The Framingham Heart Study

Precursors and Prognosis of Traumatic Brain Injury

Protocol

Introduction

The Framingham Heart Study

The Framingham Heart Study (FHS) started when a group of researchers wanted to identify the common factors or characteristics that contribute to cardiovascular disease (CVD). They sought to do this by following its development in a large group of people who had not yet developed any signs of CVD. About 5,200 men and women between the ages of 30 and 62 from the city of Framingham, Massachusetts were recruited to participate. For each participant, this entailed returning to the study every two years for a detailed medical history, physical examination, and laboratory tests. These people comprised the first cohort (group of participants). Then, a second cohort of participants was started in 1971. These 5,124 participants were the children of the participants from the first cohort. Finally, in 2002, a third generation cohort was started.

Although the study was started primarily for the purpose of discovering the risk factors for CVD, the data obtained through medical histories, examinations, and other documents is still very useful for other epidemiological studies. The FHS is unique because there are three generations of data, and that the participants mostly live in the same environment. This allows for fewer confounding factors in these epidemiological studies.

Traumatic Brain Injury

A case of traumatic brain injury (TBI) is defined as "either an occurrence of injury to the head that is documented in a medical record with one or more of the following conditions attributed to head injury: 1) observed or self-reported decreased level of consciousness 2) amnesia 3) skull fracture 4) Objective neurological or neuropsychological abnormality 5) diagnosed intracranial lesion".

TBI and spinal cord injuries are the leading causes of death among children and young adults from injury. Survivors of this injury suffer not only physical detriments to their health, but also experience hardships when it comes to relationships, work, and creativity. This is why TBI is called "the silent epidemic." These effects of the injury may be hard to pin down and attribute to the injury. Also, the effects of TBI reach far beyond the person sustaining the injury. Families of the injured may experience emotional distress and be challenged economically, affecting their futures.

Precursors and Prognosis of TBI

There are an estimated 1,700,000 new cases of Traumatic Brain Injury (TBI) admitted annually to an emergency department (ED) in the United States.[1] The majority of these injuries are mild (mTBI; often referred to as concussions). This is likely an underestimation, as many people with mTBI may not visit an ED (due to minimal or transient symptoms) while others with sub-concussive brain injuries from sports or falls may minimize or neglect symptoms. Recent reports indicate that people experiencing a single or repetitive TBI may have an increased risk for development of late-life cognitive decline or neurodegenerative disease. Which risk factors

might lead to heterogeneous profiles of late-life decline? One risk factor might reflect a persistent inflammatory response, another might reflect a genetic predisposition to neurodegenerative diseases and yet another might include cognitive reserve and co-morbid diseases. Recent post-mortem studies suggest that not only history of diagnosed TBI but also history of *exposure* to head impacts is linked to significant pathological changes. Antemortem TBI studies have been largely focused on clinically diagnosed cases or select populations (e.g., war veterans, elite athletes), but to date no community-based study has examined whether repeated exposure to head impacts may have later life clinical consequences.

Our study will capitalize on pre-existing, prospectively ascertained data from the Framingham Heart Study Generation 1 cohort to conduct a community-based study of the environmental, genetic, metabolic and inflammatory biomarkers as risk factors for traumatic brain injury and subsequent neurodegenerative outcomes.

Objectives

For this project, the goal is to determine the pre-existing prevalence of traumatic brain injury in the Generation 1 cohort of the Framingham Heart Study. This will involve a systematic and comprehensive search of participant medical records for evidence (or lack thereof) of head injury. All relevant episodes and symptoms will then be collected through Qualtrics, an online data capture tool, for the study's use. The depth of the information collected can then be used in conjunction with existing data to find possible links and risk factors.

Confidentiality

The Framingham Heart Study places great emphasis on the confidentiality of their participant's personal and medical information. As you will be accessing FHS records, you will be exposed to a significant amount of protected health information (PHI), including FHS ID numbers, names, addresses, telephone numbers, electronic mail addresses, social security numbers and personal medical records. This information is not to be shared with anyone outside of the study - verbally, electronically or otherwise. De-identified data may be shared with study-affiliated personnel through secure platforms, namely the Framingham N Drive. Do not share documents containing PHI through Dropbox or e-mail without encryption, as these methods are not HIPAA compliant.

Collecting Data

Priority Lists

We are collecting data from a very large population – 5,209 Generation 1 participants for this project, as well as several more thousands from the other cohorts in later projects. A previous research project at the Framingham Heart Study looked through the Generation 1 charts and noted the incidences of head injury along with the related ICD-9 Codes. This project did not collect the breadth of data that we will, but it does provide dates and brief descriptions of the incidents. This spreadsheet will be useful as quality control of the data entry, but direct use could bias chart reviewers to look specifically for incidents mentioned and nothing else. In order to both look at the validity of this past project and also have a reliable source for quality control, this spreadsheet will be used as part of a priority list for the order of charts to be reviewed.

Due to the large number of participants and random nature at which head injury/TBI could be found, there will first be an introductory period of increased exposure discovery. The reviewers will be blinded to this period. Using an algorithm, the list will be generated with a repeating pattern of 1-3 random IDs from the ICD-9 Head Trauma Study followed by 3-5 random IDs that are not part of that study. This means that the average ratio of non-TBI cases to TBI cases will be 2:1, with a certain degree of randomness (SD = 1.3) to make it less predictable.

This introductory period is for the purpose of closely monitoring exposure data retrieval ability of the interns, working through unforeseen issues with patients' charts, and for the overall preservation of data collection quality. Upon completion of the introductory period (1-2 weeks), the reviewers will be instructed to pull charts in a randomized fashion. Again, the interns will be blinded to both the introductory period and the randomized sequence afterwards, so that there will be no discernable pattern of record pulling.

Pulling Records

Each participant has been assigned a four-digit identification number, which is preceded by one or two digits that indicate the cohort they belong to. Generation 1 is coded with "0" (Ex. 0-0000). The new electronic system will allow reviewers to simply search a particular participant, which they will do in the order of the priority list. This list will be in the format of a shared Excel sheet or Google Sheet. One column will list the FHS ID number, while another will be filled out by the Tech ID of the person starting that case. The final column will require the Tech ID of the person who finishes that case. Having a column for the start and the finish of a case will allow us to see which cases may still be in progress at a given time. A shared workbook will ensure that cases are not accidentally done more than once.

Team Set Up/Review Flow

In order to increase the efficiency and yield of chart review, reviewers will be grouped into teams of three. The review process will resemble an assembly line where one team member

will handle the earlier core exams, then pass the chart on to the next team member to handle the middle core exams, and finally the third team member will review the remaining exams for that particular chart. Relevant head injury/TBI information will be written on a stick note that should be passed to the next person, as well as entered into Qualtrics (see **Data Entry**), so that the third team member who handles the last core examinations can do a final review of all noted sections to ensure no duplicate entries. This style of review will increase efficiency and yield by allowing a constant flow of chart review across all three team members. For example, once team member #1 has completed a review of the first core exams and passed the chart to team member #2, #1 can begin the review of the early core exams of a new chart, and so on. In the case of no head injury, the final reviewer is responsible for recording this data.

Chart Mapping

The content and set-up of the 32 Original Cohort core examinations has changed numerous times over the course of the study. Only in recent examinations have questions pertaining to neurologic health become consistently present. In order to account for the slight variations over time, every single core exam has been scrutinized and a document was generated that maps out every section of every exam that could possibly house important head injury/TBI exposure information. This document is in sequential order (both for the exams and the sections within each exam) and will be given to all team members for reference purposes. The document should be treated as a check-list and it will help to standardize the process in which interns work through charts and search for relevant exposure data.

A. Major Sections of Interest

The (Interval) Medical History and Physical Examination sections are two of the areas in the core examinations that show up the most consistently over time. The Medical History section contains important sub sections, such as (but not limited to): Headache, Vertigo, Dizziness, History of CVA, Previous Hospitalizations or Operations, Syncope/Fainting-Spells, and Additional Notes where physicians can record extra findings. The Physical Examination section also contains important sub sections, such as (but not limited to): Signs of CVA, Non-Cardiovascular Findings, Neurologic Findings, Physician's Judgment of Overall Disability, Clinical Diagnostic Impression (which becomes its own section in later exams), and Additional Notes where physicians can record extra findings.

Two more areas of note are the Cognitive Function and Activities (which later becomes Falls and Fractures) sections. They do not appear until later on (exam 19 and on), but they are important because of the questions they ask. The Cognitive Function section has an assessment of the participant's mental status while the Activities section enquires about accidental falls over the previous year. These are the four major sections that have appeared with some level of consistency over the course of the study and will contain most of the exposure data in question.

*NOTE: There are numerous other sections or sub-sections that appear sparingly throughout the 32 core examinations which may house important information. Although not

described here, they are listed on the exam-mapping document that interns will continuously reference while working through the charts.

B. Additional Documents

At the beginning of the chart there should be a Summary of Findings document with an Additional Notes section. This will briefly outline major things of note over time for each original participant and should be used for reference as interns review charts. There may also be various referral forms to different arms of the Framingham Heart Study, such as the cognitive clinic. When a participant misses a check-up at Framingham, sometimes phone interviews or home visits are conducted to maintain compliance. There may be different documents in place of a core examination if this has occurred and interns should make sure to review these too for exposure data.

Medical Records

These kinds of records appear between exams, and can range from nursing home notes to hospital face sheets to doctor's office notes. They are placed in chronological order between exams and are stamped in order to identify which exam cycle they belong to. There are too many variations to form a consistent approach, so each record should be read thoroughly and completely.

For hospital records, the admitting complaint and the diagnosis upon discharge will usually be on the first few pages. Any history or physical exam that is recorded is often very useful and often follows the face sheet. For head injuries, these notes will indicate whether the participant had any neuroimaging done. All of the information from a particular hospitalization is usually stapled together in one packet, and is one of the primary sources of information regarding the details of an incident.

Doctor's office notes and nursing home notes will vary far more than hospital records, and are not usually associated with the trauma itself. There may be references to the incident, as well as follow up appointments that detail post-traumatic symptoms. The exception is small falls that may occur in a nursing home, which are not serious enough to require hospitalization. It is important to read everything, as details about an incident could be hidden in a single small sentence.

Data Entry

For every participant and every incidence of head injury, relevant TBI data must be collected. We will be using an online data capture tool called Qualtrics. It will allow us to collect data more easily, and is also accessible from any computer and can be used by multiple people at once. Upon being opened, the survey will ask for the following information and present 3 options.

General Information

A. **Subject ID Number:** The subject's five digit identification number, including cohort identification number in the correct format (0-XXXX). Validation will insure that this is entered in exactly the right format, as it is the only identification attached to this data.
B. **Reviewer ID Number:** The reviewer's 3-digit FHS tech identification number.
C. **Flag Option:** Allows the reviewer to flag the case if they think it should be reviewed further. Also provides an option to enter the reason for flagging.
D. **Flags for Further Studies:** In order to gather data of interest for other studies, there are options to check if delirium or ALS were mentioned in the chart. This will be collected for all participants, regardless of head injury status.
E. **Data Capture Option:** This is where the choice is made on what kind of data will be entered. This alters what questions are asked of the reviewer.
    i. **No Head Injury Occurred**
    ii. **Record Head Injury Data**
    iii. **Record Post-traumatic Data**

The three options and corresponding data are discussed below.

Option 1: No Head Injury Occurred

This option indicates that the participant had NO instance of head injury. This should be used in cases where there is no data to suggest a head injury occurred.

Option 2: Record Head Injury Data

If an incidence of head injury is found, then the person who found it should immediately open the Qualtrics survey and choose the option, "Record head injury." The survey will then ask a series of questions designed to capture as much data about the incident as possible. The information should come from all of the records found up to and including that specific exam cycle. For example, if a TBI was found in a hospital record that is marked as part of the Exam 9 cycle, then any records beyond that point cannot be used. If there was a follow up appointment after the incident that is still within that time frame, it can be used. Nothing with a "10" stamp or higher should be used in that review.

This reduces the bias that may occur in evaluating the incident if a reviewer sees the outcome and changes the evaluation accordingly. A reviewer could rate symptoms as more severe if they see that someone develops a problem later in life, or conversely rate them lower if the

incident has no effect. In order to minimize this even further, the following questions try to remove any level of judgment. Only facts should be recorded, and scoring should be done behind the scenes.

A. Exam Cycle: Indicate the exam cycle during which this incident occurred. Each document in a chart belongs to an exam cycle, which is clearly marked through a stamp. This helps place the incident in a specific time-frame and allows for easier review.

B. Source Available for Review: Select the sources that reported this TBI event and related symptomology. An incident that is reported on the Exam is likely to also have medical records associated with it, but this is not always the case.

i. Medical Records: If medical records are present from a hospital or emergency room visit immediately post-trauma or, if they did not initially seek medical attention, records from a follow up with a physician specifically regarding the TBI event. These sources will provide the most information.

ii. Framingham Heart Study Exam: During their exams, patients share past medical histories, including potential cases of TBI. This source typically provides very little information about the injury and is best when supplemented by hospitalization records.

iii. Death Review: When a patient is deceased, the Framingham Heart Study creates a summary of the patient's health throughout his or her lifetime. This source provides major events in the patient's medical history, similar to an exam review. Death certificates also fall under this category.

iv. Other: This category can include any other sources from which you obtained information, of note, Medical History Updates (MHU) fall under this category. If possible, include the description and date of the source in the "other" text box.

C. Additional Record Information: These questions will come up based on what the selection above is. The idea is to figure out whether the data for any of these sources was self-reported or medically verified.

i. Medical Record Info: These questions will ask the date, and which kind of record the data was found in. The options are Hospital Records, Nursing Home, Neurologist, Other Physician, and Other. If there are nursing home records, then it will ask if multiple falls were reported in this record.

ii. Death Review Info: This will ask whether the Death Review info is from a death certificate, a FHS Death Review, or an autopsy.

iii. Other Info: A text box will ask for more information about the "Other" category.

D. History of Head Injury

i. Date of Injury: This asks for the date of the injury to the highest level of accuracy known, with medical records taking precedence over self-reported information.

ii. Cause of Accident: The mechanism of injury is documented, with the following options being based on the NINDS definition of TBI as external force acting on the brain and includes the relevant options that they use.

- Acceleration/deceleratiobn

- Head struck by/against an object: Exposure to external forces from human, animal or inanimate object.
- Falls with trauma to the head: Unintentional falls resulting in injury.
- Force generated by blast/explosion: Any injury caused by proximity to an explosive force, relevant to military exposure.
- Foreign body penetrating the brain: A penetration that goes through the skull into the brain itself.
- Motor Vehicle Accidents (MVA): Traffic or transportation accidents, including motorcycles and all-terrain vehicles (ATVs).
- Unknown: Used if the source of accident is unknown based on records.
- Other: For all possible injuries not covered in these options.

iii. Setting of Injury: Document setting of traumatic event.
- Residential: If the event occurred at ANY kind of residence, including that of a friend or a nursing home.
- Recreational: Setting that is anywhere outside of home or work and does not fit in other categories.
- Occupational: Settings related to participant's employment
- Sports: Settings related to athletics of any kind.
- Military: Setting related to military service, including blast exposure.
- Unknown: if the setting of injury is unknown
- Other: For injuries where the above options do not suffice.

iv. Highest Level of Care: This section is asking for where the highest level of care was received. Inpatient care is higher than ED care, which is higher than non-hospital based care, which is higher than no evaluation sought.
- No evaluation sought: Participant did not go for evaluation.
- Hospital: This option will bring several more options, including ICU, ER and in patient care. This will allow us to track how severe the injury may have been.
- Non-hospital: Refers to any type of care that may have taken place outside of a hospital setting, for example outpatient care, ambulance care for a patient who was not taken to the hospital, etc.
- Evaluation sought but level of care is unclear: If it is clear that a participant sought care for their injuries, but it is unclear whether they were hospitalized, seen in the emergency department or by a primary care/specialist physician. Most often used when a head injury is documented in the FHS examination medical encounter table or when Head CT/MRI dates match with the date of a reported head injury, but level of care is not specified.

v. Time between injury and presentation to care: Most often, this information will only be available when medical records are present from the traumatic event. It is only required when a medical evaluation was sought by the participant.

vi. Duration of Hospitalization: Only necessary when the highest level of care selected is hospital ED care or inpatient hospital care.

vii. Brain Surgery: Used if participant underwent brain surgery as a direct result of their head injury.

E. If medical records from the time of injury are not present or no further clinical data is available regarding clinical presentation, select to auto-populate the remaining survey questions as "unknown."

Note: For all reported symptoms, the survey also asks for verification, which is either self-report, witnessed, clinical interview, medical chart or unknown. There is also a question that asks which of the data sources (Medical records, FHS exam, etc.) were used to get this information.

F. Post Traumatic Clinical Symptoms: For each symptom, fill out if present, not, etc. Look for exact words (loss of consciousness, amnesia, etc.). To score this section:

- No: Used when doctor's notes are present AND the symptom is not noted or the doctor documents that the symptom is not present.
- Yes: Used when doctor's notes are present AND a symptom is definitely present and most likely due to the head injury.
- Suspected: Used when a doctor's note is present AND they state that they suspect a symptom but do not have verifiable evidence (e.g. self-report LOC).
- Unknown: Doctor's note is not available, or only available doctor's note does not evaluate head injury directly and symptom cannot be ruled in or out.

i. Loss of Consciousness: Defined as lack of responsiveness to people and other environmental stimuli.

- This is split into pre and post injury loss of consciousness. For posttraumatic LOC, there is also a question looking at the duration.
- The duration options are under 30 minutes, between 30 minutes and 24 hours, greater than 24 hours, and unknown.
- These options come from the VA guidelines for assessing the severity of TBI. This will allow us to assign severity to cases using a standardized method if we choose. These options also appear in the OSU TBI questionnaire.

ii. Posttraumatic Amnesia: Short term loss of memory often occurring after TBI.

- The only type of amnesia we are interested in is posttraumatic. The duration options given are under 24 hours, between 1 and 7 days, greater than 7 days and unknown. Again, these options come from the VA guidelines.
- There are questions probing for the kind of amnesia using simple language with the actual name in parentheses afterwards. It asks for anterograde, retrograde, both or unknown.
- Indicate when the seizure occurred in relation to the head injury. If it occurred after the head injury, list the duration (if known).

iii. Alteration in Mental State: This is a wide range of criteria that can be quite common following injury.

- The format of the question is a matrix with the possible symptoms listed on the left and 5 options regarding its duration: not present, under 24 hours, between 1 and 7 days, greater than 7 days, and present but duration unknown. This is also pulled from the VA severity criteria.
- The list of symptoms are adapted from an online list. There is no standardized list of what constitutes "altered mental state", but these options cover most of the bases.

iv. Focal Neurologic Deficits: Injury to specific components of CNS (brain and spinal cord) lead to localizing findings on neurologic exam (e.g. weakness in arms or loss of sensation in the distribution of a dermatome).

- For definitions of the deficits, look in the scoring section. The ones included are a general list and are not pulled from a standardized checklist. This has the same style of checklist as AMS and also is based on the durations the VA uses.

v. Strokes: These events introduce a lot of complications when they are reported near TBI. All cases with confirmed stroke will be pulled out of the main pool and reviewed separately, but this section will capture information on suspected stroke that may not have been found in Stroke Review.
   - The history of stroke as well as the suspected timing of it is important in understanding its relation to the injury. This section also asks about the provided evidence. This will give us more information to sort cases by when they are reviewed by people with clinical experience.

vi. Seizures: Caused by abnormal, excessive or synchronous neuronal activity in the brain, leading to sudden change in behavior, and can be the cause or symptom of TBI.
   - Similar to stroke, this section also asks for history of seizures as well as whether or not the participant was taking anticonvulsants. The timeframe of seizures is also asked for.
   - Though there are many kinds of seizures, this question does not ask for a type. Finding this information may confuse reviewers with limited clinical experience.

G. Glasgow Coma Score (GCS): Used by clinicians to rapidly assess level of consciousness of patient, and is used in ED to rapidly triage, monitor, and record patients who have any neurologic deficits. This system is based on three categories: eye opening, verbal response, and motor response. Each category can get a minimum of 1 and a maximum score of 4, 5, or 6 for eye, verbal and motor respectively. Therefore, the GCS can be scored anywhere from 3 to 15.

i. GCS was not published until 1974, so for many of the injuries in these patients' files a GCS will not be available, unless the injury occurred more recently.

H. Cerebral Imaging and Radiological Evidence: Patients with severe injuries require imaging for diagnosis and management. The image itself is often unavailable, but the diagnostic imaging report is. We are solely interested in imaging done on the head.
   - There are several types of useful imaging that are asked for. Head CT is very good at finding bleeds and bone injuries. Brain MRI is better at finding old strokes and differentiating soft tissue types. Head X-Ray is useful to look at bones.
   - These different imaging techniques all result in different kinds of radiological evidence for TBI, which can be instrumental in determining whether a TBI occurred. This list has several different kinds of findings which could be pertinent to this diagnosis. Because imaging reports are well marked and use medical terminology, it is more appropriate to use the full terms for this rather than simpler language.

I. Confounding Variables: Variables that interfere with our diagnosis of traumatic brain injury and the symptoms and outcomes associated with the injury.
   - Drugs and alcohol can be a major factor, so this is represented with its own choice. Physical and emotional injuries may also be a potential confound, so a few of the options relate to this as well.

- Previously diagnosed mental illness is one of the biggest confounding factors, so there are several questions that try and ask for various different kinds of mental illnesses. This ranges from neurodegenerative to anxiety disorders.

Option 3: Record Posttraumatic Data

Posttraumatic Symptoms of TBI: In addition to filling out some of the basic information required for recording a TBI (**Sections A – C** above), those choosing Option 3 will be taken to these questions. These are criteria that help support possible cases of TBI. They are split into 4 distinct categories, which are described below:

A. **Physical:** These symptoms are those that involve a change in physical functioning, ranging from headaches to photosensitivity. Different kinds of vision and balance issues are also included in this category.
B. **Sleep:** These are symptoms that relate to sleep disturbances, which can be an indicator of TBI or other neurological issues.
C. **Cognitive:** These are symptoms that relate to a noticeable decrease in cognitive skills such as attention, memory and language.
D. **Emotional:** These relate to a change in emotional states which can accompany TBI, which includes aggression, irritation and depressed mood.

The purpose of this section is to allow us to understand the timeline of symptoms for a given participant. It is designed to be filled out after a head injury has already been reported, and a reviewer finds some long term deficit that could be used to support a case for TBI. By asking for the Subject ID again, we can tie the information for a particular participant together into a cohesive set.

Standardizing Questions and Answers

The time frame that we use for symptoms comes from the "VA/DoD Clinical Practice Guideline for the Management of Concussion-mild Traumatic Brain Injury." It allows us to have a standardized and simplified reference point, which we can then later use to assign severity if we so choose.

Table 1. Classification of TBI Severity [3]

(If a patient meets criteria in more than one category of severity, the higher severity level is assigned)			
Criteria	**Mild**	**Moderate**	**Severe**
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness (LOC)	0-30 min	>30 min and <24 hours	>24 hours
Alteration of consciousness/ mental state (AOC)*	up to 24 hours	>24 hours; severity based on other criteria	
Posttraumatic amnesia (PTA)	0-1 day	>1 and <7 days	>7 days
Glasgow Coma Scale (GCS) (best available score in first 24 hours)**	13-15	9-12	<9

*Alteration of mental status must be immediately related to the trauma to the head. Typical symptoms would be looking and feeling dazed and uncertain of what is happening, confusion, and difficulty thinking clearly or responding appropriately to mental status questions, and being unable to describe events immediately before or after the trauma event.

The sources for the options in the other questions are drawn from the National Institute of Neurological Disorders and Stroke (NINDS). The NINDS website has a list of Common Data Elements (CDEs) that pertain to TBI, located at this address:

https://www.commondataelements.ninds.nih.gov/TBI.aspx#tab=Data_Standards

The "Injury Presentation – Early/Late" CDE is where the Injury Date and reliability are drawn from. The Neurological Assessment CDEs provided the bulk of the options for many of the questions. The LOC, PTA and AOC form gave the following options regarding the presence of symptoms: Yes, No, Suspected, Unknown. They also provided the following verification options presented in the survey: self-report, witness, clinical interview, and medical chart. The TBI Signs and Symptoms form provided the different categories of Posttraumatic Symptoms, as well as several of those options.

The symptoms and signs listed for the various ACRM criteria were not drawn from a standardized source, because one does not exist for this sort of information. The list was developed with the help of people with clinical expertise, and aims to cover all of the various nuances of terms such as "Altered Mental Status" or "Focal Neurological Deficits." A similar method was employed for the options given under radiological findings, as those results were the ones determined to be most clinically useful.

Scoring Procedures and Logic

Once all symptoms and data have been collected via Qualtrics, we will categorize the severity of the cases using the American Congress of Rehabilitation Medicine (ACRM) criteria. This process will take place automatically based on the data that is entered, in order to minimize any potential bias or errors of judgment.

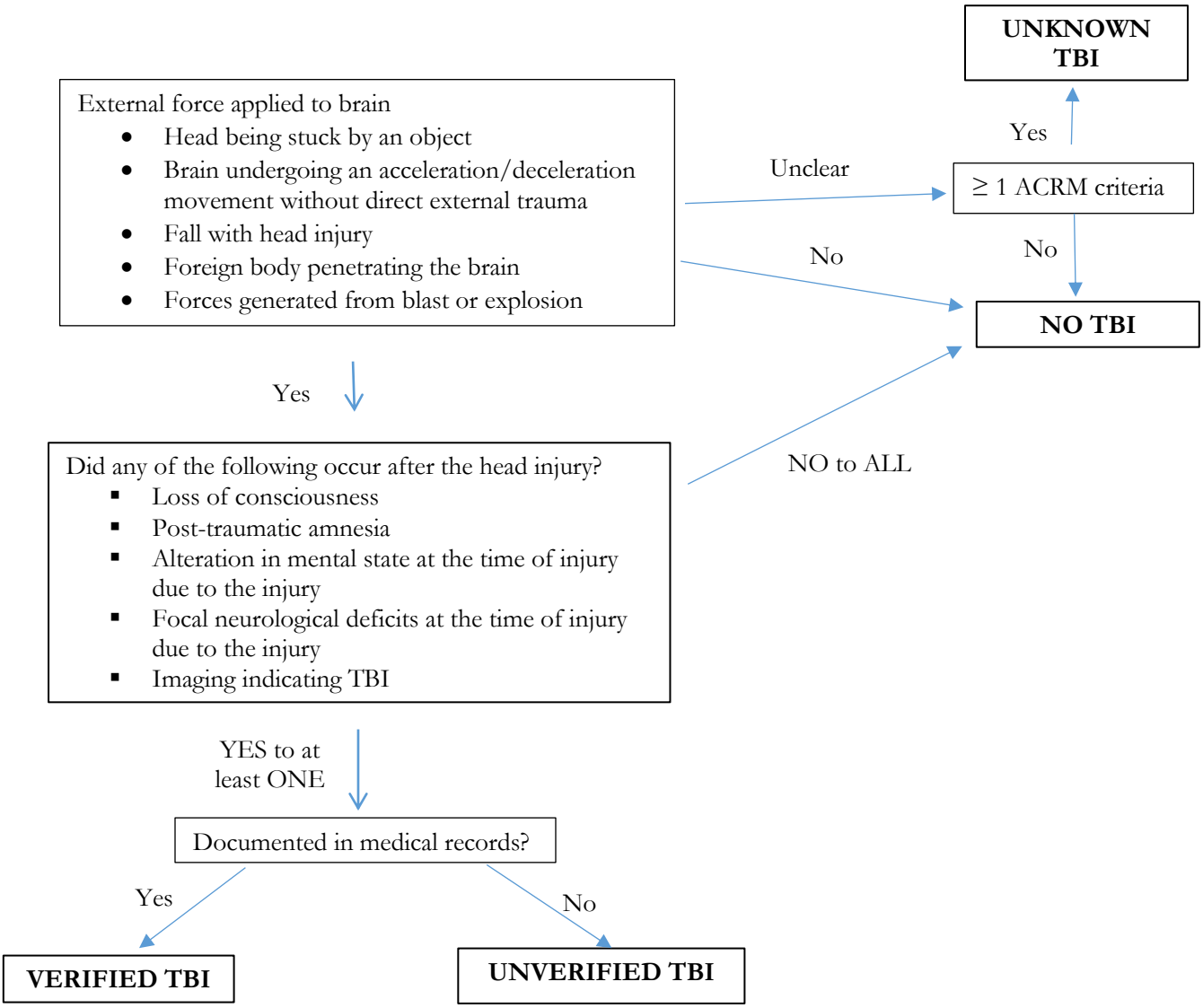
Definition of TBI

Based on the proposal of the Demographics and Clinical Assessment Working Group of the International and Interagency Initiative toward Common Data Elements for Research on Traumatic Brain Injury and Psychological Health, *TBI is defined as an alteration in brain function, or other evidence of brain pathology, caused by an external force*. Since records of brain pathology is limited in FHS charts, we will be approaching this definition in a two-folded approach to help identify the presence of TBI.

A) History of external force applied on the brain when a clear description from medical records the head strike with source and/or setting of how the head strike occurred or presence of acceleration/deceleration forces. Medical records should be from the hospitalization or ED visit directly following the traumatic event.

NOTE: Medical records from the traumatic event must be present to validate an assignment of "Verified TBI". For example, if a participant reports a head injury with loss of consciousness on a FHS exam, but no medical records from the injury are in their file, the head injury must be categorized as an "Unverified TBI." Episodes of LOC with no reported injury or unclear head injuries should be diagnosed as "Unknown TBI," unless medical records from the event are present to validate "No TBI."

B) Alteration of brain function using ACRM criteria. ACRM defines a patient with traumatic brain injury as a person who has had a traumatically induced physiological disruption of brain function, as manifested by at least one of the following:
(1) Any period of loss of consciousness
(2) Any loss of memory for events immediately before or after the accident
(3) Any alteration in mental state at the time of the accident (i.e. confusion, disorientation or slowed thinking, etc.)
(4) Focal neurological deficits that may or may not be transient. (i.e. weakness, loss of balance, change in vision, dyspraxia paresis/plegia [paralysis], sensory loss, aphasia, etc)



Confounding Factors in Determining TBI

LOC or posttraumatic amnesia caused by drugs
Recreational drugs (cocaine, alcohol, marijuana, inhalants, and opiates), severe carbon monoxide poisoning causing QT prolongation, medications

LOC or posttraumatic amnesia caused by pre-existing medical conditions
Congenital heart disease, structural heart disease, migraine syndromes, seizures, narcolepsy

LOC leading to TBI or post-TBI LOC
Defer to patient's story or physician's impression. Rule out common causes of falls (i.e. mentioning of syncope, seizure, history of passing out, low blood sugar, abnormal cardiac findings), then assume it is post TBI LOC.

Baseline dementia and intellectual disability complicating assessment of memory and LOC
Severe dementia and mental retardation makes memory and LOC difficult to assess. Stroke and seizure can also cause LOC. The key to deciding if a neurologic abnormality is TBI related is *whether any of the abnormalities are thought to be new, acute, or worsened following trauma*.
Neurodegenerative diseases before and after injury

Posttraumatic amnesia vs dissociative amnesia
Acute stress disorder or PTSD may be responsible for partial amnesia surrounding the events of injury. Preserved memory for the events of the accidents (i.e. no posttraumatic amnesia), associated with amnesia for events that begins sometime after the injury, may be accounted for in part of fully by stress or by medication administered after the injury.

Neurological signs caused by alterative cause
For example, in a motor vehicle accident with acceleration/deceleration, focal motor deficit caused by nerve injury may provide alternative causes of focal neurological deficit. However, the presence of these confounders should not preclude the diagnosis of TBI and therefore should be included in "Definite TBI".

Important Principles of Scoring

This section provides additional Q/A. For additional questions that are not present here, refer to a neurology expert.

Loss of Consciousness (LOC)

Did an injury lead to both LOC + TBI or was there post TBI LOC?
Always defer to patient's story or physician's impression. If you have ruled out the common causes of falls (i.e. mentioning of syncope, seizure, history of passing out, low blood sugar, abnormal cardiac findings), then assume that it is post TBI LOC.

Amnesia

Are memory lapses considered amnesia?
The term memory lapses may not be specific enough to describe a period of actually not being able to recall events. Forgetting keys or where they parked is not amnesia.

Is amnesia the same as dementia?
No. Amnesia in ACRM refers to memory loss immediately after TBI. Dementia is a diagnosis made based on cognitive testing. It is true that dementia can result from TBI, further down the line.

Can amnesia be coded for infants?
Infants show behavior change such as lethargy or decreased arousal and can be considered altered mental state. Amnesia cannot be assessed.

Altered Mental State (AMS)

How is AMS different from amnesia?
Mental status in AMS refers to a person's alertness and orientation to self, time and place. A person can have amnesia without AMS and vice versa. For instance, a person's memory can be intact (no amnesia) but thinks that it's 1963 (not oriented to time).

Focal neurological deficit

What counts as focal neurological deficit?
Focal neurological deficit refers to a neuro exam finding that can be explained by damage to the brain or spinal cord. A neuro exam includes cranial nerve exam (vision, visual fields, smell, face sensation and facial muscle movements, balance, hearing, etc.), strength, reflex, and sensation.

Does facial droop always mean stroke?
No, Bell palsy can also cause facial droop. Look for speech slurring and limb weakness associated with stroke.

Stroke

What causes stroke?
There are two main types of stroke.

1) Ischemic stroke: brain blood vessels occluded, resulting in brain tissue dying
- Can be treated with anticoagulation (i.e. tPA)
2) Hemorrhagic stroke: bleeding in the brain.

Intracranial hemorrhage: epidural, subdural, subarachnoid
There are three protective layers to the brain (from outside to inside): dura, arachnoid, and pia.

1) Epidural hematoma: under the skull and above the dura, shearing of middle meningeal arteries
    - Usually has associated skull fracture, most commonly temporal bone
    - Described as "lens shaped" collection of blood on CT
2) Subdural hematoma: under the dura and above arachnoid, rupture of bridging veins
    - Common in older adults, alcoholics, and blunt trauma (i.e. whiplash injuries)
    - "crescent shaped" on CT
3) Subarachnoid hemorrhage: under arachnoid
    - Can be caused by aneurysm rupture or arteriovascular malformation
    - Blood in the sulci, ventricles on CT

Is it possible for head injury to cause a stroke?
Yes, head injury can cause brain to bleed, causing hemorrhagic stroke.

Dementia

What are the different types of dementia?
Dementia refers to decrease in cognitive ability, memory, or function with intact consciousness. There are Alzheimer's disease, frontotemporal dementia (also known as Pick disease), Lewy body dementia, Creutzfeldt-Jacob disease, vascular dementia, etc.

Radiological findings

Types of imaging:

- Head CT: Rapid, very good at finding bleeds and bone injuries.
- Brain MRI: Slower, better at finding old strokes, better at differentiating soft tissue types.
- Head X-Ray: Useful to look at bones.

What are the common radiological findings suggesting TBI?
Hematoma/contusion (bruise on the brain), hemorrhage, skull fracture. Please record only imaging that involves the brain/skull.

Differentiating acute vs chronic bleed on CT
Acute means the finding is recent, likely less than a week. Chronic means that it has been there for a while, likely more than a month. Acute bleed will be bright on CT, described as "hyperdensity". Findings of acute bleed after head injury should be scored as Head injury with medical records.

How to explain atrophy?
Global atrophy refers to aging/Alzheimer's. Frontotemporal atrophy refers to Frontotemporal dementia (Pick's disease). Cerebellum atrophy in alcoholics, resulting in motor incoordination and ataxia.

Important Definitions and Acronyms for Scoring

AD: Alzheimer's disease

A&O: Alert and Orientation. A&Ox3 means that the patient is alert, and oriented to self, time and place.

Anti-Seizure Medications: Usually only used if a seizure occurs, may be given during the first week to avoid any additional brain damage that might be caused by a seizure

Aphasia: Impairment of language production or understanding (having trouble speaking, writing, reading etc.) because of damage to frontal or parietal cortex, specifically Broca or Wernicke.

Ataxia: Impairment of voluntary muscle coordination

Atonic: A short type of seizure where muscles go limp

AVM: Arteriovenous malformation, congenital defect that can lead to brain aneurysm and strokes

C: With

CC: Chief complain

Cerebral Contusion: Bruise of brain tissue

CN: Cranial nerve, usually followed by a roman numeral indicating the nerve

Complex Parietal: Type of partial seizure where a larger part of the hemisphere is affected and person may be unconscious.

C/o: Complaint of

CVA**:** Cerebrovascular accident, means stroke

Diuretics: Reduce the amount of fluid in tissues, can help reduce pressure inside the brain

Delirium: transient state of confusion or disorientation with a cause (infection, medication, electrolyte imbalance), common in older adults but NOT the same as dementia

DVT: Deep vein thrombosis, blood clot in leg that can travel to heart (causes heart attack), brain (causes stroke), or lungs (causes pulmonary embolism)

Ecchymosis: Bruising

ED care: Simply stands for emergency department care.

Epidural Hematoma: A type of TBI where blood accumulates between the dura matter and the skull.

General tonic-clonic: Type of seizure where the entire brain is affected and typically the entire body convulses.

H/A: Headache

Hemianopia: Decreased vision or blindness in half of the visual field of one or both eyes

Hemi-Spatial Neglect: A deficit in attention to and awareness of one side of space

Intraparenchymal Hemorrhage: Bleeding into the tissues of the brain

Intraventricular Hemorrhage: Bleeding into ventricles of brain.

MI: myocardial infarct, which means heart attack

MVA: Motor Vehicle Accident

Myoclonic: A short type of seizure where muscles tense up

Neuralgia: pain due to nerve injury

NPH: Normal pressure hydrocephalous

P: After

PD: Parkinson's disease

P.E.E.R.L: Pupils are equal and equally reactive to light (pupils are normal)

PMH: Past medical history

PTA: Posttraumatic amnesia

S: Without

SAH: subarachnoid hemorrhage

S/P: Status Post

Simple Parietal: Type of partial seizure where part of one lobe is affected and person is conscious

S/P: Status post

Subarachnoid Hemorrhage: Bleeding into the subarachnoid space, which is the area between the arachnoid membrane and pia matter.

Subdural Hematoma: Usually associated with TBI that causes blood to accumulate between the dura matter and the arachnoid matter (which lines the brain)

Syncopal Episode/Syncope: Fainting

TIA: transient ischemic attack, reversible and usually resolves in 15 minutes

Panel Review

Selecting Cases for Further Review

In the course of the data collection process, interns will come across cases where it is difficult to ascertain the causes or reliability of TBI. In most cases, this will be those in which a stroke is reported but it is unclear whether the stroke preceded a TBI or vice versa. In other cases, there may be several conflicting medical records. We will have a few ways to determine whether a case should be reviewed.

By default, all participants who have been confirmed to have a stroke through prior consensus review will be taken out of the main pool and set aside. Those who are marked as having a confirmed or suspected stroke or seizure during data capture will also be flagged for review. In addition to preemptively removing stroke cases, there will be an option to flag a case at the very beginning of the survey. This will also allow the reviewer to write a few sentences on the reason why they are flagging said case, which should indicate that there is something confounding or complicated for this particular incident.

Different Levels of Review

There will be 3 levels of review, which will allow the team to deal with difficult cases in the most efficient manner. First, the case will be looked at by someone who is on the level of a full time Research Assistant. The easiest cases to resolve will be those that happen due to a misreading of the chart or a lack of familiarity with the material. Research Assistants who have worked for several months will be able to see if the reviewer simply missed something that would have clarified the issue. If this is not the case and the RA cannot answer the question, then it goes up to another level of review.

The second level will consist of medical students with more clinical experience. They will have the expertise to understand more complicated cases. These will most likely involve figuring out a clinical diagnosis based on conflicting signs and symptoms, and how to categorize vague symptoms. This tier will be where most of the stroke cases will be resolved, as a medical student will likely be able to parse the language and indicate whether the stroke preceded or was caused by the TBI based on the available data. If it is still difficult to deal with a case due to a great number of confounding factors or an unusual presentation over the course of their lifetime, then it will go to the 3rd tier.

The final level of review will be done with a panel of experts. For a case to reach here, a corresponding case summary must be written (detailed below). After the number of cases requiring panel review has reached a certain threshold, a meeting will be scheduled. Everyone will be provided the case summary and will be walked through the incident. The outcome will decide how we categorize the case and how we discuss the symptoms. This will involve editing the existing data and also maintaining a form that can take more detailed data for these complicated cases.

Writing Case Summaries

In order to ensure that time is not wasted during the meetings, the initial reviewers of the case will be asked to write a summary for that particular participant. Because these cases would probably require more data to reach a conclusion, the reviewer will look through the entire charts to detail the pertinent findings.

The top section of each summary will list every FHS exam as well as the date. For each one, the reviewer will write any significant findings. This could include any minor or major accident/life event, the presence of risk factors, or the presence of symptoms. Underneath this, the reviewer will summarize all relevant medical records, organized in chronological order. Each medical encounter should be written with the exam cycle and the date of the encounter. Reviewers should quote the record as much as possible when discussing presentation after injury and what steps the participant took towards treatment. Again, this should cover all relevant details for TBI.

The overall goal is to provide an easily readable way to see all relevant TBI information over the course of that participant's lifetime. This includes the time course for symptoms, as well as the severity of those symptoms.

This section needs more information based on what is most important for the reviewers to know.

Overview

The training period for the interns will be conducted over the course of their first week on site at Framingham. It will consist of three days of content-based learning with built in assessments, followed by a two-day trial of chart review. The first half of content-based learning will cover Framingham introduction/foundational medical knowledge, information bias/standardized chart review, and proper data entry. The second half of chart review trial will serve as a run-in period to assess the overall quality of data retrieval.

By the end of the introductory week, the interns should have a baseline understanding of the Framingham Heart Study with pertinent medical knowledge, know how to use the standardized chart mapping document, and know how to properly enter data into Qualtrics.

Assessment

To ensure our interns can perform at the level we expect, we will assess them using either multiple choice or short answer test at the end of each day for the first three days of training. Interns who consistently demonstrate inability to acquire understanding of the content presented will be asked to review materials and retake tests or be asked to leave the training at the comfort of the instructors.

Day 1: Framingham Introduction and Medical Knowledge Foundation

Objectives:

1) Introduction to Framingham Heart Study and TBI study
2) Understand basics of brain anatomy, neurological signs, and neuro exam
3) Identifying head injury from presentations, clinical exam, and imaging
4) Be familiar with definition of TBI and ACRM criteria

Course of Action:
We will begin with an introduction of FHS and TBI study, focusing on their roles for the next eight weeks and our expectations, along with the training schedule. Brief break with tour of Framingham site and exchange contact information. Then we will have a series of PowerPoint lectures as follows:

a. Neuro foundation
- Big picture brain anatomy and introducing anatomical terminologies
- Common manifestations of neurological deficits, including signs and symptoms

b. Head injury
- Clinical approach in evaluating head injuries, including cause, timing, progression, alleviating/aggravating factors
- demonstrate full neuro exam and explaining how findings are documented
- reviewing a standardized chart to cover common medical abbreviations

c. Neuroimaging
- explain rationale of using different imaging modalities
- acute vs chronic findings on imaging
- basics of reading any radiology report, focusing on how to efficiently find what we need

d. TBI
- What constitute TBI using NINDS definitions
- acute vs chronic presentation of TBI
- long-term sequelae of TBI

Assessment:
A multiple choice exam focusing on first day's knowledge will be given at the end of the day.

Day 2: Information Bias and Standardized Chart Review

Objectives:
1) Introduce the general concept of information bias and how it can affect study results.
2) Introduce the chart mapping document and show interns how to use it.
3) Split interns up into five groups of three (total of fifteen interns) and teach them the mechanics of team-based chart review.
4) Emphasize the importance of standardization to ensure all teams review patient charts the same exact way.

Course of Action:
On the morning of the second day, a power-point presentation will be used for the purpose of teaching the interns general information on bias and how it affects study results. Then after a short break, the interns will reconvene and resources will be distributed to them (including the chart mapping document) which they will use for the duration of their work at Framingham. They will be walked through the documents and taught how to use them to ensure a standardized data retrieval process. Then after another short break, the interns will be split into their groups of three (using a random design). Once split up, they will be taught how the dynamics of group chart review will work (See Protocol).

Assessment:
A multiple choice and short answer test will be distributed at the end of the day covering general information from the three teaching sessions during the day.

Day 3: Data Entry

Objectives:
1) Introduce Qualtrics as the tool for data capture.
2) Walk interns through the Qualtrics form to understand questions and mechanics of data entry.

Course of Action:
On the morning of the third day, interns will be introduced to Qualtrics and the importance of proper data entry with a PowerPoint lecture, which will cover the basics of accessing and

using the program. After a short break, the interns will then be walked through the entire Qualtrics form with a brief explanation of all available options. This will ensure that certain data be entered in the proper fields on the data capture tool. After seeing and using the tools, each intern will be given a copy of a simple medical record and asked to enter in all of the relevant data. These entries can be compared to one another to ensure that there is no deviation.

Assessment:
A short test will be distributed covering general knowledge on Qualtrics and the proper mechanics of data entry.

Day 4 and Day 5: Trial Chart Review

Objectives:
1) Have interns begin the process of group chart review.
2) Assess the quality of data retrieval during run-in period to ensure quality of data retrieval.

Course of Action:
Interns will meet with their groups (assigned during day 2) and begin a group review of a patient's chart. Once all the groups have finished, the chart will be reviewed all together to make sure all interns are on the same page. This will also allow a chance for any unseen issues to be addressed. After a short break, the groups will then conduct another chart review. Upon completion by all groups, this new chart will then also be reviewed all together for the purpose of understanding and trouble-shooting. At the end of Day 5, interns should possess the skills necessary to carry out group chart review for the remainder of their internship.

Assessment:
Two known charts will be reviewed for the purpose of ensuring proper standardized data retrieval by intern groups.