Creating a Character Animation-based Interactive Frailty Model to Support Better Primary Care Implementation and Planning for Older Adults

by
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Abstract

As global populations age, it is imperative for clinicians and researchers to understand and apply measures of frailty syndrome to support healthy aging. Frailty syndrome is defined as a clinically recognizable state of increased vulnerability resulting from aging-associated declines in reserve and function across multiple physiologic systems, compromising the ability to cope with everyday or acute stressors. Frailty predicts surgery outcomes, waitlist times, cancer therapy tolerance, disability, institutionalization, morbidity, and mortality. Insufficient understanding of the complex nature of frailty from molecular changes, to physiology to clinical changes, is a major challenge for clinicians and researchers that focus on uni-dimensional (one factor at a time) molecular pathways to late-life decline connections. In a collaboration between clinicians, frailty researchers, and medical illustrators, a multidimensional, character animation-based resource was built, which articulates the aging and frailty-related changes from the cellular level to the clinical level, and provides visualizations that facilitate an understanding of a multidimensional, holistic frailty theory. With guidance from the Frailty and Multisystem Dysregulation Working Group at the Center on Aging and Health, a two-part animated, web-based, interactive 2D and 3D module was created to convey both “2D” clinical theory and “3D” real patient experience, created in ZBrush and Cinema 4D. The interactive portion of the module was created through Blender and Verge3D.
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The combination of increased lifespan and reduced fertility is leading to rapid aging of populations around the world. However, the increase in longevity does not mean an extended period of healthy life in old age (Xue et al, 2018). As worldwide populations age, it is important to understand and clinically implement the measurement of frailty syndrome, which greatly affect the older populations’ health and quality of life. Frailty syndrome is defined as a clinically recognizable state of increased vulnerability resulting from aging-associated declines in reserve and function across multiple physiologic systems, so that the ability to cope with everyday or acute stressors is compromised. In the United States, frailty syndrome affects 15% of the older non-nursing-home population aged 65 and older and between 3.5% and 27.3% of the older adult population worldwide (Xue et al, 2018). Frailty is known to be a strong predictor of disability, hospitalization, institutionalization, and mortality. It can also be used to predict surgery outcomes, transplant waitlist times, cancer therapy tolerance and recovery times for older patients (Xue et al, 2018).

i. The Physical Frailty Phenotype

Frailty can be measured using Linda Fried’s Physical Frailty Phenotype (PFP), which is a measurement of five distinct physical domains; walking speed, unintentional weight loss, exhaustion, activity levels, and grip strength (Fried et al, 2001). Frailty syndrome and its measurable phenotype is of utmost importance to understand in all clinical settings because frailty, and its association with adverse outcomes following clinical procedures, cannot be ascertained by simply looking at the patient. There is no single way a frail patient can appear, and observing a patient’s physical appearance (also known as “the eyeball test”) does not give any indication of their underlying cellular function and health. For example, frailty assessment by emergency care providers could facilitate referral to the more appropriate services and could assist with identifying patients who will not benefit from aggressive medical treatments (Theou, 2016). However, few clinics implement frailty measures and research into their care planning for older patients, and those that do are still in experimental phases (Vellas et al, 2012).
The thresholds for each PFP criteria are as follows:

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Frailty Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shrinking</td>
<td>Frailty cut point:</td>
</tr>
<tr>
<td></td>
<td><strong>Baseline:</strong> Self reported unintentional weight loss ≥10lb in previous year</td>
</tr>
<tr>
<td></td>
<td><strong>Follow-up:</strong> Unintentional weight loss ≥5% of previous year’s body weight</td>
</tr>
<tr>
<td></td>
<td>OR BMI &lt;18.5kg/m²</td>
</tr>
<tr>
<td>Physical endurance/energy</td>
<td><strong>Geriatric Depression Scale:</strong></td>
</tr>
<tr>
<td></td>
<td>1. Do you feel full of energy?</td>
</tr>
<tr>
<td></td>
<td>2. During the last 4 weeks how often you rested in bed during day?</td>
</tr>
<tr>
<td></td>
<td>Response options: Every day, every week, once, not at all.</td>
</tr>
<tr>
<td></td>
<td>Frailty cut point:</td>
</tr>
<tr>
<td></td>
<td>No to 1 and every day or every week to 2.</td>
</tr>
<tr>
<td>Low physical activity</td>
<td>Frequency of mildly energetic, moderately energetic and very energetic physical activity.</td>
</tr>
<tr>
<td></td>
<td>Response options: ≥3 times per week, 1-2 times per week, 1-3 times per month, hardly ever/never</td>
</tr>
<tr>
<td></td>
<td>Frailty cut point:</td>
</tr>
<tr>
<td></td>
<td>Hardly ever/never for very energetic physical activity AND for moderately energetic physical activity.</td>
</tr>
<tr>
<td>Weakness</td>
<td>Hand grip strength in Kg: GRIP-D hand held dynamometer, dominant hand, average of 3 measures.</td>
</tr>
<tr>
<td></td>
<td><strong>Frailty cut point:</strong> Grip strength: lowest 20% (by gender, body mass index)</td>
</tr>
<tr>
<td></td>
<td><strong>Men</strong></td>
</tr>
<tr>
<td></td>
<td>BMI ≤24 ≤29</td>
</tr>
<tr>
<td></td>
<td>BMI 24.1–26 ≤30</td>
</tr>
<tr>
<td></td>
<td>BMI 26.1–28 ≤30</td>
</tr>
<tr>
<td></td>
<td>BMI &gt;28 ≤32</td>
</tr>
<tr>
<td></td>
<td><strong>Women</strong></td>
</tr>
<tr>
<td></td>
<td>BMI ≤23 ≤17</td>
</tr>
<tr>
<td></td>
<td>BMI 23.1–26 ≤17.3</td>
</tr>
<tr>
<td></td>
<td>BMI 26.1–29 ≤18</td>
</tr>
<tr>
<td></td>
<td>BMI &gt;29 ≤21</td>
</tr>
<tr>
<td>Slow walking speed</td>
<td>Walking time in seconds (usual pace) over 15 feet</td>
</tr>
<tr>
<td></td>
<td><strong>Frailty cut point:</strong> Slowest 20%, stratified by gender and median standing height.</td>
</tr>
<tr>
<td></td>
<td><strong>Men</strong></td>
</tr>
<tr>
<td></td>
<td>Height ≤173 cm ≥7 seconds</td>
</tr>
<tr>
<td></td>
<td>Height &gt;173 cm ≥6 seconds</td>
</tr>
<tr>
<td></td>
<td><strong>Women</strong></td>
</tr>
<tr>
<td></td>
<td>Height ≤159 cm ≥7 seconds</td>
</tr>
<tr>
<td></td>
<td>Height &gt;159 cm ≥6 seconds</td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>Time to complete “timed up and go test” (TUG)</td>
</tr>
<tr>
<td></td>
<td><strong>Frailty cut point:</strong></td>
</tr>
<tr>
<td></td>
<td>TUG time ≥19 seconds</td>
</tr>
</tbody>
</table>

Table 1: Fried’s Frailty Criteria. Adapted from Fried et al, Cardiovascular Health Study Collaborative Research Study 2001, Frailty in older adults: Evidence for a phenotype.
Having crossed the threshold for 1 or 2 out of 5 measures categorizes someone as **prefrail**. A score of 3 or more active measures out of 5 characterizes someone as **frail**. Prefrailty is a state that can often be reversible with interventions such as nutritional counseling, exercise and physical therapy including forms such as yoga, tai chi, square dancing, walking, and multicomponent interventions (Walston, Buta, Xue, 2018). A comprehensive geriatric assessment (CGA) performed in response to a prefrail status can provide information about how an older adult will react to the side effects of new medications and predict other geriatric outcomes such as falls, urinary and fecal incontinence, dementia, and cognitive decline. (Xue, et al, 2018). However, an individual in a measured frail state may or may not be able to reverse the cellular aging they have accumulated through the aforementioned interventions. There is no consensus as to whether or not a frail person can be helped by interventions, although frailty remains useful for predicting many significant geriatric outcomes and reactions to stressors.

**ii. Definitions of Frailty**

The understanding of the definition of frailty and its constantly changing multidimensional nature is still evolving, but there is some consensus on frailty and aging theory. Most importantly, a delineation of frailty from comorbidity and disability, which are characteristics that are often treated as synonymous with frailty (Fried et al, 2004). It is understood that frailty causes disability, independent of clinical and subclinical diseases. Therefore, the syndrome of frailty may be a precursor to disability, due to its central features of weakness, decreased endurance, and slowed performance. Functions most likely to be affected by frailty are those dependent on energy level, muscle health, and speed of performance such as mobility. Fried et al reported that 27% of those who were disabled in activities of daily living (ADLs) tasks were frail, which suggests that frailty begins by affecting mobility tasks and energy production and storage before causing noticeable multisystem functional decline (Fried et al, 2001). For example, disability due to arthritis of the hands might very specifically affect ability to grasp or eat, without having any relationship to frailty. It is important to distinguish that frailty is not synonymous with either disability or comorbidity (Fried et al., 2001). Consequently, frailty is increasingly understood as a muscular and energy production and storage mechanism dysfunction that occurs in some vulnerable older adults.
Fried’s phenotype is widely agreed upon as a competent tool for diagnosing frailty at Johns Hopkins Medical Institutions and other research oriented medical institutions, although there are many additional frailty measurements that have been introduced to the research literature in the past two decades (Buta et al, 2016). The Center on Aging and Health (COAH) at Johns Hopkins engages frailty researchers such as Dr. Ravi Varadhan, Dr. Qin Li, Dr. Karen Bandeen-Roche, and Dr. Jeremy Walston. These researchers spearheaded the use of Fried’s Physical Frailty Phenotype (PFP) and thus the PFP was used to explain clinically recognizable frailty measures and related physiological changes.

There has also been much research on cellular and molecular aging and its links to frailty. Elevated low-grade chronic inflammation is associated with a rise in macrophage, plasma cell, and neutrophil count as well as cytokines such as IL-6, TNF-α, TNF-α receptor 1, and IL-1B, which lead to an exhaustion of cellular resources, specifically mitochondria, through oxidative stress, formation of vacuoles (Fig. 1), and blebbing (Garth, 2014). Cellular energy resource exhaustion leads to an increased vulnerability to psychosocial, physiological, and cellular stressors that can be determinants in low metabolic rate, muscle wasting. These outcomes can be linked to the development of the frail state through Fried’s cycle of frailty (Fried et al, 2001).

**Figure 1: Mitochondrial damage and dysfunction.** (A) Photomicrograph demonstrating the presence of an intracellular, vacuolated, double-membrane (black arrow) (B) Double-membrane structure surrounding an AP (white arrow). (C) AP with electron-dense granular inclusions located in proximity of clusters of mitochondria (black arrow heads). (D) Mitochondria with normal ultrastructure including intact mitochondrial membranes, cristae, and matrix. (E, F) Mitochondria with abnormal structure including disrupted membrane (white arrows), loss of cristae, and matrix dissolution (asterisks). Adapted from Ko, et. al., 2015, Impaired Mitochondrial Degradation by Autophagy in the Skeletal Muscle of the Aged Female Interleukin 10 Null Mouse.
iii. Fried’s Cycle of Frailty

Fried’s cycle of frailty (Fig. 2) is a conceptual framework to understand the physiological changes that a frail person may experience. Frailty was first defined by Fried and Walston as a state of increased vulnerability that arises from multisystem dysregulation, leading to decline in physiologic and cellular reserves, and therefore to diminished capacity to cope with every day or acute stressors (Fried et al., 2001; Fried et al., 1998). This multisystemic decline affects homeostatic mechanisms, cell repair mechanisms, and cellular defense mechanisms that are essential to health (Fried et al., 2009) and eventually leads into a self-perpetuating “cycle of frailty” that includes skeletal muscle decline (sarcopenia), lower levels of energy production, and lower nutritional intake and processing.

Figure 2: Fried’s Cycle of Frailty. Adapted from Fried and Walston, 2003, Frailty and failure to thrive.
This continuous cycle of frailty shows how immobility, disability, and dependence can occur with the involvement of the five frailty criteria of the PFP. The combination of 3 or more of these criteria can lead to a syndromic state of aggregated declines, including decreased energy expenditure (from low energy and exhaustion), weight loss, muscle wasting, and lower metabolic rate.

iv. Primary vs. Secondary Frailty

Primary frailty is defined as a clinically recognizable functional decline where the development of frailty is not associated with a specific disease, comorbidity or when there is no substantial disability (Chan, 2008). Primary frailty is useful for understanding and studying the basic model of frailty, however it is rare to encounter older persons that do not have any comorbidities but are also frail. It is important to note that the development of disability and comorbid conditions can preclude frailty because they require the person to exhaust available physiological resources with a potential consequence of exhausting homeostatic cellular functions and eventually, organ systems. Therefore, most frail older adults do have some form of chronic disease. For example, in patients with severe congestive heart failure or advanced renal failure, developing frailty is almost inevitable because of how these conditions eventually exhaust functional capacity. Often, disease can be a determinant of developing frailty however, conclusive evidence does not exist to identify disease as a causative factor of the frailty syndrome. It may only be possible to separate frailty from existing disease in a patient if frailty was assessed very early on in their care plan (Bergman et.al, 2007)

Secondary frailty occurs in concurrence with disease, multiple diseases, or disability. Of the many conditions that may render an older person unable to respond to stressors, the most conclusive evidence exists for depression, congestive heart failure, cancer, diabetes, chronic infections, and cognitive decline. These conditions in conjunction with a frail state increase an older person’s vulnerability to develop multiple conditions, which is why clinics often see frail patients who have multiple illnesses or disabilities (Bergman et.al, 2007).
Frailty is referred to as a multifactorial syndrome because of the many levels of risk factors that are involved in its development. It is difficult to draw concrete causal connections between risk factors and development of frailty, which is why the gerontology field often refers to frailty syndrome as a “complex term with multiple and slippery meanings...” (Bergman et.al, 2007). Many risk factors and correlations to frailty are bidirectional, meaning that there are no specific “causes” of frailty, rather they act as determinants and drivers (Fig. 3). For example, it is difficult to determine causality in the link between depression (which is a well-researched comorbid condition with frailty) and frailty. Depression may lead to frailty because depressed older adults tend to have exhaustion and low activity levels, and do not leave their home to exercise or engage their metabolism, causing muscle wasting and a decline in ability to cope with every day or acute stressors. On the other hand, frailty may lead to depression if cellular factors and genetics may cause an older adult to have elevated low-grade inflammation which leads to an exhaustion of cellular mechanisms and resources, decreased mobility, and functional decline, which may cause the older adult to develop depression.

Figure 3: Multidimensional Frailty Model: Adapted from Walston, 2017. A figure explains the multidimensional, bidirectional nature of links between triggers, physiology and clinical outcomes.
Moreover, risk factors or drivers of frailty exist on multiple levels of clinical significance. With the help of Dr. Peter Abadir and Brian Buta, three major “spheres” of risk for frailty were identified: **psychosocial**, **physiologic**, and **cellular and molecular** risk factors. This project mainly involves cellular and physiologic risk factors because they are closest to what primary frailty may look like, and are supported by published research.

The cellular and molecular changes associated with frailty include increased inflammatory cytokines such as IL-6, TNF-α, TNF-α receptor 1, and IL-1β which contribute to low grade chronic inflammation. Other cellular factors include increased cortisol, catecholamines, mitochondrial dysfunction, mitochondrial copy number deletions, oxidative stress, cellular senescence, epigenetic modifications, and cell injury resulting in necrosis. Low grade inflammation causes a weakened or unresponsive immune system, which can lead to oxidative stress and consequent mitochondrial damage, toxic blood byproducts, and impaired stress response. The renin-angiotensin (RAS) system and the hypothalamic-pituitary-adrenal axis (HPA-axis) are also significant cellular and molecular homeostatic mechanisms to the development of frailty. The RAS is a hormonal system that is vital to blood pressure regulation and salt balance but when dysfunctional in an aging individual, lower blood plasma concentrations of RAS components (Angiotensin Receptor I and II, renin, angiotensin converting enzyme), or an altered ratio of ATRI and ATRII are observed, potentially resulting in hypertension and inflammation (Abadir, 2013). The involvement of RAS in aging is irrevocable however there is much to be researched on how aging affects RAS.

The HPA-axis is also a significant aspect of frailty and aging. Dysregulation of the HPA-axis can cause an increase in cortisol secretion, which can in turn, increase low grade inflammation. The HPA-axis also regulates the circadian rhythm and research has shown that frailty in older adults is correlated with higher morning and nighttime cortisol levels (Varadhan et al, 2008). With respect to normal biological aging, the HPA-axis has increased adrenocorticotropic hormone (ACTH) and cortisol secretion, decreased glucocorticoids secretion, a decline in dehydroepiandrosterone (DHEA), which stimulates estrogen and testosterone formation, and flattening of diurnal pattern (daily activity and nightly inactivity) of cortisol release. The complexity of the HPA-axis needs to be further understood, however, research suggests that DHEA supplements may slow or reverse signs of biological aging, osteoporosis and depression (Gupta and Morley, 2014).

Apart from cellular triggers and changes, there are many studied psychosocial risk factors
to frailty such as social life, home environment, isolation, and pollution. Having a bleak social circle or few remaining relatives can be debilitating for an older adult, especially in a hospice or nursing home environment where the older adult no longer has a stable support system, and is more likely to develop depression and lead to frailty (Peek et al., 2012). Pollution can limit a person’s mobility and can lead to development of chronic lung disease and other conditions. “Lifespace” is a term that describes the home environment that an older person may live in (Xue, 2012). For instance, inadequate lifespace may consist of a cluttered home that does not have a seated shower, additional support handles, and a fall-safe bathtub for the older person to use and not feel limited by their home environment. With home modifications such as bathroom fittings, door handles that require less grip strength to open, staircase accessibility devices, ramps, widened doorways, and floor modifications to allow easier wheelchair mobility, an older person is more likely to feel a greater sense of autonomy in their activities of daily living (ADLs) (Kwan, 2019). In conclusion, frailty is associated with more restrictions in actual and perceived social participation, decline in life-space and mobility (Portegijs, 2016).

vi. Hallmarks of Cellular Aging

Normal biological and cellular aging includes such phenomena as cellular senescence, epigenetic changes such as DNA methylation, cell injury resulting in necrosis, and mitochondrial damage and dysfunction (Lopez-Ortin, 2013). The hallmarks of aging that often go awry with frailty syndrome are related to loss of homeostatic mechanisms for cell repair, mitochondrial function. Low grade inflammation and related interactions due to increased vulnerability is also a significant contributor to cellular and phenotypic aging however, there are also cell to cell interactions where senescent cells can induce senescence in neighboring cells through gap-junction-mediated cell-cell contacts. Mitochondrial damage is somewhat similar, as dysfunctional or damaged mitochondria can signal to each other, fuse, or undergo fission to control the amount of mitochondrial dysfunction (Lopez-Ortin, 2013).

vii. Interventions for Prefrail and Frail Individuals

Interventions to slow or reverse an individual’s clinical symptoms of frailty are most effective
in prefrail patients however serve frail patients as well. In order to discuss interventions, it is imperative to define what successful aging means. Healthy aging, which is a goal of medical and therapeutic interventions, includes a low risk of disease, disease-related disability, high cognitive and physical function, and active social, physical, and emotional engagement with life. Interventions to slow development of frailty include exercises that focus on resistance and aerobic training, weight lifting, and building back lean muscle mass in response to muscle wasting and weight loss. Physical interventions can also include square-dancing, tai-chi, which enhance balance and gait, yoga, and walking (Apostolo et al., 2018).

Other therapies include lingual exercises to improve and reinforce the swallowing mechanism, controlled and thorough oral hygiene, dietary supplements, socialization during mealtimes, and home environment modifications to improve the individual’s sense of autonomy and lessen their risk of falls (Benefield and Higbee, 2007).

viii. Existing Teaching Tools

A novel, visual, and dynamic solution to this knowledge gap in understanding and responding to frailty is highly necessary, as existing figures explaining frailty are linear, one dimensional, static, and disparate to one another, all which frailty syndrome is not (Fig. 3; Fig. 4). One such figure found in a medical textbook chapter on frailty tries to address the multidimensional, multifactorial nature of frailty syndrome however fails to show the levels of crosstalk between organ systems and other physiologic factors (Xue et al., 2018).

The proposed project is an interactive, dynamic, multidimensional clinical picture of frailty, connecting various spheres of risk factors while allowing the user to see the cellular and molecular changes occurring during frailty, as well as the connections between frailty measures and risk factors. For example, if a clinician using the interactive chooses depression as a driver of frailty, the frailty network configuration will rearrange to show: how the patient’s home life or environment is affected by depression, how their physiology changes; how their weight and activity levels change, how their body chemistry changes, and the odds ratios for how likely the patient is to show certain positive measurements of frailty in an examination, all due to depression. With the hope of spreading awareness of frailty syndrome, this interactive tool will inform clinicians by connecting many arenas of research.
and help to visualize a complex medical syndrome in a unique, dynamic form.

Figure 4: Biology Driving Frailty Syndrome in Older Adults. Adapted from Walston, 2017, 3 levels of information show how cellular/molecular changes alter physiology and cause clinically apparent symptoms/syndromes. This figure suggests the complexity and multidimensionality of frailty syndrome.
ix. Effectiveness of 3D animation as a Teaching Tool

The need for 3D animation as an effective teaching tool has been proven in many instances, and the implementation of 3D animation and graphics is growing. Increasingly, teachers and educators are turning to YouTube or TeacherTube for animated educational content. 2D and 3D animation have been proven to enhance learning experiences and simplify complex, abstract concepts in science and mathematics by providing real world situations and opportunities for the viewer to engage their critical thinking skills. Additionally, one the greatest benefits of animated learning experiences is the assurance that learning objectives will be met, because animated content can guide the viewer through the content in an informed, intentional way (Chan, 2013). It is important to note that animation is not a replacement for teaching or learning concepts by reading text; it is a stepping stone to true learning, to introduce and generate interest in the viewer and stimulate broader classroom or workplace conversations.

Animation can be a useful method of disseminating complex information with specific learning objectives, however, its limitations should be considered in the making of successful animations for healthcare professionals, as is the case in this project. Cognitive Load Theory suggests that cognition required to experience a 3D animation are split threefold: intrinsic cognitive load, extraneous cognitive load, and germane cognitive load. Intrinsic cognitive load is the natural load of information and interacting elements presented by the animation, extraneous cognitive load is the load created by the format, style, or method of the animation (e.g. character animation vs molecular animation), and germane cognitive load describes load of the learning memory resources required to learn the information in a long-term fashion (Ainsworth, 2008). Any animated content with a load too high in any one of these cognitive loads will overwhelm the viewer and cause a lapse in understanding. One method of avoiding this phenomenon is through effective instructional design such as limiting the amount of information seen at any given moment, and segmenting the animated content, allowing the viewer more control to view and learn at their own pace, or pause and play the animation as they wish (Jong, 2010).

Additionally, it is widely accepted that animation is a significant learning tool for children and adolescents, however its effectiveness in adults and especially those in high-pressure careers requiring doctoral degrees is still being explored. In a study done on the effectiveness of guided 3D simulation
and animation in adults, it was proven that adults can inductively learn from guided animations to a level of comprehension equal to a traditional lecture teaching method (Rieber and Parmley, 1995). Animated content designed for learning activities for older adults has also proven to be more effective than traditional teaching methods (Van Gerven et al, 2003). However, it is not certain if animated content on frailty presented in a light-hearted, narrative format will enhance or intrigue adults who are highly educated healthcare professionals.

x. Learning Theories

When designing an instructional module or educational experience, it is critical to identify learning theories that may be implemented to achieve the desired learning objectives for a specified audience. Of the many learning theories described in literature, this project focuses on constructivism and humanism. Constructivism describes the learner as active, in charge, and with regards to a learning environment or situation, brings their own prejudices, experiences, and thoughts to the situation. Every learner will have a different interpretation of the material according to their past experiences and cultural or social contexts. One of the tenets of constructivism is the establishment of a more knowledgeable other (MKO), that guides the learning of the learner. However, learning in a constructivist context primarily denounces “acquiring learning” for engaged learning involving the learner’s context (Learning Theories, 2015).

Humanism also applies to the endeavor of teaching frailty to a clinical audience, as the goal of the animations and interactive module is to spark conversation and contextualize frailty in the viewer’s daily clinical practice. Humanism believes that learning is a personal action to fulfill or further their growth. It suggests that people have a natural desire to learn and often, this requires looking inwards and altering the concept of self. This is applicable to a clinical audience learning about frailty because they should be prompted to question themselves internally as to why older people are underserved in healthcare, and why frailty is so often unconsidered in their treatment planning. As the animations and interactive module are built solely to introduce the values of knowing a patient’s frailty status, they do not explicitly suggest that the viewer implement frailty assessment into their clinical practice and offers no recommendations for the viewer. There is no established objective to take the “next step” of implementing frailty assessment and research into a clinician’s practice because of the humanistic
understanding that people, moreover, healthcare professionals have a desire to consistently perform well and learn more information to be able to better serve their patients (Learning Theories, 2015).

xi. Statement of Novelty

The novelty of this proposed solution is the utilization of a character animation-based, narrative format animation to educate clinicians outside of the geriatric realm about frailty syndrome. A light-hearted, animated approach can prove effective for a highly educated, busy audience such as healthcare professionals, as much of their current learning comes from journal articles, case studies, and clinical experiences. According to a study conducted in 1989, clinicians do not prefer separate tutoring or learning experiences outside of their clinical practice due to wanting to spend time with family or relax outside of the hospital, and increasingly turn to private reading or learning (Lewis and Bolden, 1989). While reading is a significant part of private learning, animation can simplify and distill learning rather than having to read multiple journal articles. Animation can also direct the viewer to further in-depth learning resources such as more specific journal articles, the point of the animation being to get the clinician interested in this geriatric phenomenon as a significant clinical issue.

Many medical syndromes are increasingly complicated by comorbidity, genetics, environment and social factors and frailty syndrome is an ideal multifactorial syndrome to visualize via animation and interactive modules. Medical and biocommunication experts often view syndromes and disease processes as signaling cascades and flow charts, all of which are highly effective but do not allow for an understanding of the complexity of the disease process. The methods used in this project will provide a model for creating a user-driven learning experience that aids the user in understanding complex syndromes as moving pictures so that multiple manifestations, pathways, and outcomes of the syndrome can be explored. This project aims to create a macro to micro picture of frailty syndrome that is also clinically relevant to healthcare providers with older patients.
xii. Audience

As frailty measures and associated research have not yet been universally integrated into primary care practices, care planning, or surgical considerations, the audience of this interactive tool will be primary care physicians, clinicians, specialty care professionals, surgeons, and researchers. Targeting this product to a clinician and researcher audience would aid to decrease this knowledge gap and subsequently the gap in care for elderly patients. It is imperative that the concept of frailty be introduced and understood in the clinical care setting so as to impact how older individuals are given care. Additionally, learning about frailty syndrome could be useful and informative for patients and family members of patients who may be frail or prefrail. Understanding their loved ones physical and cognitive changes will help caregivers such as hospice workers, family members, or nursing staff anticipate other physiological changes that the elderly patient will experience in the cycle of frailty.

xiii. Objectives

The goal of this project is to create a user-driven, interactive web resource that presents a clinical picture of frailty syndrome as a stressor-induced moving network while providing clinically relevant statistical information. This project’s objectives include:

1. Create a complete, integrated clinical picture of frailty syndrome which includes frailty research from the last decade to educate clinicians on the value of understanding frailty syndrome.

2. Educate clinicians and researchers on frailty syndrome and the frailty phenotype so that they are aware of the benefits of integrating frailty assessments into their clinical practice.

3. Describe the cellular and molecular, physiological, and clinical changes that occur in frail individual on a macro to micro scale. This resource should utilize user experience design principles and easy to follow hierarchy of information to direct the user through the content.

4. Justify and promote the need for frailty-informed, personalized care for older patients.
III. Materials and Methods

The workflow for this project was as follows:

1. Script development
2. Storyboard creation in Storyboarder, wireframe development in Adobe XD, animatic creation
3. 3D modeling of characters, cellular components and environments
4. Voice over production
5. Animation in C4D, Rendering
6. Post-processing in Adobe After Effects
7. Development of website subdomain
8. Importing models into Blender, Verge3D-based web hosting of interactive frailty model elements.

i. Script Development

Script development was primarily directed by what Dr. Abadir, a geriatrician at the Bayview campus of JHH, considered to be important for a clinician to understand about frailty syndrome to implement in their clinical practice. It was originally planned to create one 3-to-4 minute animation explaining the concepts behind frailty however, with feedback from the FWGMD, more information was needed to be added to properly convey what is currently known and unknown about frailty. Therefore, much of the script writing was dictated by what the FWGMD researchers deemed appropriate language around frailty in order not to suggest consensus on hypotheses that have not yet been proved.

In order to engage clinicians who are often already involved in reading journal articles and watching and learning clinical content related to their clinical practice, a jovial 3D character animation approach was used. Character animation in the style of Pixar or Disney films such as Up served as a model for creating the characters and the bulk of the story-telling. Because the topic of frailty connotes death and loss of loved ones, it is often a hard topic to discuss with clinicians and patients.
alike: This was another reason for choosing light-hearted 3D character animation to depict this subject matter. The storyline centers a character names Ernesto Gomez, who is 75 years old and has a history of hypertension and falls, especially in the last few months. Ernesto can be characterized as somewhat curmudgeonly but with a wholesome demeanor in order to avoid stereotyping a certain kind of older adult. Ernesto’s healthcare journey is depicted as follows:

1. Frailty syndrome is introduced along with its global significance.
2. The benefits of frailty are listed (medical phenomena frailty can predict).
3. Ernesto visits his primary care practitioner Dr. Lee and tells her about his falls.
4. Dr. Lee asks him more questions and finds out he has been feeling lower energy.
5. She refers him to a geriatric specialist to undergo frailty assessment.
6. Ernesto is diagnosed as prefrail.
7. Ernesto’s physiology and cellular changes are shown, with low grade chronic inflammation, a buildup of cytokines TNF-alpha, IL-6, and toxic byproducts in his blood.
8. Other hallmarks of aging significant to frailty are introduced: cell senescence, or the cease of cell proliferation, epigenetic changes such as DNA methylation, and cell injury, resulting in necrosis.
9. Ernesto is shown having options for rehabilitation and physical therapy to decrease his vulnerability to other life stressors, as he is prefrail and has opportunities for intervention.

A narrative of an older person’s patient experience was chosen for the animations because it is important for a clinician to know what to do if they suspect a patient is frail. They may not have to conduct a frailty assessment themselves if the primary care clinic does not have the appropriate equipment, but should be able to refer the patient to a geriatrician. Moreover, universal frailty assessment and scoring in all healthcare institutions is yet to come. Ernesto, the main character, was depicted as prefrail because it provided the opportunity to discuss interventions for early frailty assessment and detection of potential functional decline (Appendix A). After approval of the script by researchers in the FWGMD, the final voice-over was recorded by Dacia Balch of the department of Art as Applied to Medicine.
ii. Animation and Interactive Module Ideation

To break down Ernesto’s healthcare journey further, the animations were split into four smaller clips in order to allow the user to skip between animations, view related research articles, and read a linked, written transcript of the script. The first animation titled “What is Frailty?” introduces frailty and its significance as a global healthcare issue. Statistics of those affected in the United States are shown and the reasons why frailty status and frailty assessment are discussed to add significance to the gravity of frailty syndrome. After the first animation, the viewer is prompted to view the second animation, titled “What does Frailty Look Like?”

The second animation introduces the narrative of Ernesto Gomez, who is 75 years old, has a history of hypertension, and more recently, falls. The keyword in this introduction to Ernesto is geriatric falls, and thus the purpose of this animation is to present a scenario from both patient and doctor viewpoints to arrive at a treatment decision or conclusion for the falls. The doctor picks up on key phrases from Ernesto such as “exhaustion” and “less exercise” and knows that these clinical presentations are in line with a possibly frail or prefrail older adult. This allows a potential clinician viewing this animation to learn what symptoms or physiological factors to pay attention to in clinic as well as gives insight into how a patient in Ernesto’s condition may feel about the entire experience. The doctor, Dr. Lee, refers Ernesto to a geriatric clinic for frailty assessment and the narration lists the frailty measures and the meaning of different frailty scores.

The third animation, titled “Cellular and Molecular Changes in Frailty” zooms into Ernesto’s cellular and molecular makeup, and the changes he is undergoing with his development of prefrailty. These changes include low grade chronic inflammation with an increase in cytokines TNF-a and IL-6, mitochondrial dysfunction shown as oxidative stress and blebbing, cell injury resulting in necrosis, epigenetic changes such as DNA methylation, and increased cell senescence. Most importantly, these changes are stressed as changed occurring system-wide, not localized in specific body systems. These cellular changes are then tied into Fried’s cycle of frailty, which is a cycle of physiological changes
that occur in frailty. The physiological changes Ernesto is experiencing is then related back to his recent falls, because of his low energy and muscle wasting, thus, coming full circle in a macro to micro exploration of frailty.

Lastly, the fourth animation, “How Does Frailty Impact Geriatric Health?” shows that Ernesto has hope for possible therapeutic interventions such as yoga, tai-chi, comprehensive geriatric assessment (CGA), and nutritional counseling. Once the fourth animation finishes, the user is prompted by a button to explore the interactive frailty module. It has been prototyped (Appendix E) as a case-study based method of viewing multiple presentations of the frailty phenotype. The user will be able to choose from any of the four characters seen in the first animation and will be able to look through their social environment, current medications, and frailty assessment score. Testing is necessary to determine the effectiveness of this almost “learn as you please” resource however should allow the user to familiarize themselves with various frailty phenotypes as well as shed any preconceptions or stereotypes they may have about how a frail individual may look or present in clinic.

iii. Storyboards, Wireframes, Animatics

Storyboards were created in Storyboarder, a free storyboarding app that allows the user to work with Adobe Photoshop to sketch, organize, and further develop frames (Fig. 5 ;Appendix B). Then, animatics were created through the “export video” option in Storyboarder with rough voiceover. These animatics were shown to the FMDSWG for feedback, which mostly had to do with the imagery of Ernesto’s journey through being diagnosed as frail. It was after this feedback that Ernesto’s story was changed to him being diagnosed as prefrail, because it was supported by more conclusive research and it left the viewer on a positive note, knowing that Ernesto would live on with the help of some interventions. Thus, the original animatics were changed after the Frailty Working Group presentation. Wireframes were made for the original idea for the interactive component of the module in Adobe XD. The wireframes allowed for recognizing doubts in the necessity of showing a clinical picture of secondary frailty where most clinicians and healthcare professionals do not yet know about primary frailty. The wireframes aided in making a switch to focus on primary frailty, which is the first model of
frailty and is supported by the most research.

Figure 5: Selected Storyboards from Animation 3. Cellular and Molecular Changes in Frailty (text not intended to be read).
iv. 3D Modelling

The four characters featured in the first animation were modelled in Pixologic ZBrush using preset body part brushes and subsequently dynameshing afterwards (Fig. 6, 7). ZBrush brushes used mainly to sculpt are shown in Fig. 8. 3D assets that were modelled in Cinema4D include the cellular and molecular animation sequences.

Figure 6: Character Building in ZBrush using preset body parts.

Figure 7: Character Building in ZBrush using preset body parts. Character building using basic shapes to create torso shape.
The characters sculpted in ZBrush were created using the brushes highlighted in red boxes (fig. 8). Body frames were built using IMMToon, which includes preset body parts to create fantasy creatures and inhuman characters with exaggerated facial features, and IMM BParts, which includes preset body parts to create a more natural looking human mesh. Hands, feet, torso, and legs were created using IMM Toon parts and facial features were created using IMM BParts.

Once the characters’ main body frames and appendages were sculpted, the Extract function in ZBrush was used to create clothing and hair. First, the area desired to be extracted was masked using the Mask Pen and the mask was sharpened by holding down Ctrl and clicking on the sculpting canvas. Then, an extract thickness was set for the clothing depending on the intended clothing material. Pants and shirts were extracted at 0.02 thickness and seaters and lab coats were extracted at 0.5 thickness. Then, the accept option was selected and the masked area became a separate subtool to manipulate and sculpt upon. IMM Clothing, IMM ZipperM, IMM Zipper F, and StitchBasic brushes were used to create details on the characters’ clothing such as sewn seams between pieces of cloth, buttons, zippers on pants, belt buckles and belts.
Care was taken to preserve the linework and soft, friendly quality of the original sketches (Fig. 9) and the character designs done in Adobe Illustrator (Fig. 10).

**Figure 9: Original Pencil Sketch Character Design**

**Figure 10: 2D Character Design.** Done in Adobe Illustrator.
Characters were created by using the multimesh brush preset body part brushes and subsequently dynameshing and subdividing to sculpt features of the characters. Clothing, head, neck, hair, hands, and footwear were all separated into subtools so that they could later be textured and painted individually in Maxon Cinema 4D. Hair generator experiments were done to test if the cartoon quality of the original sketches of Ernesto could be enhanced with the “grow hair” function in ZBrush.

**Figure 11: Character Sculpting Using Dynamesh.** Red box indicates that different body parts and clothing were separated into their own subtools (text not intended to be read).

**Figure 12: Hair Generator Test.** The image on the left shows character with hair generated in ZBrush, and the image on the right shows extracted, smoothed and sculpted hair.
Ernesto’s expressiveness was mainly controlled by his eyebrows and mustache so it was suggested that the quality and depth of his expressions could be improved by having lifelike, moving hair. The hair generator worked well however it was difficult to comb into a lifelike head of hair and contrasted with the smooth clay-like quality of the rest of the mesh. It was decided against using lifelike hair for all the characters to set up for more straightforward animation, as the style of the animation was cartoon-like, soft, and reliant on subtle textures. After all characters were modelled in ZBrush, ZRemesh was used to reduce the polygon count of the mesh to allow for smoother animation and joint rigging. ZRemesher causes some loss of detail because of reduction in polygons, so a high resolution mesh duplicated before ZRemesh was completed was used to project details back onto the low polygon, low resolution mesh (Fig. 13). Projecting detail is not always a reliable way of retrieving fine sculpting back onto the low-resolution mesh, so ultimately some detail was lost, but resculpted in Cinema4D.

Figure 13: ZRemeshed and High Polygon Count Models. The image on the left shows character of high resolution before optimization, and the image on the right shows ZRemeshed character with some loss of detail.
Other characters were subsequently modelled and lightly textured in ZBrush. The characters were created to reflect an ethnically diverse crowd of older adults, as frailty affects older adults of different ethnicity, gender and sexuality in many ways. Moreover, frailty studies have been done in older adults of many different ethnicities and it is important to acknowledge this. Research for the look and clothing style was done by attending frailty assessment clinic appointments with nurse practitioners at the Bayview Johns Hopkins Hospital. Observations served two purposes: first, to observe real older adults (with attention to clothing, demeanor, and posture) to base illustrations off so as not to stereotype a “typical, frail” older adult, and second, to observe frailty assessment, take notes on the equipment used, and how a frail or prefrail person may present in clinic. It is important to note that before the clinic visits, initial illustrations of the characters done in Adobe Illustrator were met with some disagreement by the FWGMD (Fig. 10). Criticism was mainly regarding facial expressions and clothing choice: In figure 10, the third character from the left wearing jean cut-off shorts was deemed an unlikely patient look, as cut off shorts are clothing from a younger crowd. The initial expressions of the illustrations of older adults were melancholy, somber, and tired, which ultimately stereotypes older adults as constantly in disdain for their declining health and quality of life. As this is not the case for many older adults, expressions for the 3D modelled characters were made to look cheerful with a smile, and simple, friendly eye creases to demonstrate that older adults can already have a good quality of life even if frail, and that not all older adults are miserable in their condition. Later on, eyeballs were added to the sculpts to give the characters a friendlier, more realistic look. All final sculpts including improved clothing design are shown in Figure 14.
Figure 14: All 4 Final Character Sculpts. Finished character sculpts in industry standard “T-pose” before ZRemeshing.
In modelling the cellular aspects of the animation, the main challenge was to create realistic cellular dynamic effects to depict necrosis and dysfunction. Research was done to capture these cellular effects and were based on scanning electron micrographs (SEM) and transmission electron micrographs (TEM) (Fig. 15). Modelling these dynamic effects was achieved by using Cinema 4D R20’s volume builder functionality. Cellular scenes and effects such as necrosis, senescence, inflammation and DNA repair were created with Cinema4D’s volume builder function. In the case of creating vessels such as arteries and veins, volume builder and volume mesher were used to mesh together spline sweep functions of varying radii, to make vessels appear as if they are branching off larger vessels, becoming thinner. For effects such as cell membrane disintegration or mitochondrial dysfunction, the object being affected was placed in a volume builder, which was nested in a volume mesher function. Then, a random field was added to the hierarchy of objects underneath the volume builder. The mode on the random field was switched to noise, and the effect option for the random field was switched from “box” to “object” so that the entire object intended to be affected by the noise field will be affected. Once the random field was set to “noise”, a noise pattern was chosen that mimics a disintegration or crumpling effect. Once a noise pattern is chosen, the entire object under the volume builder will be affected by the noise pattern. To control and manipulate where on the object the noise appears, a linear field must be applied to the volume builder above the random field. The hierarchy thus should look like this: object > random field > linear field. Once the linear field has been applied, the move tool can be used to move the field to affect specific parts of the volume object. For the blending modes of the functions underneath the volume builder, the random field was set to “min” and the linear field was set to “add”. In the case of cellular and mitochondrial effects, the linear field was switched to a spherical field and the radius of the spherical field was keyframed to create the effect of increasing disintegration. It should be noted that the radius of the random field can be increased to have the object appear as if it has no effect applied whatsoever. Once the effect was keyframed using the sphere radius, a hardware preview under the setting HardWareGL Preview should be created to ensure proper movement and speed of animation. Additionally, pose morph tags can be added to objects nested in the volume mesher and can also be keyframed along with noise fields. All materials should be applied to the volume mesher, which is highest in the hierarchy of nested volume builder function. Cloners can also be affected by the volume builder functions without significant lag or slowness occurring.
Figure 15: Cellular Animation and Imaging. Finished cellular and molecular animation stills (left-hand column) and the SEM and TEM images they were based on and modelled after (right-hand column) (text not intended to be read).
Figure 16: **Organization of Objects in Volume Builder.** Red box indicates hierarchy of volum objects. The object named “inner” represents the inner mitochondrial membrane where the effects were occurring.

Figure 17: **Settings and Hierarchy of objects and fields in the Volume Builder.** The upper red box indicates that the volume type should be set to “fog” and the lower redbox shows the hierarchy and blending modes of the volume builder objects.
Figure 18: **Settings in the Random Field.** Used to create mitochondrial dysfunction effects.

Figure 19: **Settings in the Spherical Field.** Used to create mitochondrial dysfunction effects.

Figure 20: **Mitochondria Model:** The left-hand image depicts the mitochondrial model with the random field applied, creating the disintegration effect, and the right-hand image shows the model once the spherical field has been applied.
v. Texturing

After 3D modelling in ZBrush, each element of each character was brought into Cinema4D using File>Merge. The merge function puts all character elements at (0,0,0) coordinates and imports their relative size and coordinates of meshes from ZBrush, so the characters can be easily “reassembled” in Cinema4D. After importing each character, clothing, skin, hair, and footwear were colored and textured in Cinema4D. Texturing was intentionally created to appear clay-like and soft (Fig. 23). Texture mapping was done by using the noise function under the texture tab in the material menu, and “cell voronoi” was used at a small global scale with 7-9% texture strength (Fig. 24). Once all characters were textured, BodyPaint3D in Cinema4D was used to add details in the character’s clothing to reflect more of their personalities and to add interest to the look of the characters. First, the clothing item was UV unwrapped using the BodyPaintUV interface in Cinema4D using the unwrap function (Fig. 25). In the unwrapping, optimal remapping was chosen and texture map quality was set to 1024x1024 (Fig. 26). Depending on the size of the mesh, UV mapping can take a few minutes to complete. Once UVs were unwrapped for the clothing meshes, care was taken to make sure no elements of the UV map were overlapping, which can cause breakage in the painted textures when applied to the mesh. Once UV maps were generated, the Cinema4D interface was switched to BodyPaint3D to begin painting (Fig. 27).

BodyPaint is a robust tool for painting 3D meshes, and features a lengthy brush menu and layering functions. To use BodyPaint, adequate lighting was needed to make sure colors sampled from the characters matched their true color in the viewport. Lighting is also important to BodyPaint because painting the whole mesh requires rotating the mesh, and if color is resampled in a different or uneven lighting setup, coloring will not be consistent. Patterns painted on the characters’ clothing was done with a simple, free-drawn line quality. Stripes, checkered shirt patterns, and floral and paisley patterns were painted on the clothing meshes to reflect the clothing’s aesthetic quality of observed older adults (Fig 23). For the character third from the left, a Johns Hopkins University School of Medicine (JHUSOM) logo was placed on her sweatshirt as a nod to the frailty and aging research done here (Fig. 21). Placing this logo as a texture in the color channel proved difficult because the character’s UV map did not allow for the full logo to appear on her chest. Instead of choosing the texture mapping option “Unwrapped UVs”, “Cylinder” was used to overcome the inconsistent UV
map (Fig. 22). Placing the logo on cylinder mode looked better and mapped well, but later in the rigging process it was found that this character could not move her arms farther than her head, as the logo would map onto her shoulders and upper arms. To resolve this, the character’s movement was restricted although alternatively, the texture could have been baked.

**Figure 21: Texture Settings Under Reflectance.** These are the texture settings for one of the characters’ sweatshirt. The Johns Hopkins logo is placed via the color channel under texture, with the blending mode set to Multiply. The cloth type is set to polyester.
Figure 22: Projection of Surface Textures for Clothing. The JHU logo on the pink sweatshirt was set to cylindrical projection (shown in red box) in order to ensure more accurate mapping of the logo onto the material of the sweatshirt.

Figure 23: Texturing Characters in the View Port. All four characters and their final clothing design and texturing.
Figure 24: Skin Texture. Texturing accomplished by using the noise pattern “Cell Voronoi.”
Figure 25: BodyPaint 3D Setup Wizard. This window opens when the startup wizard icon is selected (outlined in red box). The object desired to unwrap UVs for is chosen, and next (outlined in the red box) is chosen.

Figure 26: BodyPaint 3D Setup Wizard. This window opens when the object to be unwrapped is chosen, and the next button is selected. The minimum and maximum texture heights and widths should be set to 1024 px or more so as to allow for clarity of the texture mapping on the object with minimal pixelation.
Figure 27: BodyPaint 3D Workspace. Upon choosing the BP3D workspace, options for colors and brushes appear on the righthand panels (text not intended to be read).

Figure 28: BodyPaint 3D Texture Material. This texture map is generated from the BodyPaint workspace.
Figure 29: Texture Map Resulting From UV Unwrap. The texture for Ernesto’s shirt is shown above and is generated once exiting out of the BodyPaint 3D workspace and entering the Standard workspace.

Figure 30: Additional Cloth Texturing. Cloth types like wool, jeans, and silk were achieved using a reflectance preset in the reflectance channel. For Ernesto’s pants, Irawan (Woven Cloth) type was chosen and the pattern was set to Wool Gabardine.
Figure 31: Evolution of Character Design and Texturing. Shown are three iterations of the final character designs and the last image in the column is the final rigged and textured character design set.
Additional cloth texturing was achieved using the reflectance channel in the materials editor. Clothing types such as jeans, wool, courdoroy, and silk were achieved by changing the reflectance channel to a cloth type under the option “type” (Fig. 29). The pattern, for example, for Ernesto’s thick and soft pant fabric was set to Wool Gabardine, and the texture size was changed accordingly to suite the size of the 3D model, in this case, the pants (Fig. 30). All final character designs, texturing, and facial characteristics are shown in Figure 31.

vi. Character Rigging

After texturing was completed, all the elements of each character were merged using the “Connect Objects and Delete” function. Once each character’s mesh became one single object, the rigging toolkit in Cinema4D (Fig. 34) was used to build a skeleton unique to each character’s topology. The joint tool was used while carefully checking placement of bones in the top, side, and front viewports to assure even and symmetrical skeletons (Fig. 33). Joint placement is significant because if a mesh has an uneven or poorly placed joints, the binding and weighting of the now rigged mesh will be inaccurate and will not allow for smooth movement, resulting in breakage of polygons. Joint placement is first started by placing a joint point in the pelvic region of the character, or their center of gravity. Then, two joints on either side to fill out the hip region, a knee joint, and ankle joint are placed. The upper half of the character must start with placing a point in the clavicle area, as centered as possible. Then the shoulder, forearm, and wrist joints are placed. Joints were not placed in the fingers of each character as movements storyboarded previously did not require fine movement in the fingers (Fig. 32). The joint hierarchy should look similar to Figure 34.

Alternatively, the symmetry function under the character animation menu can be used to perfectly mirror and align half of a skeleton to the opposite side. However, the skeleton should still be checked manually in all viewports that all joints are placed inside the mesh. The spine should also be placed carefully on a slight diagonal, as human spines are curved at different angles, and to balance weight at the center of gravity. Once all joints were checked for symmetry, the bind function under the character animation menu was run to bind the mesh geometry to the skeleton, resulting in a color-differentiated weighting map which shows the surface area of how much of the mesh is affected by each joint (Fig. 35; Fig. 36).
Figure 32: Skeleton Joint Placement. The left-hand image shows joint placement in the skeleton and the right-hand image shows the bound skeleton.

Figure 33: All Viewport Views of Rigged Characters. (text not intended to be read)
Figure 34: Hierarchy of Joints. Smaller joints are nested underneath main joints. Binding joints will generate a skin object and a weight tag.

Figure 35: Character Building Menu. Weight tool used to paint weights is highlighted in blue.
Rigging can prove to be difficult because no matter how symmetrically the skeleton is placed, additional weight adjustment must be manually done to correct any improper weighting to correct, for example, an arm joint that also places weight on the forearm, so more geometry moves than is necessary when the arm joint is rotated. Most of the characters created needed significant weight adjustment, perhaps because they were still too high resolution for Cinema4D (30,000–40,000 polygons). Weight adjustment was done using the Weight Painting tool in the character animation menu (Fig. 35). Weight painting allows the user to manually paint weights for each joint to improve movement quality later in the animation phase. With the weight painting tool selected, the fully rigged model can be selected in the object menu to view the current weighting of the model. Selecting individual joints will show the geometry affected by each joint via color, and it is important to paint weights in a joint by joint fashion while checking the overall weight map and by testing the rotation and movement of each joint (Fig. 37). Because the characters modelled were of a more organic quality and not perfectly symmetrical, weighting calculation and binding of the skeleton initially caused jarring movement with significant polygon stretching and breakage. Weight painting can also be difficult because some incorrectly weighted polygons can only be erased from the inside of the model as well as by constantly rotating and erasing polygons from various angles. This can often happen at edges where a jacket edge may cause a slight height difference between the jacket’s mesh and the shirt’s mesh, such that weighting will be incorrectly calculated at these edges and the chest or clavicle joint will not move smoothly (Fig. 38). Weight painting was mostly contingent on constantly testing rotational movements, seeing which polygons were incorrectly weighted, and then painting those polygons to the joint they should belong to.

Figure 36: Weighted Mesh Coloration. Joints are colored by weight distribution after joints are bound.
Figure 37: Selected Weights: The left-hand image shows the joints of the character before weight painting, and the right-hand image shows the joints after weight painting. It is to note that the forearm joint is weighted to only affect the polygons in the forearm in the right-hand image.

Figure 38: Improperly Rigged Model. This image shows the polygon breakage and stretching that will occur if the model is not weighted properly.
Character rigging often involves creating spline or basic nurb shape or null-based rig controls to allow for easier movement control. This process often involves using the IK joint handle function in Cinema4D and linking it to a circular control, for example, at the hip. This allows the animator to manipulate the hip joint solely with the circular control, without needing to individually move each joint’s position, scale, and rotation. Because the characters in this animation engaged in non-complex idle animation and simple arm, head, and hand movements, this rig control system was not used and individual joints were moved, rotated, and keyframed in the animation process.

vii. Environment and 2D Asset Creation

Once character rigging was complete, environments for each scene were built. The environments included a doctor looking down at a patient’s chart, a clinic room, and a neutral backdrop to discuss statistics and flowcharts. The clinic room was created as simply as possible with four walls textured by drawings made in Adobe Illustrator (Fig. 39; Fig. 40). A clinic bed and stool were sculpted in ZBrush and textured in Cinema4D (Fig. 41). 2D assets such as icons for frailty consequences and predictors were created in Adobe Illustrator. To ensure that the 2D assets would match the aesthetic of the 3D assets, a grain texture was placed on many of the 2D icons to echo the 3D character’s texturing (Fig. 42; Fig. 43). Thin quality of line was also used to match the hand drawn and hand sculpted quality of the characters.

Figure 39: Example of 2D Asset Creation. These four artboards were created to map onto a simple 3D model of a clinic room.
Figure 40: Viewport View of Clinic Room. The mapped Illustrator artwork is shown here on each wall in the viewport view of Cinema4D.

Figure 41: Final Rendered Still of Clinic Room. The resulting texture-mapped clinic room with wall art.
Figure 42: 2D Anatomy Drawings. This drawing was created to show the multi-organ changes that occur in a frail person.

Figure 43: 2D Icon Creation. These icons from the first animation explain how frailty status can predict various geriatric health outcomes.
After carefully rigging the characters and checking for adequate movement in all joints, the characters were placed in a simple lighting setup consisting of physical sky and two warm orange and cool purple lights to fill in the shadows in some of the characters faces. The Cinema4D interface was switched to the animation workspace and character animation was primarily led by the timing of the voiceover so that characters could react to the voiceover with appropriate timing. The character animation process was initiated before approval of the script so as not to waste any time, so a third of animation 1 had to be keyframed again to match the pace of the voice over. Each sentence of the animation sequence was timed, and an average number of frames needed to animate the sentence was calculated using 30 fps. For example, an 11 second dialogue would require at least 330 frames, and knowing this is crucial to character animation both for efficiency and so the animator can allow for extra animation and movement cushioning the beginning and end of the dialogue. On average, an extra 30 to 50 frames were added to each dialogue’s animation sequence as a time buffer. An 11 second animation might approximately need 360 frames including a time buffer in case the post processing phase requires for more or less fade - in or fade - out of the animation sequence.

The first few animated sequences created appeared unrealistic and had an animatronic quality, which was jarring and distracting to watch while simultaneously paying attention to the voice-over. Idle animation sequences used in game characters were studied and it was noted that most movement of single limbs often involves multiple joints. For example, a character lifting their arm will use their clavicle or chest joint, the arm joint, and the forearm will rotate because of the rotation of the radius and ulna, depending on the angle of the lift. Human movements are never singular and often involve many other muscles outside of the muscle group performing the action. It was important to recreate believable, exaggerated movements because the characters themselves were simple models and without exaggeration, the movements would be subtle and hard to read. Disney’s Twelve Principles of Animation were studied and referenced to further create human-like movements. For example, the second principle is known as Anticipation, which calls for animated movements in anticipation of a major movement, such as bending of the characters’ knees before they jump into the air. These principles and study of human and game character movement allowed for more realistic animation (Thomas and Johnston, 1981).
Animation of the characters’ facial expressions, eyes, mouth, and eyebrows were controlled using Pose Morph tags under Cinema4D’s character animation tag menu (Fig. 44). Pose morph tags allow the animator to sculpt different expressions and poses from a base pose. These sculpted poses can be activated or deactivated during the animation process using percentage based sliders. The percentage based pose sliders allow for mixing of two or more poses to create a unique, more nuanced expression. Unfortunately, Pose-morphing could not be used to sculpt back a muscle’s deformation after rotating a joint because of a bug in the R20 version of Cinema4D. Pose morph contains a feature known as Correctional PSD, which allows a rigged mesh to be sculpted back into a realistic state once a joint has been posed or moved, which will end up deforming unrealistically (Fig. 38). Pose morphs were useful in creating facial expressions, especially Ernesto’s eyebrows. Ernesto’s eyebrows each had a base pose, a worried pose, and a surprised or smiling pose (Fig. 46). Keyframing the slider bars between poses created realistic and smoothly transitioned facial expressions. After keyframing each scene of all four animations, the Cinema4D files were packaged with assets, which generates a textures folder. Both the C4D file and the texture files were uploaded to the Cinema 4D Render Farm, which allowed for comparatively faster animation renders.

Figure 44: Pose Morph Tag. Three main expressions were sculpted for each character: happy, neutral, and sad/concerned.
Figure 45: Expression Control With Pose Morph Tag. The upper left-hand image shows the character in her base pose and the upper right-hand corner image shows the character once Pose.0 (pose for neutral), was keyframed in the animate settings of the tag, shown in the bottom image.

Figure 46: Rendered Facial Expressions. Ernesto is shown here with facial control movements in his eyebrows achieved by using the Pose Morph tag.
ix. Post-processing

The rendered animation sequences were imported into Adobe AfterEffects using File>Import>Multiple files to create a composition from the PNG sequence generated by the Cinema4D render farm. Slight lighting and color adjustments were made in AfterEffects but was mostly used for compositing the render sequences, keyframing fade in and fade out effects between scenes, and matching the animation sequence with the voiceover audio. Masks were created and animated to hide and show text and images in accordance with the voiceover audio.

Photoshop files are extremely compatible with AfterEffects as it imports all layers in the photoshop file. Layered Photoshop files containing each body part or joint of a 2D character were imported to AE and were animated using movement and rotation and subsequently keyframed for these values. It was important to ensure that the 2D elements matched the 3D elements, so care was taken to apply color correction, levels, and exposure channels to sequences mixing 2D and 3D animation. AfterEffects was also used to mask videos to create video insets in certain scenes (Fig. 48). Painted Photoshop layers were created to add texture, form, and light to parts of the renders in post-processing.

Figure 47: Post-processing of Cellular Processes and 2D Art. Here, Ernesto’s body outline and anatomy were composited with rendered 3D animations using precompositions and masking the animations to a circle shape.
The organization of precomposed scenes and compositions was significant to the organization of the animation structure. For example, in animation 3 “Cellular and Molecular Changes in Frailty,” each cellular process was made into a precomposition so as to unclutter the larger main composition which contains every scene of the animation. This was done because many of the cellular scenes were rendered in layers for better manipulation during post-processing, which created multiple layers in AfterEffects. In addition to these layers, Photoshop adjustment layers were added to the rendered cellular process layers and so layers were grouped into a precomposition, which allows for editing short scenes and all of their associated layers without affecting the larger composition. Layers were also color-coded to further organize animation sequences (Fig. 49).
x. Website Development

The interactive website was established as a subdomain under Dr. Abadir’s lab website. The website is intended to provide the user with a series of case studies based on the characters featured in the animation that apply the frailty knowledge taught in the introductory animations to mock patient case studies. Each of the four featured characters presents with a specific frailty phenotype and is shown with associated comorbid conditions, relevant psychosocial details such as home life and pollution, and information about current medications. Depending on the frailty phenotype present in the character, a frailty assessment will show the patient’s results and criteria for frailty that have been reached. There is no testing component of this learning module in the website, rather the purpose is to apply the knowledge to various scenarios and allow the user to explore the information in non-punitive, low-stress ways (no in-module post or pre testing).

A WordPress theme was chosen that allowed for a video background, featuring video composites of scenes from the animations. Two buttons will be featured on this landing page: one that will allow the user to access the animations, and one that will take the user to the interactive module. For interactive content in the module, Verge3D was used to create manipulatable models and were placed in the webpage by embedding its iFrames in the visual editor of WordPress. The models optimized for interactivity on the web were first imported into Blender, animated with a simple idle animation sequence, and published using Verge3D and a puzzles-format code to create an interactive module inside the webpage. All animations and the interactive module can be found at frailtymodule.abadirlab.org

xi. Measurement of Success

Comments and feedback from the Frailty and Multisystem Dysregulation Working Group (FMDW) were taken into consideration through all phases of production. The FMDWG is a group of Hopkins researchers from the Center on Aging and Health (COAH) that meet weekly to discuss new developments in frailty research, and have been an excellent group of consultants for this project’s development thus far. Keeping in mind that this resource is made for clinicians outside of frailty, this project will also be tested by a group of outside clinicians including transplant surgeons, oncologists, and general practitioners organized by Dr. Mariah Robertson, a frailty specialist at Hopkins.
The clinician group would be given a pre- and post-knowledge test to assess information learned, which is separate from the web module. This resource will be used by both the clinician and researcher groups and their feedback about the content, flow of information, usefulness, and ease of use will be taken into the development and editing processes.
IV. Results

The challenge unique to this subject matter and its subsequent educational purpose was distilling the research, information, clinical practices, and uncertainties in frailty syndrome studies for the purposes of a clinical audience: clinicians, nurses, healthcare professionals, and if applicable, hospice workers and even family members who may care for their older relatives. In total, the final assets completed and implemented in the website were four animations titled “What is Frailty?”, “What Does Frailty Syndrome Look Like?”, “Cellular and Molecular Changes in Frailty”, and “How Does Frailty Impact Geriatric Health?”. Each animation runs approximately one and half minutes long and features educational content in a chalkboard infographic style with 3D animated characters (Appendix C). The interactive website created features this animation and an abridged version of the frailty interactive module (due to time constraints) that allows viewers to explore various phenotypes of frailty.

In addition to the final products, 4 animatics, 1 set of wireframes (Appendix E), a site map of the website and web module (Appendix D) and 8 sets of storyboards (Appendix B) were created in preparation for the animations and interactive module, however four of the storyboard sets were not used in the process of creating the final products so they are not included in the appendices. The purpose and presentation of this resource changed considerably due to too large of a scope, so storyboards were redrawn but animatics for these new storyboard sequences were not created for lack of time. The final script and voiceover are included in the final products as well (Appendix A). The interactive resource is intended to serve as a prototype and companion to the four animations, and with more time and resources, can be developed to be a more robust learning module.

i. Effectiveness of Character Animations to Teach Frailty

The four character animations were very well received by the FWGMD, but the effectiveness of the learning content is yet to be tested. For future consideration, a pre- and post- test may be administered to a random group of clinicians who work outside of geriatrics. Building upon past theses produced by graduate students in the medical and biological illustration program, cartooning and 3D animation approaches have been well received and enjoyed by their target audiences, however, informal feedback is needed to see if this light-hearted, narrative animation approach is favorable to healthcare professionals and their more rigorous learning styles.
ii. Access to Assets Created

Acess to the website, animations, interactive frailty module, and animatics resulting frkom this thesis can be viewed at this address: frailtymodule.abadirlab.org, or by contacting the author through the contact form on their website: lohithakethu.com. The author may also be reached through the Department of Art as Applied to Medicine via the website www.hopkinsmedicine.org/medart.
V. Discussion

The methods used in this project provide a workflow to create a 3D animation which flows from a macro to micro scale, aided by 2D illustrated assets. Basic frailty independent of any comorbid conditions or specific social situations was chosen to first introduce the workings of frailty syndrome. Upon this foundation of basic frailty, one can start to understand the multidimensionality of psychosocial, physiological, and cellular and molecular drivers and risk factors that interact when a comorbid disease develops with frailty or vice versa. Most of the project schedule was dedicated to 3D modelling, animating, and compositing because the purpose of the animations is to introduce the topic of frailty and aging to healthcare professionals, most of whom see this as foreign and outside of their knowledge or clinical practice. Originally, it was planned to spend the bulk of the project schedule building the interactive module but it was decided that without introducing the context of frailty and aging in healthcare via the animations, the module would have little teaching value.

i. Idea Development

The project created a character animation-based, interactive, model of frailty syndrome to educate clinicians outside of geriatrics. However, the initial plan for this project was to create a dynamic resource that visualized frailty syndrome as a constantly moving, rearranging network with associated odds ratios to provide clinical relevance and support frailty knowledge with published research. This model would connect three dimensions of risk factors (molecular, psychosocial, and physiological) to the frailty phenotype, against the backdrop of normal biological aging. The user would be introduced to frailty via an animation, and then would be invited to affect the model by choosing one of six well recognized stressors (heart disease, diabetes, infection, cancer, depression, and cognitive decline). The stressor would cause the model to reconfigure to show: frailty progression, (ii) outcomes (disability, dependence, or death), and (iii) ratios of likelihood of occurrence for studied connections between risk factors. Odds ratios and hazards ratios for each studied connection would provide insight to the user on how likely a comorbid condition or trigger is likely to develop and what other risk factors these triggers are connected to (e.g. a high correlation between cardiovascular disease and low grade chronic inflammation may suggest that certain frailty criteria will be met in a given individual). Through exploring this interactive frailty model, the user would be able to understand how specific stressors drive frailty, where there are gaps in research, and the value
of viewing frailty as a dynamic network. However, the leg work of teaching such an abstract, complicated concept as frailty had to be animating and simplifying the past decade of frailty research for the purposes of a clinician. As with any field of research, there is a plethora of research publications that are relevant to clinical practice, however, to bring awareness to the importance of frailty, the previous clinically relevant, statistics-based interactive frailty model was substituted for a friendly and eye-catching animation style to first and foremost generate interest. The basic concept, site map, odds ratio table, and wireframes are shown in Figures 50 - 53.

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1A) Introduction to frailty. 1B) The frailty progression model. 1C) Possible frailty progressions.

Figure 50: Frailty Model Schematic
## Cardiovascular Disease Odds Ratios and Comprehensive Review

<table>
<thead>
<tr>
<th>Outcomes affected by Frailty</th>
<th>Association</th>
<th>Frailty Assessment</th>
<th>Population</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Readmission, rehabilitation after cardiac surgery</td>
<td>3.2-13 OR</td>
<td></td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Arrythmia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resistance to medication (Diuretics and Beta blockers)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower exercise tolerance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Likelihood of hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Likelihood of Chronic Kidney Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transient Ischemia</td>
<td>1.5 OR</td>
<td></td>
<td>Cardiovascular Health Study (CHS), a cohort</td>
<td><a href="https://academic.ncbi.nlm.nih.gov">https://academic.ncbi.nlm.nih.gov</a></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.9 OR</td>
<td></td>
<td>Cardiovascular Health Study (CHS), a cohort</td>
<td><a href="https://academic.ncbi.nlm.nih.gov">https://academic.ncbi.nlm.nih.gov</a></td>
</tr>
<tr>
<td>CHF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 month mortality/morbidity TAVR</td>
<td>4.2 OR</td>
<td></td>
<td>Prospective, multicenter cohort of patients undergoing TAVR</td>
<td></td>
</tr>
</tbody>
</table>

Figure 5.1: Frailty Model Odds Ratios Spreadsheet
<table>
<thead>
<tr>
<th>Row</th>
<th>Description</th>
<th>Odds Ratio</th>
<th>Population</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>Coronary Artery Disease 6 month mortality</td>
<td>1.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td><strong>Depression</strong> Odds Ratios and Comprehensive Review</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Outcomes affected by Frailty</td>
<td>Odds Ratio</td>
<td>Population</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>likelihood of institutionalization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Readmission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>lower exercise tolerance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Antidepressant use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>persistence of depression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26</td>
<td><strong>Cancer</strong> Odds Ratios and Comprehensive Review</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>Outcomes affected by Frailty</td>
<td>Odds Ratio</td>
<td>Population</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>Metastasis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>Readmission</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Figure 51.2: Frailty Model Odds Ratios Spreadsheet*
Figure 52: Original Frailty Model Site Map
Figure 53.1: Selected Wireframes. The red boxes indicate the button or option that was chosen to move to the next page (smaller text not intended to be read).

Figure 53.2: Selected Wireframes. The red boxes indicate the button or option that was chosen to move to the next page (smaller text not intended to be read).
Figure 53.3: Selected Wireframes. The red boxes indicate the button or option that was chosen to move to the next page (smaller text not intended to be read).

Figure 53.4: Selected Wireframes. The red boxes indicate the button or option that was chosen to move to the next page (smaller text not intended to be read).
**Figure 53.5: Selected Wireframes.** The red boxes indicate the button or option that was chosen to move to the next page (smaller text not intended to be read).

**Figure 53.6: Selected Wireframes.** The red boxes indicate the button or option that was chosen to move to the next page (smaller text not intended to be read).
Figure 53.7: Selected Wireframes. The red boxes indicate the button or option that was chosen to move to the next page (smaller text not intended to be read).
ii. “Branding” Frailty Syndrome

Furthermore, the final animations created for the COAH frailty website also proved to be an exercise in branding an area of research. As certain retail stores have recognizable, friendly mascots or logos, research labs, medical associations and institutions may also adopt similar branding schemes to maintain relevance in the public sphere and to gain familiarity. The colors, textures, and characters created for the animations are consistent throughout the subdomain that hosts them, and creates a mood or tone around the topic of frailty. The friendly visuals and calm, soft purple, pink, orange, and blue hues suggest a seriousness and somber hopefulness around frailty research. Ernesto, the patient who the viewer follows on a healthcare journey, has been discussed as being almost a mascot for frailty research because of his easily recognizable appearance and good-natured, curmudgeonly personality translated through his facial and body movements. Although it is unlikely that frailty will evolve a character-related branding scheme, it is an interesting study in how animation style, color, texture, pacing, and sound can create a mood around a specific area of research that engages the viewer.

iii. Reflections on Character Animation

The character animation style used in this project was enjoyable to create and view, however, its limitations and challenges should be noted. A large part of animation troubleshooting was re-weighting the skeleton rigging and painting geometry to affect the correct joints. Without a script to do this in Cinema4D, this process can be extremely time-consuming, especially for unsymmetrical meshes such as the characters modelled for the animations. There are scripts such as Mixamo and open source rigging programs sponsored by visual effects schools, however many of these are mostly compatible with Autodesk Maya and require a significantly low polygon count model for the skeleton to bind and weight the character appropriately.

Additionally, rigging proved to be harder in heavy-set characters as opposed to thin and tall characters. When there is more space between limbs and overlying clothing (thin limbs, thin torso), the rigging calculations in Cinema4D produce better results and the final weighted character moves smoothly without polygon displacement. Seeing as three out of four of the characters made for these animations were intended to be portly or overweight, a great deal of weight readjustment had to be done to achieve smooth movement, because there was less space between limbs and clothing. Additionally, rigging with complicated clothing styles was also a challenge. For example, in the case of the character in orange sporting a South Asian style scarf, the scarf’s weight had to be painted to match the movement of the
neck, to appear as if the scarf was moving with the turn of the character’s head and neck. This was not a complete solution however, because individual polygons were ultimately displaced in the final renders and were masked and blurred in AfterEffects to hide the distracting polygon displacement.

The four 3D characters were created and rendered in 3D to make a distinction between “2D” clinical theory and “3D real life” clinical situations; the clinical theory being the statistics and research supporting the implementation of frailty assessment, and the “real life” patient journey of an individual who may be frail. In line with this intention, the characters’ realism and aesthetics were prioritized over their movement ability. Cinema4D’s preset material library and versatile material options allowed for complex and seemingly tangible skin, cloth, and upholstery textures. Cinema4D texturing and ZBrush soft-sculpting allowed for organic and sympathetic characters, but with limited movement. Conversely, creating a low resolution, less realistic character aesthetic may have appeared simple, but would have allowed for a greater range of movement due to the ease of rigging such low polygon count models. 3D character animation can be an impactful tool to convey complicated concepts however, more research and testing could have been done to achieve a time-efficient rigging and weighting workflow, time permitting. The workflow used in this project was intensive but produced smooth movement throughout the animations.

iv. Future Considerations

To develop this project further, the original interactive, dynamic, multidimensional frailty model may be implemented. With the completion of the four animations and limited-functionality interactive frailty module, a viewer now has the context for understanding primary frailty and basic frailty theory. The next step of this education journey would be to introduce the viewer to secondary frailty and the associations between risk factors and comorbid diseases. This side of frailty is increasingly complex and without the foundation provided by the assets created, the viewer would get lost in the research and intricacies of frailty syndrome without understanding its underlying causes on a macro to micro scale.
## Appendix A: Script

**Final Script for Frailty Intro Animation (Projected 4-5 min total)**

<table>
<thead>
<tr>
<th>Narration</th>
<th>Visual</th>
<th>Audio/Assets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scene 1: Introduction</strong>&lt;br&gt;Narrator: One of the biggest global healthcare challenges is the medical and economic burden of caring for older adults. In the US, healthcare for older patients accrues approximately 50 billion dollars per year in medical costs. (citation). However not everyone ages the same way and simply looking at an older person is not enough to determine their health or functional status. Substantial research has identified that certain individuals are especially vulnerable to poor health outcomes such as dependence, disability, and death. <em>(On screen text: Frailty Syndrome)</em>&lt;br&gt;&lt;br&gt;Narrator: Frailty syndrome can affect upwards of 15% (citation: frailty txt) of the older adult population in the US.</td>
<td><em>(all graphics will be done in blocky 3d style, similar to simpler pixel character animation)</em>&lt;br&gt;Animated text and icons describing outcomes</td>
<td>Narration mostly but with pings and click sound effects as icons or graphics pop onto screen</td>
</tr>
<tr>
<td><strong>Scene 2: What does frailty syndrome look like?</strong>&lt;br&gt;Narrator: Imagine an individudal, Ernesto, 75 years old, with a history of hypertension and more recently, falls.</td>
<td>Populate screen with frail and prefrail animated characters (icons and numbers hovering over their heade)&lt;br&gt;Zoom into intro of character, looks normal.&lt;br&gt;Conversation exchange via text bubbles and images <em>(2D art)</em></td>
<td>Assets to be created:&lt;br&gt;<strong>Scene 1:</strong>&lt;br&gt;3D: character guys(4)&lt;br&gt;Ernesto (full)&lt;br&gt;Clinician&lt;br&gt;Clipboard+chart&lt;br&gt;Syringe&lt;br&gt;Cross sign&lt;br&gt;Diabetic sugar meter&lt;br&gt;2D: disability, institutionalization, transplant success, waitlist times, surgery outcomes, mortality icons.</td>
</tr>
<tr>
<td>Narrator: Ernesto visits his primary care practitioner Dr. Lee, and reports that he has experienced a couple of falls in the past six months. Dr. Lee asks Ernesto a few more questions and finds out that Ernesto is increasingly exhausted and has little energy. Concerned that Ernesto may be frail or becoming frail, Dr. Lee refers him to a geriatrics clinic for frailty assessment.&lt;br&gt;&lt;br&gt;Narrator: The clinical assessment for frailty includes five measures: unintentional weight loss, exhaustion, activity levels, walking speed, and grip strength <em>(needs citation)</em>. Ernesto’s assessment shows that he meets two criteria for frailty based on these measures: slow walking speed and low grip strength. Having one or two frailty criteria characterizes him as pre-frail. A score of three or more out of five criteria would characterize him as frail.</td>
<td>Chart appears with checks marking every measure as narrated&lt;br&gt;Don’t need to show whole frailty assessment but show via quick vignettes or icons</td>
<td><strong>Scene 2:</strong>&lt;br&gt;3D:&lt;br&gt;-dr.lee&lt;br&gt;-clipboard&lt;br&gt;-exam table&lt;br&gt;2D: all icons for frailty measures</td>
</tr>
<tr>
<td><strong>Scene 3:</strong>&lt;br&gt;3D:&lt;br&gt;-dr.lee&lt;br&gt;-simplified cell&lt;br&gt;-mitochondrial dysfunction (how to show this)</td>
<td>Cellular changes animated in 3D are shown as each hallmark is explained.</td>
<td></td>
</tr>
</tbody>
</table>

---

Figure 54.1: Narrated Script for all four animations. Each scene described is one animation’s narrated content and notes about asset creation.
Figure 54.2: Narrated Script for all four animations. Each scene describes one animation’s narrated content and notes about asset creation.

**Scene 3: Molecular changes**
Ernesto’s pre-frail state may be the result of many factors. Over the past few months, a multisystemic build-up of chronic low grade inflammation with an increase in cytokines IL-6 and TNF-alpha exhaust his cellular energy resources which impairs cell repair mechanisms, and is associated with an overall build-up of toxic byproducts in his body systems. With time, these energy demanding chronic changes could also lead to mitochondrial dysfunction. Other factors that also play roles in the development of frailty syndrome include cell senescence, epigenetic changes such as methylation, and cell injury resulting in necrosis.

(needs citation)

How do these molecular changes relate to frailty and geriatric health?
Over time, these chronic multi-organ changes can lead to system failure, muscle wasting, which are related to lower resting metabolic rate, less energy expenditure, and clinically apparent physical declines such as impaired balance, low strength, and slow walking speed. These combined molecular, physiological, and functional declines are predictive of common geriatric health outcomes such as falls, incontinence, and cognitive decline. (needs citation)

**Scene 4: Interventions and Conclusion**
Dr. Lee discusses with Ernesto options for medical and therapeutic interventions such as physical therapy, nutrition counseling, medication screenings, and optimization through a comprehensive geriatric assessment. (needs citation)

These interventions can decrease his vulnerability to other stressors in his life.

Conclusion:
Frailty syndrome is a series of complex, multifactorial and non-linear interactions between cellular and molecular changes and physiological factors. Other determinants can include psychosocial factors such as loneliness, home environment or “lifespace”, as well as comorbid conditions and life stressors. Understanding and screening for frailty early on can result in better care and treatment options for older adults.

<Button prompt to view thresholds for frailty measures/interactive case studies>

<table>
<thead>
<tr>
<th>Related to Fried’s cycle of frailty through moving icons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Show ernesto again, positive atmosphere, show icons of therapeutic measures as they are narrated.</td>
</tr>
<tr>
<td>Show possible stressors like infection, sickness. Etc?</td>
</tr>
</tbody>
</table>

(2D: sarcopenia, RMR, energy expenditure, balance, two frailty measures, falls.

**Scene 4:**
- icons for therapies
- stressors = infection(show ernesto coughing)

- show Fried’s cycle of frailty again with icons in place
One of the biggest global healthcare challenges is the medical and economic burden of caring for older adults.

In the US, healthcare for older patients accrues approximately $50 billion dollars per year in medical costs.

However, not everyone ages the same way and simply looking at an older person is not enough to determine their health or functional status.

55.1: Storyboards for Animation 1 (text not intended to be read).
Substantial research has identified that certain individuals are especially vulnerable to poor health outcomes such as dependence, disability, and death.

Frailty syndrome can affect upwards of 15% of the older adult population in the US. If you are a clinician or healthcare professional, you may have older patients that may benefit from frailty assessment.

Frailty is a strong predictor of disability, falls, medication side effects, and death.

55.2: Storyboards for Animation 1 (text not intended to be read).
55.3: Storyboards for Animation 1 (text not intended to be read).
Imagine an individual, Ernesto, 75 years old, with a history of hypertension and more recently, falls.

Ernesto visits his primary care practitioner Dr. Lee and reports that he has experienced a couple falls in the past six months.

Dr. Lee asks Ernesto a few more questions and finds out that Ernesto is increasingly exhausted and has little energy. Concerned that Ernesto may be frail or becoming frail, assessment.

Concerned that Ernesto may be frail or becoming frail, assessment.

The clinical assessment for frailty includes five measures: unintentional weight loss, exhaustion, low activity levels, slow walking speed.

56.1: Storyboards for Animation 2 (text not intended to be read).
56.2: Storyboards for Animation 2 (text not intended to be read).
Ernesto’s pre-frail state may be the result of many factors.

Over the past few months, a multisystemic buildup of chronic low grade inflammation with an increase in cytokines IL-6 and TNF-alpha.

57.1: Storyboards for Animation 3 (text not intended to be read).
FRAILTY SCENE 3

exhausted his energy resources and body systems.

and is associated with an overall buildup of toxic byproducts in his blood.

With time, these energy demanding chronic changes

could also lead to mitochondrial dysfunction.

Other factors that also play roles in the development of frailty syndrome include cell senescence.

57.2: Storyboards for Animation 3 (text not intended to be read).
Frailty Scene 3:

- Epigenetic changes such as methylation.
- Cell injury resulting in necrosis (citation).
- and cell injury resulting in necrosis (citations).
- Over time, these chronic multi-organ changes can lead to system failure.
- Muscle wasting, which is related to lower resting metabolic rate, less energy expenditure.
- Muscle wasting which is related to lower resting metabolic rate, less energy expenditure.
- And clinically apparent physical declines such as impaired balance.
- And slow walking speed.
- These combined molecular, physiological, and functional declines.
- Are predictive of common geriatric health outcomes such as falls, incontinence, and cognitive decline.

57.3: Storyboards for Animation 3 (text not intended to be read).
Dr. Lee discusses with Ernesto options for medical and therapeutic interventions such as physical therapy, nutritional counseling, medication screenings, and optimization through a comprehensive geriatric assessment. These interventions can decrease his vulnerability to other stressors in his life.

Frailty syndrome is a series of complex, multifactorial and non-linear interactions. Other determinants can include psychosocial factors such as loneliness, home environment or "lifespace", as well as comorbid conditions and life stressors.

Understanding and screening for frailty early on can adults.

58: Storyboards for Animation 4 (text not intended to be read).
Appendix C: Selected Stills

Animation 1: What is Frailty Syndrome?

Figure 59.1: Animation stills. Narrator: One of the biggest global healthcare challenges is the medical and economic burden of caring for older adults. dependence, disability, and death.

Figure 59.2: Animation stills. Narrator: In the US, healthcare for older patients accrues approximately 50 billion dollars per year in medical costs. However not everyone ages the same way and simply looking at an older person is not enough to determine their health or functional status.
Figure 59.3: Animation stills. Narrator: Frailty syndrome can affect upwards of 15% of the older adult population in the US.

Figure 59.4: Animation stills. Narrator: Substantial research has identified that certain individuals are especially vulnerable to poor health outcomes such as dependence, disability, and death.
Figure 59.5: Animation stills. Narrator: If you are a clinician or healthcare professional, you may have older patients that may benefit from frailty assessment.

Figure 59.6: Animation stills. Narrator: Frailty is a strong predictor of disability, falls, medication side effects, poor wound healing, hospitalization, institutionalization, surgery outcomes and mortality.
Figure 59.7: Animation stills. Narrator: Understanding your patient’s frailty status can provide crucial health information for their adequate care...

Figure 59.8: Animation stills. Narrator: ...and treatment planning.
Animation 2: What Does Frailty Syndrome Look Like?

Figure 60.1: Animation stills. Narration: Imagine an individual, Ernesto, 75 years old, with a history of hypertension and more recently, falls.

Figure 60.2: Animation stills. Narration: Ernesto visits his primary care practitioner Dr. Lee, and reports that he has experienced a couple of falls in the past six months.
Figure 60.3: Animation stills. Narration: Dr. Lee asks Ernesto a few more questions and finds out that Ernesto is increasingly exhausted and has little energy.

Figure 60.4: Animation stills. Narration: Concerned that Ernesto may be frail or becoming frail, Dr. Lee refers him to a geriatrics clinic for frailty assessment.
Figure 60.5: Animation stills. Narration: Concerned that Ernesto may be frail or becoming frail, Dr. Lee refers him to a geriatrics clinic for frailty assessment.

Figure 60.6: Animation stills. Narrator: Ernesto’s assessment shows that he meets two criteria for frailty based on these measures: slow walking speed and low grip strength. Having one or two frailty criteria characterizes him as pre-frail. A score of three or more out of five criteria would characterize him as frail.
Animation 3: Cellular & Molecular Changes in Frailty

Figure 61.1: Animation stills. Narrator: Ernesto’s pre-frail state may be the result of many factors.

Figure 61.2: Animation stills. Narrator: Over the past few months, a multisystemic buildup of chronic low grade inflammation...
Figure 61.3: Animation stills. Narrator: ...With an increase in cytokines IL-6 and TNF-alpha exhaust his cellular energy resources which impairs cell repair mechanisms, and is associated with an overall buildup of toxic byproducts in his body systems.

Figure 61.4: Animation stills. Narrator: With time, these energy demanding chronic changes could also lead to mitochondrial dysfunction.
Figure 61.5: Animation stills. Narrator: Other factors that also play roles in the development of frailty syndrome include cell senescence,...

Figure 61.6: Animation stills. Narrator:...epigenetic changes such as methylation,...
Figure 61.7: Animation stills. Narrator: ...and cell injury resulting in necrosis.

Figure 61.8: Animation stills. Narrator: Over time, these chronic multi-organ changes can lead to system failure, muscle wasting, which is related to lower resting metabolic rate, less energy expenditure, and clinically apparent physical declines such as impaired balance, low strength, and slow walking speed.
Figure 61.9: Animation stills. Narrator: These combined molecular, physiological, and functional declines are predictive of common geriatric health outcomes such as falls, incontinence, and cognitive decline (text not intended to be rerad).

Animation 4: How Does Frailty Affect Geriatric Health?

Stills for Animation 4 can be found at lohithakethu.com or through frailtymodule.abadirlab.org. The author may also be contacted regarding these files through www.hopkinsmedicine.org/medart.
Appendix D: Site Map

Figure 62: Site Map. Contains 4 animations and frailty module
Appendix E: Website Wireframes

Figure 63.10: Website Wireframes. Landing page for frailty module. The long buttons featured here direct the viewer to view each of the animations, learn frailty vocabulary, and access the interactive module.

Figure 63.20: Website Wireframes. The frailty module is prototyped here under the tab “Explore Phenotypes.” Each of the four phenotypes or characters is a case study on how frailty commonly presents in older adults.
Figure 63.30: Website Wireframes. When “View Frailty cycle” is clicked, a popup of a frailty cycle relevant to the particular phenotype will show how these physiological changes affect the individual’s

Figure 63.40: Website Wireframes. When “View Frailty cycle” is clicked, a popup of a frailty cycle relevant to the particular phenotype will show how these physiological changes affect the individual’s
Figure 63.50: Website Wireframes. When “View Frailty cycle” is clicked, a popup of a frailty cycle relevant to the particular phenotype will show how these physiological changes affect the individual’s
Figure 63.70: Website Wireframes. When “View Frailty cycle” is clicked, a popup of a frailty cycle relevant to the particular phenotype will show how these physiological changes affect the individual’s
Figure 63.90: Website Wireframes. The frailty module is prototyped here under the tab “Explore Phenotypes.” Each of the four phenotypes or characters is a case study on how frailty commonly presents in older adults.

Figure 63.91: Website Wireframes. The frailty module is prototyped here under the tab “Explore Phenotypes.” Each of the four phenotypes or characters is a case study on how frailty commonly presents in older adults.
Figure 63.92: Website Wireframes. The frailty module is prototyped here under the tab “Explore Phenotypes.” Each of the four phenotypes or characters is a case study on how frailty commonly presents in older adults.

Figure 63.93: Website Wireframes. The popup that is seen when the “Instructions” button is clicked.
VII. Cited References


Shaaron Ainsworth School of Psychology, Learning Sciences Research Institute, University of Nottingham, University Park, Nottingham, NG7 2RD, & UK. How do animations influence learning?


Varadhan, R., Walston, J., & Bandeen-Roche, K. (2018). Can a link be found between physical resilience and frailty in older adults by studying dynamical systems? Journal of the American Geriatrics Society,


General References


Lohitha Kethu was born in the city of Hyderabad, Andhra Pradesh, a southern state in India. She is a second year medical illustration graduate student at the Johns Hopkins University School of Medicine. Previously, she received a BFA in scientific and preparatory medical illustration with a minor in biology from the VCU School of the Arts. She was drawn to the profession through her own studies of biology, the stunning images she found in cell biology textbooks, and from a lifelong appreciation of medicine. With these interests, she completed internships at the Smithsonian Museum of Natural History and did freelance work for surgical textbooks, book chapters, cancer research presentations, and patent applications. Under the guidance of many incredible medical illustrators at Hopkins, she learned surgical illustration, segmentation and 3D modeling, and animation with an inclination towards cellular and molecular visualization and patient education. Throughout her education, Lohitha developed a love of graphic novels and children’s books and aims to infuse these styles into her patient education work. She hopes to soon publish her first graphic novel for children about type 1 diabetes, Jaci Has Diabetes. Her other research interests include patient education, cancer biology, basic science research, and molecular biology. Lohitha also hopes to infuse an understanding of ethnic, gender, and sexual diversity in all of the work she creates to further represent the multitude of communities that medicine serves. She will receive her Master’s degree in Medical and Biological Illustration in May, 2019.