

PRELIMINARY VERSION, THE PRESENTATION WILL BE
SUBJECT TO CHANGES

Familias 3.0 – Exploring new features

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Familias 3.0 - Outline

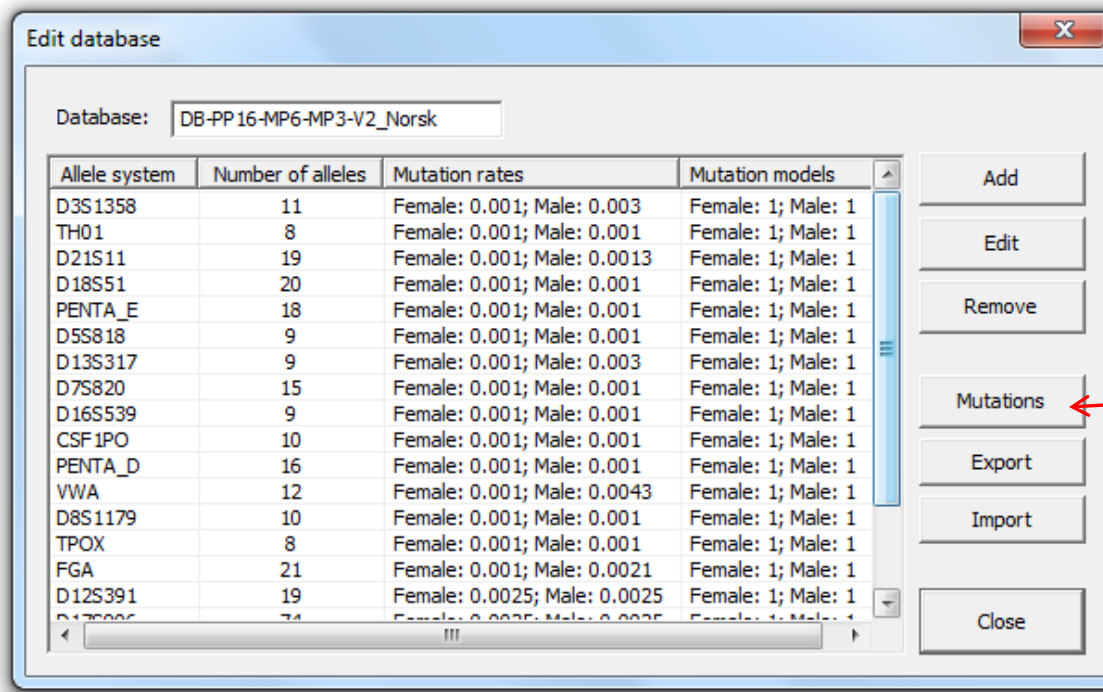
- Brief overview
- New mutation model
- Simulation interface
- DVI module
- Blind search module

Familias 3.0 – Introduction

- Developed from the old core
- Based on user input
- Validation article (Drabek)
- Subject to further improvements based on user input

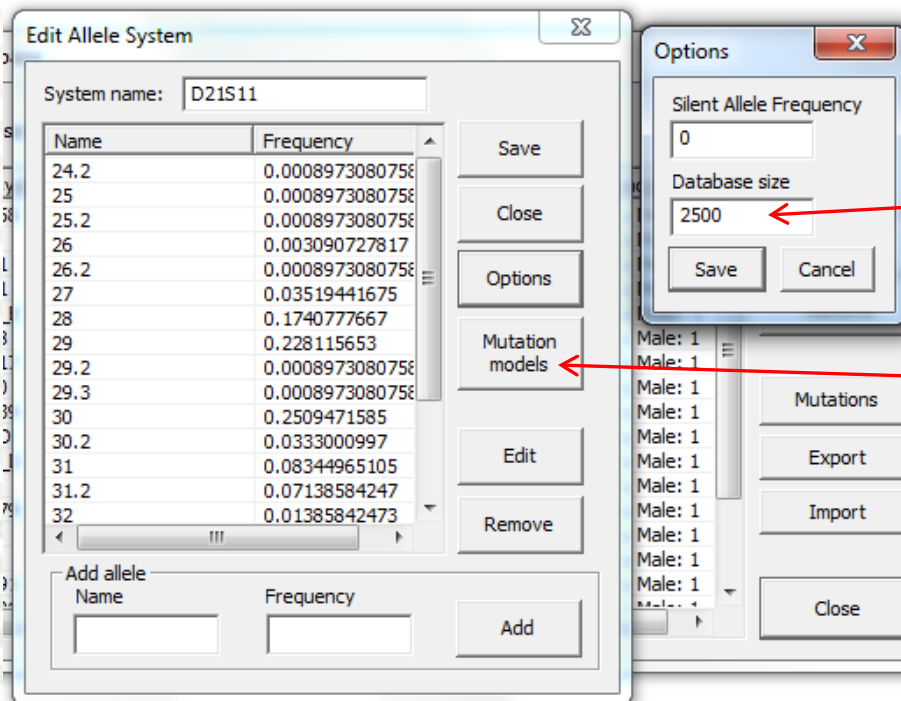
Familias 3.0 – At a glance

- Define general database
- Change mutations



Familias 3.0 – At a glance

- Define marker specific database sizes
- New allele dialog
- New mutation dialog



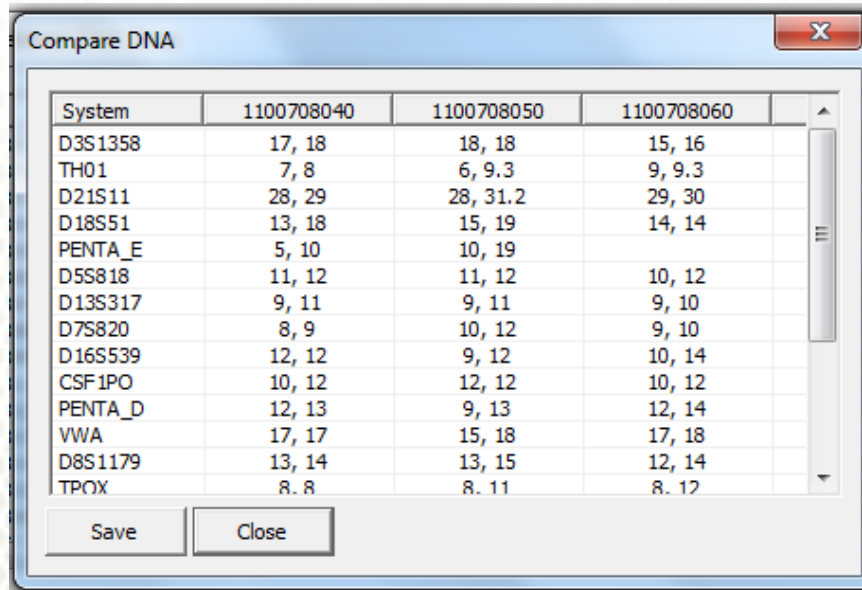
Familias 3.0 – At a glance

- New import options
- Case data dialog
- Compare profiles



Familias 3.0 – At a glance

- Compare data



System	1100708040	1100708050	1100708060
D3S1358	17, 18	18, 18	15, 16
TH01	7, 8	6, 9.3	9, 9.3
D21S11	28, 29	28, 31.2	29, 30
D18S51	13, 18	15, 19	14, 14
PENTA_E	5, 10	10, 19	
D5S818	11, 12	11, 12	10, 12
D13S317	9, 11	9, 11	9, 10
D7S820	8, 9	10, 12	9, 10
D16S539	12, 12	9, 12	10, 14
CSF1PO	10, 12	12, 12	10, 12
PENTA_D	12, 13	9, 13	12, 14
VWA	17, 17	15, 18	17, 18
D8S1179	13, 14	13, 15	12, 14
TPOX	8. 8	8. 11	8. 12

Familias 3.0 – At a glance

- Definition of pedigrees

Project name: 0_NORSK_20_ Number of pedigrees: 2

Pedigree	Prior	Posterior	Likelihood Ratio	Ln likelihood
Ped 1	0.5	8.003991e-017	8.00399075e-017	-976.1204
Ped 2	0.5	>0.999999	1	-939.0564

Actions

Calculate

Add

Edit

Remove

Remove all

Generate

Simulate

Options

Parameters

Included systems

Display

Scale

Save results

Simulation

Will be genotyped

Not genotyped

Options

Number of simulations: 1000

Save raw data

Data for all markers

Seed

Random seed

Simulate

Results

Close

Display

Static

Prior

Posterior

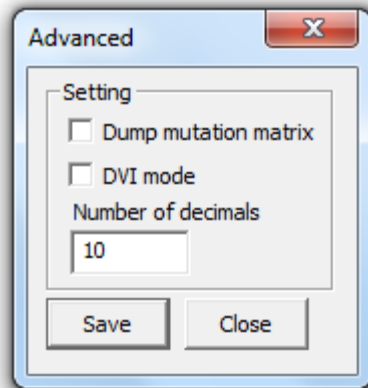
LR

Ln likelihood

Close

Familias 3.0 – At a glance

- Advanced settings



Familias 3.0 – New mutation model

- Theory
 - Steps
 - Microvariants
- Parameters
 - Mutation rate (μ)
 - Range (r)
 - Secondary mutation rate (α)

Familias 3.0 – New mutation model

- Mutation matrix

$$M = \begin{matrix} & 12 & 13 \\ 12 & 1-\mu & \mu \\ 13 & \mu & 1-\mu \end{matrix}$$

List of alleles

12.1
13
13.1
14
17

- Example

$$M = \begin{bmatrix} (1-\mu)(1-\alpha) & \alpha/3 & (1-\alpha)k_1r^1 & \alpha/3 & \alpha/3 \\ \alpha/2 & (1-\mu)(1-\alpha) & \alpha/2 & (1-\alpha)k_2r^1 & (1-\alpha)k_2r^4 \\ (1-\alpha)k_3r^1 & \alpha/3 & (1-\mu)(1-\alpha) & \alpha/3 & \alpha/3 \\ \alpha/2 & (1-\alpha)k_4r^1 & \alpha/2 & (1-\mu)(1-\alpha) & (1-\alpha)k_1r^3 \\ \alpha/2 & (1-\alpha)k_5r^4 & \alpha/2 & (1-\alpha)k_5r^3 & (1-\mu)(1-\alpha) \end{bmatrix}$$

For first row: $1 = (1-\mu)(1-\alpha) + \alpha/3 * 3 + (1-\alpha)k_1r \Leftrightarrow k_1 = \frac{1-(1-\mu)(1-\alpha)-\alpha}{(1-\alpha)r} = \frac{\mu}{r}$

Familias 3.0 – Simulations

- What is a simulation?
 - Based on a model
- Why do we want to simulate?
 - Find distributions of LRs
 - What can we expect
- The utility of simulations
 - Assisting tool in decision prior to obtaining a case
 - Assisting tool after a case is complete
- Further uses
 - Use raw data to perform statistical calculations
 - Use simulated data in other settings

Familias 3.0 – Simulated example

- Steps in a simulation

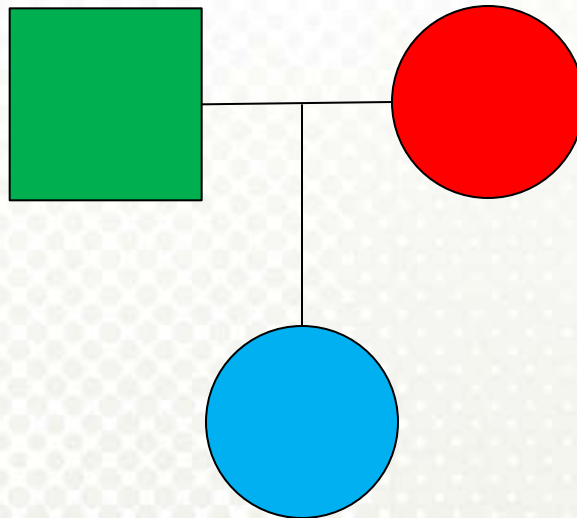
1. Define allele frequencies and mutation models
2. Define all persons we need
3. Define hypotheses (i.e. pedigrees)
4. Start simulations

- Algorithm

1. Define founders and non-founders
2. Sample founder alleles from allele frequencies (Account for kinship)
3. Randomly sample the non-founder alleles based on the parents alleles and the mutation models (i.e. allele may change/mutate given a mutation rate >0)
4. Repeat 2. such that all non-founders are sampled
5. Calculate likelihoods for the simulated data given all hypotheses
6. Repeat 1-4 for all hypotheses, i.e. we must simulate all pedigrees as true

Familias 3.0 – Simulated example

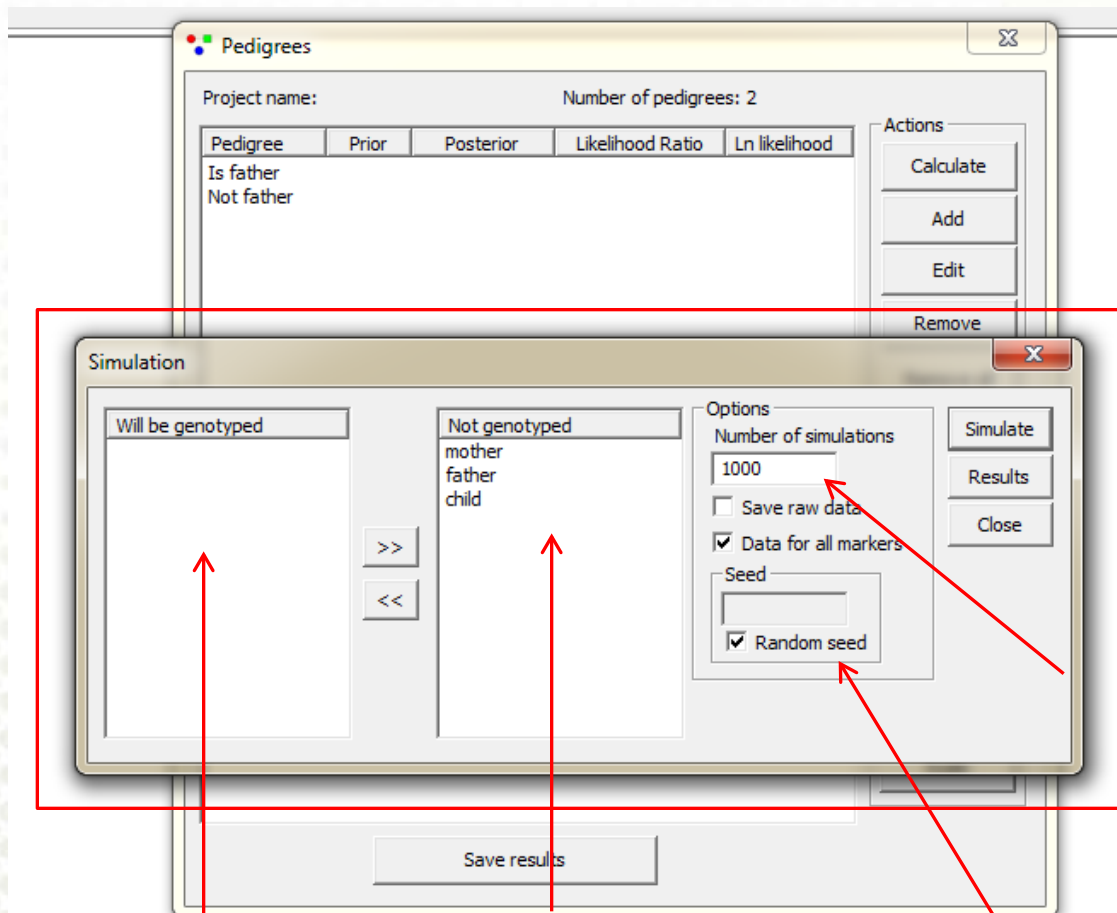
- Consider a paternity case



Familias 3.0 – Simulated example

- We define a marker S1
 - Alleles 12, 13, 14 and 15. (Uniform allele frequencies 0.25)
 - Simple mutation model with mutation rate 0.0
- We define the necessary persons
 - Mother, child and the father
 - We do NOT define any DNA data for the persons
- We define the pedigrees
 - Two different hypotheses

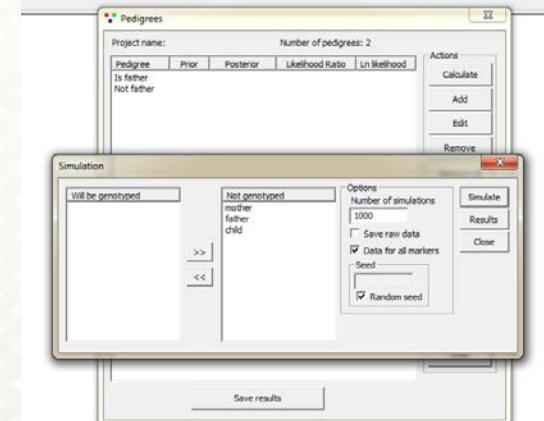
Familias 3.0 – Simulated example



Familias 3.0 – Simulated example

Options

- Number of simulations
 - Greater is often better
- Save the raw data
 - Use in other studies
 - Calculate your own statistics
- Random seed or non-random seed
- Select genotyped persons



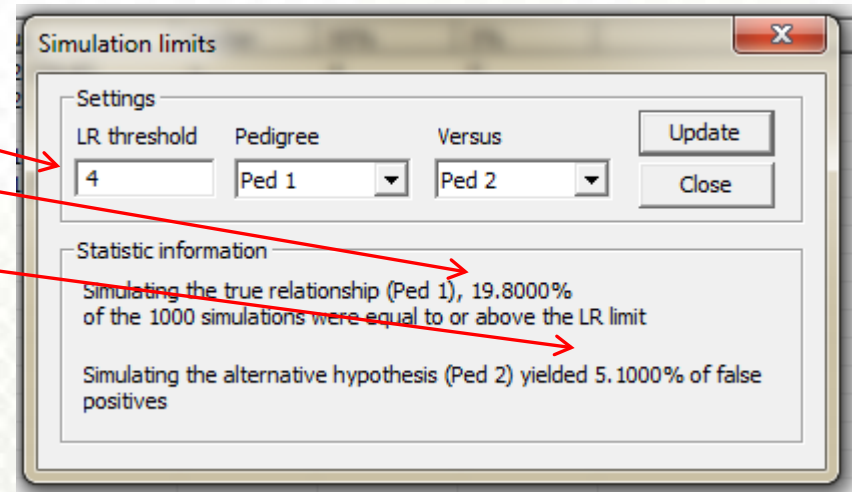
Familias 3.0 – Simulated example

- Simulate data
 - Simulate data given both hypotheses
 - In reality 1000*2 simulations are performed
 - Calculate likelihood for both hypotheses

Pedigree	Versus	Median	95%	5%
Ped 1	Ped 2 (TRUE)	1	4	0
Ped 1 (TRUE)	Ped 2	2	4	1
Ped 2 (TRUE)	Ped 1	1	NaN/Inf	0.25
Ped 2	Ped 1 (TRUE)	0.5	1	0.25

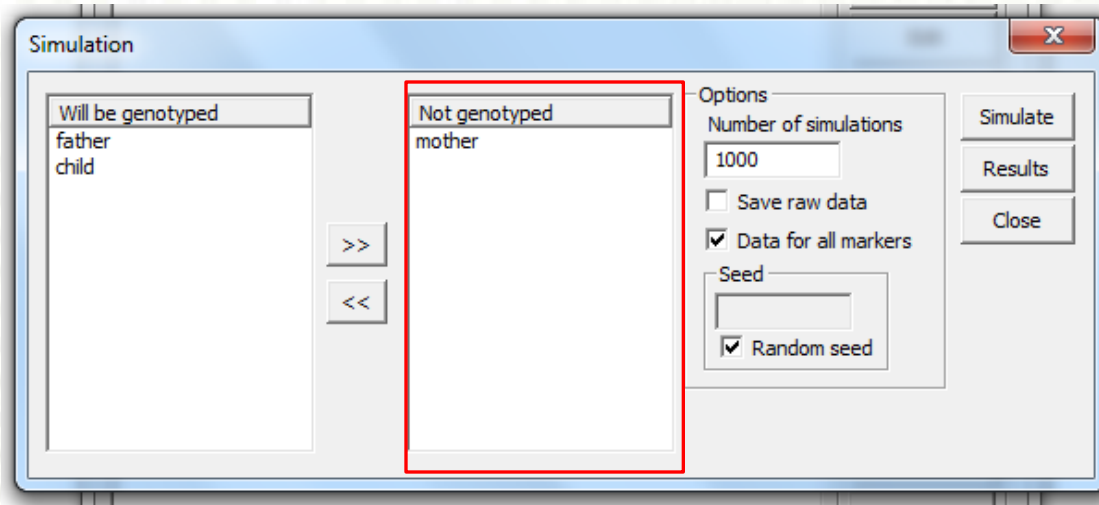
Familias 3.0 – Simulated example

- Threshold
- False negative rate
- False positive rate



Familias 3.0 – Simulated example

- Return, the mother is not genotyped!



Familias 3.0 – Simulation summary

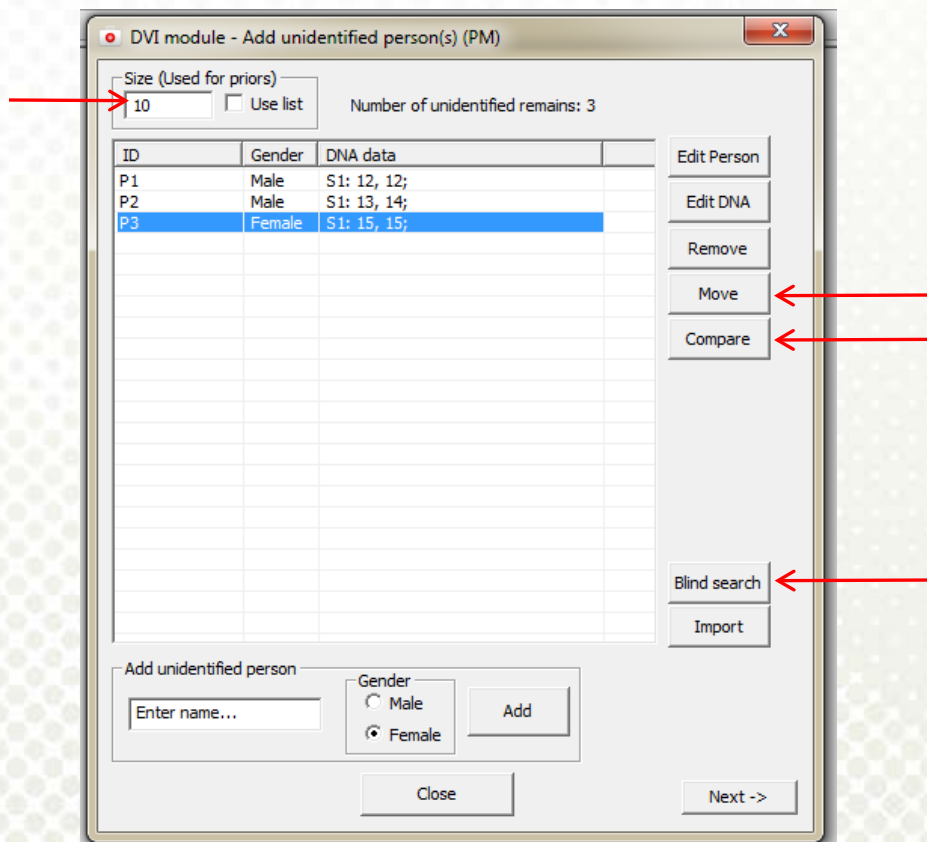
- Find good thresholds
 - False positive/negative rate
- Investigate what we can expect
- Include
 - Kinship
 - Mutations
 - Silent alleles
 - Multiple pedigrees
- Investigate the number of persons we must genotype
- Investigate the number of markers we must include

Familias 3.0 – Disaster Victim Identification (DVI)

- What is a DVI operation?
- What is the purpose of developing a DVI module?
- “Alternative” softwares
- Brief overview
- Blind search module

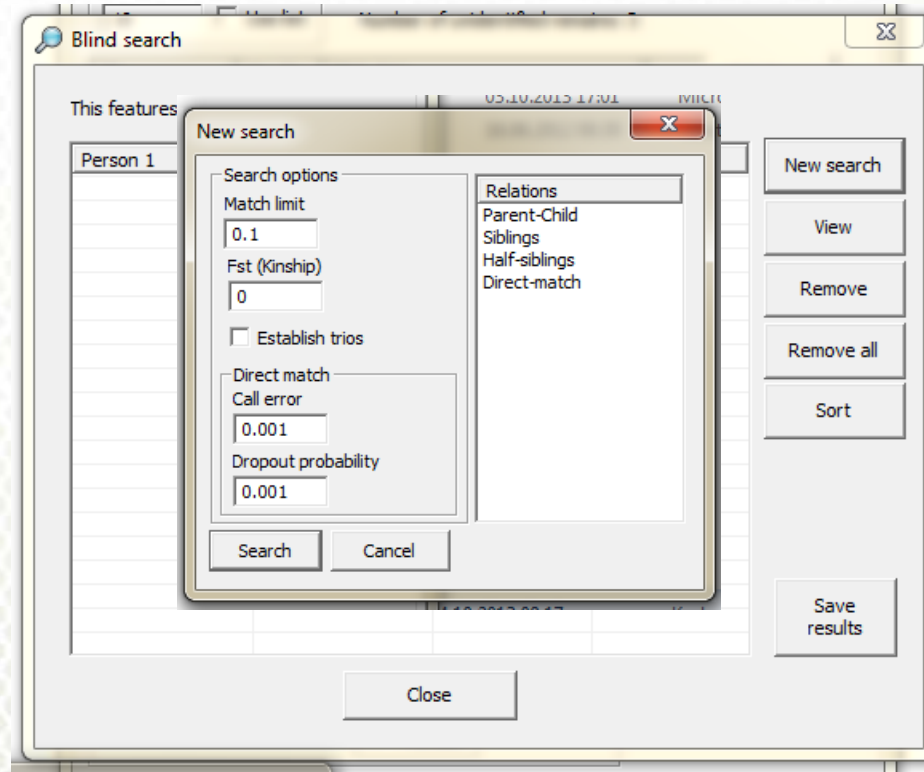
Familias 3.0 – DVI example

- Add Unidentified persons



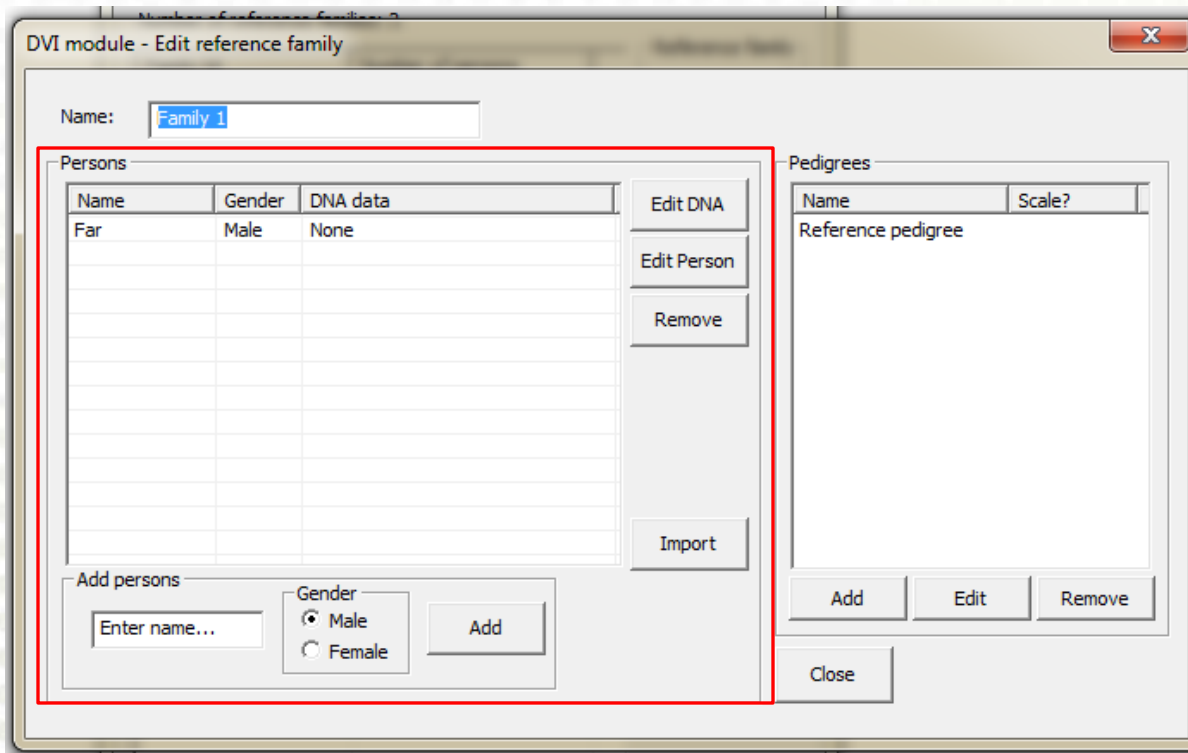
Familias 3.0 – DVI example

- Blind search



Familias 3.0 – DVI example

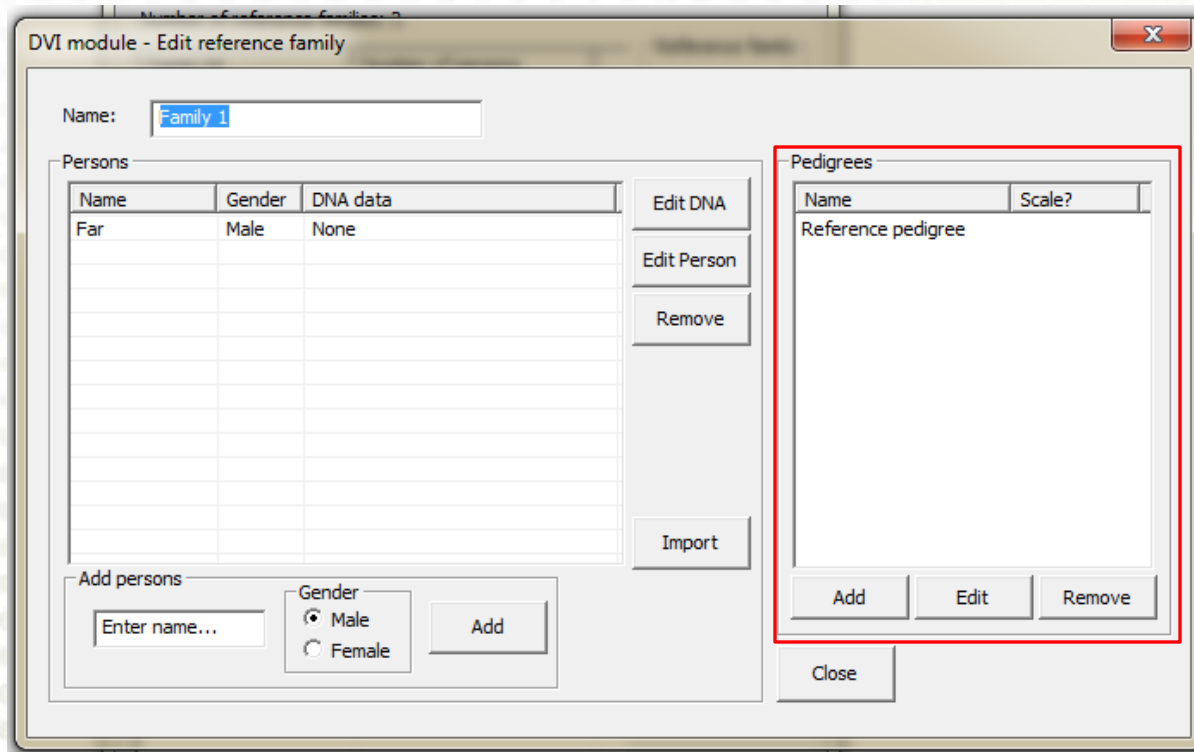
- Edit reference family



- Add persons

Familias 3.0 – DVI example

- Edit reference family



- Add pedigrees

Familias 3.0 – DVI example

- Add pedigree

Add new template pedigree

Name:

Parent	Child	Direct match?
Far	Missing person	No

Close

Extra persons

Remove

Add relation

Direct match

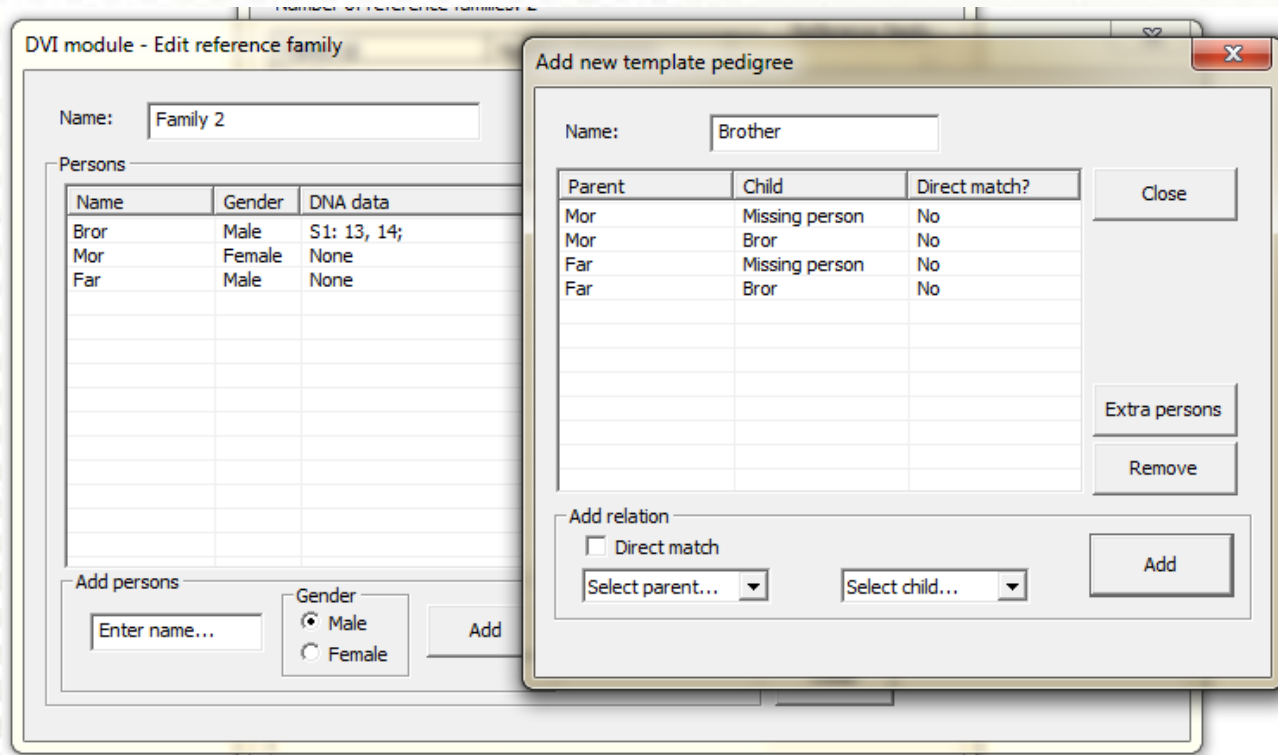
Select parent...

Select child...

Add

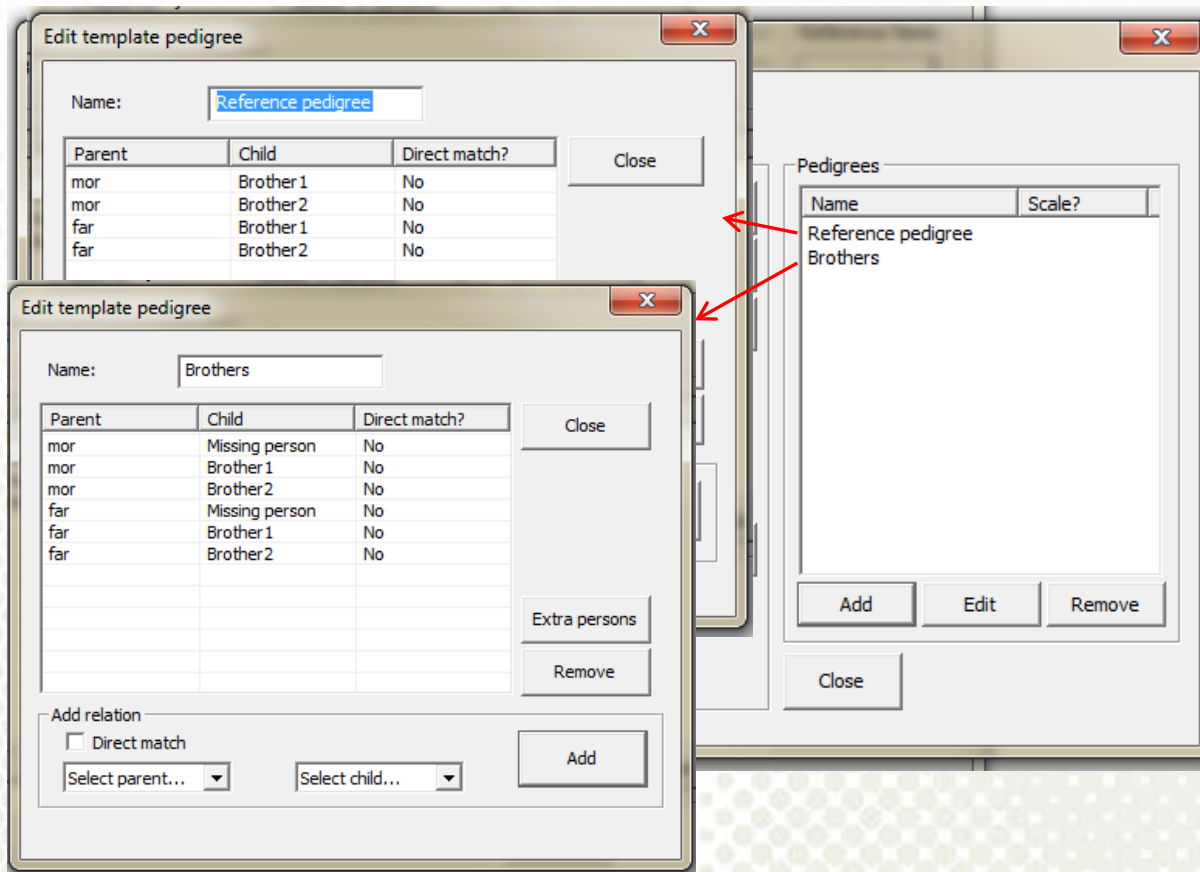
Familias 3.0 – DVI example

- What if we have more complicated relationships?
- Brother



Familias 3.0 – DVI example

- Two brothers as reference persons!?



Familias 3.0 – DVI example

- Matching

DVI module - Results

Project name is: familias_dvi_example

Family id	Unidentified person	Prior	Posterior	LR
Family 1	Reference pedig...	0.72727	0.2	1
Family 1	P1 (Father)	0.090909	0.8	4
Family 2	Reference pedig...	0.72727	0.210526	1
Family 2	P1 (Brother)	0.090909	0.0526316	0.25
Family 2	P2 (Brother)	0.090909	0.684211	3.25
Family 2	P3 (Brother)	0.090909	0.0526316	0.25
Family 3	Reference pedig...	0.72727	0.10917	1
Family 3	P1 (Brothers)	0.090909	0.0174672	0.16
Family 3	P2 (Brothers)	0.090909	0.0174672	0.16
Family 3	P3 (Brothers)	0.090909	0.855895	7.84

Search

Search

Sort

Limit list

Display

Match

View match

Confirm match

Remove

Save results

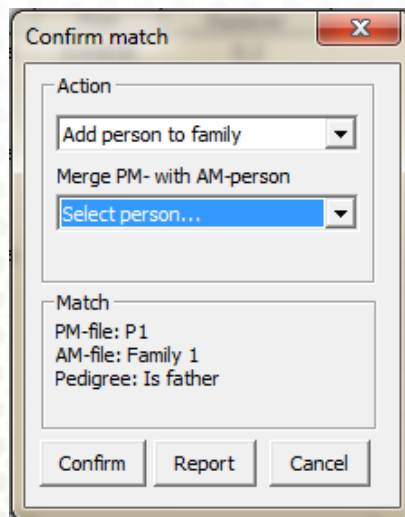
<- Previous

Close

The screenshot shows a software window titled "DVI module - Results" with a close button (X) in the top right. The window displays a table of results for a project named "familias_dvi_example". The table has five columns: "Family id", "Unidentified person", "Prior", "Posterior", and "LR". There are 12 rows of data. To the right of the table is a control panel with two sections: "Search" and "Match". The "Search" section contains buttons for "Search", "Sort", "Limit list", and "Display". The "Match" section contains buttons for "View match", "Confirm match", and "Remove". Below these sections is a "Save results" button. At the bottom of the window are buttons for "<- Previous" and "Close". Red arrows point to the "Search", "View match", and "Confirm match" buttons.

Familias 3.0 – DVI example

- Confirm match // Write report



Familias 3.0

- Questions?
- Exercises
- New file format

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