

Table S II: 56 families with BD in their reproductive history.

Family n°	BD	2007-2010 (3,5y)				2004-2006 (3y)				2001-2003 (3y)				1991-2000 (10y)			
		<i>normal</i>	<i>BD</i>	<i>SB</i>	<i>MS</i>	<i>normal</i>	<i>BD</i>	<i>SB</i>	<i>MS</i>	<i>normal</i>	<i>BD</i>	<i>SB</i>	<i>MS</i>	<i>normal</i>	<i>BD</i>	<i>SB</i>	<i>MS</i>
116	CHD		1														
118	NT		1		1												
148	O	1	1														
153	CHD	2	1														
120	NT	1	1			1											
121	NT		1			1			3								
123	NT-NT-NT		1				2							9			
124	CHD	2	1			1			1								
125	CLP	1	1		1												
146	CHD	1	1			1											
145	CHD-CHD	2	1		1		1		4								
156	NT		1											4			2
139	CHD	3	1			4			1					1			
136	CHD	2	1						2					2			
104	O		1														
112	NT		1		2	1			1	1				4			
113	CLP	1	1														
115	CHD	1	1		1				1								
126	NT		1														
127	CHD	2	1														
128	O	1	1			1											
102	CHD		1						1	2				2			
129	NT		1														
130	NT	1	1														
135	CHD	1	1							1				4			
151	SK		1		2												
152	NT	2	1														
154	CHD	2	1														
155	CLP		1														
157	O	1	1														
107, two generations	CHD-O-SK	2	3			1				1			2	4			
119	CHD		1											4			

131	SK-O	1				1	1			1				2	1		1
134	CHD						1							6			
137	SK		1		2												
138	CHD		1			3				2				3			
142	O	1	1		1												
122	NT	2	1														
149	CHD		1			1				2							
150	CHD										1			6			
106	CHD-O		2			1											
147	O		1														
117	O		1														
109	CHD		1			1								3			
110	CHD		1			2											
103	NT	1									1						
101	O-NT		2														
140	SK		1			1				1				1			
133	CHD	1								1							
1	CHD	1			1					1	2						
132	CLP-SK		1		1	2			1	2	1			1			
141	O	1	1														
143	CHD	2									1						
144	CHD	1	1							3				1			
105	NT-NT	2	1								1						
114	NT	1	1			1											
Total live births		42	50	0	14	23	10	2	16	17	2	0	2	57	1	0	3
%BD			54,3				30,3				10,5				1,75		
%MS/total births					15,2				45,1				10,5				5,2

Legend: normal-healthy child; BD-birth defect; MS miscarriage. CHD congenital hearth disease, NT neural tube, CLP cleft Lip/Palate, SK skeletal malformation, kidney is atrophic.

Prevalence of BD (black columns) and MS (grey columns) on total live births in three time windows in all the families with a BD in the last 7 years.

Trend of BD significance is $p < 0.001$, of MS significance is $p < 0.0003$.

