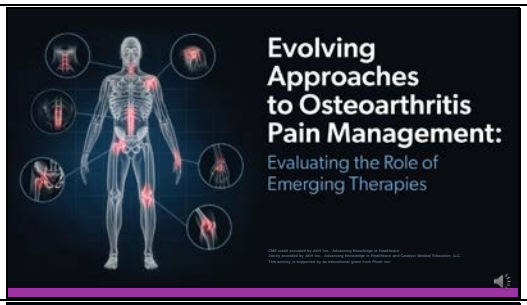
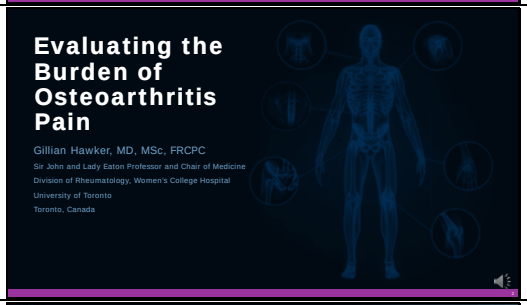
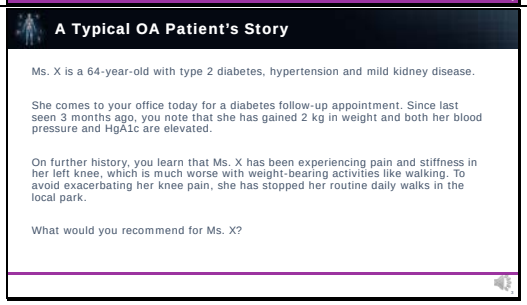
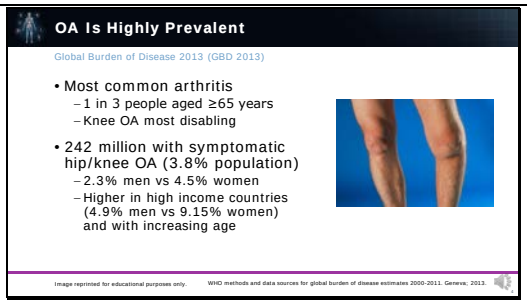
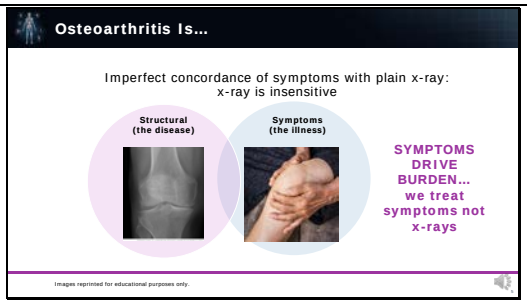
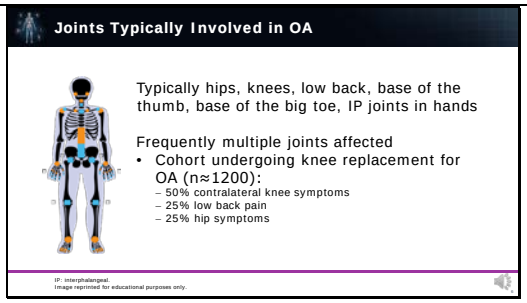
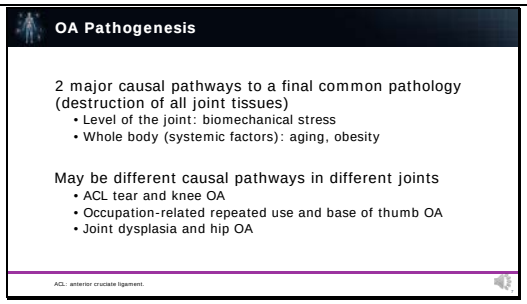
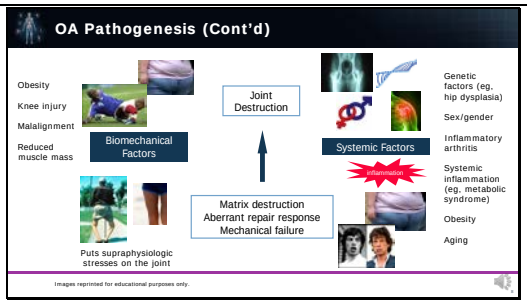
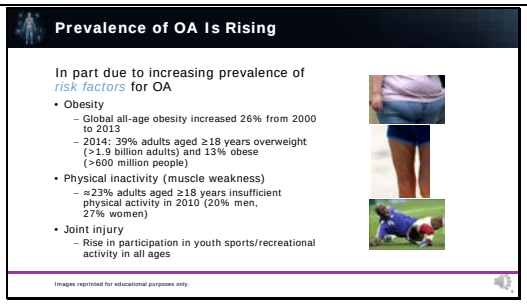
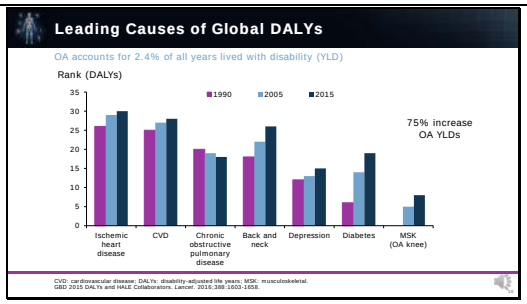
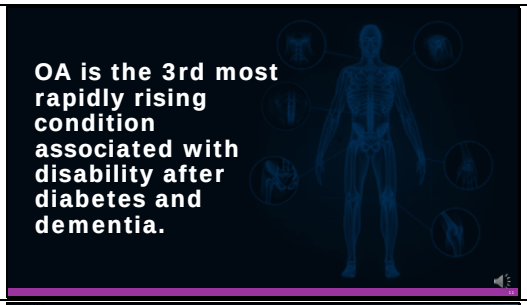
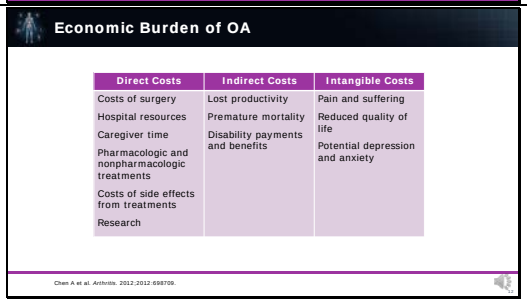
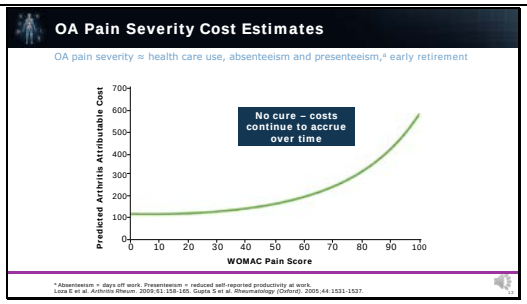
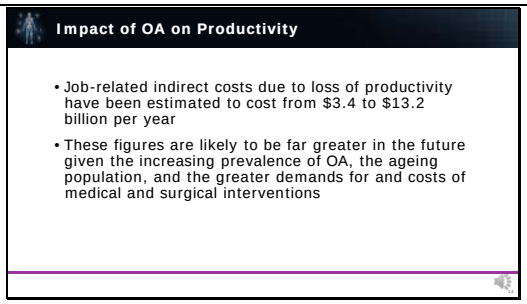
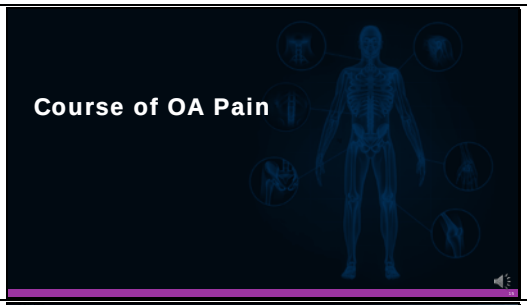
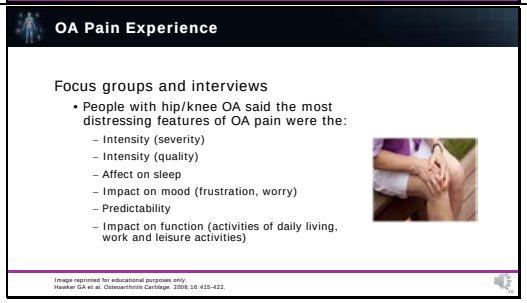
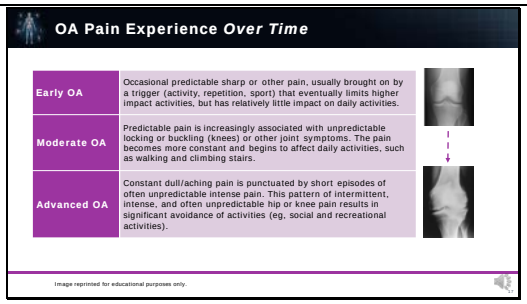
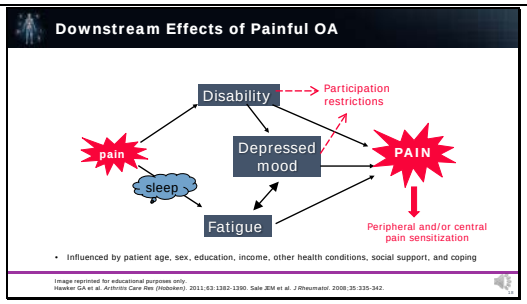
1		
2		My name is Gillian Hawker. I'm a rheumatologist and professor of medicine at the University of Toronto.
3		We hope these modules will help you with the management of people with osteoarthritis. So let's start with a typical case history. Ms. X is a 64-year-old woman with type 2 diabetes, hypertension, and mild kidney disease. She comes to your office today for a diabetes follow up. Since last seen 3 months ago, you note that she has gained 2 kilograms in weight and both her blood pressure and hemoglobin A1c are elevated. On further history, you learn that Ms. X has been experiencing pain and stiffness in her left knee, which is much worse with weight-bearing activities like walking. To avoid exacerbating her knee pain, she's given up her routine daily walks in the local park. What would you recommend for Ms. X? As we go through this module, we hope to give you the tools and resources to answer that question.
4		I think we all know that osteoarthritis is highly prevalent. It's the most common arthritis, affecting approximately one in three individuals, 65 years of age or older. And when it affects the knee, it is most likely to cause disability. From the Global Burden of Disease Study in 2013, close to four percent of the worldwide population was estimated to have symptomatic hip or knee osteoarthritis. Roughly twice as many women or men are affected. And the prevalence is higher in high income countries and with increasing age.

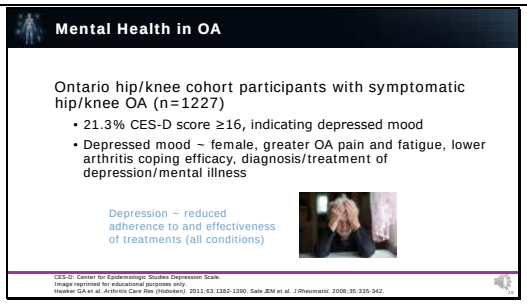
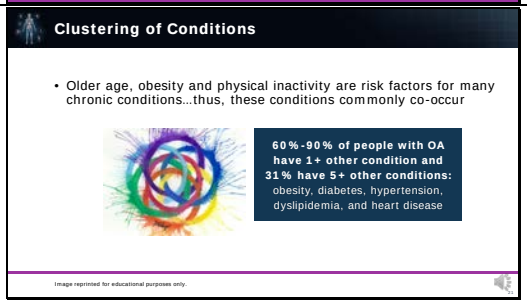
5		Unlike inflammatory arthritis, there is an imperfect relationship between the symptoms experienced by people with osteoarthritis and what is seen on plain x-ray. X-ray is insensitive, which means that people with early osteoarthritis may have substantial symptoms associated with their osteoarthritis in the presence of a normal x-ray. But we know that its symptoms, pain presents principally, which drive healthcare use and health-seeking behavior, and which cause the burden of illness in the population. We treat symptoms, not x-rays. And for the remainder of this talk, I will be talking about symptomatic osteoarthritis.
6		The joints typically involved in osteoarthritis are the hips, knees, low back, base of the thumb, base of the big toe, and the interphalangeal joints of the hands, as shown in blue on this homunculus. But frequently, multiple joints are involved. In a recent cohort of people with knee osteoarthritis undergoing knee replacement, 50 percent complained of symptoms of OA in the other knee, 25 percent in the low back, and 25 percent in one or both of their hips.
7		We now understand that there are two major causal pathways which lead to a final common pathology, which we see as, and characterize as, osteoarthritis. One at the level of the local joint related to biomechanical stress, and the second due to whole body or systemic factors, like aging or obesity, which I'll talk about a little bit more. What makes osteoarthritis much more complicated than perhaps other conditions, is that there may be different causal pathways operating in different joints at the same time.

8		On the left we see several of the biomechanical factors that are associated with increased risk for osteoarthritis. These factors include obesity, knee-related injury, malalignment, and reduced muscle mass, which is often due to physical inactivity. Each of these puts a supraphysiologic stress on the joint, increasing the risk for OA. On the right hand side, we have systemic factors, which include genetic background, sex, the final common pathway of inflammatory arthritis, the effects of aging, and inflammation associated with metabolic syndrome or morbid obesity. Together, these factors result in matrix destruction, an aberrant repair process, which is unsuccessful, and ultimately leads to mechanical failure and joint destruction.
9		The prevalence of osteoarthritis is on the rise. This is in part due to the increasing prevalence of three risk factors, obesity, muscle weakness, and joint injury. Between 2000 and 2013, the global prevalence of obesity increased 26 percent. In 2014, almost 40 percent of adults were overweight, and 13 percent obese. Physical inactivity, causing muscle weakness, has been found in about 23 percent of adults 18 and over in 2010, disproportionately higher numbers in women than men. And finally, joint injury is also rising in incidence due to increased participation in youth sports and recreational activities across all ages, particularly individuals who are less fit and more likely to experience injury.

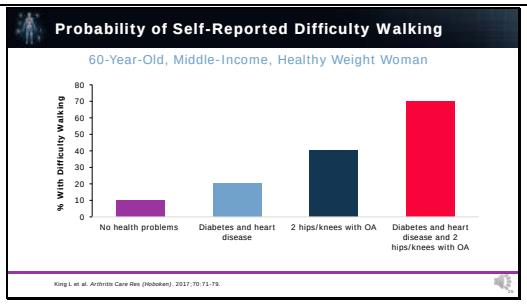
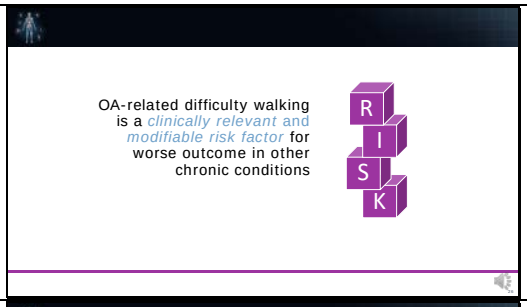
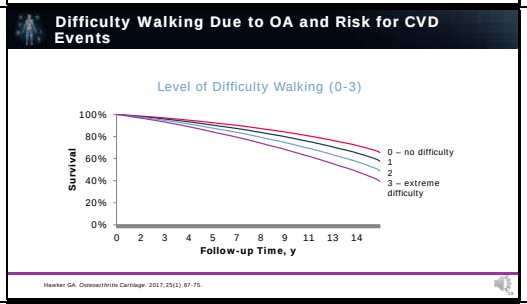
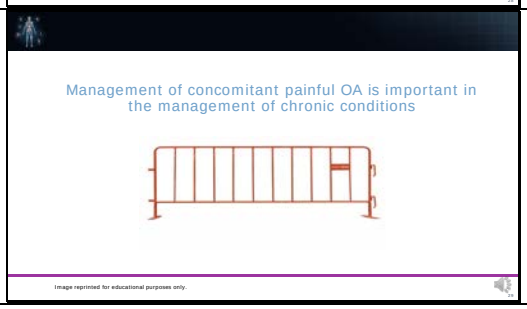
10		Osteoarthritis is one of the leading causes, globally, of disability-adjusted life years. That is, years of life lived with a disabling condition. OA, over all accounts, for about two and a half percent of all years lived with disability. What's important, however, is that while the overall prevalence of contributions to years lived with disability are greater for cardiovascular disease, this slide shows, from the Global Burden of Disease, the back and neck complaints, diabetes, and musculoskeletal disease, in particular osteoarthritis of the knee, are on the exponential rise, in terms of the prevalence of, or contribution to years lived with disability. And, in fact, it's been estimated that there has been a 75 percent increase in years lived with disability, attributable to OA, particularly knee OA, between 1990 and 2015.
11		As a result, osteoarthritis is currently the third most rapidly rising condition associated with disability after diabetes and dementia.
12		The economic burden of osteoarthritis is incredibly large. It's characterized by costs that are direct healthcare costs to the healthcare system, including the costs of surgery and other hospital resources, caregiver time, both drug and nondrug therapies that are covered byt the healthcare system or insurance, the costs of managing side effects from treatments, such as gastrointestinal bleeds from anti-inflammatory drugs, and the costs for research invested in osteoarthritis prevention and treatment. But there are also substantial indirect costs due to osteoarthritis. These include lost ability to work or work productively, so lost productivity, premature mortality or shortened lifespan, and the costs of disability and loss of benefits as a result of being unable to work.

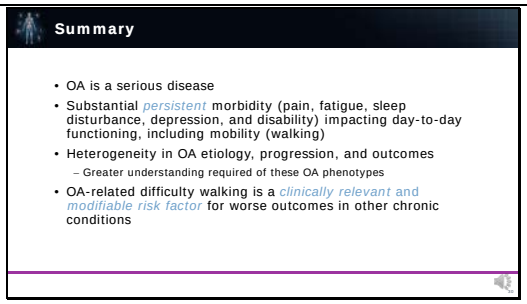
		But there are also intangible costs at the level of the individual experiencing this condition. These include pain and suffering over long periods of time that reduce their quality of life, and put them at increased risk for depression and anxiety.
13		There is a close relationship between osteoarthritis pain and the costs and burden to society. On the x-axis here we show the WOMAC Pain Score, or level of pain with activity from zero to 100, where 100 indicates the worst possible pain. On the y-axis, we see predictable arthritis attributable costs, which include healthcare costs, costs due to lost productivity, and early retirement. With an exponential relationship showing that, with increased pain come increased burden. As there's no cure for osteoarthritis, the costs continue to accrue over many, many years.
14		The impact of osteoarthritis on work-related productivity is enormous. Job-related indirect costs due to loss of productivity have been estimated at $3 ½ to $13 billion dollars per year. And these figures are likely to be far greater in the future, given the increasing prevalence of OA, the aging population, and the greater demands for, and costs of, both medical and surgical interventions.
15		Let’s talk a little bit about the course of osteoarthritis pain.
16		From focus groups and interviews of people with hip and knee osteoarthritis, we've learned that the most distressing features of living with OA pain are the severity or intensity of the pain, the quality of the pain, such as whether or not it causes pins and needles, or is burning, or radiates. The effect of the pain on sleep and mood, its predictability, and its impact on function, including ability to perform activities of daily living, to work, and to engage in leisure or recreational activities.

17		Qualitative research has enabled us to understand the osteoarthritis pain experience from the perspective of people with hip and knee OA, as it progresses over time. Early OA is characterized by occasional, predictable, sharp or other pain, usually brought on by a trigger, in particular an activity or sport, or repetitive use of the joint. This type of pain eventually limits high impact activities but has relatively little impact on day to day activities. As the disease progresses, moderate OA is characterized by predictable pain increasingly associated with unpredictable locking or buckling of the knees in some patients, or other symptoms. The pain becomes more constant and starts to affect daily activities, such as walking and climbing stairs. Advanced OA pain is characterized by constant dull or aching pain, punctuated by short episodes of often unpredictable intense pain. This pattern of intermittent, intense, and often unpredictable hip or knee pain results in significant avoidance of activities, including both social and recreational activities. When these patterns of pain have been correlated with changes on x-ray, we see the early OA progression to stage or grade 3 Kellgren/Lawrence OA is characterized by these changes in pain symptoms.
18		Longitudinal studies have shown that there's a causal relationship between pain and fatigue and pain and disability. When people are experiencing osteoarthritis pain, which is generally worse with joint use, they tend to give up doing those activities, in order to avoid experiencing the pain, leading to disability. Pain also interrupts sleep, which contributes further to fatigue. The combination of disability and fatigue are causally related to a higher prevalence of depressed mood in people with a chronic OA pain. Depressed mood and disability result in participation restrictions, and in particular, an

		effect on the ability to walk, which affects independence and mobility. Depressed mood, in combination with disability and fatigue, lead to an exacerbation of pain. And over time, this predisposes to changes in the peripheral and central pain pathways, which cause a syndrome called pain sensitization and widespread pain. This downstream pathway is influenced by patients' sociodemographic factors, comorbidity, social support, and coping.
19		As previously noted, osteoarthritis pain is causally related to depressed mood. In multiple cohorts, including ours, approximately 21 to 25 percent of individuals living with chronic hip or knee osteoarthritis pain, have depressed mood. Depressed mood is associated with female sex, greater pain and fatigue, lower arthritis coping efficacy, and a prior diagnosis of a mental health disorder. This is particularly concerning, as in all conditions, depression is associated with reduced adherence to, and lower effectiveness of treatments.
20		
21		Older age, obesity, and physical inactivity are risk factors for many chronic conditions, and thus these conditions commonly co-occur. We now know that 60 to 90 percent of people with osteoarthritis have at least one other chronic condition, and 31 percent, or close to a third, have five or more conditions. Due to the risk factors, obesity and physical inactivity, the most common comorbid conditions in OA are obesity, diabetes, hypertension, dyslipidemia, and heart disease.

22	**OA Is Underdiagnosed and Undertreated, Especially in Setting of *other* Conditions** • Competing demands/priorities • Beliefs about OA as "normal aging" with no effective treatment • Physician uncertainty about diagnosis and treatment of OA – Contraindications to OA therapies (eg, NSAIDs) – Lack of awareness of safe OA treatment options  NSAID: nonsteroidal anti-inflammatory drug. Images reprinted for educational purposes only.	The problem with the high prevalence of comorbidity in people with OA is that osteoarthritis tends to be under-diagnosed and under-treated in the setting of other conditions. This is partly due to competing demands or priorities, both from the perspective of the patient and the healthcare provider. Societal beliefs about OA is normal aging, with no effective treatment. And physician uncertainty about the diagnosis and treatment of OA, particularly in the setting of comorbidities, which might present contraindications to therapies, or lack of awareness of how safely to manage OA in the setting, for instance, of renal disease or heart disease.
23	**People With OA Avoid Activities That Exacerbate Their Symptoms** Qualitative studies: • Not offered other options • Desire to avoid "risky" pain killers • Other conditions prioritized as more important (patients, family, doctors) Physical activity plays a pivotal role in chronic disease management  Image reprinted for educational purposes only. Sale JEM et al. *Arthritis Rheum.* 2006;55:272-278. Cheraghi-Sohi S et al. *Arthritis Care Res (Hoboken).* 2013;65:920-927.	From qualitative studies, we know that people with osteoarthritis often are left with avoidance of activities that exacerbate their symptoms as their best management approach. This is the result of not being offered other therapies, possibly because of comorbid conditions, their own personal desire, or that of their physician to avoid risky painkillers, and the fact that they've prioritized other conditions like their diabetes or heart disease as more important. This is a problem, however, as physical activity plays a pivotal role in chronic disease management. And sedentary behavior, which may result from lack of use of joints because they're painful, may be a barrier to physical activity.
24	**Physical Activity** Core element of *all* chronic disease programs • In OA – Pain, function, joint load, stiffness, muscle weakness, depressed mood, and balance • In cardiometabolic diseases (diabetes, CVD, hypertension, obesity) – Lipid metabolism and lipid levels – Glucose control (HbA1c) – Systemic inflammation  Image reprinted for educational purposes only.	Physical activity is core to all chronic disease programs. In osteoarthritis, physical activity has been shown to improve pain, function, reduce joint load and stiffness, improve muscle strength, improve mood, and balance. In cardiometabolic diseases, in addition to these benefits, there is an improvement in lipid metabolism and lipid levels, glucose control, and reduction in systemic inflammation.

25		Under-treated osteoarthritis pain is the number one cause of walking-related difficulty. What's seen here is the probability that a 60-year-old, middle-income, healthy weight women—woman will experience difficulty walking. With no health problems, her likelihood is 10 percent. With diabetes and heart disease it's 20 percent. With two hips or knees affected by symptomatic OA, it's 40 percent. And if she has diabetes, heart disease, and osteoarthritis, the likelihood is 70 percent.
26		Thus, we believe that osteoarthritis-related difficulty walking is a clinically relevant and modifiable risk factor for worse outcome in other chronic conditions.
27		A number of studies have therefore looked at the relationship between OA-related physical inactivity or difficulty walking, and the risk for cardiovascular events and diabetes complications.
28		This study, and others, have shown that baseline level of difficulty walking is associated with subsequent risk for cardiovascular events and all-cause mortality. In this particular study, a greater level of baseline difficulty walking in people with hip and knee OA was associated with shorter survival and higher likelihood of experiencing a cardiovascular event.
29		The management of concomitant painful OA is therefore important in the management of other common chronic conditions.

30		In summary, osteoarthritis is a serious disease associated with substantial and persistent morbidity, characterized by pain, fatigue, sleep disturbance, depression, and disability. It impacts day-to-day functioning, and mobility, and independence. It's a heterogeneous disease, in terms of etiology progression and outcomes. And we're only just beginning to understand osteoarthritis phenotypes. Osteoarthritis-related difficulty walking is common, particularly in the presence of knee OA, and is a clinically relevant and modifiable risk factor for worse outcomes in people with OA, and for their other chronic comorbid conditions. Thank you.