


RISCALW a windows program for risk calculation in Duchenne muscular dystrophy

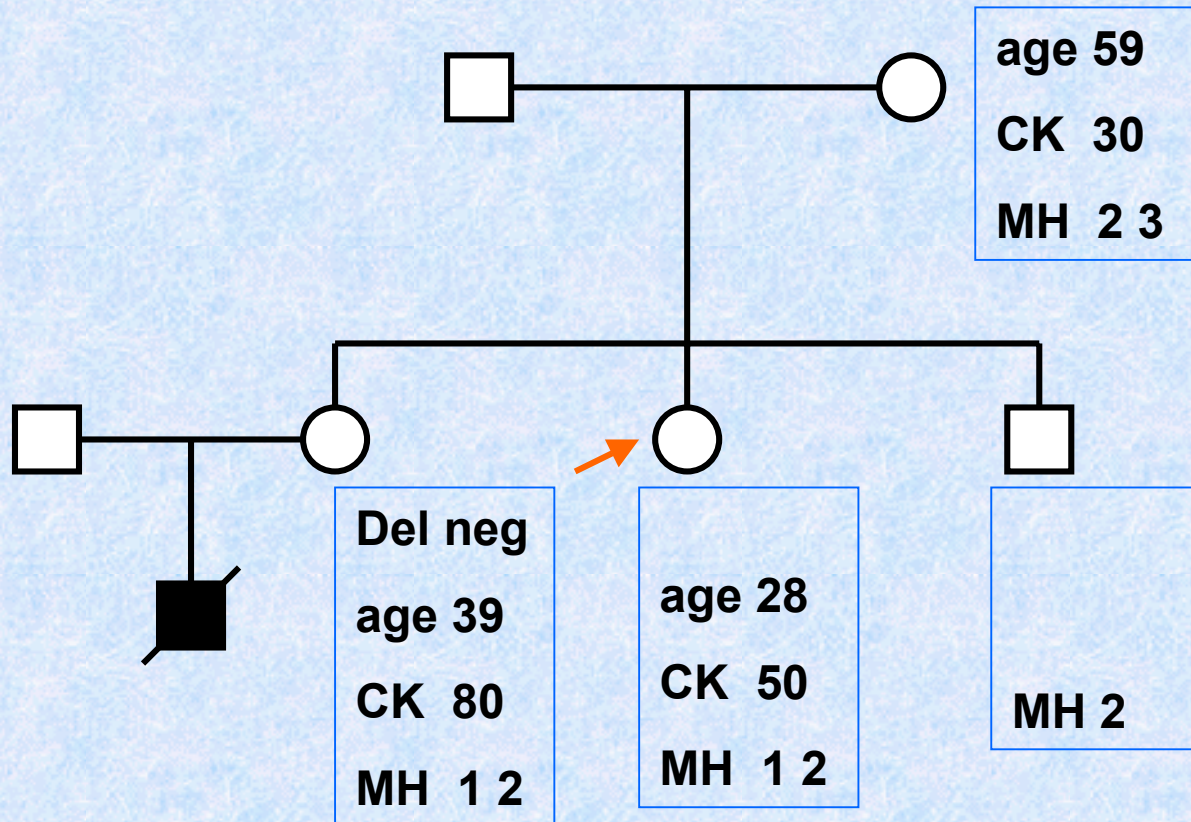


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Calculation with paper and pencil may be errorprone

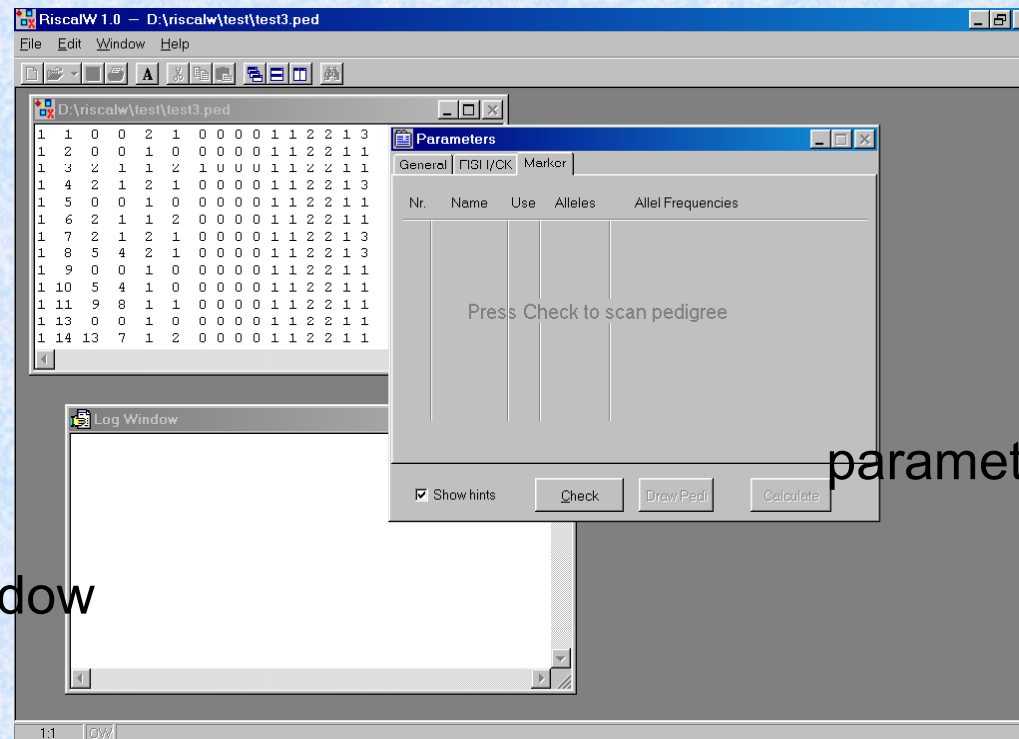


Principle features of RISCALW

pedigree window

output window

parameter window



Possibilities for the genetic model

Parameters dialog box showing the following values:

Incidence	0.0003	Fem. Del. Mos-R	0
Pt-Mutation RR	1	Male Del. Mos-R	0
Del-Mutation RR	1	Fem. Gam. Pt-Mut. Mos-R	0
Del/Pt-Mutation R	1.5	Male Gam. Pt-Mut. Mos-R	0
Fem. Pt-Mut. Mos-R	0	Fem. Gam. Del. Mos-R	0
Male Pt-Mut. Mos-R	0	Male Gam. Del. Mos-R	0

Buttons: Show hints, Check, Draw Ped, Calculate, Load, Save.

simple model

Parameters dialog box showing the following values:

Incidence	0.0003	Fem. Del. Mos-R	0
Pt-Mutation RR	3	Male Del. Mos-R	0
Del-Mutation RR	0.3	Fem. Gam. Pt-Mut. Mos-R	0
Del/Pt-Mutation R	1.5	Male Gam. Pt-Mut. Mos-R	0
Fem. Pt-Mut. Mos-R	0	Fem. Gam. Del. Mos-R	0
Male Pt-Mut. Mos-R	0	Male Gam. Del. Mos-R	0

Buttons: Show hints, Check, Draw Ped, Calculate, Load, Save.

sex specific
mutation rates

Parameters dialog box showing the following values:

Incidence	0.0003	Fem. Del. Mos-R	0.48
Pt-Mutation RR	3	Male Del. Mos-R	0.48
Del-Mutation RR	0.3	Fem. Gam. Pt-Mut. Mos-R	0.47
Del/Pt-Mutation R	1.5	Male Gam. Pt-Mut. Mos-R	0.47
Fem. Pt-Mut. Mos-R	0.48	Fem. Gam. Del. Mos-R	0.47
Male Pt-Mut. Mos-R	0.48	Male Gam. Del. Mos-R	0.47

Buttons: Show hints, Check, Draw Ped, Calculate, Load, Save.

mosaicism and
sex specific mutation
rates

FISH test and CK measurements

The screenshot shows a 'Parameters' dialog box with the 'FISH/CK' tab selected. The 'FISH Del-Detection Rate' is set to 0.75. The checkbox for 'CK quantitative?' is unchecked. The bottom of the dialog has buttons for 'Show hints', 'Check', 'Draw Pedi', and 'Calculate'.

Parameter	Value
FISH Del-Detection Rate	0.75
CK quantitative?	<input type="checkbox"/>

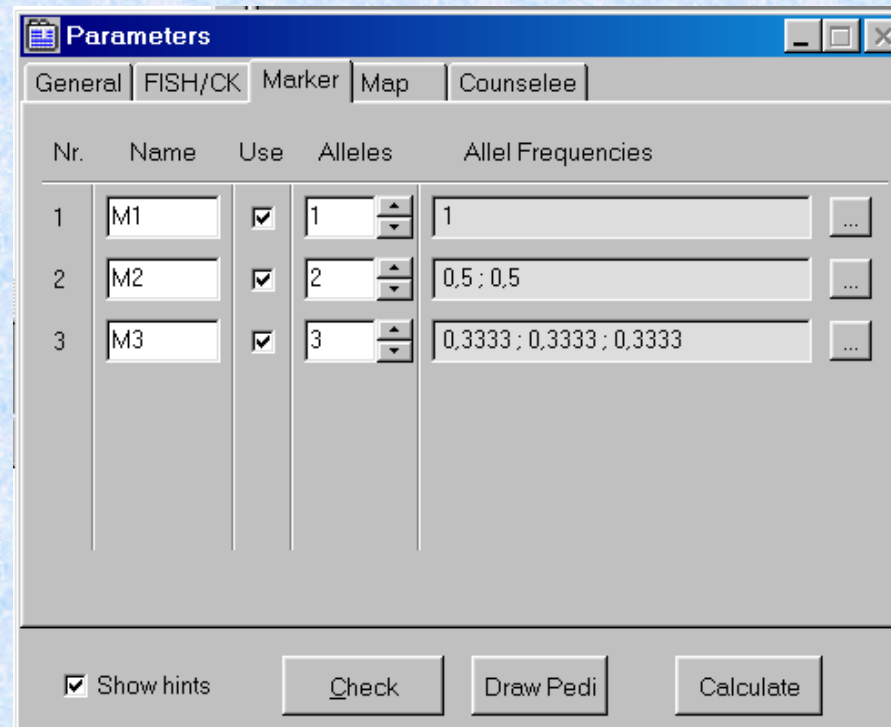
CK as odds ratios

The screenshot shows the same 'Parameters' dialog box, but with 'CK quantitative?' checked. A 'log(CK) Distribution' section is visible, containing a table with mean and standard deviation values for 'Normal' and 'Heterozygote' categories. The bottom of the dialog has buttons for 'Show hints', 'Check', 'Calculate', and 'Help'.

	Mean	Std-Deviation
Normal:	1.524	0.209
Heterozygote:	1.956	0.379

CK quantitatively

Marker characteristics

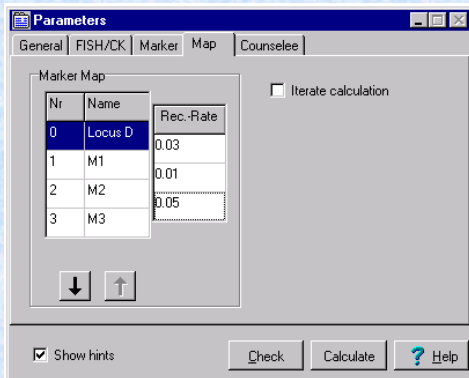


The screenshot shows a 'Parameters' dialog box with a tabbed interface. The 'Marker' tab is selected. It contains a table with columns for 'Nr.', 'Name', 'Use', 'Alleles', and 'Allel Frequencies'. Below the table are four buttons: 'Show hints' (checked), 'Check', 'Draw Pedi', and 'Calculate'.

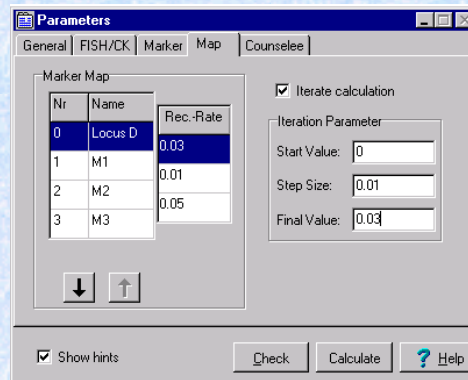
Nr.	Name	Use	Alleles	Allel Frequencies
1	M1	<input checked="" type="checkbox"/>	1	1
2	M2	<input checked="" type="checkbox"/>	2	0,5 ; 0,5
3	M3	<input checked="" type="checkbox"/>	3	0,3333 ; 0,3333 ; 0,3333

Show hints

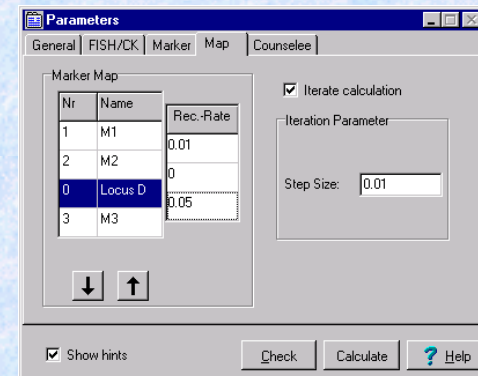
Marker map



a

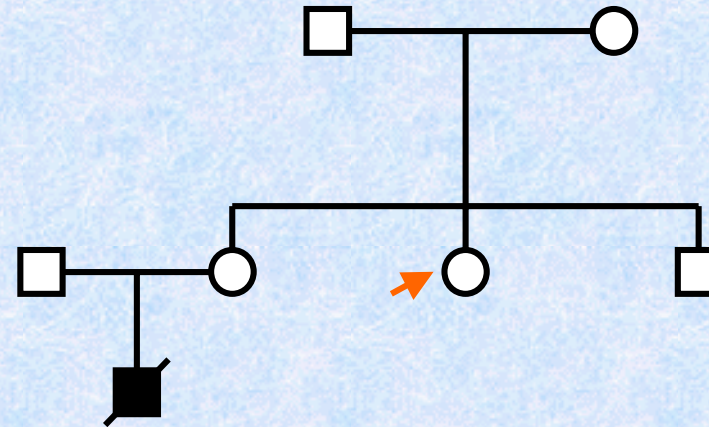
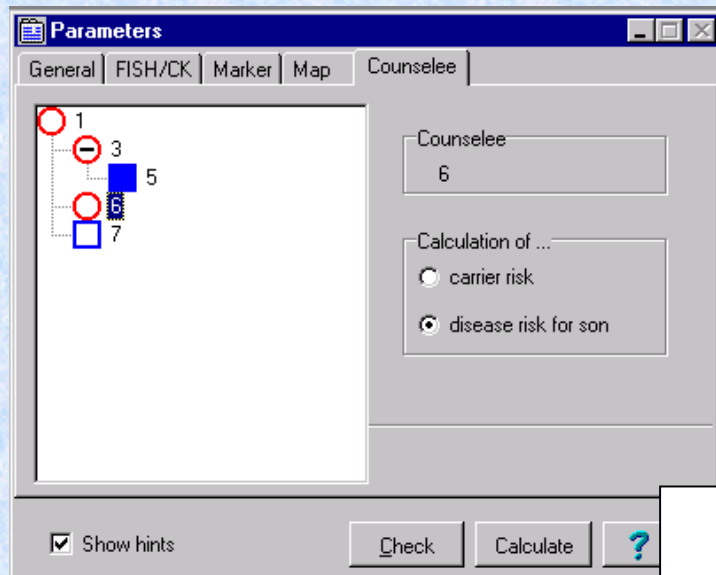


b



c

Choice of counselee and calculation start



Carrier probabilities for

Son of 6:

Mutation (PM+Del)	=	4,5680%
Deletion	=	0,6185%
Mosaicism (PM+Del)	=	0,0059%
Del-mosaicism	=	0,0014%

Technical details



- ⌘ RISCALW is programmed in Delphi
- ⌘ runs on PC under any WIN.. operation system
- ⌘ uses a new model to account for germline mosaicism and sex specific mutation rates

Program validation



- ⌘ extensively tested
- ⌘ compared with LINKAGE
- ⌘ compared with hand calculations

Concluding remarks

- ⌘ easy to use risk calculation for DMD
- ⌘ flexible
- ⌘ only program which is able to account for mosaicism, heterogenous new mutation rates
- ⌘ incorporation of negative deletion tests, CK-values and marker genotypes possible
- ⌘ sensitivity analysis very convenient