

# EPIDEMIOLOGICAL SURVEY ON HUNTINGTON'S DISEASE IN THE PROVINCE OF FERRARA: INCIDENCE AND PREVALENCE STUDY

E. Carrassi, M. Pugliatti, V. Govoni, MC. Sensi, I. Casetta, E. Granieri.

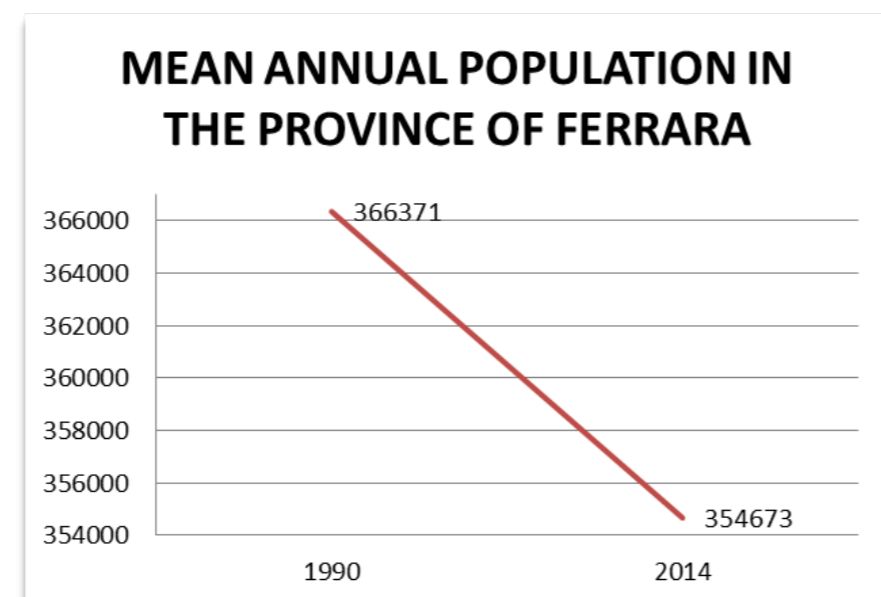
Department of Biomedical and Specialty Surgery, Section of Neurology - University of Ferrara – Ferrara

## INTRODUCTION

Huntington's Disease (HD) is an autosomal dominant (AD) degenerative disease of the central nervous system caused by an unsteady amplification of repeated sequences of CAG triplets on the IT15 gene first exon, located on chromosome 4p16.3. Up to the early 1990s, HD was diagnosed merely on clinical basis. The introduction of genetic tests has represented a turning point in diagnostic work-up, making it possible to perform preclinical and antenatal diagnoses. An increase in incidence and prevalence of HD has been observed in Italian and European population ascribable to the new diagnostic era (1) (2) (3) pointing out how the lack of a specific test had led to an underestimation of the actual disease burden.

## METHODS

### Study Area



### Case Definition

**FAMILIAL HISTORY OF HD**

**- CHOREIFORM MOVEMENTS AND/OR RIGIDITY**  
**- PROGRESSIVE MENTAL DETERIORATION**

**DNA TESTING**

### Case Ascertainment

- Health data archives and outpatient records from the Units of Neurology, Ferrara University Hospital
- Anonymous data supplied by the Medical Genetics Section
- Administrative data from the Hospital Health Statistics Office.
- Information System of Health and Social Policy Service (SISEPS) of the Emilia-Romagna Region

## RESULTS

### Incidence

| Age class (years)    | Mean annual population |                |                | N. cases  |           |           | Incidence            |                      |                      |
|----------------------|------------------------|----------------|----------------|-----------|-----------|-----------|----------------------|----------------------|----------------------|
|                      | Men                    | Women          | Total          | Men       | Women     | Total     | Men                  | Women                | Total                |
| <25                  | 35,387                 | 33,326         | 68,713         | 0         | 0         | 0         | -                    | -                    | -                    |
| 25-34                | 25,450                 | 24,285         | 49,734         | 0         | 2         | 2         | -                    | 0.4                  | 0.2                  |
| 35-44                | 26,484                 | 26,055         | 52,539         | 2         | 3         | 5         | 0.4                  | 0.6                  | 0.5                  |
| 45-54                | 24,591                 | 25,440         | 50,031         | 4         | 3         | 7         | 0.8                  | 0.6                  | 0.7                  |
| 55-64                | 23,692                 | 25,895         | 49,587         | 3         | 3         | 6         | 0.6                  | 0.6                  | 0.6                  |
| 65-74                | 20,124                 | 25,099         | 45,224         | 0         | 0         | 0         | -                    | -                    | -                    |
| 75+                  | 13,606                 | 24,562         | 38,168         | 2         | 0         | 2         | 0.7                  | -                    | 0.3                  |
| <b>Total (95%CI)</b> | <b>169,334</b>         | <b>184,662</b> | <b>353,996</b> | <b>11</b> | <b>11</b> | <b>22</b> | <b>0.3 (0.1-0.5)</b> | <b>0.3 (0.1-0.5)</b> | <b>0.3 (0.2-0.5)</b> |

Table 1. Sex- and age-specific mean annual crude incidence rate (per 100,000) of HD in the province of Ferrara, Northern Italy in 1990-2009

The overall mean (SD) age at onset was 50.2 (12.7) years, ranging from 32 and 82 years, 54.9 (14.6) for men and 45.8 (9.4) for women (p=ns).

The mean (SD) duration of the disease (i.e., period elapsed between clinical onset and prevalence year (2014), was 14.6 (4.5) years, 13.8 (3.9) for men and 15.8 (5.2) for women, respectively (p=ns). Eleven patients manifested neurological symptoms, 8 only psychiatric symptoms and 4 both symptoms.

The type of the first symptom did not significantly affect the mean (SD) age of onset, which was 50.8 (12.9) years for HD patients with psychiatric symptoms, and 48.8 (15.8) for neurological symptoms (p= ns).

To overcome differences deriving from the recent availability of genetic tests, the incident cases were divided into cases with onset before year 2000 and cases with onset after that date. The mean (SD) time period elapsing between the clinical onset and diagnostic tests showed statistically significant differences in the two groups: it was 6.7 (3.4) years in the first group, and 2.5 (1.7) years in the second group (p= 0.01).

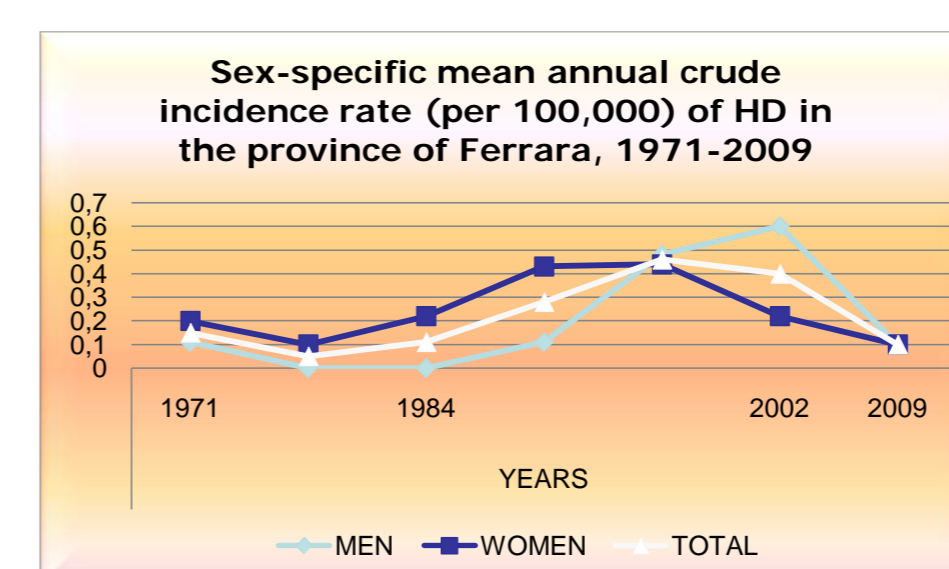
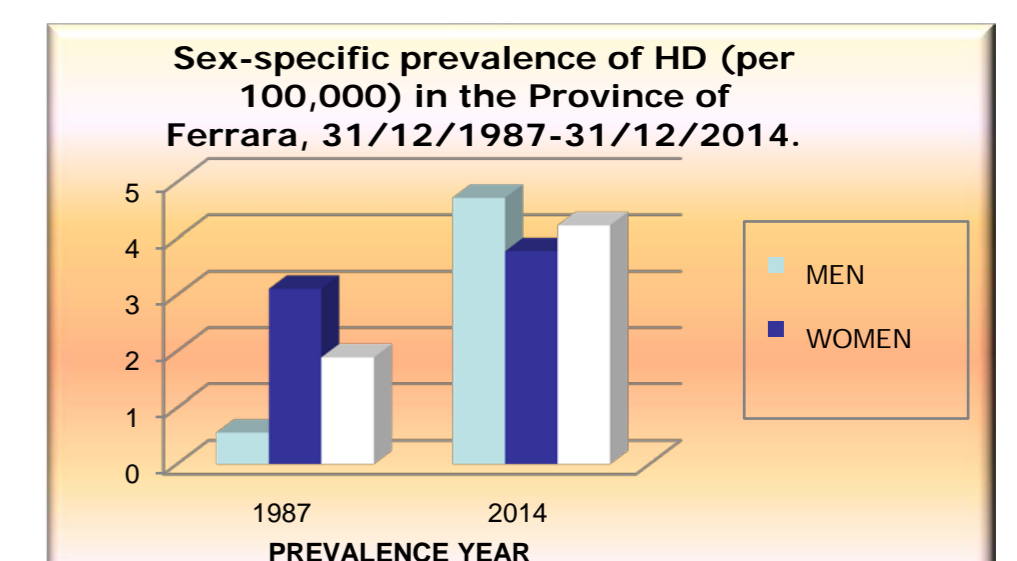
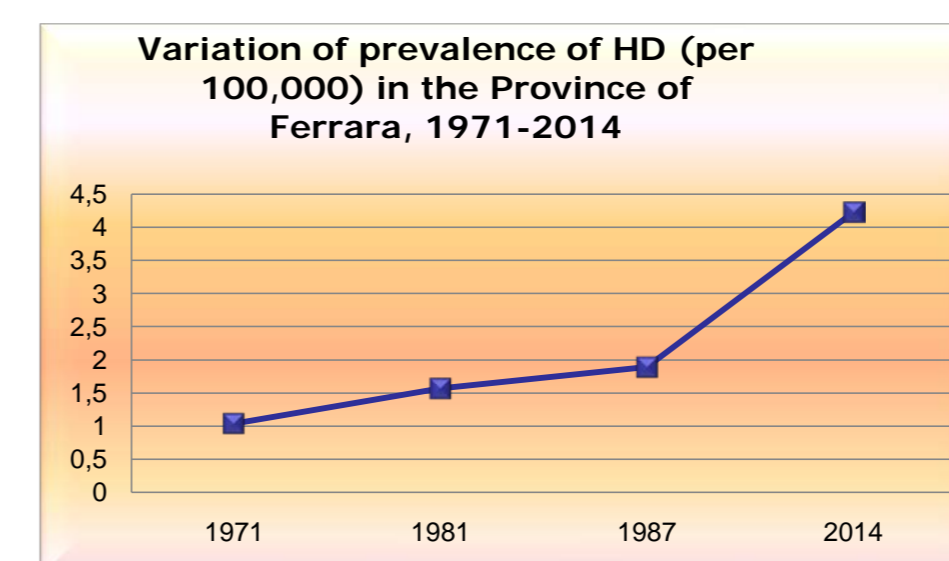
### Prevalence

| Age class (years)    | Population     |                |                | N. cases |          |           | Prevalence           |                      |                      |
|----------------------|----------------|----------------|----------------|----------|----------|-----------|----------------------|----------------------|----------------------|
|                      | Men            | Women          | Total          | Men      | Women    | Total     | Men                  | Women                | Total                |
| <25                  | 36,833         | 34,921         | 71,754         | -        | -        | -         | -                    | -                    | -                    |
| 25-34                | 20,069         | 20,139         | 40,208         | -        | 1        | 1         | -                    | 5.1                  | 2.5                  |
| 35-44                | 31,144         | 30,812         | 61,956         | -        | -        | -         | -                    | -                    | -                    |
| 45-54                | 29,139         | 30,852         | 59,991         | 2        | 2        | 4         | 6.9                  | 6.5                  | 6.7                  |
| 55-64                | 24,755         | 27,795         | 52,550         | 2        | 1        | 3         | 8.1                  | 3.6                  | 5.7                  |
| 65-74                | 18,679         | 23,474         | 42,153         | 3        | 2        | 5         | 16.1                 | 8.5                  | 11.9                 |
| 75+                  | 8,891          | 17,170         | 26,061         | 1        | 1        | 2         | 11.3                 | 5.8                  | 7.7                  |
| <b>Total (95%CI)</b> | <b>169,510</b> | <b>185,163</b> | <b>354,673</b> | <b>8</b> | <b>7</b> | <b>15</b> | <b>4.7 (2.0-9.3)</b> | <b>3.8 (1.5-7.8)</b> | <b>4.2 (2.4-6.9)</b> |

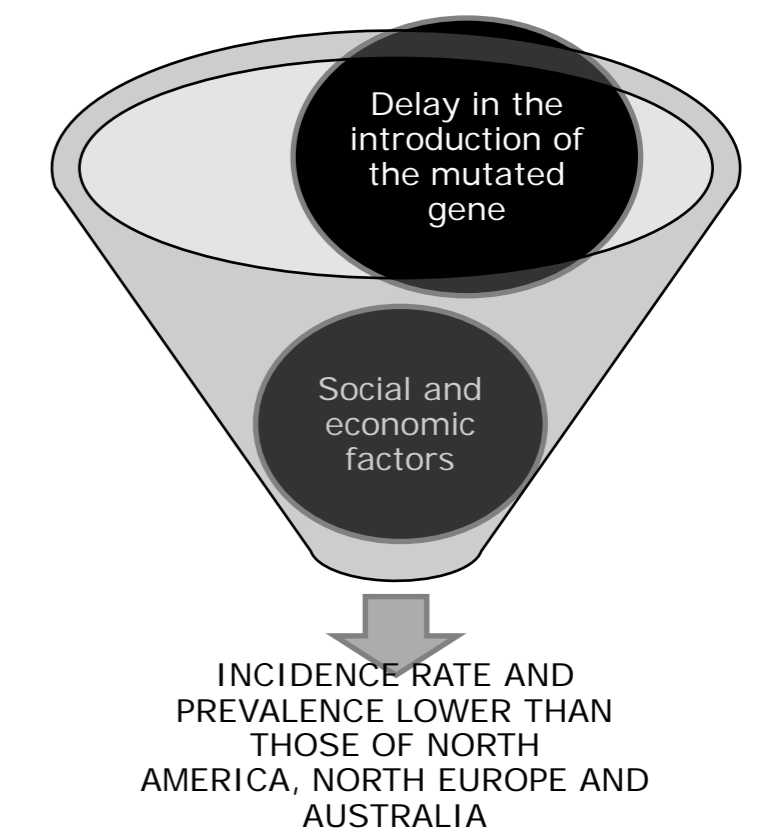
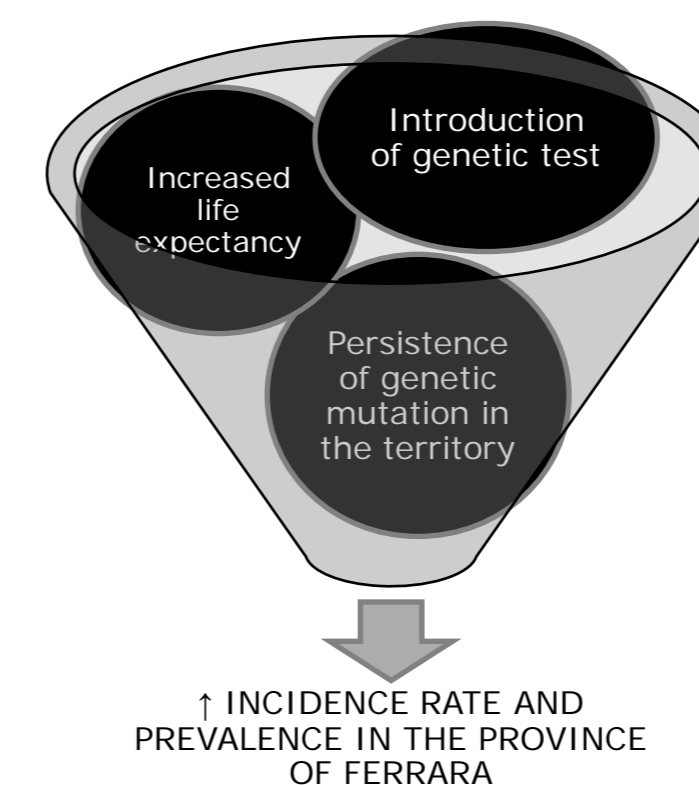
Table 2. Sex- and age-specific crude prevalence (per 100,000) of HD in the province of Ferrara, northern Italy, on prevalence day 31 December 2014.

The age at study time ranged from 30 to 87 years with a mean (SD) of 60.7 (14.4), 57.6 (16.1) for women and 63.4 (13.3) for men (p=ns). Among prevalent cases, symptoms involved all functional domains affected by the disease (motor, cognitive and psychiatric).

## CONCLUSIONS



Compared to previous data obtained for the same population (province of Ferrara) for year 1987 (4), our study shows an increase of HD prevalence and indirectly allows for a description of HD incidence temporal trend in this population from 1971 to 2009.



| Study                          | Location                  | Incidence year(s) | Incidence per 100,000 persons-year | Prevalence year | Prevalence per 100,000 persons       |
|--------------------------------|---------------------------|-------------------|------------------------------------|-----------------|--------------------------------------|
| Govoni et al. [1988] (4)       | Ferrara, Italy            | 1971-1987         | 0.1                                | 1978            | 1.89                                 |
| Chang et al. [1994] (5)        | Hong Kong                 | 1984-1991         | 0.05                               | 1991            | 0.3                                  |
| McCusker et al. [2000] (6)     | NSW, Australia            | 1991-1996         | 0.7                                | 1996            | 6.3                                  |
| Almqvist et al. [2001] (7)     | British Columbia, Canada  | 1996-1999         | 0.7                                | -               | -                                    |
| Ramos-Arroyo et al. [2005] (8) | Navarra and Basque, Spain | 1994-2002         | 0.5                                | -               | -                                    |
| Chen et al. [2010] (9)         | Taiwan                    | 2000-2007         | 0.1                                | 2007            | 0.4                                  |
| Panas et al. [2011] (10)       | Greece                    | 1995-2008         | 0.4                                | 2009            | 2.5                                  |
| Sackley et al. [2011] (11)     | UK                        | 2004-2008         | 0.6                                | 2008            | 6.3                                  |
| Sveinsson et al. [2012] (12)   | Iceland                   | 1988-2007         | 0.1                                | 2007            | 1.0                                  |
| Sipila et al. [2014] (13)      | Finland                   | 1987-2010         | -                                  | 2010            | 2.12                                 |
| Wexler et al. [2016] (14)      | UK                        | 1990-2010         | 0.7                                | -               | -                                    |
| Baine et al. [2016] (15)       | South Africa              | 1995-2014         | -                                  | 2014            | 5.1 white<br>2.1 mixed<br>0.25 black |

Table 3. HD Incidence and prevalence studies

The distribution of HD in the World is uneven. The incidence and prevalence of the disease in the province of Ferrara showed an incremental trend in the past 30 years. These estimates are lower than those found in Northern Europe, but higher than those of Asia and Africa. The introduction of genetic testing and the increase in life expectancy contribute to reduce the underestimation of HD.

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