

# **The EMQN Huntington's disease EQA scheme (1997- 2007): 10 years' lessons and experiences**

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# EQA: Aims

- 1997: measure quality and encourage raising of standard of molecular genetic testing in Europe
- Huntington's disease as a pilot
  - technically straightforward (CAG-repeat)
  - allows a range of difficulties in technical competence and interpretation complexity
- 2006: Provide EQA for (accredited) molecular genetic testing laboratories around the world

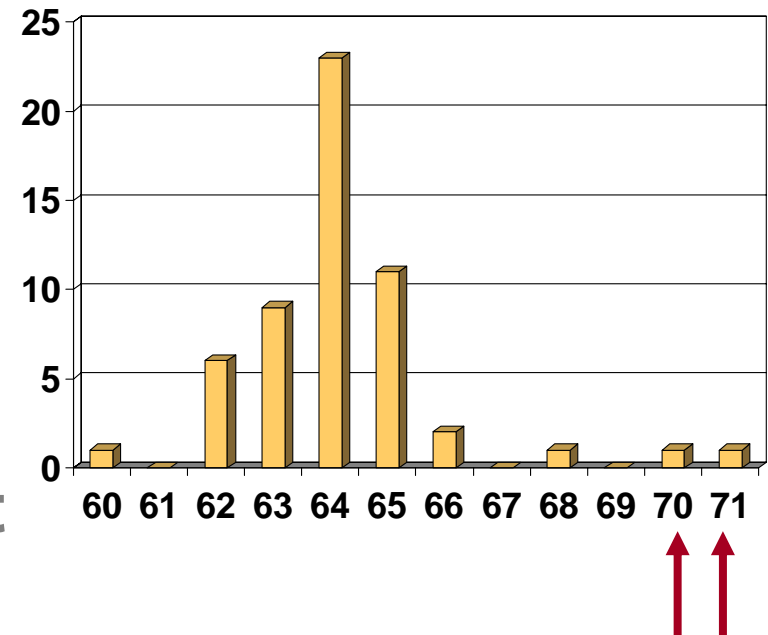
# How does it work?

- A laboratories output is compared to a fixed standard: **Anonymous!**
- Cases
  - 3 DNA samples matched to mock clinical referrals are distributed
  - Genotyping results and reports in normal laboratory format returned
  - Returns marked by 3 assessors

- Marking criteria:
  - Genotyping (max 2 points)
    - Allel outside error limit: -0.5
    - Outside allele range: 0 for that case
  - Interpretation (max 2 points)
    - Case specific remarks formulated and scored
    - Point not adequately covered: -0.5/-1.0

# What do we test technically (genotyping)?

- Straightforward cases
  - 17 and 43 CAG repeats
  - 18 and 21 CAG repeats
- Large repeats
  - >60 CAG repeats (2006)
- Alleles with one repeat difference
  - 17-18 CAG repeats
  - 2006: **5/57** typed a homozygote



2007: **4/55** typed a homozygote

Based on publications, best practice guidelines, labs own documented experience

- Diagnostic test by neurologist
  - Refer for genetic counselling
  - (2006: **6/57** failed to do so)
- Interpretation of specific alleles (Intermediate, reduced penetrance, homozygotes etc)
  - 2003: **19/42** (45%) and 2007: **11/55** (20%) failed to discuss implications of intermediate allele

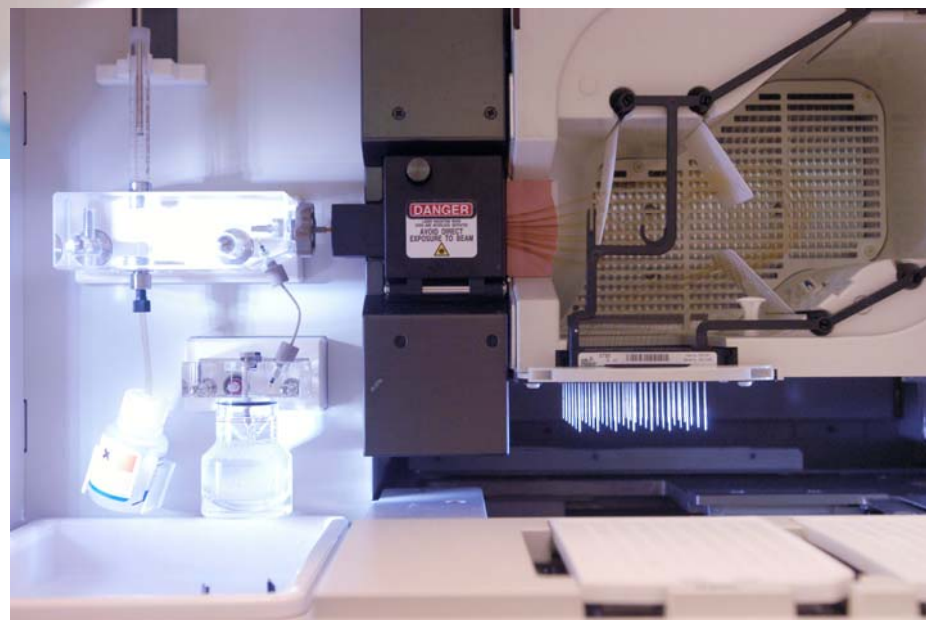
- Phrasing of the conclusion
  - Should be clear and unambiguous**
  - Predictive test:
    - will develop/is at risk of developing HD
    - will not/is not at risk .....
  - Diagnostic:
    - Diagnosis of HD is confirmed
    - Patient is affected with HD
    - Result is consistent with diagnosis of HD
- Immediately clear that prenatal test is reported
  - 2000: **11** out of **39** reports this was not clear

# Changes over the years

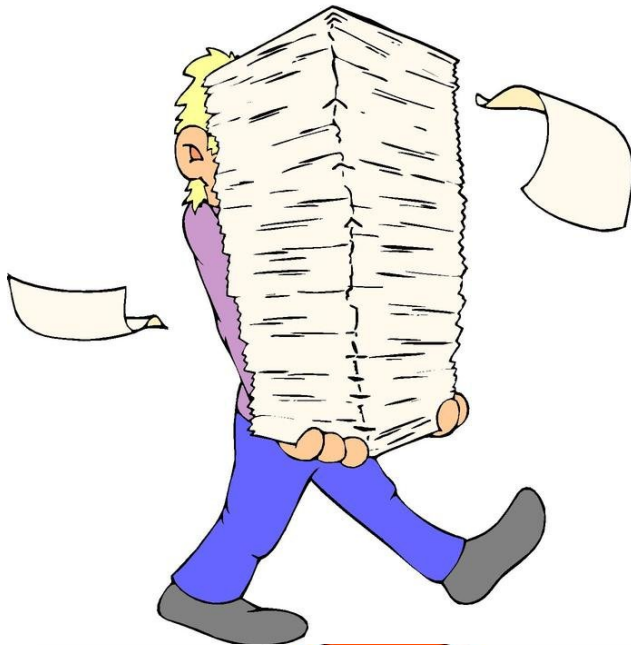


Leiden...

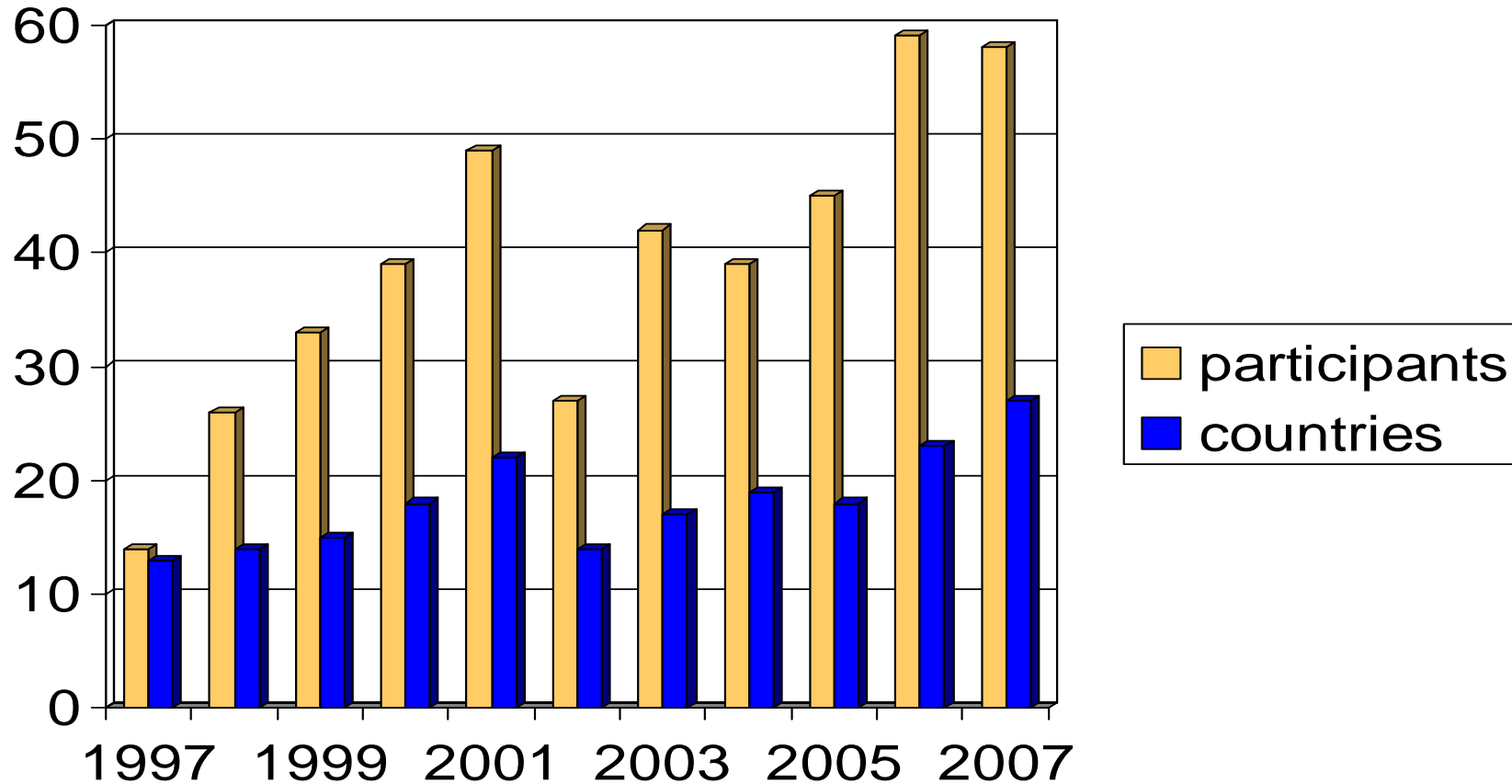
.....Manchester



# Changes over the years: organisation



# Changes over the years: Participants



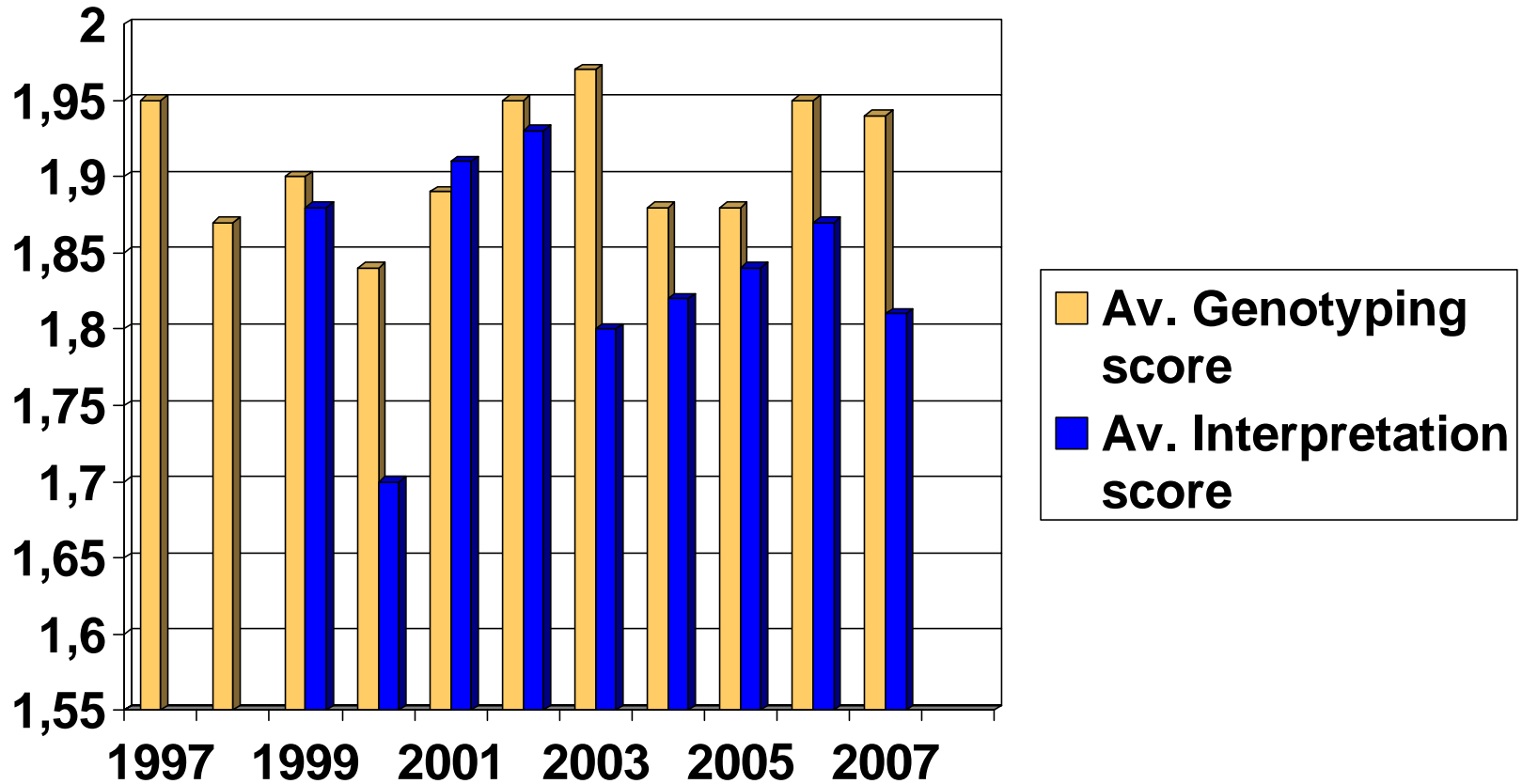
Note: Almost all participants return reports (usually all-but 2)

# Repeated participation

Number of years participated (2005-2007)	Number of laboratories (total 77)
One	33 (43%)*
Two	18 (23%)
Three	26 (34%)

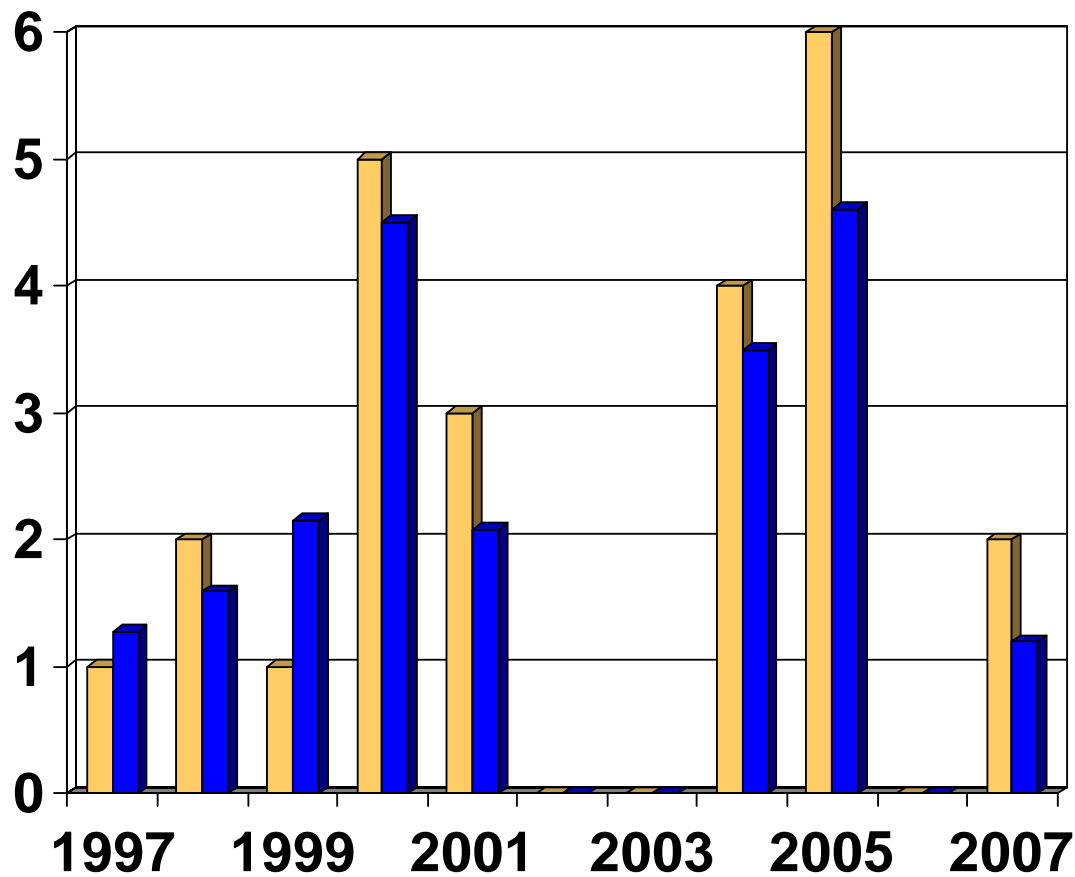
Note: ~50% first year participant in 2007

# Changes over the years: Scores



Note: Criteria have become more stringent over the years

# Changes over the years: Diagnostic errors



■ number of diagnostic errors  
■ Error rate (%)

# Type of errors

## 1. Swapping of samples

- 2 errors at once
- Usually one can deduct from the case description that the samples were swapped

## 2. Finding an extra allele

- 1999: 48 repeats typed instead of 18
- 2001: 43 .....20

## 3. Missing an allele

- 1999: allele of 56 repeats missed

# Conclusions

- EQA scheme demonstrates potential level of misdiagnosis (1-4.6%) among labs offering molecular testing for HD
- Way of reporting varies widely
  - Partly due to
    - local policies
    - Language
    - outside ordinary lab routine
  - Participating in EQA reduces differences
- Gradual improvement both at genotyping and interpretation level
- Number of participants is increasing
- We keep learning.....also scheme organiser and assessors

# Who did the work?

## EMQN

(administration, sample distribution, software..)

Simon Patton

Outi Kamarainen

National Genetics Reference  
Laboratory, St Mary's Hospital,  
Manchester, UK

And...

Franco Laccone (Göttingen)

Bert Bakker (Leiden)

Rob Elles (Manchester)

**All participants!!!!!!!!!!!!**

## Assessors

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