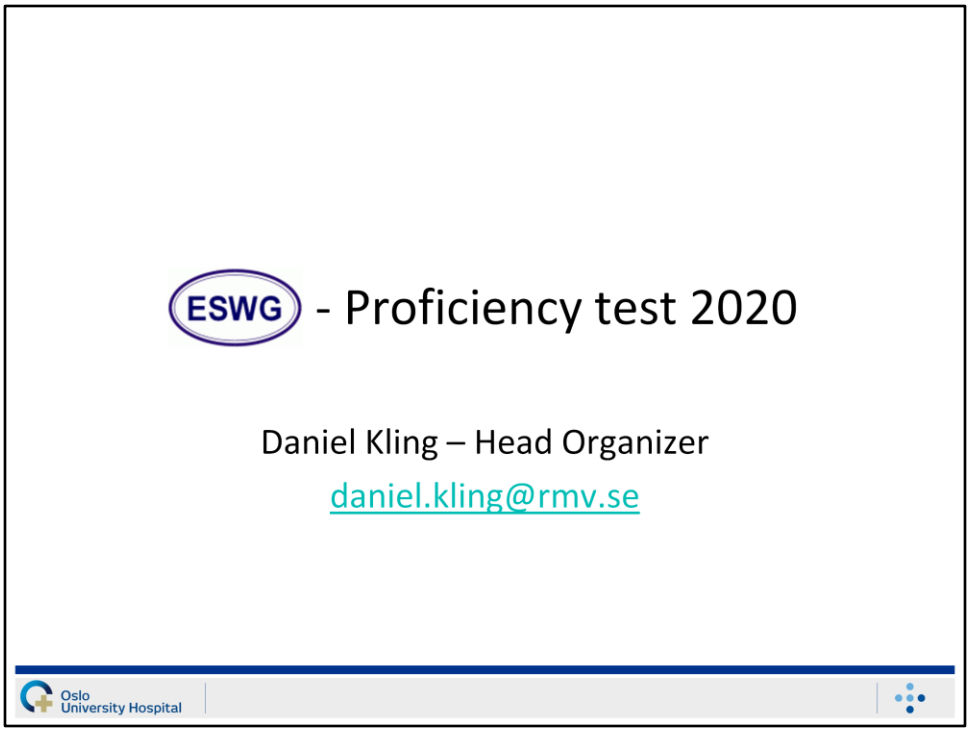
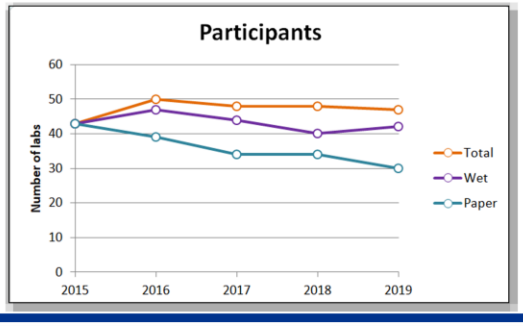


This is a summary of the ESWG proficiency test 2020. Complete results are contained in the Excel summary. A video is available through https://familias.name/ESWG/presentation_eswg_2020.mp4

Summary

- 47 labs participated
- 30 completed paper challenge
- 42 completed wet exercise



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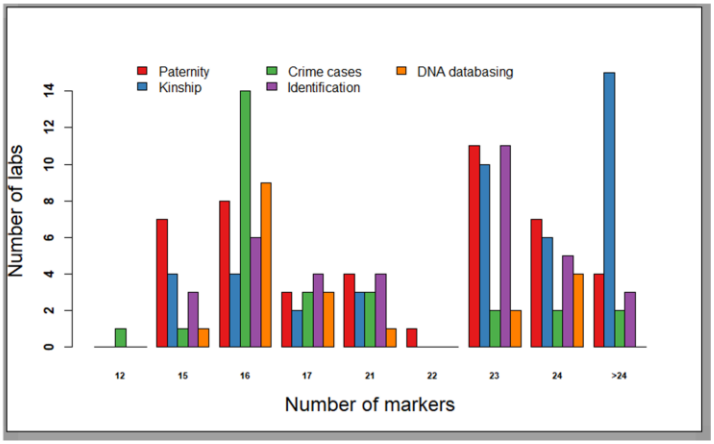
We observe a steady-state for the number of participating labs. Paper challenge is seeing a decrease – partly explained by the Pandemic.

Questionnaire – Markers used



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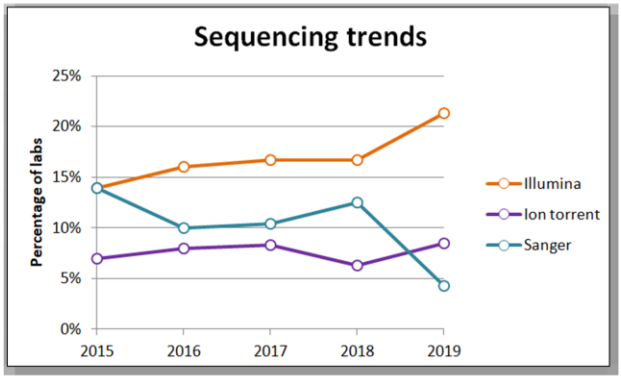
Questionnaire – Sequencing trends

- 16 labs (34%) own sequencing instrument. 2 planning to buy (4%)



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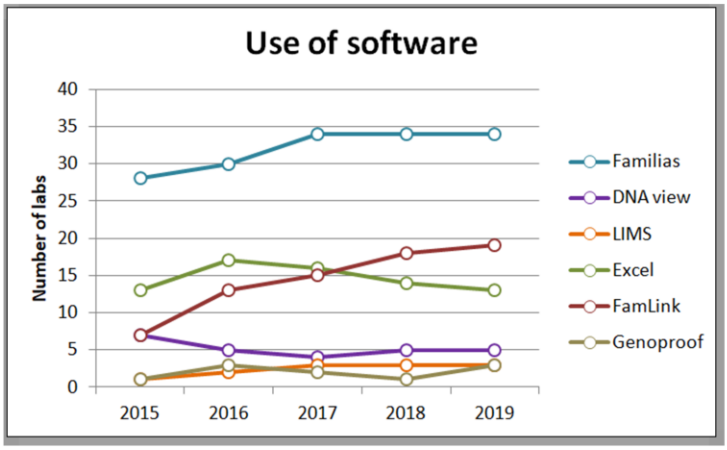
An increase in NGS/MPS/2nd generation sequencing and a drop in Sanger.

Questionnaire – Software trends



Questionnaire – Linked markers

Not accounted for: 12

Not used: 12

Exclude one: 14

Accounts for: 9

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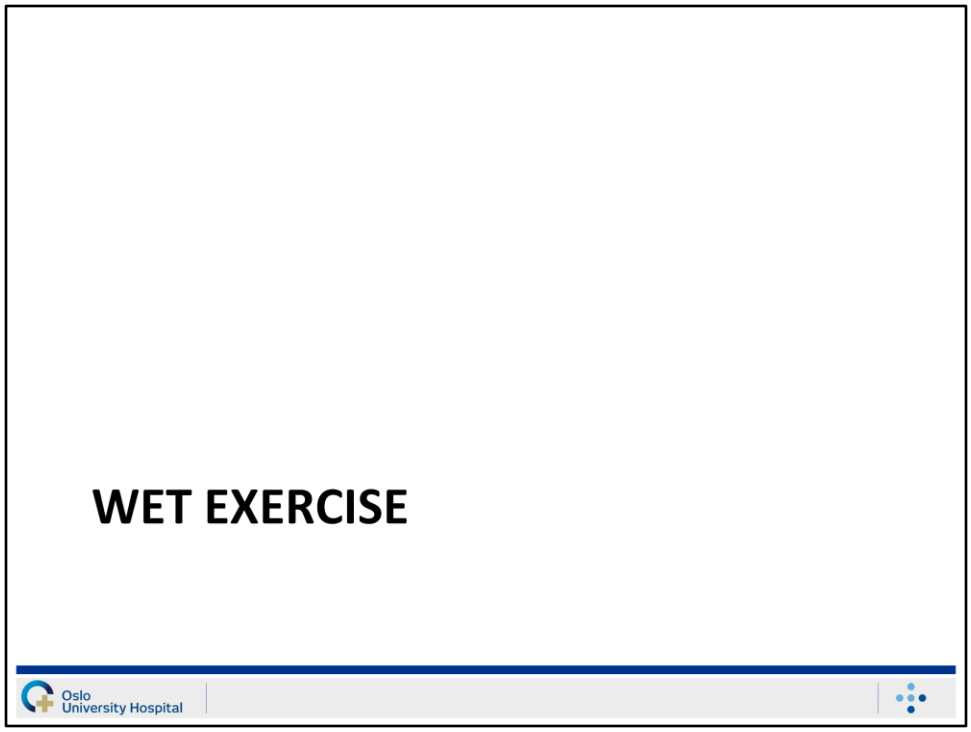
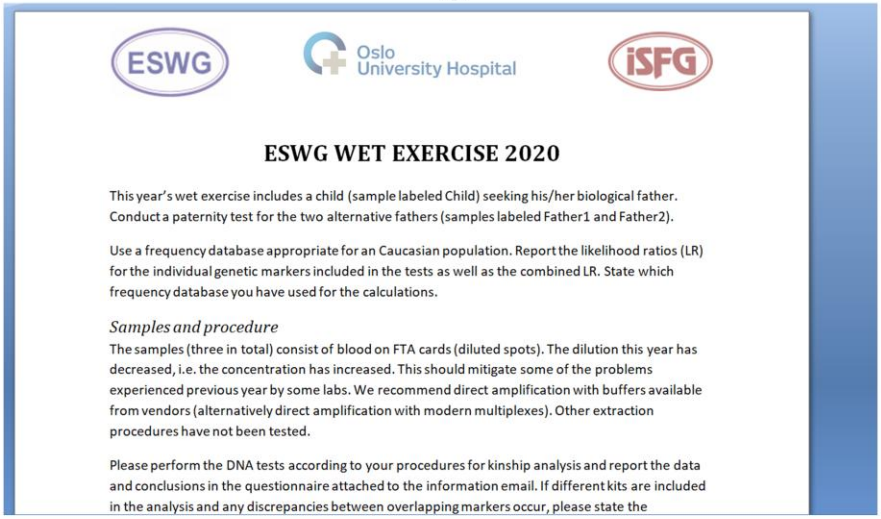
Linkage is becoming increasingly relevant with the expanded marker panels used. We see that only 9 of the participating labs account (or adjust) the LR accordingly. This is something that needs further attention in the next few years.



The following slides summarizes the wet exercise

Wet exercise - Background



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ESWG WET EXERCISE 2020

This year's wet exercise includes a child (sample labeled Child) seeking his/her biological father. Conduct a paternity test for the two alternative fathers (samples labeled Father1 and Father2).

Use a frequency database appropriate for an Caucasian population. Report the likelihood ratios (LR) for the individual genetic markers included in the tests as well as the combined LR. State which frequency database you have used for the calculations.

Samples and procedure

The samples (three in total) consist of blood on FTA cards (diluted spots). The dilution this year has decreased, i.e. the concentration has increased. This should mitigate some of the problems experienced previous year by some labs. We recommend direct amplification with buffers available from vendors (alternatively direct amplification with modern multiplexes). Other extraction procedures have not been tested.

Please perform the DNA tests according to your procedures for kinship analysis and report the data and conclusions in the questionnaire attached to the information email. If different kits are included in the analysis and any discrepancies between overlapping markers occur, please state the

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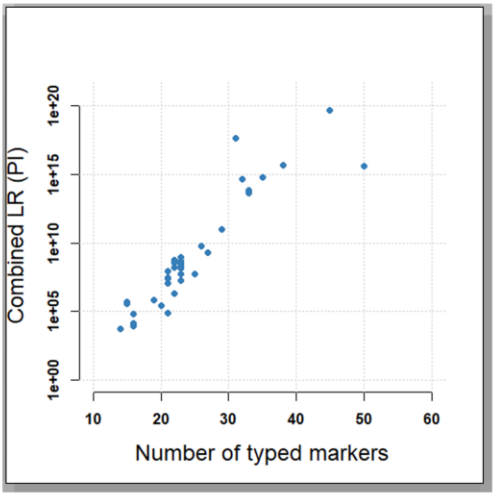
Wet exercise - Summary

- Overall very concordant results (despite the use of potentially different databases)
- A lower blood dilution was used. No labs reported unsuccessful amplification.
- 43 labs participated
- Consult the Excel summary for details
- For the wet exercise some labs' results have been highlighted (red or orange) which indicates a result that deviates. Certificates will still be issued. To obtain "successful participation" no red fields are allowed.

Wet exercise – Part a)

- Father could be exluded in 23 out of the total set of reported markers (markers with only a single lab excluded)
- Combined LR well below 1E-10
- No lab reported a false paternity inclusion

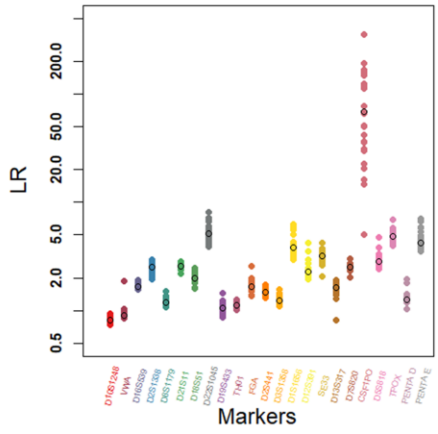
Wet exercise – Part b)



All labs report combined LR>10.000

Wet exercise – per marker LR variation

Per marker results



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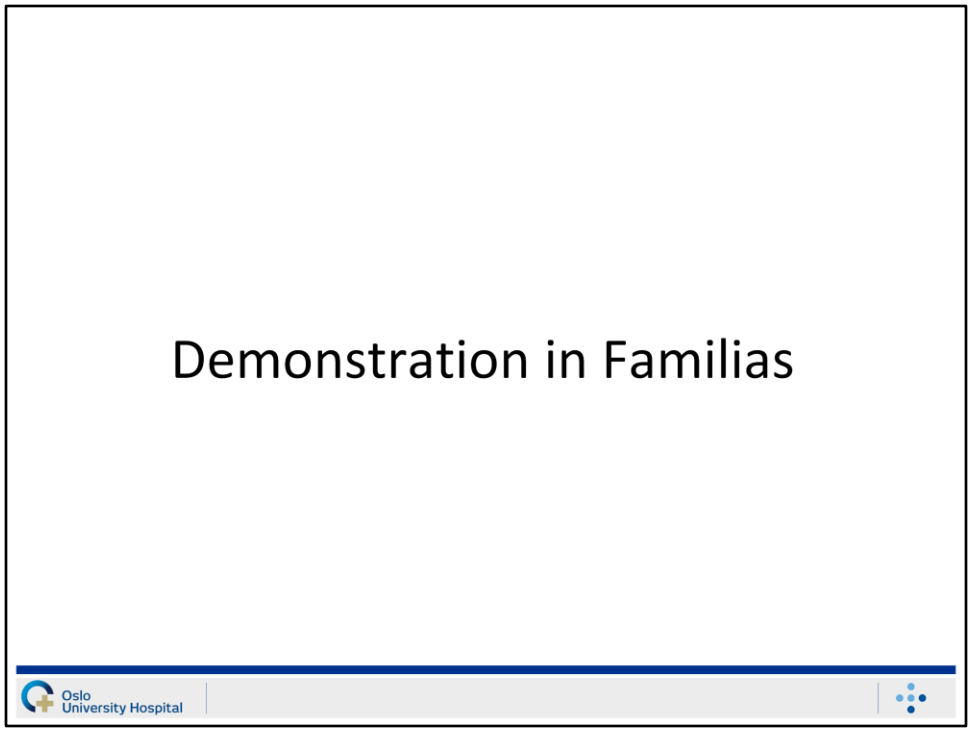
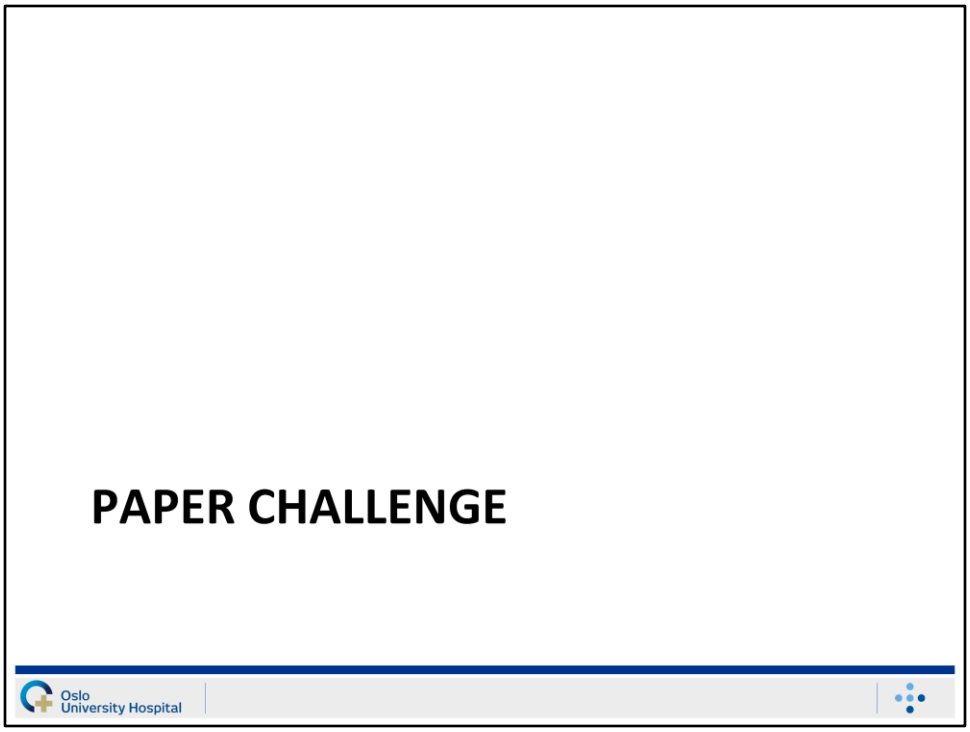
Big variation in CSF1PO. A rare allele is shared between the father and the child.



See online video for demonstration



We start with the paper challenge. Solutions files (available for Familias and FamLinkX) are available through http://familias.name/ESWG/ESWG_2020_solutions.zip

Paper challenge - Background

- The paper challenge consisted of 4 cases
  - Case 1 was a complex kinship case with autosomal and X-chromosomal markers
  - Case 2 was a mixture case with relatives
  - Case 3 was a case with an expanded marker panel
  - Case 4 was a case with multiple hypotheses
- This year's paper challenge was particularly tricky

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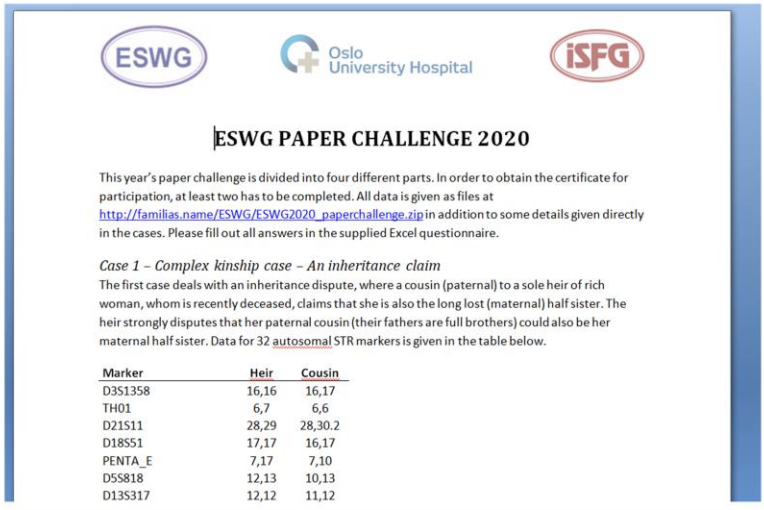
Brief description of this year's paper challenge. It is divided into four different cases, each with its own complexity.

Paper challenge – Case 1



ESWG PAPER CHALLENGE 2020

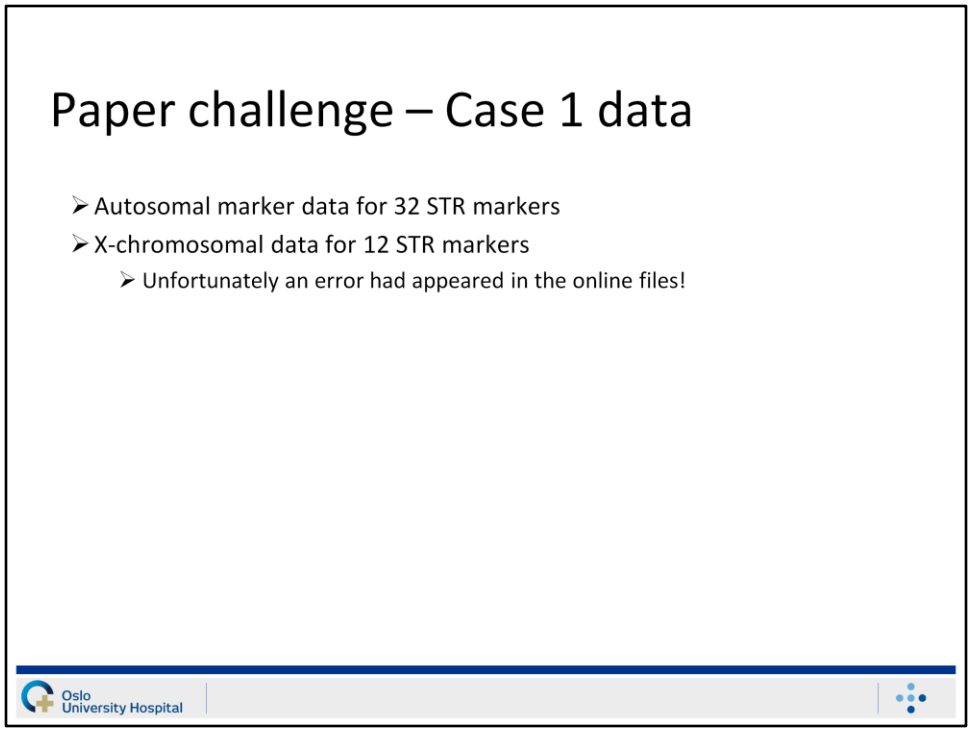
This year's paper challenge is divided into four different parts. In order to obtain the certificate for participation, at least two has to be completed. All data is given as files at http://familias.name/ESWG/ESWG2020_paperchallenge.zip in addition to some details given directly in the cases. Please fill out all answers in the supplied Excel questionnaire.

Case 1 – Complex kinship case – An inheritance claim

The first case deals with an inheritance dispute, where a cousin (paternal) to a sole heir of rich woman, whom is recently deceased, claims that she is also the long lost (maternal) half sister. The heir strongly disputes that her paternal cousin (their fathers are full brothers) could also be her maternal half sister. Data for 32 autosomal STR markers is given in the table below.

Marker	Heir	Cousin
D3S1358	16,16	16,17
TH01	6,7	6,6
D21S11	28,29	28,30.2
D18S51	17,17	16,17
PENTA_E	7,17	7,10
D5S818	12,13	10,13
D13S317	12,12	11,12

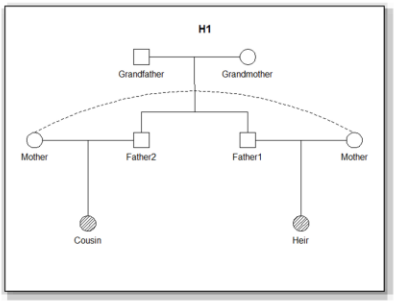
Some background.

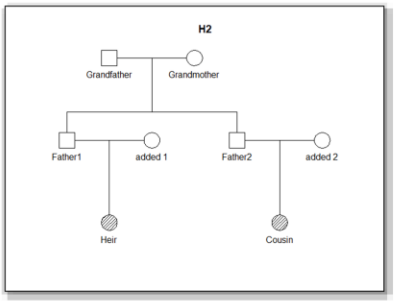


Brief summary of the genetic marker data. There was an error in the X-chromosomal data given in the online files.

Paper challenge – Case 1

a) Plot the pedigrees and discuss what type of markers could be used to solve the case (Not reported in the questionnaire).





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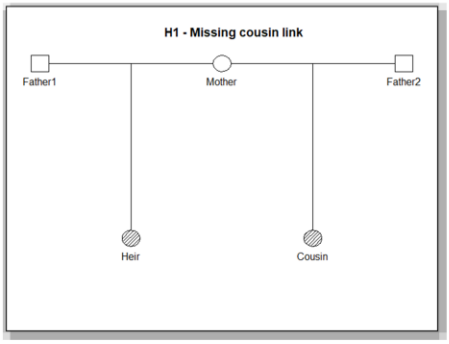
Correct formulation of the hypotheses

Paper challenge – Case 1

a) Plot the pedigrees and discuss what type of markers could be used to solve the case (Not reported in the questionnaire).



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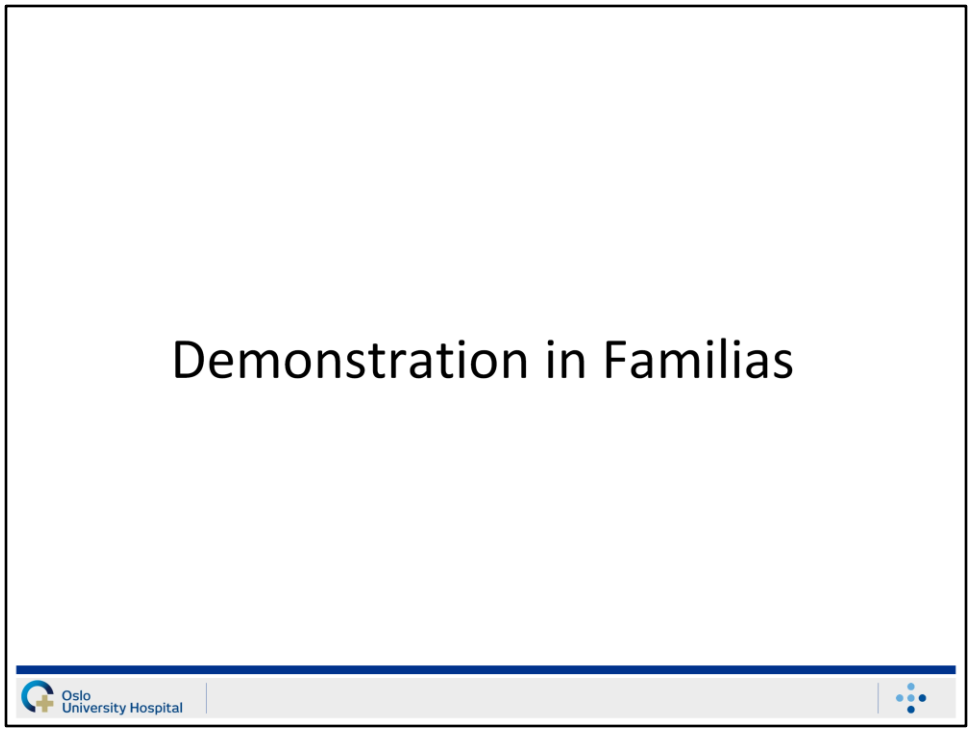
Errounous H1 with missing cousin link



Available in the online video

Paper challenge – Case 1

b) Compute the LR for the given autosomal markers comparing.
H1: The heir and her paternal cousin are maternal half sister.
H2: The heir and her paternal cousin are unrelated on their maternal side.

For b) we can ignore complicating factors such as mutations, silent alleles and linkage.

The LR becomes approximately 65 (when not considering any linkage or mutations, as stated). If the cousin link is not accounted for, the LR becomes 159502 instead.

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An overestimation of the evidence if the cousin link is not accounted for.

Paper challenge – Case 1

c) Compute the LR for the X-chromosomal data using the same hypotheses as in a). Mutations and silent alleles can be ignored while linkage and linkage disequilibrium should be accounted for if relevant.

d) Combine the LRs from b) and c) into a total LR. What is your verbal verdict in the case?

Marker	Heir	Cousin
DXS10148	18, 25.1	25.1, 25.1
DXS10135	20, 23	23, 27
DXS8378	10, 11	10, 11
DXS7132	13, 13	13, 13
DXS10079	19, 22	19, 22
DXS10074	16, 16	16, 16
DXS10103	16, 18	16, 17
HPRTB	13, 14	13, 14
DXS10101	25.2, 28.2	25.2, 31
DXS10146	27, 28	27, 28
DXS10134	34, 37	37, 38
DXS7423	13, 14	13, 15

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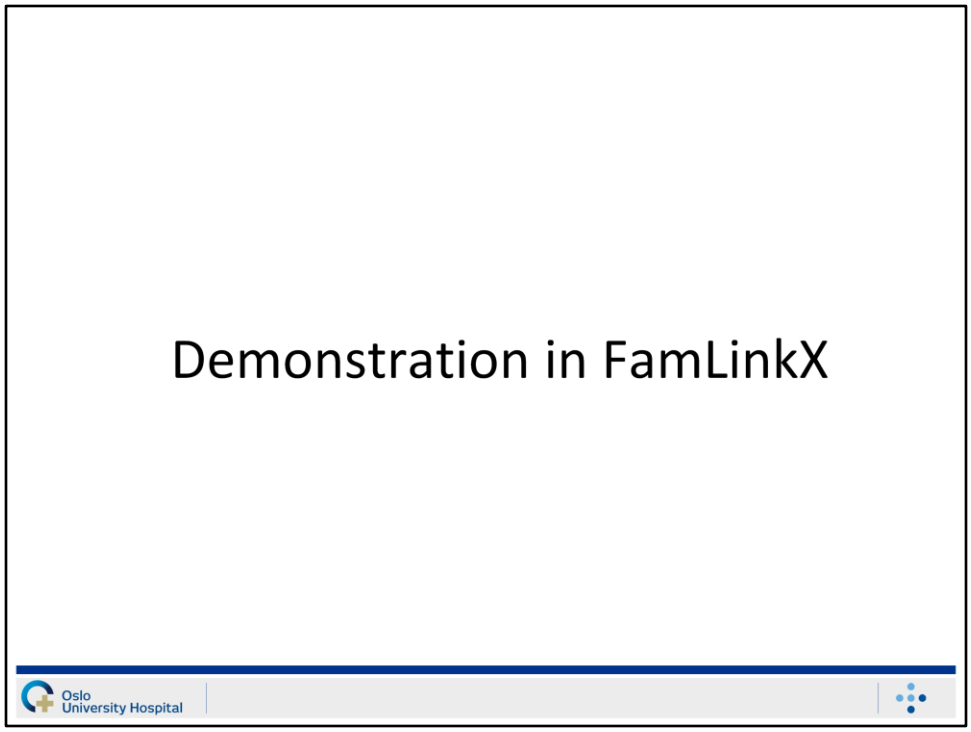
X-chromosomal data (correct alleles in the table while the online files contained an error).



Available in the online video.

Paper challenge – Case 1

c) Compute the LR for the X-chromosomal data using the same hypotheses as in a). Mutations and silent alleles can be ignored while linkage and linkage disequilibrium should be accounted for if relevant.

The LR becomes 38 if the cousin link is accounted for. This required the creation of pedigrees in FamLinkX. Without the cousin link an LR of >200,000 is obtained.

d) Combine the LRs from b) and c) into a total LR. What is your verbal verdict in the case?

The combined LR becomes 65 times 38 = 2470. So the data is more than 2000 times more likely of H1 is true compared to if H2 is true. If equal prior probabilities are assumed this translates to a greater then 99.9% posterior probability for H1.

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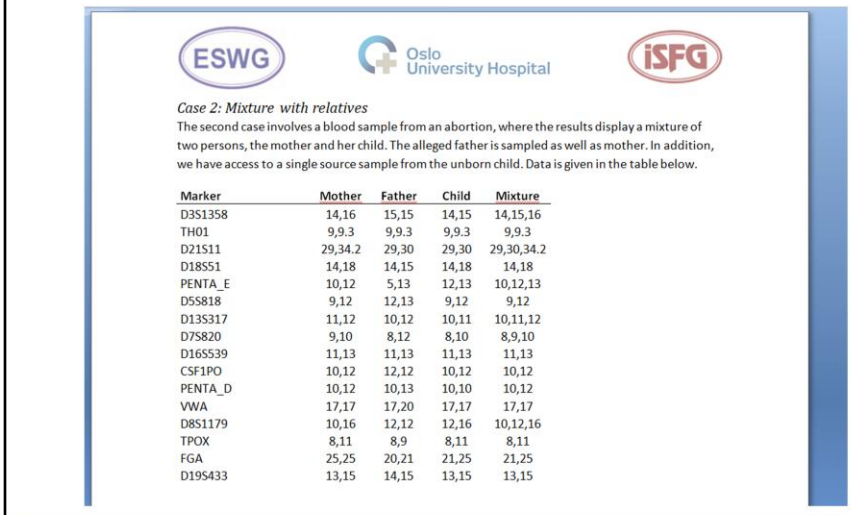
Again, an overestimation of the evidence if the cousin link is not accounted for. The total LR is greater then 2000 an therefore provides strong support for H1.

Paper challenge – Case 2



ESWG Oslo University Hospital iSFG

Case 2: Mixture with relatives

The second case involves a blood sample from an abortion, where the results display a mixture of two persons, the mother and her child. The alleged father is sampled as well as mother. In addition, we have access to a single source sample from the unborn child. Data is given in the table below.

Marker	Mother	Father	Child	Mixture
D3S1358	14,16	15,15	14,15	14,15,16
TH01	9,9.3	9,9.3	9,9.3	9,9.3
D21S11	29,34.2	29,30	29,30	29,30,34.2
D18S51	14,18	14,15	14,18	14,18
PENTA_E	10,12	5,13	12,13	10,12,13
D5S818	9,12	12,13	9,12	9,12
D13S317	11,12	10,12	10,11	10,11,12
D7S820	9,10	8,12	8,10	8,9,10
D16S539	11,13	11,13	11,13	11,13
CSF1PO	10,12	12,12	10,12	10,12
PENTA_D	10,12	10,13	10,10	10,12
VWA	17,17	17,20	17,17	17,17
D8S1179	10,16	12,12	12,16	10,12,16
TPOX	8,11	8,9	8,11	8,11
FGA	25,25	20,21	21,25	21,25
D19S433	13,15	14,15	13,15	13,15

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Second paper challenge case - background

Paper challenge – Case 2 data

- Autosomal marker data for 16 STR markers
- Data given for mother, father, child and a mixture (two contributors)

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Brief summary of the genetic marker data.

Paper challenge – Case 2 background

The hypotheses we will consider is given by.

H1: The alleged father is the biological father of the child (either the single source or the mixture).

H2: The alleged father is unrelated to the child.

Maternity for the mother can be assumed in both hypotheses. There will be some slight variations when the mixture is considered. see details in the exercises below.

In all computations we will disregard any further complicating factors such as mutations. population substructure etc. Frequency data as well as the genotypes (single source only) are also given as files at http://familias.name/ESWG/ESWG2020_paperchallenge.zip

Paper challenge – Case 2

a) Compute the LR comparing using the single source sample for the child.

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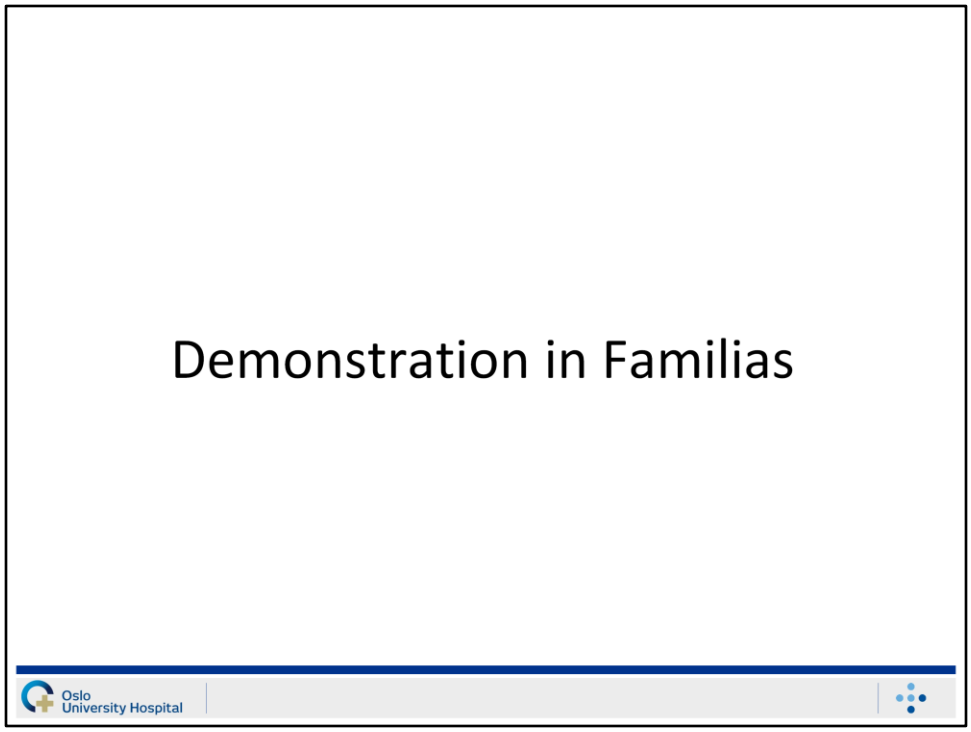
First part is a regular paternity case. We compute the LR for the trio and for paternity only (disregarding the mother)



Video available online, see first slide.

Paper challenge – Case 2

b) Now consider the mixture (abortion sample), compute the LR in the same manner. Use the sample for the mother as a known contributor in the mixture (both hypotheses)..

c) Consider the mixture again, compute the LR as in b), but disregard the known profile of the mother (both hypotheses).

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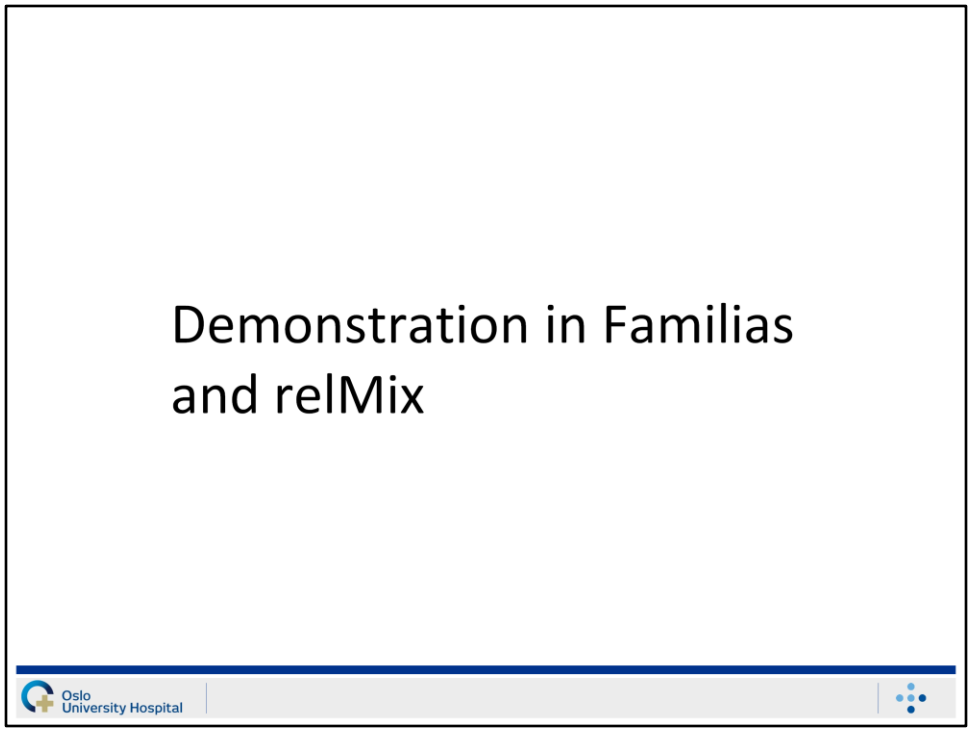
For the next part of the exercise we work with the mixture (mother and child). We will provide demonstration in the R package relMix



See online video. Script for relMix is available through http://familias.name/ESWG/ESWG_Case2_solution.R. Data for the mixture table is available through http://familias.name/ESWG/ESWG2020_paperchallenge_case2_genotypedata_R.txt

Paper challenge – Case 2 results

Marker	LR a)	LR a) paternity	LR b)	LR b) no maternity	LR c)
D3S1358	3.79	1.90	3.79	2.40	1.34
TH01	2.11	2.61	2.11	2.11	2.33
D21S11	2.00	2.12	2.00	2.07	1.59
D18S51	1.89	1.33	1.89	1.89	1.65
PENTA_E	6.11	3.06	6.11	3.47	1.89
D5S818	1.29	0.71	1.29	1.29	1.01
D13S317	5.62	2.81	5.62	3.44	2.23
D7S820	3.13	1.56	3.13	1.81	1.00
D16S539	2.09	2.26	2.09	2.09	2.16
CSF1PO	1.73	1.52	1.73	1.73	1.64
PENTA_D	3.98	3.98	1.39	1.39	1.65
VWA	1.69	1.69	1.69	1.69	1.69
D8S1179	7.20	3.60	7.20	4.93	2.77
TPOX	0.62	0.45	0.62	0.62	0.55
FGA	2.90	1.45	2.90	2.19	1.73
D19S433	1.23	1.37	1.23	1.23	1.29
Total	1619722	9940	564300	38336	1158

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Likelihood ratios calculated with different methods. a) is calculated in Familias (both the second and third column). b) is calculated in relMix (both fourth and fifth column). c) is calculated in the familial searching module of Familias.

Paper challenge – Case 2 results

Single marker manual calculation – consider Penta D

$$LR = \frac{\Pr(Data \mid H_1)}{\Pr(Data \mid H_2)}$$

Marker	Mother	Father	Child	Mixture
D3S1358	14,16	15,15	14,15	14,15,16
TH01	9,9.3	9,9.3	9,9.3	9,9.3
D21S11	29,34.2	29,30	29,30	29,30,34.2
D18S51	14,18	14,15	14,18	14,18
PENTA_E	10,12	5,13	12,13	10,12,13
D5S818	9,12	12,13	9,12	9,12
D13S317	11,12	10,12	10,11	10,11,12
D7S820	9,10	8,12	8,10	8,9,10
D16S539	11,13	11,13	11,13	11,13
CSF1PO	10,12	12,12	10,12	10,12
PENTA_D	10,12	10,13	10,10	10,12

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Manual calculations for one marker using different methods and approaches. Formal definition of the LR.

Paper challenge – Case 2 results

Single marker manual calculation – consider Penta D

Marker	Mother	Father	Child	Mixture
D3S1358	14,16	15,15	14,15	14,15,16
TH01	9,9.3	9,9.3	9,9.3	9,9.3
D21S11	29,34.2	29,30	29,30	29,30,34.2
D18S51	14,18	14,15	14,18	14,18
PENTA_E	10,12	5,13	12,13	10,12,13
D5S818	9,12	12,13	9,12	9,12
D13S317	11,12	10,12	10,11	10,11,12
D7S820	9,10	8,12	8,10	8,9,10
D16S539	11,13	11,13	11,13	11,13
CSF1PO	10,12	12,12	10,12	10,12
PENTA_D	**10,12**	**10,13**	**10,10**	**10,12**

Part a) – Trio

$$LR_{Trio} = \frac{\Pr(G_{Mother})\Pr(G_{Father})\Pr(G_{Child} \mid G_{Father}, G_{Mother})}{\Pr(G_{Mother})\Pr(G_{Father})\Pr(G_{Child} \mid G_{Mother})} = \frac{0.5 \cdot 0.5}{0.5 \cdot p_{10}} = \frac{1}{2p_{10}}$$

Genotypes of parents in both hypotheses, cancel out!

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Straight-forward derivation of the LR for a trio. Some steps are omitted for brevity.

Paper challenge – Case 2 results

Single marker manual calculation – consider Penta D

Marker	Mother	Father	Child	Mixture
D3S1358	14,16	15,15	14,15	14,15,16
TH01	9,9.3	9,9.3	9,9.3	9,9.3
D21S11	29,34.2	29,30	29,30	29,30,34.2
D18S51	14,18	14,15	14,18	14,18
PENTA_E	10,12	5,13	12,13	10,12,13
D5S818	9,12	12,13	9,12	9,12
D13S317	11,12	10,12	10,11	10,11,12
D7S820	9,10	8,12	8,10	8,9,10
D16S539	11,13	11,13	11,13	11,13
CSF1PO	10,12	12,12	10,12	10,12
PENTA_D	**10,12**	**10,13**	**10,10**	**10,12**

Part a) – Paternity only

$$LR_{Paternity} = \frac{\Pr(G_{Father})\Pr(G_{Child}|G_{Father})}{\Pr(G_{Father})\Pr(G_{Child})} = \frac{0.5p_{10}}{p_{10}^{\ 2}} = \frac{1}{2p_{10}}$$

Genotypes of father in both hypotheses, cancel out!

Oslo University Hospital

Straight-forward derivation of the LR for the paternity (mother is disregarded). Some steps are omitted for brevity. Conditioning on the mother does not add any information for this particular marker.

Paper challenge – Case 2 results

Single marker manual calculation – consider Penta D

Marker	Mother	Father	Child	Mixture
D3S1358	14,16	15,15	14,15	14,15,16
TH01	9,9.3	9,9.3	9,9.3	9,9.3
D21S11	29,34.2	29,30	29,30	29,30,34.2
D18S51	14,18	14,15	14,18	14,18
PENTA_E	10,12	5,13	12,13	10,12,13
D5S818	9,12	12,13	9,12	9,12
D13S317	11,12	10,12	10,11	10,11,12
D7S820	9,10	8,12	8,10	8,9,10
D16S539	11,13	11,13	11,13	11,13
CSF1PO	10,12	12,12	10,12	10,12
PENTA_D	**10,12**	**10,13**	**10,10**	**10,12**

Part b)

A contributor to the mixture can have genotypes 10,10 10,12 or 12,12

Mother is a known contributor and the mother of the other contributor

$$LR_{Maternity\ assumed} = \frac{\sum_{G_{Child}} \Pr(G_{Child} \mid G_{Father}, G_{Mother})}{\sum_{G_{Child}} \Pr(G_{Child} \mid G_{Mother})} = \frac{\Pr(G_{Child} = 10,10 \mid G_{Mother}, G_{Father}) + \ldots}{\Pr(G_{Child} = 10,10 \mid G_{Mother}) + \ldots} =$$

$$= \frac{0.5 \cdot 0.5 + 0.5 \cdot 0.5 + 0.5 \cdot 0}{0.5 p_{10} + 0.5(p_{10} + p_{12}) + 0.5 p_{12}} = \frac{0.5}{p_{10} + p_{12}} = \frac{1}{2(p_{10} + p_{12})}$$

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Less straight-forward derivation of the LR for the mixture. We enumare all possible genotype of the child (second contributor) in the mixture. The mother's genotype is a known contributor.

Paper challenge – Case 2 results

Single marker manual calculation – consider Penta D

Marker	Mother	Father	Child	Mixture
D3S1358	14,16	15,15	14,15	14,15,16
TH01	9,9.3	9,9.3	9,9.3	9,9.3
D21S11	29,34.2	29,30	29,30	29,30,34.2
D18S51	14,18	14,15	14,18	14,18
PENTA_E	10,12	5,13	12,13	10,12,13
D5S818	9,12	12,13	9,12	9,12
D13S317	11,12	10,12	10,11	10,11,12
D7S820	9,10	8,12	8,10	8,9,10
D16S539	11,13	11,13	11,13	11,13
CSF1PO	10,12	12,12	10,12	10,12
PENTA_D	**10,12**	**10,13**	**10,10**	**10,12**

Part b)

A contributor to the mixture can have genotypes 10,10 10,12 or 12,12

Mother is a known contributor but not assumed as the mother

$$LR_{Maternity\ not\ assumed} = \frac{\sum_{G_{Child}} \Pr(G_{Child} \mid G_{Father})}{\sum_{G_{Child}} \Pr(G_{Child})} = \frac{\Pr(G_{Child} = 10,10 \mid G_{Father}) + \ldots}{\Pr(G_{Child} = 10,10) + \ldots} =$$

$$= \frac{0.5p_{10} + 0.5p_{12} + 0p_{12}}{p_{10}^{\ 2} + 2p_{10}p_{12} + p_{12}^{\ 2}} = \frac{0.5(p_{10} + p_{12})}{(p_{10} + p_{12})^2} = \frac{1}{2(p_{10} + p_{12})}$$

Conjugate

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Less straight-forward derivation of the LR for the mixture where we only consider the paternity. We enumare all possible genotype of the child (second contributor) in the mixture. The mother's genotype is a known contributor.

Paper challenge – Case 2 results

Single marker manual calculation – consider Penta D

Marker	Mother	Father	Child	Mixture
D3S1358	14,16	15,15	14,15	14,15,16
TH01	9,9.3	9,9.3	9,9.3	9,9.3
D21S11	29,34.2	29,30	29,30	29,30,34.2
D18S51	14,18	14,15	14,18	14,18
PENTA_E	10,12	5,13	12,13	10,12,13
D5S818	9,12	12,13	9,12	9,12
D13S317	11,12	10,12	10,11	10,11,12
D7S820	9,10	8,12	8,10	8,9,10
D16S539	11,13	11,13	11,13	11,13
CSF1PO	10,12	12,12	10,12	10,12
PENTA_D	**10,12**	**10,13**	**10,10**	**10,12**

Part c)

A contributor to the mixture can have genotypes 10,10 10,12 or 12,12

Mother is not a contributor and not assumed as the mother. Unknown second contributor assumed.

$$LR_{Paternity} = \frac{\sum_{G_{Child},G_{Unknown}} \Pr(G_{Child} \mid G_{Father}) \Pr(G_{Unknown})}{\sum_{G_{Child},G_{Unknown}} \Pr(G_{Child}) \Pr(G_{Unknown})} = \frac{\Pr(G_{Child} = 10,10 \mid G_{Father}) \Pr(G_{Unknown} = 10,12) + \ldots}{\Pr(G_{Child} = 10,10) \Pr(G_{Unknown} = 10,12) + \ldots} =$$

$$= \frac{0.5p_{10}(2p_{10}p_{12} + p_{12}^2) + 0.5p_{12}(p_{10}^2 + 2p_{10}p_{12} + p_{12}^2) + 0p_{12}(p_{10}^2 + 2p_{10}p_{12})}{p_{10}^2 \cdot (2p_{10}p_{12} + p_{12}^2) + 2p_{10}p_{12}(p_{10}^2 + 2p_{10}p_{12} + p_{12}^2) + p_{12}^2(p_{10}^2 + 2p_{10}p_{12})} = \frac{0.5\left[2p_{10}^2 + p_{10}p_{12} + (p_{10} + p_{12})^2\right]}{p_{10}\left[4p_{10}^2 + 6p_{10}p_{12} + 4p_{12}^2\right]}$$

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Least straight-forward derivation of the LR for the mixture where we only consider the paternity and where the mother's genotypes are disregarded. This requires a second unknown contributor.

Paper challenge – Case 2 results

Single marker manual calculation – consider Penta D

Marker	Mother	Father	Child	Mixture
D3S1358	14,16	15,15	14,15	14,15,16
TH01	9,9.3	9,9.3	9,9.3	9,9.3
D21S11	29,34.2	29,30	29,30	29,30,34.2
D18S51	14,18	14,15	14,18	14,18
PENTA_E	10,12	5,13	12,13	10,12,13
D5S818	9,12	12,13	9,12	9,12
D13S317	11,12	10,12	10,11	10,11,12
D7S820	9,10	8,12	8,10	8,9,10
D16S539	11,13	11,13	11,13	11,13
CSF1PO	10,12	12,12	10,12	10,12
PENTA_D	**10,12**	**10,13**	**10,10**	**10,12**

Part a) $LR_{Trio} = \frac{1}{2\,p_{10}}$ $\quad p_{10}$=0.1256, p_{12}=0.2349

$LR_{Paternity} = \frac{1}{2\,p_{10}}$

Part b) $LR_{Maternity\ assumed} = \frac{1}{2(p_{10} + p_{12})}$

$LR_{Maternity\ not\ assumed} = \frac{1}{2(p_{10} + p_{12})}$

Part c) $LR_{Paternity} = \frac{\left[2\,p_{10}^{\,2} + p_{10}p_{12} + (p_{10} + p_{12})^2\right]}{4\,p_{10}\left[2\,p_{10}^{\,2} + 3\,p_{10}p_{12} + 2\,p_{12}^{\,2}\right]}$

Marker	LR a)	LR a) paternity	LR b)	LR b) no maternity	LR c)
D3S1358	3.79	1.90	3.79	2.40	1.34
TH01	2.11	2.61	2.11	2.11	2.33
D21S11	2.00	2.12	2.00	2.07	1.59
D18S51	1.89	1.33	1.89	1.89	1.65
PENTA_E	6.11	3.06	6.11	3.47	1.89
D5S818	1.29	0.71	1.29	1.29	1.01
D13S317	5.62	2.81	5.62	3.44	2.23
D7S820	3.13	1.56	3.13	1.81	1.00
D16S539	2.09	2.26	2.09	2.09	2.16
CSF1PO	1.73	1.52	1.73	1.73	1.64
PENTA_D	**3.98**	**3.98**	**1.39**	**1.39**	**1.65**
VWA	1.69	1.69	1.69	1.69	1.69
D8S1179	7.20	3.60	7.20	4.93	2.77
TPOX	0.62	0.45	0.62	0.62	0.55
FGA	2.90	1.45	2.90	2.19	1.73
D19S433	1.23	1.37	1.23	1.23	1.29
Total	1619722	9940	564300	38336	1158

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Manual calculations for one marker using different methods and approaches

Paper challenge – Case 2 conclusion

1. *Known contributors does not always increase the LR (see Penta D and TH01) but generally will, see rest of the STR markers (compare last two columns of right table)*
2. *Modelling that the mother is the mother of the child (as contributor to the mixture) can increase the LR but does not necessarily (compare third and fourth column of right table)*
3. *The mixture only has a minor impact on the LR if we model the known contributors and maternity (compare first and third column of the right table)*

Marker	Mother	Father	Child	Mixture
D3S1358	14,16	15,15	14,15	14,15,16
TH01	9,9.3	9,9.3	9,9.3	9,9.3
D21S11	29,34.2	29,30	29,30	29,30,34.2
D18S51	14,18	14,15	14,18	14,18
PENTA_E	10,12	5,13	12,13	10,12,13
D5S818	9,12	12,13	9,12	9,12
D13S317	11,12	10,12	10,11	10,11,12
D7S820	9,10	8,12	8,10	8,9,10
D16S539	11,13	11,13	11,13	11,13
CSF1PO	10,12	12,12	10,12	10,12
PENTA_D	10,12	10,13	10,10	10,12
VWA	17,17	17,20	17,17	17,17
D8S1179	10,16	12,12	12,16	10,12,16
TPOX	8,11	8,9	8,11	8,11
FGA	25,25	20,21	21,25	21,25
D19S433	13,15	14,15	13,15	13,15

Marker	LR a)	LR a) paternity	LR b)	LR b) no maternity	LR c)
D3S1358	3.79	1.90	3.79	2.40	1.34
TH01	2.11	2.61	2.11	2.11	2.33
D21S11	2.00	2.12	2.00	2.07	1.59
D18S51	1.89	1.33	1.89	1.89	1.65
PENTA_E	6.11	3.06	6.11	3.47	1.89
D5S818	1.29	0.71	1.29	1.29	1.01
D13S317	5.62	2.81	5.62	3.44	2.23
D7S820	3.13	1.56	3.13	1.81	1.00
D16S539	2.09	2.26	2.09	2.09	2.16
CSF1PO	1.73	1.52	1.73	1.73	1.64
PENTA_D	3.98	3.98	1.39	1.39	1.65
VWA	1.69	1.69	1.69	1.69	1.69
D8S1179	7.20	3.60	7.20	4.93	2.77
TPOX	0.62	0.45	0.62	0.62	0.55
FGA	2.90	1.45	2.90	2.19	1.73
D19S433	1.23	1.37	1.23	1.23	1.29
Total	1619722	9940	564300	38336	1158

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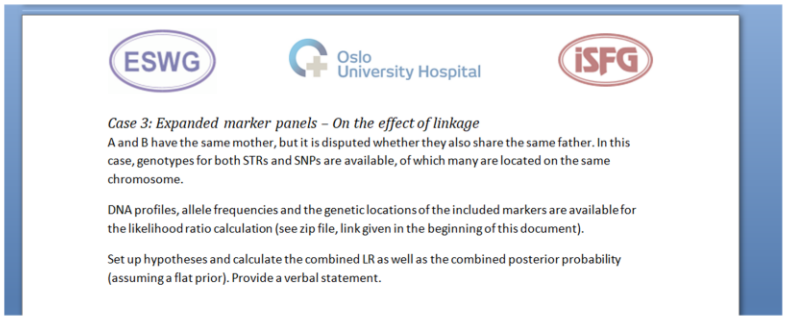
Some conclusions for Case 2.

Paper challenge – Case 3



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iSFG

Case 3: Expanded marker panels – On the effect of linkage

A and B have the same mother, but it is disputed whether they also share the same father. In this case, genotypes for both STRs and SNPs are available, of which many are located on the same chromosome.

DNA profiles, allele frequencies and the genetic locations of the included markers are available for the likelihood ratio calculation (see zip file, link given in the beginning of this document).

Set up hypotheses and calculate the combined LR as well as the combined posterior probability (assuming a flat prior). Provide a verbal statement.

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Background for the third case of the paper challenge. The exercise involves an expanded marker panel

Paper challenge – Case 3 data

- Autosomal marker data for 20 STR markers and 130+ SNPs
- Several markers located closely on the same chromosome
- Map file with marker positions (in cM) supplied

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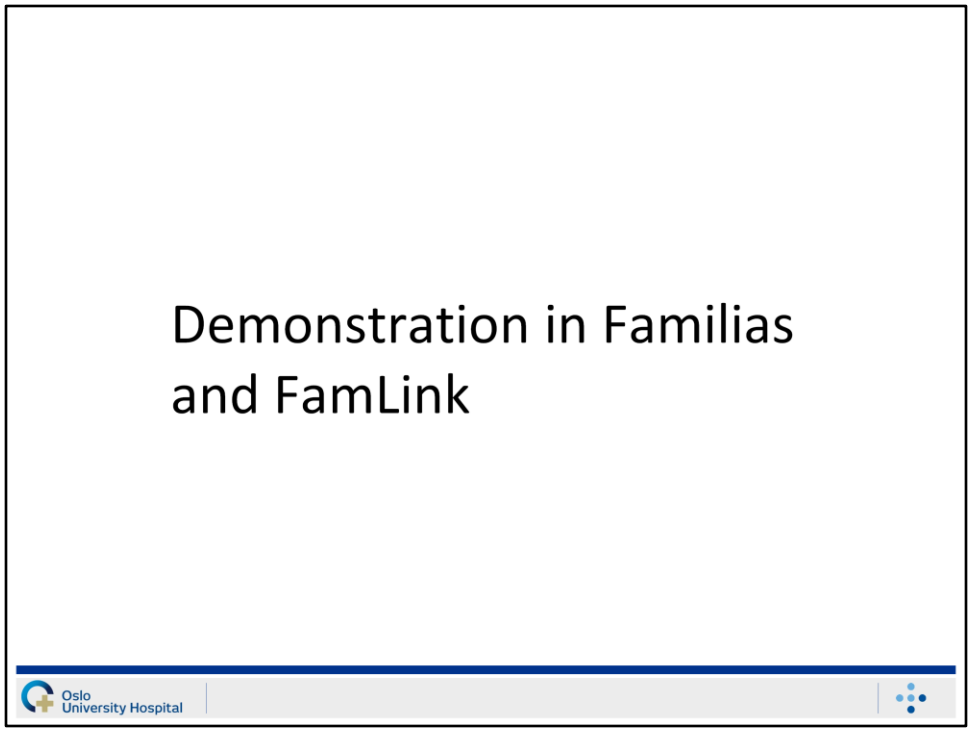
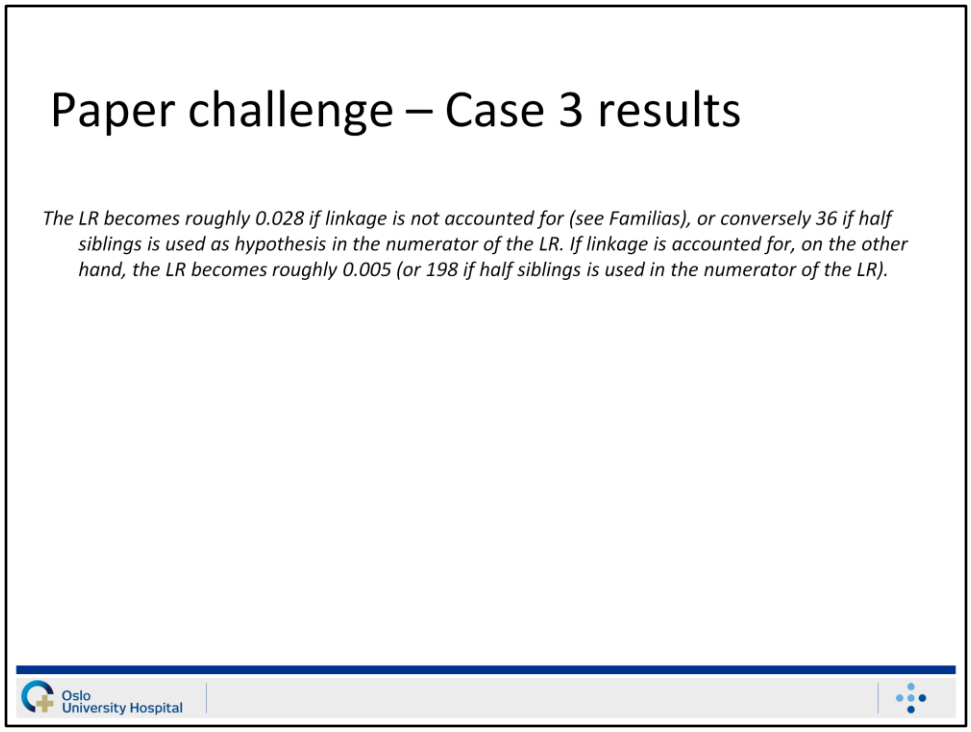
Brief summary of the genetic marker data.

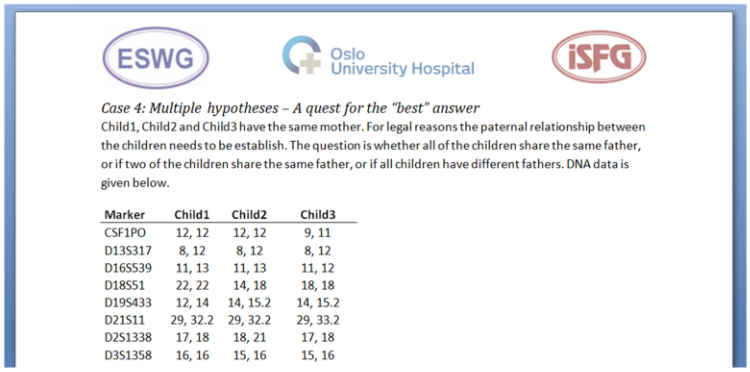


Videos available online. Link given in first slide.



Summary of the results. Accounting for linkage will increase the support for the second hypotheses (half siblings) to roughly 200, compared to only 36 if linkage is not accounted for.

Paper challenge – Case 4

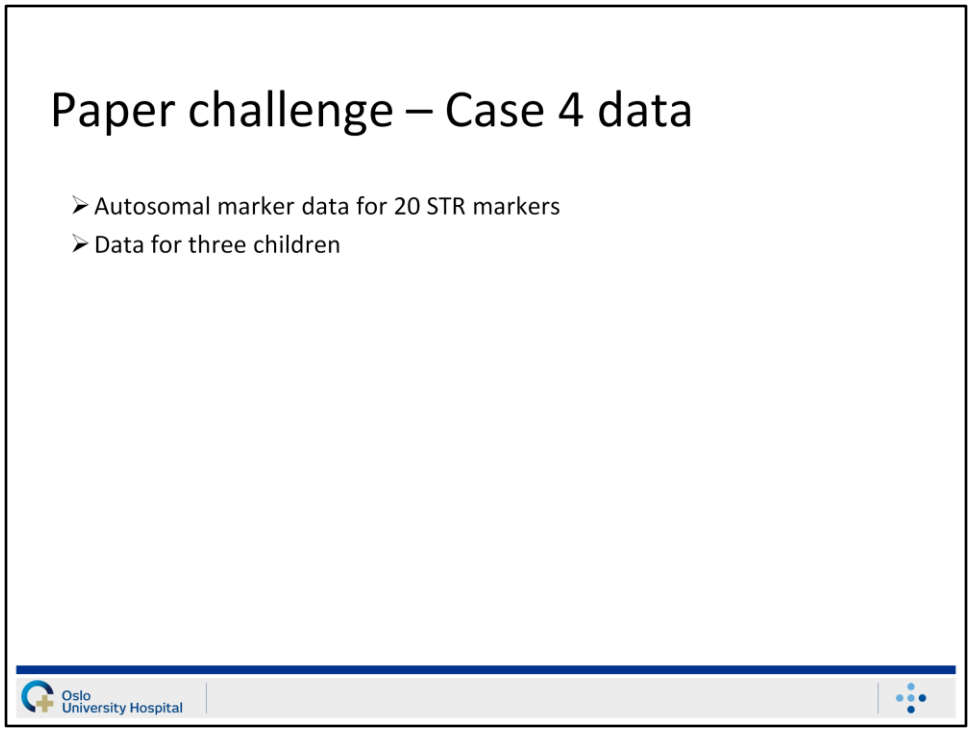


Case 4: Multiple hypotheses – A quest for the "best" answer

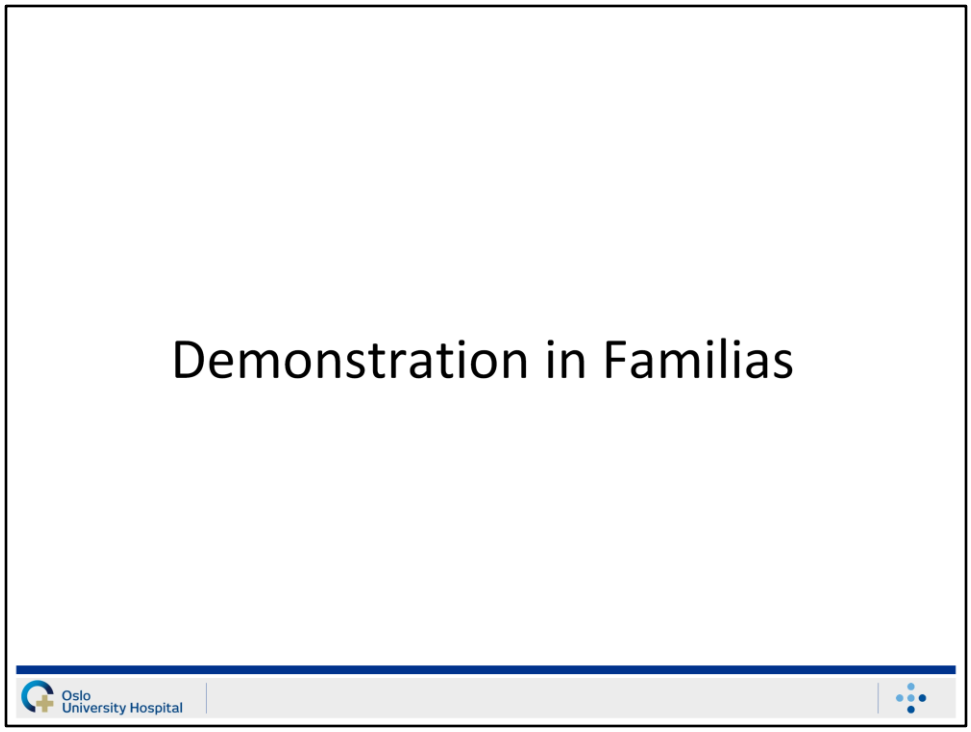
Child1, Child2 and Child3 have the same mother. For legal reasons the paternal relationship between the children needs to be establish. The question is whether all of the children share the same father, or if two of the children share the same father, or if all children have different fathers. DNA data is given below.

Marker	Child1	Child2	Child3
CSF1PO	12, 12	12, 12	9, 11
D13S317	8, 12	8, 12	8, 12
D16S539	11, 13	11, 13	11, 12
D18S51	22, 22	14, 18	18, 18
D19S433	12, 14	14, 15.2	14, 15.2
D21S11	29, 32.2	29, 32.2	29, 33.2
D2S1338	17, 18	18, 21	17, 18
D3S1358	16, 16	15, 16	15, 16

Background for the fourth case of the paper challenge. Data given for three children.

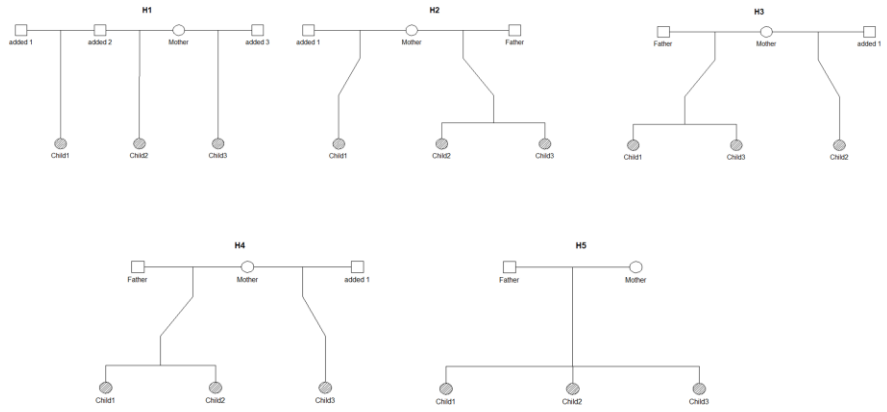


Brief summary of the genetic marker data.



Video available online. Link given in first slide.

Paper challenge – Case 4 results



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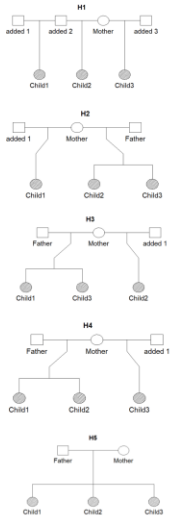
The hypotheses (pedigrees) generated for this case.

Paper challenge – Case 4 results

Compare DNA

System	LR	Child1	Child2	Child3
CSF1PO	0.3760657...	12, 12	12, 12	9, 11
D13S317	3.012455779	8, 12	8, 12	8, 12
D16S539	0.6328977...	11, 13	11, 13	11, 12
D18S51	0	22, 22	14, 18	18, 18
D19S433	3.195875489	12, 14	14, 15.2	14, 15.2
D21S11	0.7323725...	29, 32.2	29, 32.2	29, 33.2
D2S1338	3.28969025	17, 18	18, 21	17, 18
D3S1358	1.746683955	16, 16	15, 16	15, 16
D5S818	0.3433040...	11, 12	12, 13	12, 12
D7S820	0.7550753...	8, 8	8, 8	8, 12
D8S1179	0.7521977...	14, 14	14, 14	13, 14
FGA	0.7675741...	22, 22	22, 22	20, 22
TH01	0.7767790...	8, 9	8, 9	7, 9
TPOX	1.535463308	8, 12	8, 11	11, 12
D10S1248	2.426594467	15, 17	14, 16	14, 16
D12S391	0.8787964...	17, 21	17, 21	17, 17
D1S1656	6.447096544	16, 17	16.3, 17	16, 17
D22S1045	0.6245414...	11, 15	11, 15	11, 16
D2S441	2.440428589	10, 14	10, 14	10, 14
SE33	0	30.2, 33	30.2, 32	26.2, 30.2

Total LR: 0 Save Close



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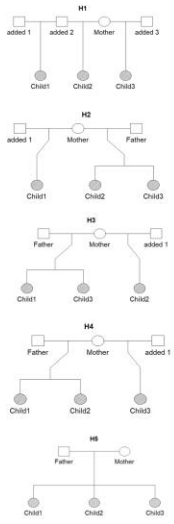
Two inconsistencies (D18S51 and SE33) given the fifth (H5) hypothesis. H5 constraints the number of alleles to four (two parents). SE33 can be explained by a single step mutation while D18S51 is more likely explained by a silent allele.

Paper challenge – Case 4 results

Compare DNA

System	LR	Child1	Child2	Child3
CSF1PO	1.515405116	12, 12	12, 12	9, 11
D13S317	3.009341631	8, 12	8, 12	8, 12
D16S539	2.23596439	11, 13	11, 13	11, 12
D18S51	0.1211116…	22, 22	14, 18	18, 18
D19S433	0.6828042…	12, 14	14, 15.2	14, 15.2
D21S11	3.917668899	29, 32.2	29, 32.2	29, 33.2
D2S1338	3.284001009	17, 18	18, 21	17, 18
D3S1358	0.7882899…	16, 16	15, 16	15, 16
D5S818	0.2598265…	11, 12	12, 13	12, 12
D7S820	3.078819711	8, 8	8, 8	8, 12
D8S1179	3.028897207	14, 14	14, 14	13, 14
FGA	3.29735637	22, 22	22, 22	20, 22
TH01	4.841025024	8, 9	8, 9	7, 9
TPOX	0.9040812…	8, 12	8, 11	11, 12
D10S1248	0.4171218…	15, 17	14, 16	14, 16
D12S391	3.216039278	17, 21	17, 21	17, 17
D1S1656	6.432688314	16, 17	16.3, 17	16, 17
D22S1045	1.93866186	11, 15	11, 15	11, 16
D2S441	2.437908449	10, 14	10, 14	10, 14
SE33	0.3143917…	30.2, 33	30.2, 32	26.2, 30.2

Total LR: 3834.375076 Save Close



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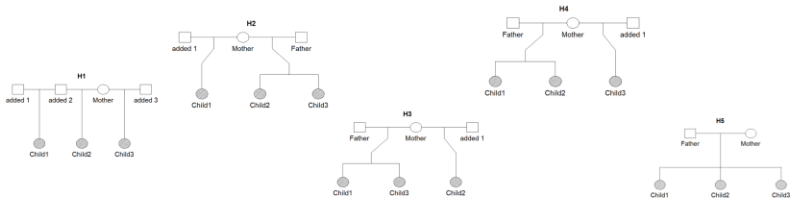
Resuls for H5 if mutations are modelled and a silent allele frequency of 0.0001 is used.

Paper challenge – Case 4 results

Hypotheses	No mutations, no silent	Mutations, no silent	Mutations and silent (0.00001)	Mutations and silent (0.0001)	Mutations and silent (0.001)
H1	0.00031	0.00024	0.00021	0.00011	0.00002
H2	0.00036	0.00028	0.00025	0.00014	0.00005
H3	0.00025	0.00019	0.00017	0.0001	0.00004
H4	0.999	0.9986	0.8857	0.449	0.104
H5	0	0.00064	0.1137	0.550	0.896

Increasing posterior for H5 →



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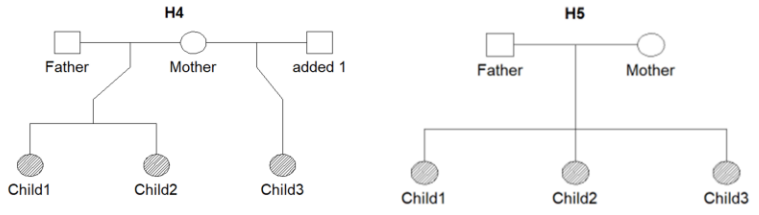
Summary of the results where different approaches to the calculations are presented. In particular, the silent allele frequency is varied, starting at 0.00001 and increasing to 0.001.

Paper challenge – Case 4 results

- 12 labs reported that H4 is most likely (and would conclude with that)
- 12 labs reported that H5 is most likely (and would in most cases conclude with that)
- 6 labs reported inconclusive or recommended additional testing



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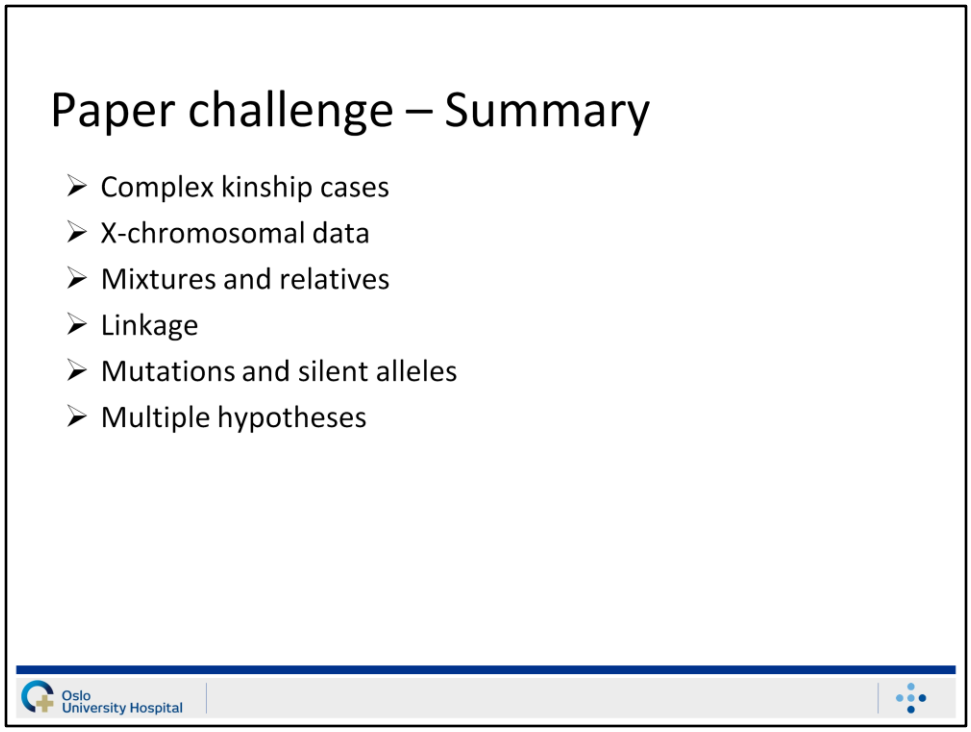
There is a 50/50 division of results favoring H4 and H5



Summary of the paper challenge

Paper challenge – Summary

Case 1

- A few labs missed the cousin link resulting in a higher LR

Case 2

- In b), several labs did not account for maternity resulting in a lower LR

Case 3

- Mostly consistent results, some labs did not account for linkage

Case 4

- 12 labs indicated conclusive results for H4 while 12 labs reported conclusive results for H5

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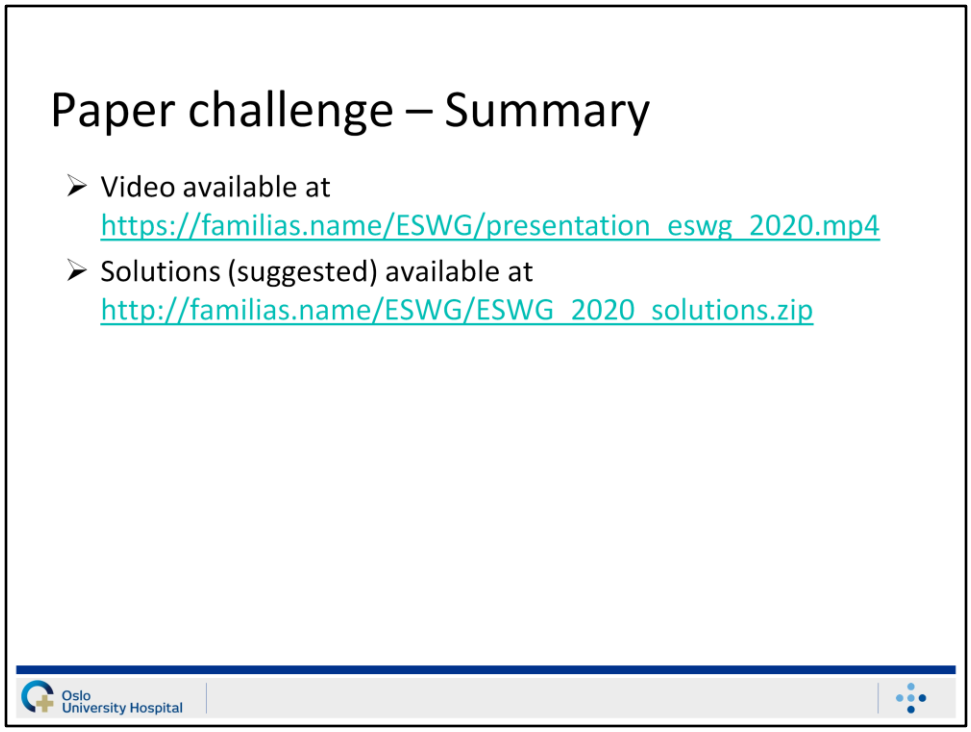
Summary of the paper challenge



Summary of the paper challenge

Proficiency test – Future

- Not determined who will organize next – ESWG board will decide

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Summary of the paper challenge

This is a brief summary of the ESWG proficiency test 2020. Complete results are contained in the Excel summary.