will be summarized using counts and percentages, and 95% Confidence Interval (CI), over the time periods of interest. Continuous data, such as age, will be summarized by using means, medians, standard deviation, minimum, maximum, and 95% CI over the time periods of interest. Routine summaries of complication data is represented by frequencies and percentages. Subgroup analysis on a variety of data will also be performed. Exploratory data analyses using statistical models to discover relationships between demographics, subject adherence, HealthKit data and outcomes will also be performed.

B. General Assumptions

The primary endpoint will be subjected to a power analysis, allowing for an estimation of the number of RCT subjects needed to demonstrate clinically significant differences between outcome measures. Below is the initial analysis on the primary endpoint.

1. Readmission Rate

A 2015 journal article in PLOS ONE used meta-analyses and the University of Wisconsin demonstrated the overall 30-day readmission rate to be 5.4%.[31] The 5.4% readmission rate is similar to the readmission rates reported in a 2016 JOA article on readmission rates for hips (% across all orthopedics 5.8%) and a 2017 JBJS article on readmission rates for knees (5.8%).

Based on an assumed readmission rate of 5.4% in both the control and study group and a non-inferiority margin of 4.5%, a total sample size of 794 patients will provide 80% power while controlling the alpha-error at 0.05.

C. Sample Size

1. RCT cohort

The RCT cohort will include 1,000 subjects. This is based on the sample size of 794 required to show non-inferiority on the readmission rate endpoint. Accounting conservatively for 20% Loss-to-follow-up, 1,000 subjects will ensure the study is adequately powered. This study is powered appropriately to show non-inferiority between the mymobility group and control group.

i. This study is designed to show that the mymobility group is non-inferior to the control group using one primary study endpoint. This will be shown using a closed testing method in which the primary endpoint of readmission rate is compared using α=0.05. Study success requires that the study group successfully demonstrates non-inferiority on this end point using the statistical methods described.

2. Apple Watch/mymobility Correlative Analytics

Although there is no well-defined method to calculate the power of a predictive model before it has been developed, the low rate of certain outcomes such as manipulation under anesthesia, readmission, embolism, etc. will increase the number of subjects needed to create a reliably predictive tool that could be used to correlate events and data in order to make claims in clinical decision making. Generally, very large numbers are required to demonstrate predictive power for a predictive statistical model. A goal of 10,000 subjects has been set, with interim analyses at 2,500, 5,000 and 7,500 subjects to determine continued need for subject enrollment. Assuming a complication rate of ~3% and a discharge rate of ~5% to postoperative rehab facility in the study population of 10,000 subjects in the Correlative Analytics Cohort, this implies that 300 subjects will have some type of complication and 500 subjects will be discharged to a rehab facility. Given the fact that our goals are to identify high positive predictive value and area under the curve (AUC) upper and lower threshold values of Apple Watch measured and transmitted biometric data (steps, stand hours, active calories, exercise minutes, heart rate - resting, walking, variability, flights climbed), using multivariate regression to correlate with post-op complications, and risks of discharge to rehab facility, we would conclude that a Predictive Signatures Study group of at least 10,000 subjects will be required.

Examples of other studies in the total joint literature that have used multivariate regression models to provide clinically useful cutoff values are provided below:

i. Study #1 – Assessing patients for joint replacement; Can pre-operative Oxford hip and knee scores be used to predict patient satisfaction following joint replacement surgery and to guide patient selection?[32]

- N = 3307 subjects
- In this study, even having an N of 3307 study subjects was not sufficient to produce receiver operating characteristics (ROC) model that was able to predict satisfaction after THA.

ii. Study #2 – The use of receiver operating characteristics analysis in determining erythrocyte sedimentation rate and C-reactive protein levels in diagnosing periprosthetic infection prior to revision total hip arthroplasty.[33]

- N = 479 subjects

- In this study, a population of 479 who had an infection (analogous to our population of 300-500 subjects who either has some type of complication or is discharged to a rehab facility) was required to produce lower limit threshold values of C-reactive protein and erythrocyte sedimentation rate to diagnose infection.

iii. Study #3 – Relation between surgeon volume and risk of complications after total hip arthroplasty: propensity score matched cohort study.[34]

- N = 37,881 subjects
- In this study, a population of ~38,000 subjects (with approximate complication rate of 2%) was required to create a received operator curve with high PPV threshold values of number of hospital and surgeon cases required to minimize risk of complications after THA.

Based on this sampling of high quality predictive and risk-modeling studies from the TJA literature, we conclude that a study population of at least 10,000 subjects is required to produce clinically useful predictive ROC curves and high PPV threshold values for passively measured Apple Watch measured and transmitted physiologic metrics. As noted earlier, interim analyses will be performed at 2,500, 5,000 and 7,500 subjects to determine emerging heuristics related to complication predictions.

XVII. Quality Control & Quality Assurance

The Investigator will be required to permit representative(s) of the Sponsor's monitoring team to inspect all Case Report Forms and corresponding sections of the study patients office records and/or hospital original medical records. These audits will be done for quality assurance purposes, i.e. verifying adherence to the Clinical Investigation Plan and the completeness and accuracy of the data being entered on the Case Report Forms.

The Clinical Investigation Plan will be provided to all participating study centers. The Investigators will be fully trained in the proper reporting and submission of trial data prior to patient enrolment. Completed Case Report Forms will be reviewed before entering the data into a central database by the Sponsor.

The Clinical Study Manager is responsible for generating data queries for missing or unclear data if needed. It is the responsibility of the Clinical Study Manager to ensure data quality.

There are regular meetings between the Investigators and Zimmer Biomet Clinical Affairs staff. Written correspondence to all sites is used to inform the Investigators of routine study details and to update them on study status.

XVIII. Suspension or Premature Termination of the Clinical Investigation

If the Sponsor decides to terminate the study early, the Sponsor will inform the Investigators of the reason for early study termination. It is the responsibility of the Investigators to inform their IRB/EC as applicable according to local and national laws/regulations. Investigator disqualification criteria leading to exclusion from the clinical study include fraud, misconduct and serial non-compliance.

A. Investigator Withdrawal

The Investigator can choose to withdraw a subject from the study if it is deemed to be in the subject's best interest or the subject does not consent to continue in the study after being informed of changes in the research that might affect them. The reason for the Investigator's withdrawal of the subject must be documented on the **Study Completion Form**.

B. Subject Withdrawal

Study subjects may choose to withdraw from the study at any time, for any reason. If possible, a final evaluation will be completed for any subject who no longer wishes to participate in the study. The reason for the subject withdrawal must be documented on the **Study Completion Form**.

C. Study Termination

Study subject participation is expected to end upon completion of the subject's last follow-up visit (365 days) unless the subject voluntarily withdraws from the study, is withdrawn from the study by the Investigator, is lost to follow-up, undergoes revision to remove the implanted device, or expires. Reason(s) for study completion must be documented on the **Study Completion Form**.

XIX. Vulnerable Populations

Per the study exclusion criteria, vulnerable and/or protected populations will not be enrolled in this study.

XX. Document History

Version	Date	Description of Change	Person in Charge of Change
1.0	15 May 2018	Initial Document	Erin Osborn
2.0	11 Jun 2019	• Updated terminology/formatting throughout • Increase number of sites to 36 • Expansion of study scope from United States to global, with applicable changes to accommodate clinical study regulations/processes outside the US	Dave Van Andel

		• Inclusion/Exclusion Criteria updated – Requirement for diagnosis of osteoarthritis removed – iPhone SE excluded from phones allowed – Language requirement updated to reflect global nature of study – Requirement for authorization for use of protected health information added where applicable – Exclusion criterion added for inflammatory arthropathies – Participation in other studies only an exclusion if it would compromise the results of this study – Exclusion criterion for staged or bilateral replacements updated/clarified to allow the second replacement to be enrolled under certain circumstances • Follow-up time frames converted from months to days • Pre-operative interval expanded to up to 90 days prior to surgery • Removal of language specifying return of watches upon study completion • Clarification of ability to use data obtained from standard of care visits for screening • Reference to crossover removed. Crossover form name changed to “Prescribed Physical Therapy” form • Addition of guidelines/documentation to allow greater flexibility in prescribing physical therapy after surgery • Download of Apple Research App added to pre-op visit • Clarification that protocol deviations will not be issued for incomplete PROMs or other patient-facing questionnaires.	
3.0	23 Jun 2020	• Protocol reformatted into current Sponsor template. Formatting, terminology, and paragraph changes throughout document • Sponsor name changed to Zimmer Biomet • Changed mymobility to a registered trademark • Clarified that Statement of Compliance signature is only required by the Principal Investigator during the site start-up process	Scott Abshagen

		• Added Netherlands address as a regional Zimmer Biomet contact location • Removed Appendix 4 – Investigational Site information • Added additional technical support email address • Added abbreviations • Expanded inclusion criteria to any commercially available THA, TKA, or PKA implant used on-label according to Instruction for Use. Removed requirement that only Zimmer Biomet implants must used. Created the "Other Device Documentation" form to collect non-Zimmer Biomet implant information. • Clarified the inclusion criteria for iPhone model requirement. • Clarified the inclusion criteria that patient must be single cane/single crutch assist preoperatively. • Added language that subjects who complete the entire study for one joint may be enrolled for a second joint. • Indicated on the data collection chart which forms can be entered directly into the EDC • Incorporated remote study activities such as informed consent, onboarding, and study assessments • Clarified the preoperative interval of up to 180 days for consent, assessments, and patient surveys or questionnaires. 90 to 14 days preop for onboarding into mymobility. • Removed TUG/SLS as a preoperative data collection point for the RCT cohort • Added Chart Review as a 90 day and 365 day form to the postoperative data collection listing • Removed the Prescribed Physical Therapy form • Clarified that the Apple Research App is officially called the Apple Health and Fitness Recorder. Added language about data sharing with Apple. • Added Medical Event / Adverse Event flowchart • Added specific Medical Event / Adverse Event instructions, including definition of readmission	

		• Added language about SAE and SADE reporting. Removed UADE definition. • Clarified that lost to follow-up process begins after patient has missed two consecutive study visits • Added that email and mymobility app can be used for contact attempts if patient is potentially lost to follow-up • Added language about protocol deviation reporting • Added Quality Control and Quality Assurance section • Added minimization of risk language specifically for Australia • Updated guideline references	
4.0	14 Feb 2022	• Updated inclusion criteria by removing total hip arthroplasty as eligible surgery • Included language about screening practices • Updated ISO reference and applicable definitions • Clarified protocol deviation reporting requirements for out of window patient surveys, missed patient surveys, and late chart reviews • Clarified preoperative interval and timing of informed consent, preoperative forms, and mymobility app registration • Clarified classification of hip resurfacing procedures • Clarified medical event and adverse event reporting requirements • Clarified patient survey dates of completion • Specified watch retrieval requirements if patient is also lost to follow-up • Clarified that subjects with tibial articulating surface exchanges may remain enrolled in the study	Scott Abshagen

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XXII. Appendices

1. Worksheets
2. Study Logs
3. Informed Consent Form (ICF) template