1 Good afternoon, my name is Manika Bansal and I'm here to speak to you about the Huntington's disease (HD) — which is not a chromosomal mutation— hence the title. Without further ado, let's dive right in.

2 I've introducing myself already, but I haven't yet introduced the main topic of this presentation. You know that it's called Huntington's disease, but do you really know what it is? For those who don't, Huntington's disease is a disorder that results in the death of brain cells.

3 The main causes for this disorder are genetic. HD is typical inherited from one's parents, however, there is a chance that the mutation could be a new one. Even though there is a chance, it's a pretty slim one, considering only 10% of cases are caused by new mutations. The disorder is caused by a dominant mutation in either parents' genes called Huntingin. This Huntington mutation is what causes an abnormal protein to form, which gradually damages cells in the brain through mechanisms that aren't fully understood yet. If we were to look at it like this, the father, for example, has the infected heterozygous alleles H and b, while the mother has the homozygous alleles t and t in the same locus on the short arm of chromosome 4. Now, if we use a punnet square, we would find out that a child of an affected person has about 50% chance of inheriting the disease.

4 Although, I wouldn't worry too much, as HD affects about 4 to 15 in 100,000 European people and about 1 in every 10,000 Americans contract this disease. I mean, you could always get a genetic test to see if you have contracted the disease as well.

5 I say we take deeper look at what actually happens for this mutation to from. A part of the Huntington gene (HTT) is a repeated section called a trinucleotide repeat. HTT contains a sequence of three DNA bases — cytosine, adenine, guanine (CAG) — repeated multiple times. CAG is the 3 letter codon amino acid glutamine. Generally, people have fewer than 36 glutamine. However, a sequence of 36 or more glutamine results in the production of a protein which has different characteristics. This altered DNA, called mutant huntingtin (mHTT), increases the decay rate of certain brain cells. When the number of glutamine crosses 36, there is a risk that a person will develop Huntington disease. When the number of glutamine is 40 or more, one will definitely develop the disease. A very large number of glutamine — 60 or more — usually indicates that the disease will be present before the age of 20. Again, this disorder is not a chromosomal mutation.

6 Just imagine that somehow, you develop this deadly disease, how could you possibly know? Even though specific symptoms usually vary from person to person, there are symptoms that are common between most. The earliest symptoms would be subtle problems with mood or mental abilities, forms of nervous activity like fidgeting and minor twitching in the fingers and toes, slight alterations in handwriting, and minor difficulty with daily physical skills like driving.

After that would come a lack of coordination, an unsteady gait — pattern of movement of the limbs, short-term memory loss, periods of depression, apathy and irritability, and impulsiveness.

As the disorder advances, uncoordinated, jerky body movements become more apparent. One's physical abilities will gradually worsen until coordinated movement becomes difficult and the person is unable to talk. Mental abilities will generally decline into dementia — a category of brain diseases that cause long-term and a gradual decrease in the ability to think and remember which is great enough to affect one's daily life.

I wouldn't worry too much if you are a child because symptoms usually begin between 30 and 50 years of age. Only about 8% of HD cases start before the age of 20. Plus, death typically occurs 15 to 20 years after the disease is first detected. These symptoms have consequences as well. Some of the probable consequences include: Pneumonia — an inflammatory condition of the lung that primarily affects the small air sacs known as alveoli — heart disease, physical injuries from falls that reduce life expectancy, and suicide, which is the cause of death in about 9% of HD cases.

There is another 'symptom' of HD. It's the production of more children. Researchers have proposed a new hypothesis to explain the prevalence of the disease. They suggested that people who have contracted the disease are healthier in childbearing years and have more children than the general population. HD strengthens the immune system during most fertile years, allowing one to produce more offspring. Symptoms caused by HD occur later in life, after the general peak reproductive age.

7 There is no cure to HD. There, I said it. There is no cure for HD. However, supportive care is the next best thing. Supportive care is a therapy that doesn't treat or improve the underlying condition, but instead increases the patient's comfort. This treatment could improve the quality of life of the patients and can relieve some of the symptoms contracted. This care is required in the later stages of the disorder. There are also medicines that can be prescribed for certain symptoms. Antipsychotics are recommended for hallucinations, delusions, and violent outbursts. Antidepressants are recommended for depression and obsessive-compulsive behaviour. However, the best treatment for movement, specifically for HD patients, is Tetrabenazine. A lot of people

worry about the life expectancy of HD, but there is no way of telling what that is. Life expectancy depends on when you were diagnosed.

8 Speaking of life expectancy, Juvenile Huntington's Disease is a disease within the normal Huntington's Disease. It has the same symptoms and does the same thing as HD, but this disease begins in one's adolescence or childhood. It occurs before the age of 20. Juvenile HD also progresses much faster, with death typically occurring in about 10 years, instead of 15 to 20 years.

9 I have been blabbing on and on about HD, when you don't even know anything about how it was discovered! So, let me tell you now. The first recorded mention of it was in 1842, in a letter written by Charles Oscar Waters which was published in *Practice of Medicine*. Later on in 1860, Johan Christian Lund gave a description of the disease, noting that dementia along with jerking movements were symptoms of the disease. In 1872, George Huntington gave the first complete description of the disease based on his studies of one family which displayed similar symptoms. He also described the dominance of the HD gene in inheritance. William Osler was impressed by Huntington's description of the disorder. Osler's interest in the disorder combined with his influence in the medical field brought mass amounts of awareness to the disorder. By the end of the 19th century, the illness gained worldwide acknowledgement.

In 1911, Charles Davenport hired Elizabeth Muncey to construct family pedigrees of people with Huntington's disease along the east coast of the Unites States. He then used the data he gathered to discover the different times that the disorder kicks in and the range of symptoms it has.

The understanding of the disease advanced over the next few decades. However, the next big break through happened in 1983, when an approximate location of a HTT gene was discovered as a result of the US–Venezuela Huntington's Disease Collaborative Research Project. In 1993, the group reported the exact locus of the gene, the short arm of chromosome 4. That's it for now. There is still a lot left to discover about this disease. Hopefully, we will make more ground breaking discoveries to move us further in the field of science and technology.

10 Rebecca Ambrose is a 29 year old lady who suffers from HD. You may be wondering, why am I talking to you about her? A lot of people have this deadly mutation. But there is something special about Ambrose. Ambrose knew that there was a very high chance that she would inherit this disorder as her mother, three uncles and two aunts all carried the dominant allele. However, before she made the big decision to take the genetic test, she had a son. When she found out that she had HD, she didn't just accept her fate. Sure, she knew that there was no cure for HD, but instead of doing nothing, she decided that people needed to know more. Ambrose took it upon herself to make a movie to raise awareness of HD. "It is regretful that families in our area suffering

from what has been called the most devastating disease known to mankind lack the ability to network with each other and do not have the support or understanding of the community, medical professionals, nursing homes or law enforcement," Ambrose said. The move is call called "Alive and Well" and was show cased on January 20th, three years ago.

11 Fate whispers to the warrior "you cannot withstand the storm" and the warrior whispers back "I am the storm" This is what HD victims need to feel, this is what they need to hear, this is what they need know.