Supporting Knee Joint Health to Promote Longevity and Wellbeing

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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STS Research Paper

Introduction

Health experts and physicians are constantly highlighting cancer, heart disease, obesity, mental health, and more recently, the threat of pandemics, as the leading healthcare challenges facing the world today. All certainly warrant significant research and discussion to develop effective treatments that promote public health. However, as healthcare spending in the United States continues to increase to exceedingly high levels as a result of countless complex inefficiencies, perhaps a large-scale shift in how healthcare is approached is long overdue (McCullough et al., 2020). Preventative approaches to medicine are far from new in modern healthcare, but they are often left neglected or at the very least underutilized. Instead, our healthcare system appears to prioritize the treatment of disease after is has arisen rather than the prevention of the disease from arising to begin with, as evidenced by the steady rise in the use of prescription medication in the United States over the last few decades. As of 2012, an astounding 39 percent of individuals over the age of 65 took more than 5 prescribed drugs – a statistic that has certainly only increased since then (Kantor et al., 2015).

The deterioration to knee health and mobility is a large-scale health issue that plagues countless Americans, and investing into the development of ways in which to slow or reverse knee health deterioration could reap significant public health benefits. Poor knee joint health lowers a patient's activity levels, leading to a host of other health problems. Most obvious, perhaps, is the vulnerability of such patients to obesity, but reductions in physical activity have even been shown to negatively impact mental health (Sharma et al., 2006). Current medical procedures and surgeries can promote good knee health, but the knee braces used for recovery introduce risks that limit the success of the surgeries themselves. My technical work has focused on designing a post-operation knee brace that minimizes these risks and allows for a more effective and physiologically mindful recovery.

Perhaps most importantly, this brace is custom-built for each patient – part of a larger push within the medical field to make care more personalized. Studies suggest that investment into personalized preventative healthcare results in "positive expenditure outcomes" within just 3 years for a majority of patients, meaning that although initial expenses might be greater than expenses for general care, in the long-term, patients and providers will spend less money on recurring health issues (Musich et al., 2016). Thus, personalized medicine constitutes just one promising way in which the longevity and overall well-being of patients can be maximized, and healthcare expenditures can be minimized.

Literature Review

Incidence and Economic Burden of Knee Pain

As a person ages, the knee joint accumulates natural wear-and-tear from everyday activities. Most significantly, the cartilage in the knee joint – which is responsible for the cushioning and facilitation of smooth contact between bones in the joint – can degrade. Without a proper layer of cartilage, the bones of the joint rub directly against one another, often causing pain that hampers one's ability to lead an active and healthy lifestyle (Clynes et al., 2019). This condition is known as knee osteoarthritis (OA), and it affects 19 percent of adults in the United States over the age of 45 years old (Wallace et al., 2017).

Other knee conditions are also common. Combined, total knee arthroplasty (TKA) and anterior cruciate ligament (ACL) reconstruction surgeries constitute nearly one million surgeries performed annually in the U.S. alone, and the demand for total knee replacement surgeries is projected to grow by 673 percent to nearly 3.5 million operations by 2030 (Hewett et al., 2010; Kurtz et al., 2007).

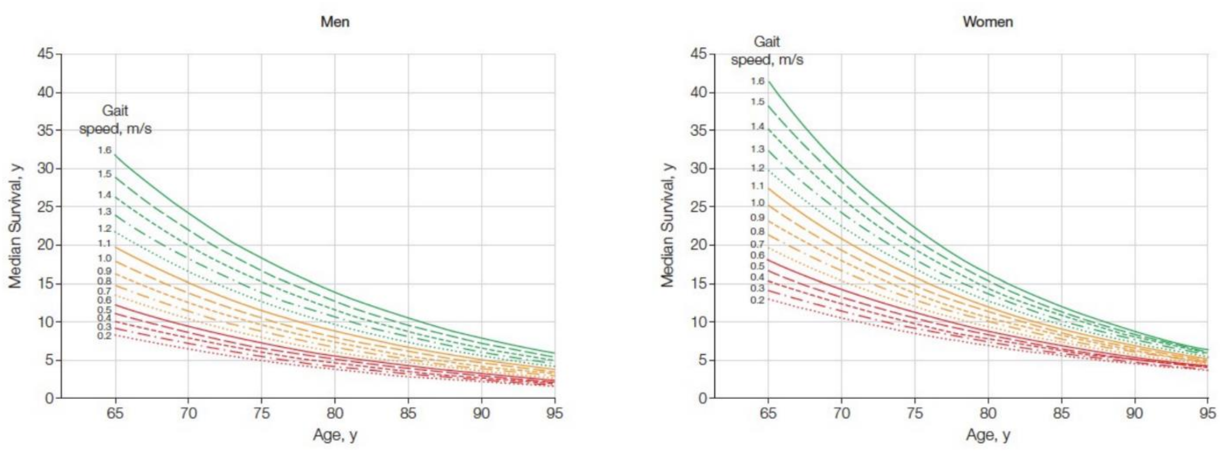
With so many individuals requiring treatment for chronic and acute knee pain and instability, it is no surprise that these conditions place a large economic burden on U.S. citizens. In fact, in 2013, spending on osteoarthritis treatments alone resulted in an average direct cost of 11,500 dollars per person, with spending reaching a total of 136 billion, of which 27 billion can be attributed to knee osteoarthritis specifically (*OA Prevalence and Burden*, n.d.). For reference, the U.S. GDP in 2013 was 16.84 trillion dollars, meaning that nearly 1 percent of the country's GDP came from spending on osteoarthritis treatment (*The World Bank | Data*, n.d.). Spending has continuously increased since 2013 and is projected to continue to increase in the future, so any means by which this economic burden might be eased would significantly benefit millions of people.

Longevity and Physical Activity

One of the most significant and far-reaching effects of osteoarthritis and other knee conditions is a marked loss in an individual's ability to maintain normal activity. Nearly half of all those with osteoarthritis report arthritis-attributable activity limitations (AAALs), which are defined as limitations to normal, daily activities, and by 2040, a projected 11.4 percent of adults will report AAALs (*OA Prevalence and Burden*, n.d.). The reduction in physical activity caused by OA leads to hypertension, depression, heart disease, diabetes, and a host of other aforementioned health issues, many of which are leading causes of death in the United States (Marshall et al., 2019). The progression that ultimately leads to the exhibition of these diseases should not be surprising, but it certainly warrants serious thought when considering how to best promote health and longevity.

The discovery of the link between physical activity and general health is not new. Extensive research into the benefits of an active lifestyle has proved what common sense holds to be true: active individuals are happier, healthier, and live longer than their more sedentary counterparts. Take walking speed, for example. A simple measurement that accounts for a wide variety of physical factors, including balance, strength, and coordination, walking speed unsurprisingly acts as one of the best indicators of longevity. In a study that looked at the walking speed, also known as gait speed, of over 34,000 individuals, gait speed was found to have a positive correlation to life expectancy in older adults (Studenski et al., 2011). In other words, an individual with a faster gait speed is predicted to live significantly longer than an individual with a slower walking speed (Figure 1).

Figure 1. Gait speed and median survival from 65 to 95 years old.



Faster gait speeds, in turn, are positively correlated with heightened physical activity. Taken as a whole, frequent physical activity increases longevity significantly: by up to 6.9 years according to some studies (Reimers et al., 2012). Furthermore, the risk of death is 30 to 35 percent lower in physically active individuals compared to inactive individuals, in part due to the lowered risk of developing conditions such as diabetes mellitus type 2, coronary heart disease, arterial hypertension, stroke, and cancer (Reimers et al., 2012).

Physical activity not only helps one live longer, but it also makes one live better too. Exercise has been shown to improve mental health by boosting self-efficacy and cognition, thereby reducing anxiety and depression (Sharma et al., 2006). Moreover, physical activity has been linked to increases in neuroplasticity, or the process of forming and remodeling new neural connections in the brain that boosts learning and improves mental health (Smith & Merwin, 2021). Exercise can even reduce the risk of dementia or slow its development in individuals who are already symptomatic (Ahlskog et al., 2011).

Preventative Care and Maximizing Healthcare Spending Value

According to CDC data, the leading causes of death in the United States are chronic conditions, including heart diseases, cancer, and stroke. Additionally, the prevalence of obesity has grown at an alarming rate over the past few decades – by 16.5 percent among all U.S. adults from 1988 to 2018 (*FastStats*, 2022). Pharmaceutical companies spend large sums of money to develop treatments for each of these diseases and conditions, but they often neglect the root issues that lead to their development. As a result, the burden falls on patients to pay for drugs that treat their symptoms – often a costly and repetitive cycle. For example, in 2017, adults in the United States spent an estimated $108.7 billion to treat heart disease alone (Muhuri, 2020). This figure could be significantly reduced if upstream factors that lead to heart disease were thoroughly researched and controlled.

The same holds true for health behavior-based diseases, such as obesity. Nearly 40 percent of all deaths in the United States can be attributed to such diseases, highlighting the need for preventative interventions to curb disease-causing behavior before the diseases themselves develop (Yong et al., 2010). In some calculations, large-scale use of various preventative medicine measures could save the United States up to $45 billion per year, while others contend that spending on the implementation of preventative treatments would match the costs associated with the diseases they are intended to reduce (Yong et al., 2010).

However, from an ethical perspective, perhaps simply reducing spending on healthcare is a misguided goal. Even if little to no savings came because of large-scale preventative medicine being adopted, the shift in spending would improve the overall health of the public, maximizing the value of each dollar spent on healthcare. Not only that, but projections that suggest a negligible sum of savings in the short-term ignore the inevitability of preventative medicine treatments becoming more refined, accurate, and cheap in the long-term.

Methodology

The goal of my research will be to investigate the burden that knee pain and instability places on the healthcare industry by increasing the prevalence of other diseases. I seek to understand the comorbidities associated with knee osteoarthritis and to draw preliminary conclusions that outline how significantly knee pain can influence longevity and long-term health. A successful study should provide a better and more complete understanding of the relationship between knee instability and immobility and life-threatening conditions such as heart disease and obesity.

Much research has been conducted surrounding osteoarthritis and related diseases, and since collecting personal health data from patients poses a substantial challenge with HIPAA regulations, I will collect information by conducting a thorough literature search using previously collected data, and I will analyze trends between the occurrences of different diseases.

Using these data, a correlation will be established and modeled that will provide clues about the importance of investing in new ways to promote knee joint health as a preventative measure.

Following my investigation into the relationship between knee pain and other diseases, I will begin to examine the current state of the art surrounding knee joint repair and maintenance, including surgical interventions, tissue engineering approaches, and bracing technology. I will compare these methodologies and outline the benefits and drawbacks of each. I will then give an outline of potential innovations that might emerge in coming years that might bring about significant improvement in the prevention of knee deterioration, and using the model developed earlier in my research, I will predict the effects that such an innovation will have on healthcare spending per capita and on the overall state of public health in the United States.

Much of the data will be qualitative because knee pain and instability are difficult metrics to quantify clinically. However, statistics surrounding the incidence of comorbidities on a large scale and the economic burden such comorbidities place on the public offer ways in which a societal effect might be quantified, and therefore modeled. A simple model could be used to assess the impact of technologies and methodologies on healthcare.

I predict that a significant coincidence will be present between chronic knee conditions and leading health concerns, including heart disease, obesity, and mental health. Furthermore, I expect that investments in personalized preventative care to promote knee joint health and stability will reduce healthcare spending by decreasing the incidence – and therefore the economic burden – of chronic conditions with comorbidities to knee osteoarthritis and other degenerative knee joint diseases.

Analysis

Chronic Knee Pain Comorbidities

As previously discussed, good knee health allows for exercise, and an active lifestyle helps delay or mitigate the risk of development for a host of diseases. So, when knee health deteriorates, either through chronic conditions such as osteoarthritis or acute injuries such as tendon or ligament tears, the risk of developing many diseases increases. Thus, when considering the impact that poor knee health has on society, comorbidities must also be considered.

Some of these diseases, with which a comorbidity with osteoarthritis is common include hypertension, depression, obesity, heart disease, chronic obstructive pulmonary disease (COPD) and cerebrovascular disease (Calders & Van Ginckel, 2018; Marshall et al., 2019; Swain et al., 2020). All have significant and far-reaching effects that not only further lower quality of life but can also lead to death, but five stand out in particular. In the analysis of hundreds of studies looking at comorbidities among populations with osteoarthritis, hypertension, obesity, depression, COPD, and diabetes have shown the greatest frequency of coincidence (see Table 1). Notably, hypertension has a comorbidity incidence with osteoarthritis of over 41 percent and obesity sits at just over 31 percent. Both are precursors to heart disease, which itself has a comorbidity incidence of 11 percent and is also the largest cause of death in the United States year after year (Calders & Van Ginckel, 2018; Marshall et al., 2019; Swain et al., 2020).

Comorbidity only indicates the frequency at which two or more diseases are present simultaneously rather than the order in which they arose, but a causal relationship can be inferred among many of the diseases listed. For example, it would be more reasonable to assume that the decrease in physical activity caused hypertension, depression, diabetes, and COPD rather than the reverse because the symptoms of these diseases would have negligible effect on the deterioration of the knee joint tissues. However, determining the causality between obesity and osteoarthritis is more difficult. A reduction in physical exercise could lead to obesity, but obesity is also one of the most significant risk factors for osteoarthritis (King et al., 2013). Indeed, one study found that obese individuals with a body mass index (BMI) greater than 30 kg/m^2 were nearly seven times more likely to develop osteoarthritis as individuals in a healthier weight range. The study also posited that if all individuals who were overweight or obese reduced their BMIs into a normal range, almost a quarter of all knee osteoarthritis surgeries could be avoided (Coggon et al., 2001).

Table 1. Comorbidities of various diseases with osteoarthritis (Calders & Van Ginckel, 2018; Marshall et al., 2019; Swain et al., 2020)

Comorbidity	Fraction of OA Patients with Comorbidity (%)
Hypertension	41.33
Depression	17.0
Obesity	31.9
Heart Disease (General)	11.0
Chronic Obstructive Pulmonary Disease	14.8
Diabetes	15.8
Congestive Heart Failure	5.6
Peripheral Vascular Disease	6.0
Myocardial Infarction	1.0
Cerebrovascular Disease	3.1

Developing a Model of the Comorbidity Network

As discussed, causality can be assumed for all the conditions in Table 1 aside from obesity, which presents a more complicated dynamic. It is more likely that obesity causes osteoarthritis rather than the reverse, so in developing a model to reflect the impact of chronic knee pain on the incidence of these diseases, measures must be taken to account for this unique relationship.

According to the CDC, obesity is defined as having a BMI greater than or equal to 30 kg/m^2 (CDC, 2022). Furthermore, Coggon et al. predicts that if all overweight and obese individuals reduced their BMI into a healthy range, 57.1 percent of osteoarthritis cases would be eliminated. (Coggon et al., 2001). Overweight individuals account for 47.1 percent of osteoarthritis comorbidities, whereas obese individuals account for 33.7 percent. By these statistics, and removing overweight individuals from consideration, 23.8 percent of osteoarthritis cases arise due to individual's being obese (Coggon et al., 2001). Therefore, if the total comorbidity between obesity and osteoarthritis is 31.9 percent, as shown in Table 1, then osteoarthritis causes obesity in the remaining 8.1 percent of comorbid cases (Calders & Van Ginckel, 2018; Marshall et al., 2019; Swain et al., 2020).

Values in Table 1 reflect the comorbidities of each disease with osteoarthritis wholly, not knee osteoarthritis specifically. Knee osteoarthritis accounts for 80 percent of all osteoarthritis cases, so rough estimates can be made regarding this specific comorbidity by multiplying each comorbidity value in Table 1 by 0.8 (Wallace et al., 2017). To avoid redundancy in the effect equation, it will be assumed that the comorbidities of myocardial infarctions and congestive heart failure are accounted for by the comorbidity between osteoarthritis and heart disease. Table 2 summarizes the adjusted comorbidities of these diseases to knee osteoarthritis as well as the adjusted obesity comorbidity frequency that accounts for the causality, and Figure 2 graphically demonstrates the causal relationships that will be used to generate a representative model for the larger effect of osteoarthritis on public health.

An equation can be developed from the relationships shown in Figure 2 that estimates the total burden knee osteoarthritis has on the United States population of 373 million individuals, noting the total incidence of knee osteoarthritis in the United States among all age groups is roughly 8.1 percent (CBO, 2023; Cui et al., 2020). Equation 1 below models this relationship.

Table 2. Adjusted comorbidities of various diseases with knee osteoarthritis (Calders & Van Ginckel, 2018; Marshall et al., 2019; Swain et al., 2020)

Comorbidity	Fraction of OA Patients with Comorbidity (%)
Hypertension	33.1
Depression	13.6
Obesity	6.5
Heart Disease (General)	8.8
Chronic Obstructive Pulmonary Disease	11.8
Diabetes	12.6
Peripheral Vascular Disease	4.8
Cerebrovascular Disease	2.5

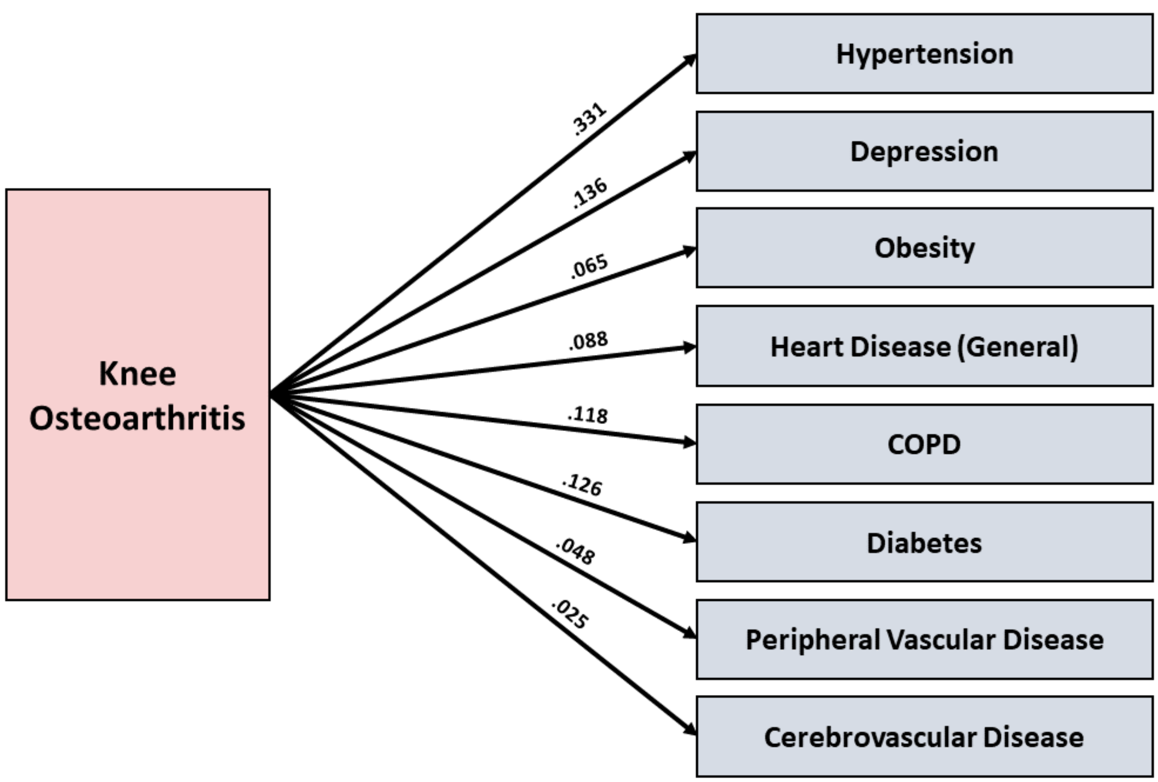


Figure 2. Comorbidity causality incidence probabilities.

$$\textbf{Equation 1}: \quad B = P_K\,[1 + I_T]$$

where B is the total burden, in number of individuals, $I_T = \{I_{Hypertension} + I_{Depression} + \cdots + I_{Cerebrovascular\ Disease}\}$ and is the total incidence of all comorbidities, and P_K is the total population with knee osteoarthritis

From Equation 1 and considering that P_K is 30.24 million and I_T is 0.99, the total burden of osteoarthritis is 60.17 million individuals, or about 16 percent of the population of the United States. Using the same equation: among individuals within the United States greater than or equal to 45 years of age, 37.8 percent are affected by the burden of knee osteoarthritis.

This equation has a limited scope, only accounting for 8 comorbidity metrics, and includes many assumptions that restrict its accuracy. The burden produced by Equation 1 is likely to be slightly higher than the true value of individuals affected by osteoarthritis because the equation fails to consider multiple iterations of causal morbidities. That is, the equation does not account for an individual who has multiple comorbidities, and rather includes each comorbidity present as a separate case. However, when considering the overall sum effect of the presence of each disease, perhaps treating the burden of each disease separately, even when present in the same individual, is a more accurate representation of the burden. Even with its limitations, the equation provides a useful estimate of the true public health burden inflicted by knee osteoarthritis. Analysis of the burden could also be taken a step further to analyze the deaths attributable to knee osteoarthritis and its effects.

State of the Art – Treating Knee Pain

Treating acute and chronic knee pain can be difficult given the unique properties of connective tissue often damaged in the knee joint. The current standard of care revolves around surgical interventions, tissue engineering approaches, and bracing technology, but none of these treatments have significant long-term success. Although most of this paper has been concerned with chronic knee pain and more specifically, osteoarthritis of the knee, many patients suffer from chronic knee pain because of their injury, even after repair or reconstruction. Thus, effective treatment of acute knee pain due to injuries would effectively reduce the risk of chronic knee pain in a patient and will therefore be examined in this section.

The most common injuries of the knee joint are to connective tissues within the joint. These include cartilage tissue, tendon tissue, and ligament tissue, and each has a unique structure and mechanical properties to support its function. Cartilage covers the ends of bones at the joint to lubricate contact movements and prevent bone degradation, and it is mostly comprised of a dense extracellular matrix (ECM) proteins and proteoglycan molecules (Horkay, 2012). Cartilage is also noticeably avascular and aneural, and there are very few cells within the tissue.

Ligaments connect bones to other bones, and they are also made up primarily of tightly packed ECM components, namely collagen I fibers. Both ligaments and tendons have tenocytes within their ECM, but tendon tissue is distinct in that the collagen fibers within the ECM are uniaxially aligned. This alignment creates unique viscoelastic properties that facilitate the storage of transfer of forces between muscles and bones – the primary function of tendons. Both tendons and ligaments are poorly vascularized and lack significant cellularization (Asahara et al., 2017).

The lack of vascularization and cellularization within connective tissues combined with the dense ECM makes it extremely difficult for the tissues to heal naturally on their own because transport of nutrients and resources necessary for tissue rebuilding and modeling is more difficult and even with adequate resources, there are few cells to initiate the healing process (Fenwick et al., 2002).

Currently, surgical interventions offer the best chance for a recovery of the function of damaged connective tissue, although reinjury and complications following surgery are both common, and often, full strength and function is not restored (Kim et al., 2020). Total knee arthroplasties (TKAs) are frequently performed to treat chronic conditions such as knee osteoarthritis, and significant strides have been made to improve the patient outcomes of these surgeries. However, surgery is both expensive and very invasive, and can be dangerous for elderly individuals or those with health complications.

Tissue engineering approaches address many of the concerns surrounding surgical interventions. These methods involve the development of an organic or synthetic scaffold, in which the cells, proteins, and nutrients required for effective healing are stored. The scaffold is then implanted either surgically or by way of injection into the damaged tissue. Although promising, there are significant challenges in trying to replicate the mechanical properties of connective tissue within the developed scaffold. Treatments must also contend with immune responses and ethical stem cell sourcing for tissue growth.

Finally, knee bracing technology offers a cheaper and more convenient option for managing knee pain. Limited mostly to reducing more mild pains, many knee braces can vastly reduce the rate at which connective tissue within the knee is damaged, and some can even reverse the damage entirely. In fact, many braces are so effective that they can reduce the need for surgery entirely (Mistry et al., 2018).

Bracing is also needed following surgeries to limit the incidence of complications and reinjury. However, current technologies are lacking. Current post-operative knee braces act only to immobilize or restrict the range of motion of the joint only, and subsequent braces need to be purchased during recovery. With complete, long-term joint immobilization also comes complications. Patients who have undergone TKA can lose up to 62 percent of their quadriceps strength due to the atrophy, and some patients have permanent physiological limitations to their knee's range of motion, a condition known as knee flexion contracture, as a result of the long-term immobilization of the joint (Anania et al., 2013; Mizner et al., 2005).

For our technical project, my team and I designed an adaptable post-operative knee brace that addresses all stages of the recovery process and allows a patient to gradually reload force into their knee. The brace will be custom fit to the patient in an effort to bring personalized medicine into the bracing technology field. The brace will also initially immobilize the joint completely, and then for later stages of the recovery will have an adjustable range of motion and adaptable force unloading at the joint. We believe that our brace will address the shortcomings of current technology by allowing the patient to exercise their mobility at all stages with assistance from the brace, thereby fostering a better recovery of the knee joint following intrusive knee surgeries.

Still, treatments to relieve knee pain are clearly lacking, as evidenced by the ever-growing number of individuals with knee osteoarthritis. As seen in the previous section, Equation 1 indicates that any reduction in the total number of patients with knee osteoarthritis will double in its influence by reducing the health burden of other comorbid diseases, but a reduction in the incidence of knee osteoarthritis is only possible if treatments or preventative care measures are significantly improved.

Conclusion

Knee pain and osteoarthritis affect millions of individuals across the world, and as life-expectancy rises, the prevalence of these conditions projects to increase too (Clynes et al., 2019). Poor knee health can result in a host of other diseases that affect longevity, from obesity and diabetes to depression and heart disease, and through these comorbidities, knee osteoarthritis has a burden of over 60 million individuals in the United States alone. Not only are millions of people affected, but tens of billions of dollars each year are spent in efforts to treat knee osteoarthritis, placing a substantial financial burden on patients and an economic burden on the country. Knee health supports an active and healthy lifestyle, which in turn promotes longevity and well-being. Therefore, investing in the development of new preventative measures to avoid the degradation of connective tissues within the knee is critical.

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