TARGETING DISEASE: MUSCULOSKELETAL CONDITIONS

Prepared for the Project

Focusing the Presidential Debates

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Much of the public debate about health care in America has focused on access to care. This is, of course, an important issue. But it is also important that we focus on basic research holding promise for cure or reduction in the burden of disease. This is particularly so for diseases where a substantial percentage of the US population is affected, where the total cost of the disease is high, where existing research funding has been relatively low, and where new biological and medical knowledge offers promise for reduction in the disease burden. Enhanced research in such settings offers promise for cost savings which are potentially an order of magnitude greater than the research costs. Further, greater success in cures or treatments would mean that millions of Americans would no longer be condemned to a lifetime of pain and disability.

Our Nation should consider whether individual groupings of diseases today meet criteria where substantially increased research funding could both return many times the costs, and increase the quality of life for millions of Americans. That is, are we at a point where more rapid advances in biological and medical knowledge suggest that the Nation should embrace a more robust approach to *Targeting Disease?* This paper will recommend that Musculoskeletal Conditions, including osteoarthritis and rheumatoid arthritis, which are the top causes of disability among US adults, should initiate such a national effort.

Musculoskeletal (MS) conditions are among the most disabling and costly conditions affecting the American population. They include a diverse group of disorders that affect the bones, joints, tendons, ligaments and muscles and encompass a broad spectrum of conditions, from those of acute onset and short duration related to injury and/or overuse to chronic disorders that include arthritis, bone diseases and low back and neck pain.

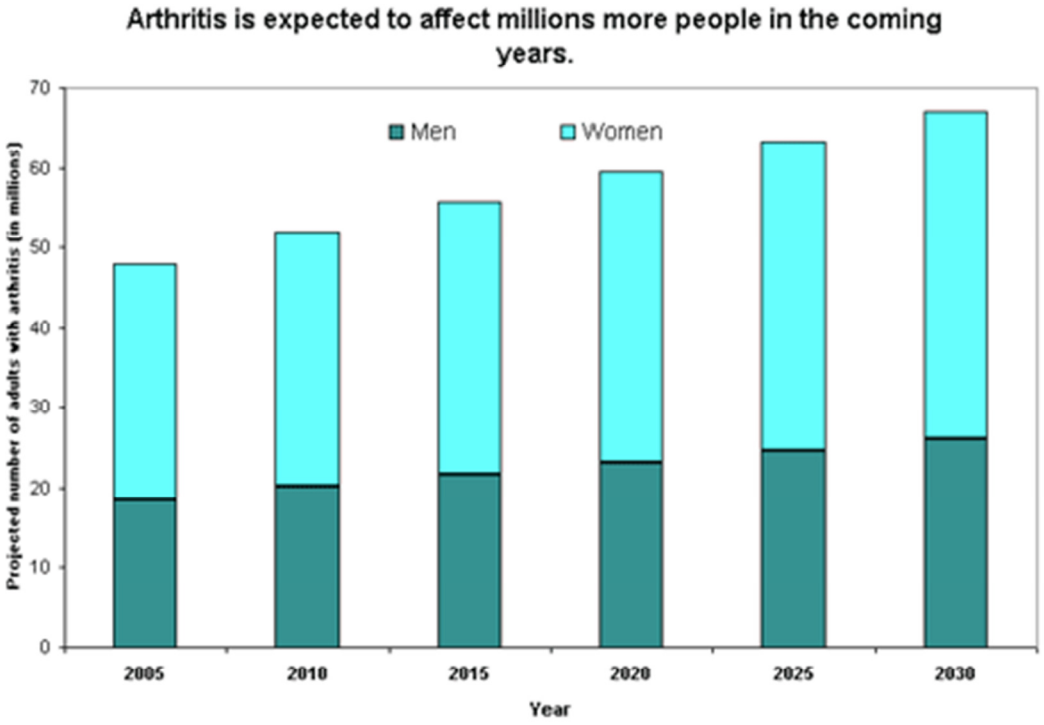
In the 1990s, the World Bank commissioned the first global burden of disease (GBD) study, which resulted in the assessment of disease burden for over 100 diseases and injuries, including musculoskeletal conditions (1-9). This study and a follow-up analysis completed in 2010 (GBD 2010) found that musculoskeletal conditions affected more than 1.7 billion people worldwide. Five major musculoskeletal conditions were studied in detail, including osteoarthritis (OA), rheumatoid arthritis (RA), gout, low back pain (LBP) and neck pain (NP). Data

from other musculoskeletal disorders including autoimmune and inflammatory rheumatic diseases such as systemic lupus erythematosus, psoriatic arthritis, ankylosing spondylitis and juvenile inflammatory arthritis were also captured. Globally, all musculoskeletal disorders accounted for 21.3% of the total years lived with disability (YLDs), which was second to mental and behavioral problems (23.2%) (1,9).

In North America, musculoskeletal conditions are responsible for more functional limitations than any other group of disorders and are the major cause of years lived with disability. Data from a representative study in Canada revealed that musculoskeletal conditions accounted for close to 40% of all chronic conditions and 54% of all long-term disability, and 24% of all restricted activity days (10). Importantly, the pain and physical disability associated with musculoskeletal conditions affects social functioning and mental health, further compromising an individuals' quality of life.

In 2010-2012 the CDC analyzed data from the National Health Interview Survey (NHIS), which revealed that 52.5 million (22.7%) of adults aged ≥18 years had self-reported doctor-diagnosed joint symptoms, and 22.7 million (9.8%, or 43.2% of those with arthritis) reported arthritis-attributable activity limitation (AAAL) (11). With the aging of the US population, the prevalence of arthritis is expected to increase so that by the year 2030, an estimated 67 million adults aged 18 years and older will have doctor-diagnosed arthritis. **Figure 1** shows that by 2030, an estimated 25 million adults (37% of adults with arthritis or 9.3% of all US adults) will report arthritis-attributable activity limitations. These estimates may be conservative, as they do not account for the current trends in obesity, which may contribute to future cases of arthritis.

Figure 1. Estimated number of adults with arthritis
http://www.cdc.gov/arthritis/data_statistics/national-statistics.html



Osteoarthritis (OA) is by far the most common form of arthritis and accounts for a majority of the patient and physician reported cases of arthritis (11). OA is characterized by loss of joint cartilage and alterations in adjacent weight bearing bone tissues that leads to loss of function and progressive disability. Pain is the most prominent symptom in most people with OA (12), and is the most important determinant of disability (13). OA most commonly affects the knees, hips and hands, although all joints can be affected. Close to 10% of men and 18% of women aged >60 years are affected by OA. Age is the strongest predictor of the development and progression of OA, and the predicted increase in life expectancy in this country will result in greater numbers of individuals at risk. The ability to replace joints destroyed by the osteoarthritic process has revolutionized the treatment of patients with end-stage OA, but the projected increase in the number of individuals undergoing joint replacement will place an increasing financial burden on the healthcare system in this country and there is a need for interventions that can slow or even halt the progression of OA.

Rheumatoid arthritis (RA) and gout are inflammatory conditions that characteristically affect multiple joints, leading to acute and chronic inflammation and deformity (2,7). Major research discoveries and the development of new and effective therapeutic agents have dramatically improved the outcomes in patients with RA (14-16). However, even with these new therapeutic advances, over one third of individuals with RA continue to experience symptoms and progressive loss of joint function (16). Similar advances in the development of drug therapies hold the promise of reducing the disease burden of gout, but despite these

advances, the incidence of gout and associated joint disease is increasing in the general population (7,17).

Osteoporosis, is a systemic skeletal disorder that is characterized by low bone mass and deterioration in bone structure and strength. It is a major risk factor for fractures of the hip, spine, and distal forearm (6). Hip fractures are particularly debilitating and may be associated with close to 20% mortality and 50% permanent loss in function (18). Research in the field of bone diseases has led to the development of multiple drug therapies that can improve bone health and substantially reduce the risk of fracture and disability (19,20). The present therapies have been shown to reduce the rate of bone loss but additional so called anabolic therapies are needed to increase bone mass in individuals who present with fractures and reduced bone mass (20).

Low back and neck pain are the final categories analyzed in the GBD 2010 study (4,5,18). They are the most prevalent of the musculoskeletal conditions, affecting nearly all individuals at some point in their lives and about 4–33% of the population at any given point. Most episodes of low back pain resolve or improve within several weeks, but recurrences are common with further acute episodes affecting 20–44% of working individuals within one year and a lifetime recurrence rate of up to 85%. Low back pain is associated with age, physical fitness, smoking, obesity, and strength of back and abdominal muscles. Occupational factors such as heavy lifting, bending, and twisting are additional risk factors (21,22).

The rate of musculoskeletal conditions is 76% greater than that of chronic circulatory conditions, which include coronary disease and heart conditions, and nearly twice that of all chronic respiratory conditions (11, 23). On an age-adjusted basis, musculoskeletal conditions are reported by 54 persons per every 100 in the population. This compares to a rate of 31 and 28 persons per every 100 in the population for circulatory and respiratory conditions, respectively. These incidence rates are reflected in the impact of the conditions on disability as shown in **figure 2** (23).

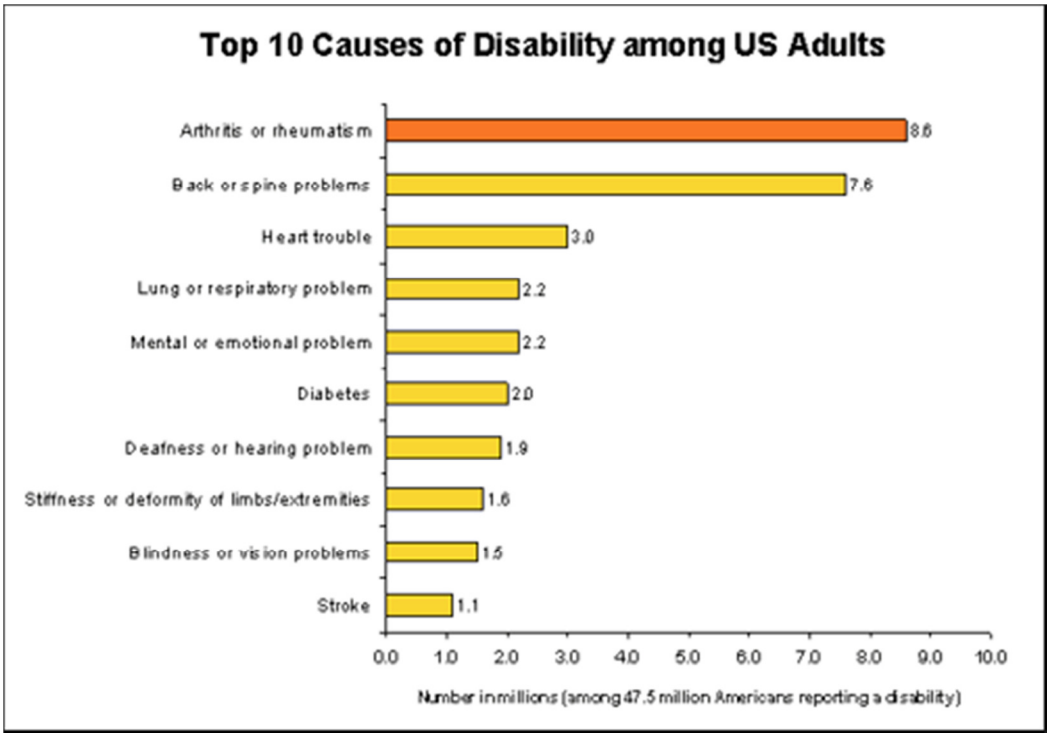


Figure 2. Top 10 Causes of Disability Among US Adults, 2005 (ref. 11, 23)

In the US in 2012, twenty eight million individuals with a musculoskeletal condition between the ages of 18 and 64, reported lost work days in the previous 12 months, totaling more than 216 million days. On average, workers lost nearly 8 days in a 12-month period. This accounts for more than four times as many lost work days as depression, which is the second most common condition associated with lost work days. Chronic circulatory conditions, including high blood pressure and other cardiovascular conditions, accounted for 32.3 million lost work days. Chronic respiratory conditions accounted for 16.5 million lost work days. The impact of musculoskeletal injuries and conditions compared to other major illnesses and disorders is in **Figure 3.**

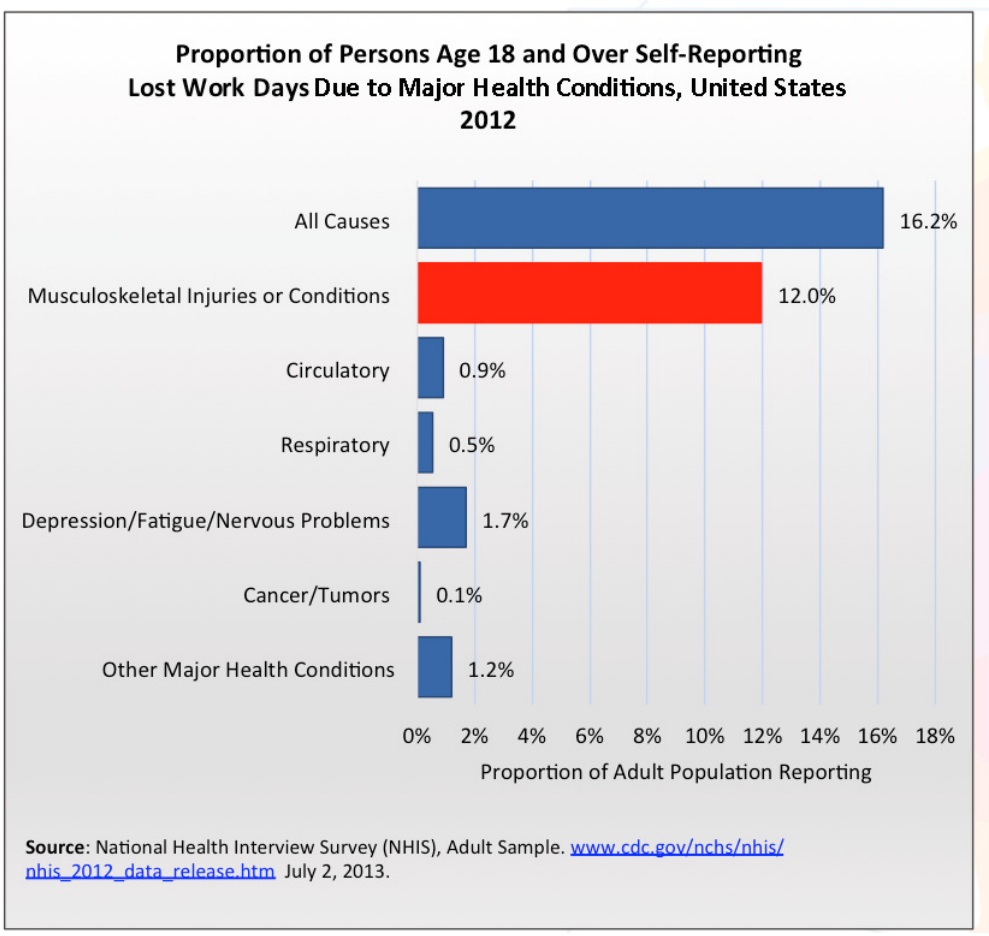


Figure 3. Proportion of Lost Work Days due to Major Health Conditions

The annual average proportion of the US population with a musculoskeletal condition requiring medical care now constitutes more than 33% of the population (24). This is an overall rate of increase of 19%. The majority of the growth is in the 45 to 64-year age bracket. The annual estimated direct and indirect cost attributable to persons with a musculoskeletal disease is $213 billion (24). Taking into account all costs for persons with a musculoskeletal disease including other comorbid conditions, the cost of treating these individuals and the direct cost to society is currently estimated to be nearly $874 billion, or 5.73% percent of the U.S. gross national product (24).

In spite of the widespread prevalence of musculoskeletal conditions, they are not among the top ten health conditions receiving research funding (25). In part, this is attributable to the low mortality from musculoskeletal conditions in comparison with other health conditions. However, because musculoskeletal conditions restrict activities of daily living, cause lost work days, and are a source of lifelong pain, the morbidity and cost to society of musculoskeletal conditions is tremendous.

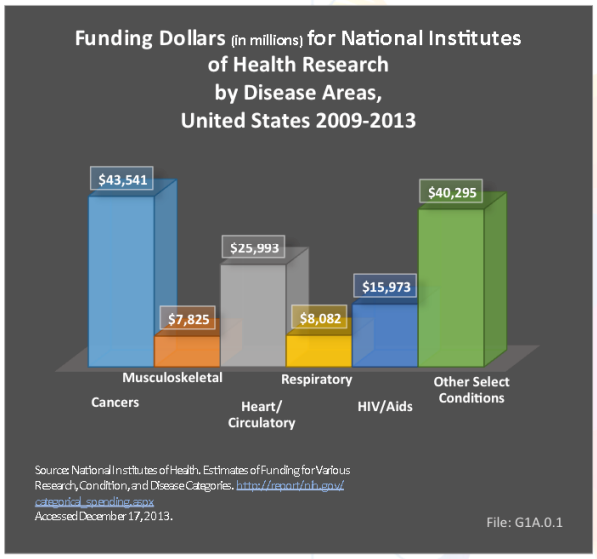
Despite the enormous financial and personal impact of musculoskeletal conditions, research funding to alleviate these major health conditions remains substantially below that of other major health conditions such as cancer, respiratory and cardiovascular diseases. The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) was formed in 1987 and is the principle NIH Institute that provides extramural financial support for musculoskeletal research. Research funding for musculoskeletal conditions has declined in relative terms, so that presently less than 2% of the annual NIH budget is appropriated to musculoskeletal disease research. Over the last five years (2009 to 2013), funding for musculoskeletal research from the NIH totaled $7.8 billion, while that of cancers and heart/circulatory disorders totaled $43.5 billion and $25.9 billion, respectively. **Figure 4** illustrates the relative distribution of funding for several major disease categories including musculoskeletal diseases.

Figure 4. Distribution of NIH Research Support for Major Diseases

Research Funding to NIAMS*

$7.8 billion = Total research funding for years 2009 to 2013.

- Less than 2% of annual National Institutes of Health (NIH) research budget allocated to NIAMS
- Annual average share of funding declining since 2000
- In spite of prevalence and high morbidity, musculoskeletal diseases research dollars a fraction of allocations for other common conditions



*National Institute of Arthritis and Musculoskeletal and Skin Diseases

In March 2002, President George W. Bush proclaimed the years 2002–2011 as the United States Bone and Joint Decade, providing national recognition to the fact that musculoskeletal disorders and diseases are the leading cause of physical disability in this country. At the end of the decade, the United States Bone and Joint Initiative (USBJI), a part of the Global Alliance for Musculoskeletal Health, was created. The goal of USBJI is to improve the quality of life for people with musculoskeletal conditions and to advance understanding and treatment of these conditions through research, prevention, and education.

The USBJI, conducted a strategic planning process that solicited input from a panel of experts in the fields of musculoskeletal research, education and care to set priorities ‘‘beyond the decade.’’ This was accomplished by six task groups (Arthritis, Bone Health and Osteoporosis, Pediatric Musculoskeletal Conditions, Spinal Disorders and Low Back Pain, Trauma and Injury, and Research). It is beyond the scope of this review to provide a detailed description of the recommendations of the task force, which were recently published (26), and therefore, only the key points of the recommendations will be highlighted:

Priority Area 1.2: Education of Policy Makers (Government and Non-Government)
Policy makers need to be made aware of the personal and financial impact of musculoskeletal conditions and Federal funding for arthritis-related public health initiatives, as well as for professional training, research, and health-care systems. for arthritis care, should be substantially increased.

Priority Area 1.5: Research
Given the enormous impact of musculoskeletal disorders on individuals and society, funding for arthritis-related research needs to substantially increase across the full spectrum of basic, translational and clinical research, including epidemiology, outcomes, and comparative effectiveness of arthritis treatments.

Priority Area 4.2: Establishment of Infrastructure for Multidisciplinary Collaboration on Research and Education
There are large gaps in our knowledge of the causes of many spinal disorders and low back pain. Multidisciplinary evidence-based guidelines for diagnosis and treatment need to be established and research involving partnership with industry, public health organizations, and government need to be expanded.

Priority Area 6.1: Basic Research
Musculoskeletal conditions are under-researched relative to the burden of disease and the discrepancy between research funding and the prevalence of disease impairs progress in reducing the burden of musculoskeletal disease. The primary goal should be to increase the quantity, quality, and relevance of musculoskeletal research. A secondary goal should be to foster translation of basic results into new prevention measures, risk assessment tools, and therapies.

Priority Area 6.2: Comparative Effectiveness Research
One mechanism to facilitate translation of research to clinical practice is through comparative effectiveness studies that provide data on how to choose among therapeutic strategies. There is a need to define identify and prioritize research needs such as evaluation of treatments for osteoporosis and osteoarthritis, that can allow investigators to assess differences in effectiveness of treatments.

Priority Area 6.3: Clinical Research and Innovative Trial Designs

There is a need for more innovative clinical trial designs than randomized controlled trials, which can be prohibitive because of difficulty attaining an appropriate sample size and because of cost. There is a need to foster more collaborative public private partnerships to allow for the breadth and depth of expertise necessary to design, implement, and analyze clinical data and to provide greater financial support for important trials.

Summary and conclusion

Musculoskeletal disorders are the major cause of disability in the United States. Given the enormous impact of musculoskeletal disorders on individuals and society, there is a urgent need to substantially increase Federal funding and non-governmental support for arthritis-related public health initiatives, as well as for professional training, research, and optimization of health-care systems. Research funding for musculoskeletal research needs to be increased across the full spectrum of basic, translational and clinical research, and the discoveries and findings translated into new prevention measures, risk assessment tools, and therapies. Research discoveries have profoundly altered and improved the natural history of many musculoskeletal disorders, including for example the development of effective biological and small molecule therapies for rheumatoid arthritis and identification and testing of new drugs for the treatment of osteoporosis. These discoveries highlight the impact that research can have on improving the lives and outcomes of individuals suffering from the disabling effects of musculoskeletal disorders and should stimulate and incent policy makers to allocate more resources to address the unmet needs for these conditions.

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