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## Functional analysis of young patients with desmoid-type fibromatosis: Initial surveillance does not jeopardize long term quality of life

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### ► To cite this version:

G. Duhil de Bénazé, M. Vigan, N. Corradini, V. Minard-Colin, A. Marie-Cardine, et al.. Functional analysis of young patients with desmoid-type fibromatosis: Initial surveillance does not jeopardize long term quality of life. *EJSO - European Journal of Surgical Oncology*, 2020, 46 (7), pp.1294-1300. 10.1016/j.ejso.2020.02.028 . hal-03477950

**HAL Id: hal-03477950**

**<https://hal.science/hal-03477950>**

Submitted on 16 Jun 2022

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3 **FUNCTIONAL ANALYSIS OF YOUNG PATIENTS WITH DESMOID-TYPE**  
4 **FIBROMATOSIS: INITIAL SURVEILLANCE DOES NOT JEOPARDIZE LONG**  
5 **TERM QUALITY OF LIFE**

6

7 **Running title:** Functional sequelae in desmoid-type tumor

8

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33  
34 **Funding statement:** This study is supported by “SOS Desmoïde association” who did not take  
35 part in any analysis of this manuscript.

36  
37 **Author contributions statement:** GDB and DO conceived and designed the analysis, collected  
38 the data, contributed data or analysis tools, performed the analysis and wrote the paper. MV and  
39 MC conceived and designed the analysis and performed the analysis. NC, PM, VM, AMC, NS,  
40 AP collected the data and wrote the paper. CV, ASD, ET, MPC, DB, LM, AR, DP, AJ collected  
41 the data.

42  
43 **Acknowledgments:** SOS Desmoïde association, EpSSG, SFCE

44  
45

46 **Abstract**

47 **Background:** With recent conservative strategies, prognosis of patients with desmoid-type  
48 fibromatosis (DTF) is about function preservation. We analyzed the long-term quality of life  
49 (QoL) of pediatric patients with DTF.

50 **Methods:** All French young patients (<21years) treated between 2005-2016 for a DTF in the  
51 EpSSG NRSTS-05 study were analyzed. A first wait-and-see strategy was recommended.  
52 Patients' QoL was analyzed with the internationally validated Child Health Questionnaire (CHQ).  
53 We focused on the relevant subscales scores: physical functioning (PF), role social limitations  
54 physical (RP), bodily pain (BP), general health perception (GH) and physical (PhS) and  
55 psychosocial (PsS) summary measures.

56 **Results:** Among the 81 patients, 52 families answered the CHQ (median delay since  
57 diagnosis=6.2years; min2.2-max13.3years). Median age at diagnosis was 11.5years. Primary site:  
58 limbs (52%), head/neck (27%), or trunk (21%). Five year-Progression Free Survival was 39.1%  
59 (95%CI: 27.7-50.5%). As initial management for these 52 patients, 30 patients were first  
60 observed (57%), 13 had surgery (25%) and 9 received chemotherapy (18%). Total burden of  
61 therapy was exclusive surgery (9pts/18%), exclusive chemotherapy (18pts/35%),  
62 surgery+chemotherapy (13pts/25%), chemotherapy+radiotherapy (1pt),  
63 surgery+chemotherapy+radiotherapy (1pt), wait and see (10pt). Regarding the parent forms,  
64 patients have significant lower PF (86.0vs.96.1; p=0.03), RP (82.0vs.93.6; p=0.04), GH (60vs.73;  
65 p<0.005) and PhS (46.2 vs.53; p=0.02) scores compared to healthy population. Comparison of  
66 QoL subscales scores according to initial strategy (wait-and-see vs.surgery/chemotherapy) did  
67 not reveal any difference (PF=87.3vs.84.9; p=0.80/RP=83.4vs.78.7; p=0.72/BP=78.9vs.78.2;  
68 p=0.95/GH=59.7vs60; p=0.97). Similar results were found using the children or adult forms.

69 **Conclusions:** Initial wait-and-see strategy does not affect long term functional impairment.

70

71 **Key words:** desmoid-type tumor; children; conservative strategy; quality of life; Child Health  
72 questionnaire.

73

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75 Number counts: Table=4, supplemental Table=1; Figure=2, abstract word=246, total words=2355

76

77 **Introduction**

78 Desmoid-type fibromatosis (DTF) are rare benign tumors of soft tissues, they can be locally  
79 invasive, but without any metastatic potential. The incidence of desmoid tumors in general  
80 population is low. It usually affects children (6-15years) and women (puberty-40years) (1–4).  
81 Because DTF are often large and infiltrative, complete resection is rarely feasible (6-25% in  
82 children) (1,5). DTF can spontaneously stabilize or resolve after diagnosis, but relapses are  
83 common (until 60%) (6–8). Surgery has been hypothesized to stimulate the onset and growth of  
84 DTF (9–11). This hypothesis and the observation of relapses after surgery lead to a conservative  
85 approach in the EpSSG (12–14). Between 2005 and 2016, European children and adolescents  
86 (age at diagnosis  $\leq$  21 years) with proven diagnosis of DTF were prospectively registered in the  
87 EpSSG Non-Rhabdomyosarcoma Soft Tissue Sarcoma study (NRSTS). Results of this protocol  
88 regarding DTF have been recently published (4). The EpSSG NRSTS Committee recommended  
89 a minimally aggressive strategy and considered as first approach the wait-and-see strategy. A  
90 treatment should be considered in case of rapid tumor growth, uncontrollable symptoms or tumor  
91 located in a threatening site. Primary resection should be considered for small tumors if it appears  
92 to be complete without mutilation. In large extensive tumors, when a medical therapy was  
93 indicated, chemotherapy (methotrexate-vinblastine) was recommended. Radiotherapy was  
94 discouraged. This group suggests initial wait-and-see strategy (4), which did not compromise  
95 outcomes. But “*outcome could be better assessed by a combination of progression-free survival*  
96 *and functional sequelae.*”(4). This study aims to assess the long term quality of life (QoL) of  
97 children and adolescents affected by DTF and analyze functional consequences according to  
98 initial therapeutic strategy.

99

100 **Material and methods**

101 ***Study design and Population***

102 We conducted a retrospective, multicenter cohort study in which we selected all French patients  
103 with DTF included in the NRSTS protocol treated in 19 different oncology centers.  
104 Parental/guardians written consent was collected at the inclusion in the study.

105

106 ***Methods***

107 All clinical and outcome data were prospectively registered in the EpSSG NRSTS 2005  
108 databases and updated for this analyze. Patients were classified by tumor site and clinical staging  
109 was defined using the TNM system (15). Study (IRS) grouping system was used (16).

110 Patients' quality of life was analyzed by the internationally quality of life (QoL) questionnaire:  
111 Child Health questionnaire (CHQ) (17–20). We picked the 50 items parents form (CHQ-PF50),  
112 and the 87 items for children $\geq$ 10 years old (CHQ-CF87). For young patients that become adults  
113 during the follow-up, this questionnaire has been adapted to age (professional activity and family  
114 life). After agreement of their reference center, the questionnaire was sent to families.

115 Long term adverse events were reported accorded to the Common Terminology Criteria for  
116 adverse Events (CTCAE) (21) by sending a case report form to all the clinicians. Data was  
117 updated at the time point of 1st September 2018.

118

119 ***Statistical analysis methods***

120 We compared clinical data for patients/families who answered to CHQ and the ones who did not  
121 with Chi-2 or Fisher test. We separated answers depending if it were parents; patients still  
122 remaining children, or patients who had become adults. The CHQ was scored using the  
123 customary algorithm, which calculates subscale scores ranging from 0 to 100, with higher scores  
124 indicating better health status (22). Comparison of scores with general US population was

125 available for CHQ-PF50 and CHQ-CF87. The link between variables of the treatment and QoL  
126 was tested with Wilcoxon test. Other variables (radiotherapy, number of surgeries, localization of  
127 the tumor, mutilating surgery, 2 or more lines of chemotherapy, chemotherapy during more than  
128 2years) were described but not tested because of insufficient number of patients. We focused the  
129 analysis on the most relevant subscale scores: physical functioning (PF, presence and extent of  
130 physical limitations), role social limitations physical (RP, extent of limitations in school-related  
131 activities and activities with friends), bodily pain (BP, intensity and frequency of general pain),  
132 and general health perception (GH, subjective assessment of overall health and illness). We also  
133 used the physical (phS) and psychosocial (psS) summary measures which aggregate CHQ-PF50  
134 items and scales (parent form). Subscale scores are presented as mean (standard deviation). All  
135 tests were bilateral (cut-off 5%) and R software version 3.4.4 (<http://www.R-project.org>) was  
136 used for the statistical analyses. PFS was estimated using the Kaplan–Meier method, and median  
137 follow-up duration using the reverse Kaplan–Meier method.

138

## 139 **Results**

140 Overall, 81 patients with DTF at a median age at diagnosis of 11.6 years (1month- 18.3years)  
141 were included in the EpSSG NRSTS 2005 study in France. Patients' characteristics of the whole  
142 cohort are described in **Table 1**. Sex ratio was 1:1. Palpation of a pain-free mass was the only  
143 symptom leading to the diagnosis in 49 (60.5%) patients. The majority of DTF primaries were on  
144 extremities (47%). The tumor size was mainly large with 63% larger than 5 cm at diagnosis.  
145 Overall, 82% of patients had first a biopsy to reach diagnosis; the other ones had a tumor  
146 resection.



147 After a median follow-up of 5.5 years (range 0.8-13), 49 tumor events occurred in 81 patients (all  
148 progressive disease) and one accidental death occurred in a patient leading to a 5y-PFS of 39.1 %  
149 (95%CI: 27.7%-50.5%; [figure 1](#)).

150  
151 CHQ questionnaires were sent between February and April 2018 to all parents and/or alive  
152 patients (n=80), except one patient with a complex social situation. Overall, 29 parents answered  
153 the questionnaire, of which 22 children completed the CHQ-CF87 form. In addition, 23 patients  
154 who reached adult age answered the questionnaire, giving a total of 52/80 participations (65%).  
155 Median delay between diagnosis and answer to the questionnaire was 6.2years (2.2-13.3). Overall  
156 characteristics of the subgroup with QoL analysis available were quite similar to the entire cohort  
157 ([supplemental Table 1](#)). Median follow-up for this population was 5.4years (0.8-13).

158 Among these 52 patients, 30 were first observed (group A; 58%), 13 underwent immediate  
159 surgery (group B; 25%), and 9 received immediate chemotherapy (group C; 17%). Treatment  
160 according to tumor evolution and overall tolerance are detailed in [Table 2](#). In group A, only  
161 10/30 patients did not receive any treatment after biopsy (except non-steroid anti-inflammatory  
162 drugs, n=4) and are still currently monitored, the other ones required chemotherapy (n=13),  
163 surgery (n=3), chemotherapy and surgery (n=4). In group B, 7/13 patients were operated on more  
164 than one time. Among these 13 patients, 7 received chemotherapy and one required radiotherapy  
165 (50.4Gy). All 9 patients in group C received methotrexate and vinblastine for a median duration  
166 of 11.9 months (range=1.5-29.1). Among them, 7 started chemotherapy due to the threat to an  
167 adjacent organ, and two because of refractory pain. Chemotherapy was prematurely stopped in 5  
168 patients (tumor progression n=2; persistence of pain n=1, partial response after 8 months n=1,  
169 stable disease after 11 months n=1). Two patients of the group C received a second line of  
170 chemotherapy for non-improvement of pain or tumor progression. Overall 2 patients received

171 radiotherapy; one (50.4Gy) for tumor progression (DTF of the arm) despite 4 surgeries and two  
172 lines of chemotherapy, and another one (DTF of the knee) after one line of chemotherapy  
173 because of severe uncontrolled pain (21Gy). No mutilating surgery was performed.

174

175 CHQ global scale and subscales scores results for the 52 patients with DTF are detailed in **Table**  
176 **3**. Comparison between our subjects and the normative sample of healthy children shows that  
177 they have significant lower PF and RP scores according to both parents and child forms, and  
178 lower MH, GH, PE and PhS scores according to the parent's forms (**Figure 2**). Comparisons of  
179 QoL subscales scores (PF, RP, BP, GH) between patients first observed (30 cases), and the ones  
180 who received immediate first-line treatment (surgery n=13, or chemotherapy n=9) do not reveal  
181 any significant difference (**Table 4**).

182 Between patients who received at least one line of chemotherapy (n=33) and those who did not  
183 (n=19), we were able to show a trend via the CHQ-PF50: patients who did not receive  
184 chemotherapy tend to present a better PF and PsS scores, however not significant (p=0.09 and  
185 0.16). It was also the case for PF scores evaluated by children (CHQ-CF87): 93.7 vs 77.8  
186 (p=0.13). RP score analyzed by patients who had become adults was better if they did not receive  
187 chemotherapy (73.6 vs 100, p=0.028). Among 3 patients who received 3 or more lines of  
188 chemotherapy (1 adult, 2 children), only one children had a low RP score (RP=44) compared to  
189 US healthy population (mean score 93.7), while PF/BP/GH scores were globally satisfactory  
190 (100/85/70, 80/90/100, 70/82/61).

191 When comparing QoL subscales scores between 23 patients who underwent at least one surgery  
192 and 29 never operated patients, no significant difference was found (CHQ-PF50: PF score  
193 85.7vs86.9, p=0.89; RP score 81.9vs81.4, p=0.97; BP score 80.8vs77.1, p=0.72; GH score  
194 57.5vs61.4, p=0.57; PsS score 44.1vs50.2, p=0.24; PhS score 46.1vs46.4, p=0.96). Notably, two

195 patients who underwent 3 surgeries and one patient who underwent 4 surgeries answered the  
196 questionnaire. We can notice that these three patients have poorest BP (40, 70, and 40) and GH  
197 (88, 43, and 59) scores compared to mean scores in healthy population (BP 81.7; GH 73).

198 Two patients received RT, associated to 2 lines of chemotherapy for both and 4 surgeries for one  
199 of them. These two patients had decreased GH scores (43 and 59). RP and BP scores were low  
200 for one of them (respectively 44 and 40) while the PF score was correct (100 and 89).

201 Finally, we compared QoL scores between non-treated patients (n=10), and those who received  
202 treatment (chemotherapy, surgery or radiotherapy), and no significant difference was found  
203 (CHQ-PF50: PF score 83.4vs98.2, p=0.15; RP score 78.3vs94.5, p=0.28; BP score 78.3vs80,  
204 p=0.91; GH score 58.1vs66.4, p=0.21).

205  
206 We obtained additional information from clinicians for 42/52 patients. Overall, 3 had at worse a  
207 grade 1 long term adverse event (AE) (pain or musculoskeletal deformity or paresthesia), 15  
208 patients had a grade 2 (pain n=2 and/or musculoskeletal deformity n=6 and/or asthenia n=1  
209 and/or unequal limb length n=2 and/or muscle weakness n=4) and 3 a grade 3 (pain n=2,  
210 musculoskeletal deformity n=1). These 18 patients with grade 2 or 3 sequelae had lower mean  
211 scores compared to general population: PF score (67.6 vs 96.1), RP score (67.0 vs 93.6), BP  
212 score (58.3 vs 81.7), and GH score (51.5 vs 73.0).

213

## 214 **Discussion**

215 DTF should be considered a chronic disease, but not a life-threatening one. The important  
216 outcome remains morbidity. This is the first study which describes and analyses QoL with a well  
217 validated tool in children. Recently, a study reported interviews of 27 adults suffering from DTF  
218 (23); it reports difficulties such as long delayed diagnosis, treatment uncertainty, treatment-

219 related side-effects, debilitating symptoms, limitations in physical and psychosocial functioning  
220 affecting daily activities. This study showed how much QoL can be affected by a chronic disease.  
221 But a non-validated QoL questionnaire was used, and no children were included.  
222 Management of this tumor has changed over the last years. In the past, it was first recommended  
223 surgery, leaving chemotherapy and/or radiotherapy for recurrent disease or inoperable tumors.  
224 But complete resection is often quite impossible, and local recurrences after surgery are common  
225 (5–7,24,25). Moreover, it has been suggested that surgery may activate tumor progression.  
226 Furthermore, DTF can spontaneously stabilize or regress (9,26). This finding has been confirmed  
227 in a study including patients with refractory DTF in a randomized trial comparing sorafenib vs.  
228 placebo. An objective tumor regression was observed in 20% in the placebo group (95% CI, 8-  
229 38%)(27). Initial wait-and-see strategy seems to be now the recommended first line attitude in  
230 children and adults (28). To avoid any unnecessary surgery, chemotherapy is recommended in  
231 cases of progression or unacceptable symptoms. Orbach *et al.* recently showed that this wait-and-  
232 see strategy doesn't affect outcomes in terms of OS and PFS in children (4).

233 The overall characteristics of our cohort were in accordance to literature data (1,4,29,30), except  
234 that there were less patients with IRS stage I tumors than expected. Patients who responded to the  
235 questionnaire were nevertheless representative of the whole population. Not surprisingly in a  
236 chronic disease, our long-term analysis demonstrated that children with DTF have significant  
237 lower scores in QoL than the general population. Analyzing QoL of patients after initial wait-  
238 and-see strategy, we did not find any difference in comparison to patients who underwent more  
239 aggressive initial therapies (surgery or chemotherapy), showing that this conservative strategy  
240 does not jeopardize the long-term outcome of children with DTF. Overall, the type of initial  
241 strategy does not seem to strongly influence long-term outcome. Nevertheless, patients who

242 underwent several surgeries or several lines of chemotherapy seem to have lower QoL global  
243 scores. These patients are probably more severe at diagnosis, and that could induce a bias.

244 We recognize that this present study has some limitations. The total number of patients included  
245 remains low to draw definitive conclusions, that's why our results must be confirmed in a largest  
246 European population. That can be partly explained by the rarity of this disease in the children.  
247 Moreover, we have only included French patients from the EpSSG group, and QoL may be  
248 differently perceived in different European countries. A large part (64%) of families included in  
249 the original study answered but not all of them. This may give a potential bias, even if analysis  
250 showed that our population was clinically representative of the whole cohort.. Some patients in  
251 our cohort were adults at the time of analysis and no specific validated QoL questionnaire exist  
252 for both adults and children. Due to the limited number of patients, we have not been able to  
253 study the association between QoL and some clinical factors. International prospective studies  
254 with a larger number of patients and systematic QoL analyze are needed to validate these results.  
255 In summary, our study showed that an initial wait-and-see strategy does not affect outcomes in  
256 term of functional impairment, pain or social behavior. These results encourage to first observe  
257 children with DTF like it was suggested by Orbach and all (4). Medical management of adults'  
258 patients affected by DTF is currently changing. Tyrosine kinase inhibitors drugs are currently  
259 tested and appear to be really effective (27,31–36). These drugs seem to be well tolerated and  
260 could change the tolerance of treatment. Nevertheless, long-term effects of these drugs in  
261 children are not well known and should be strongly considered in the overall strategy deciding to  
262 treat patients.

263

264 **Role of the funding source:** This study was supported by SOS Desmoid association. The  
265 funders had no role in study design, data collection and analysis, decision to publish, or  
266 preparation of the manuscript.

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271 **References**

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**Table 1.** Patients and DFT characteristics

Abbreviations: QoL=quality of life. Actual age is the age at the time of QoL analyses.

	National cohort (n=81)	QoL analysis (n=52)
Sex:		
Male	41 (51%)	24 (46%)
Female	40 (49%)	28 (54%)
Actual age:		
<18 years	42 (52%)	28 (54%)
≥18 years	39 (48%)	24 (46%)
Familial history of desmoid-type fibromatosis	1 (1%)	1 (2%)
Germline APC mutation	5 (6%)	4 (8%)
Tumour size > 5cm	51 (63%)	32 (62%)
Presence of pain	17 (21%)	11 (21%)
Tumour stage:		
T1	56 (69%)	33 (63%)
T2	25 (31%)	19 (37%)
IRSG stage:		
I	5 (6%)	1 (2%)
II	9 (11%)	7 (13%)
III	67 (83%)	44 (85%)
Primary site:		
Head and neck	22 (27%)	14 (27%)
Limbs	38 (47%)	27 (52%)
Trunk	21 (26%)	11 (21%)
Multifocal sites	5 (6%)	5 (10%)
At least one surgery	34 (42%)	23 (44%)
At least one line of chemotherapy	54 (67%)	33 (63%)

**Supplemental Table 1.** Comparison between initial patients and tumor characteristics according the response or not to the CHQ.

	Answers available to CHQ (n=52)	No answer (n=29)	p value
Sex:	24 (46%)	17 (59%)	0.3
Male	28 (54%)	12 (41%)	
Female			
Actual age:	28 (54%)	14 (48%)	0.6
<18 years	24 (46%)	15 (52%)	
≥18 years			
Familial history of desmoid-type fibromatosis	1 (2%)	0	1
Germline APC mutation	4 (8%)	1 (3%)	0.7
Tumour size> 5cm	32 (62%)	19 (66%)	0.8
Pain	11 (21%)	6 (21%)	1
Tumour stage:	33 (63%)	23 (79%)	0.2
T1	19 (37%)	6 (21%)	
T2			
IRSG stage:	1 (2%)	4 (14%)	0.09
I	7 (13%)	2 (7%)	
II	44 (85%)	23 (79%)	
III			
Primary site:	14 (27%)	8 (28%)	0.6
Head and neck	27 (52%)	11 (38%)	
Limbs	11 (21%)	10 (34%)	
Trunk			
Multifocal site	5 (10%)	0	0.1
At least one surgery	23 (44%)	11 (38%)	0.6
At least one line of chemotherapy	33 (63%)	21 (72%)	0.5

**Table 2.** Treatments delivered for patients with DTF who answered to the CHQ according to initial strategy adopted.

Treatment delivered	Initial therapeutic strategy			Total
	Wait-and-see strategy Group A n=30	Immediate surgery Group B n=13	Immediate chemotherapy Group C n=9	Entire Cohort n=52
<b>Medical therapies:</b>				
1 <sup>st</sup> line chemotherapy <i>Median duration</i>	17 (57%) <i>12.3 months</i>	7 (54%) <i>8 months (one still ongoing)</i>	9 (100%) <i>11.9 months</i>	33 (63%)
2nd line chemotherapy <i>Median duration</i>	10 (33%) <i>14.8 months</i>	3 (23%) <i>13.6 months</i>	2 (22%) <i>9.4 months</i>	15 (29%)
3rd line chemotherapy <i>Median duration</i>	2 (7%) <i>8.4 months</i>	1 <i>8.1 months</i>	0	3 (6%)
4th line chemotherapy <i>Median duration</i>	1 (3%) <i>Unknown</i>	1 <i>0.9 month</i>	0	2 (4%)
Non steroid anti-inflammatory drugs	14 (47%)	1	1	16(31%)
<b>Tumor resection:</b>				
Delayed surgery n°1	7 (23%)	13 (100%)	3 (33%)	23 (44%)
Surgery n°2	2 (7%)	4 (31%)	0	6 (12%)
Surgery n°3	1 (3%)	2 (15%)	0	3 (6%)
Surgery n°4	0	1 (8%)	0	1 (2%)
<b>Radiotherapy:</b>	0	1 (8%)	1 (11%)	2 (4%)
<b>Total burden of therapy:</b>				
Wait-and-see, no further treatment	10 (33%)	0	0	10 (19%)
Exclusive chemotherapy	13 (43%)	0	5 (56%)	18 (35%)
Exclusive surgery	3 (10%)	6 (46%)	0	9 (17%)
Surgery + chemotherapy	4 (13%)	6 (46%)	3 (33%)	13 (25%)
Radiotherapy + Chemotherapy	0	0	1 (11%)	1 (2%)
Surgery + chemotherapy + radiotherapy	0	1 (8%)	0	1 (2%)
<b>Long term effects:</b>				
Grade 1 or 2 sequelae	12 (40%)	3 (23%)	3 (33%)	18(35%)
Grade 3 sequelae	1 (3%)	1 (8%)	1 (11%)	3 (6%)

**Table 3.** CHQ global scale and subscales scores for 52 patients treated for DFT during childhood : mean, SD, and p compared to healthy population.

Abbreviations: GGH = General Health perceptions ; PF = physical Functioning ; REB = Role/social limitation emotional behavior ; RE = Role/social Emotional ; RB = Role/social Behavior ; RP = Role/Social limitations physical ; BP = Bodily pain ; BE= General behavior ; GBE = Global behavior item ; MH = Mental health ; SE= Self Esteem ; GH = General health ; PE = Parental impact-emotional ; PT = Parental impact-time ; FA = Family – limitation in activity ; FC = Family cohesion ; PhS = Physical summary score ; PsS = Psychosocial summary score

	General US population Mean	Parents form n=29			Child form n=22			Adult form n=23	
		Mean	SD	p value	Mean	SD	p value	Mean	SD
GGH	-	76,9	23.1	-	76	23.8	-	73	23.4
PF	96.1	86	23.2	<b>0.03</b>	83	23.3	<b>0.02</b>	78	25.5
REB	92.5	82	30.4	0.07	-	-	-	-	-
RE	-	-	-	-	87	19.6	-	83	20.8
RB	-	-	-	-	83	22.7	-	83	23.7
RP	93.6	82	30.7	<b>0.04</b>	88	17	<b>0.04</b>	81	27
BP	81.7	78,6	26.6	0.5	73	27.1	0.08	67	31.7
BE	75.6	75	14.8	0.8	80	9.5	0.9	83	11.5
GBE	-	80	16.6	-	72	15	-	77	15.2
MH	78.5	72	16.3	<b>0.05</b>	78	11.1	0.7	65	20.1
SE	79.8	74	19.5	0.1	71	14.8	<b>0.01</b>	66	16.1
GH	73.0	60	17.8	<b>0.0004</b>	67	22.3	0.1	62	22
PE	80.3	68	27,6	<b>0.03</b>	-	-	-	-	-
PT	87.8	79	27	0.1	-	-	-	-	-
FA	89.7	85	23	0.3	89	16.7	0.2	92	14.4
FC	72.3	71	21.6	0.8	75	23.2	1	77	29.3
PhS	53.0	46.2	14.5	<b>0.02</b>	-	-	-	-	-
PsS	51.2	47.6	10.7	0.09	-	-	-	-	-

**Table 4.** Quality of life scores according to the initial strategy adopted : Wait-and-see strategy (n=30) vs. surgery or chemotherapy (n=22)  
 Abbreviations: *WS*= wait-and-see strategy; *PF* = physical Functioning; *RP* = Role/Social limitations physical; *BP* = Bodily pain; *GH* = general health

		Parents form (n=29)					Children form (n=22)					Adults form (n=23)				
	First line of treatment	Min	Median	Max	Mean	p-value	Min	Median	Max	Mean	p-value	Min	Median	Max	Mean	p-value
PF	WS	22	100	100	87.3	0.80	70.4	88.9	100	88.7	0.48	37	88.9	100	82.6	0.46
	Surgery or chemotherapy	17	100	100	84.9		0	81.5	100	70.4		7.4	77.8	100	74.1	
RP	WS	0	100	100	83.4	0.72	44.4	100	100	85.2	0.15	22.2	100	100	82.4	0.77
	Surgery or chemotherapy	0	100	100	78.7		66.7	100	100	95.2		33.3	88.9	100	78.9	
BP	WS	20	90	100	78.9	0.95	20	80	100	76	0.49	20	80	100	68.5	0.69
	Surgery or chemotherapy	0	90	100	78.2		0	70	100	65.7		10	65	100	63	
GH	WS	30.8	64.2	80.8	59.7	0.97	34.2	69.6	100	67.2	0.96	10.8	55.6	91.7	56.4	0.19
	Surgery or chemotherapy	26.7	60	89.2	60		25	82.1	93.8	67.7		44.6	70.6	97.9	68.5	

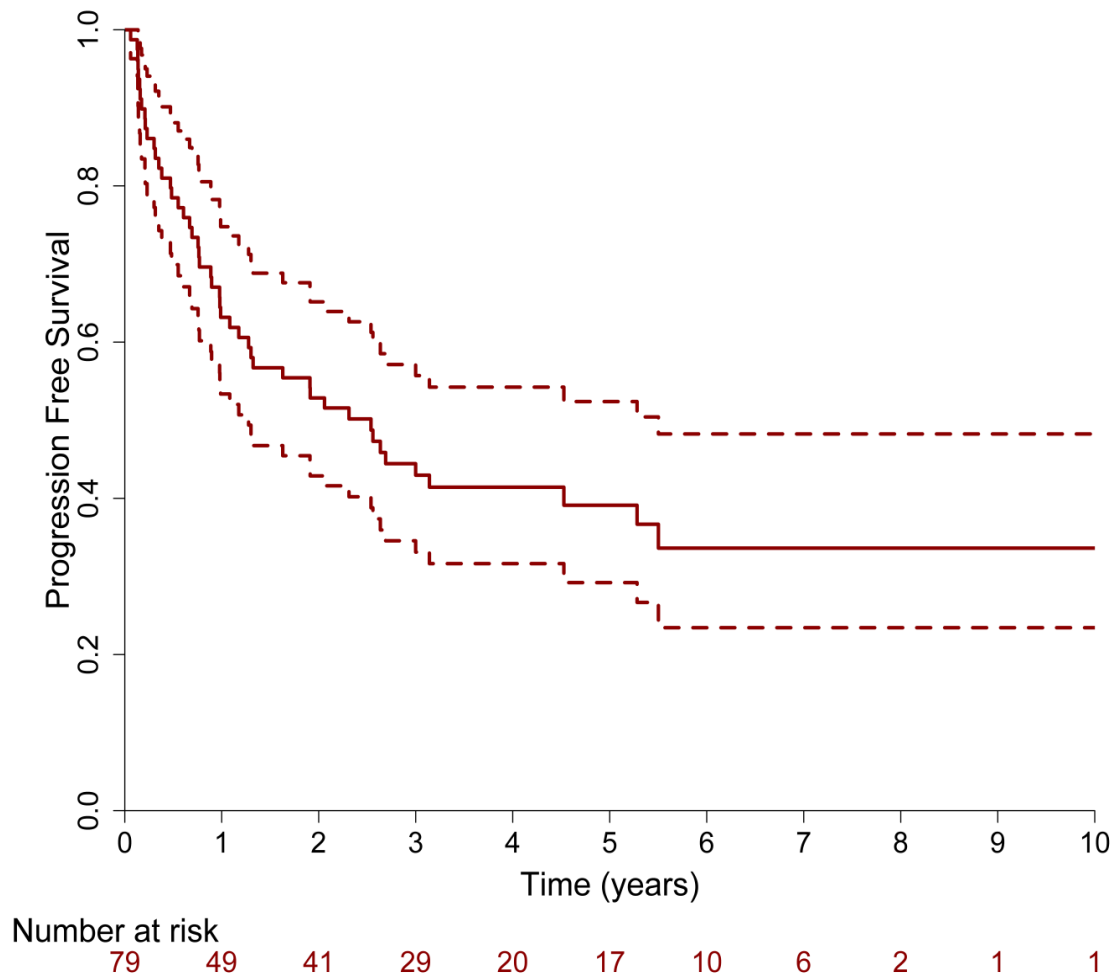
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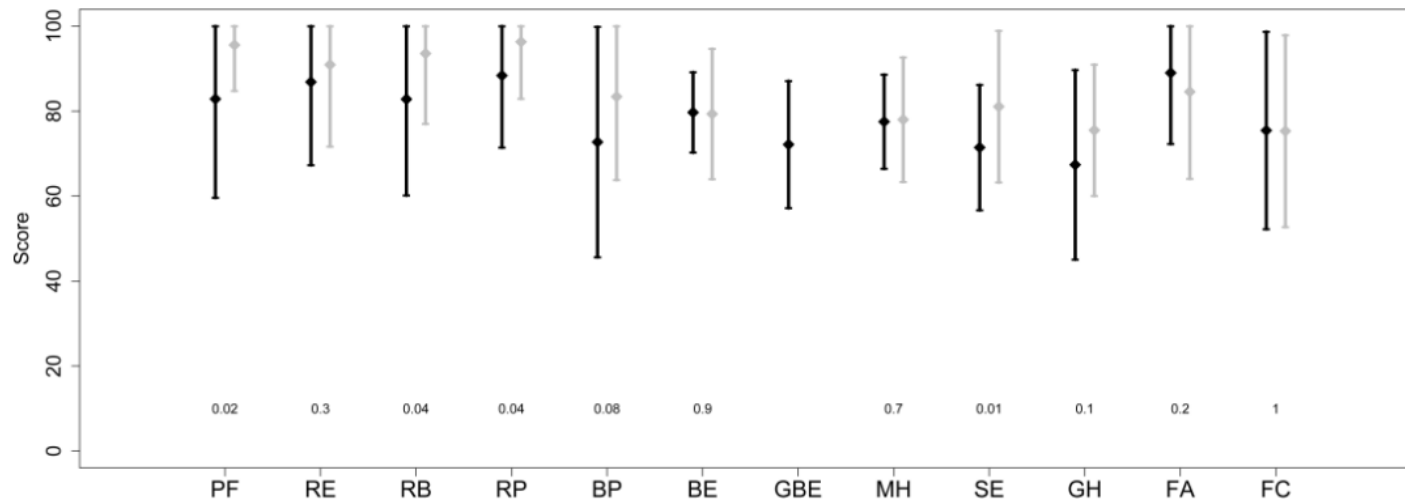
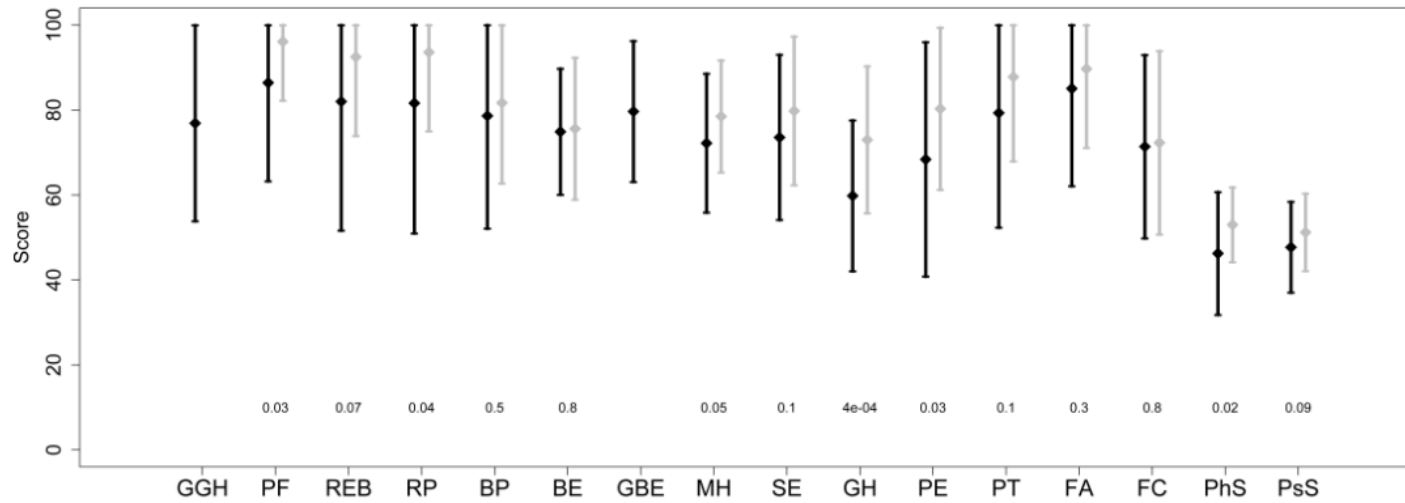
**Figure 1:** Progression-free survival (PFS) for the whole cohort (solid line) and 95% confidence interval (dotted line).

**Figure 2:** Mean (+SD) of CHQ global scale and subscales scores for 52 patients treated for DTF during childhood for parent form (Top) and child form (Bottom) in black for cohort study and grey for US healthy population. Numbers are p-values of Wilcoxon tests of comparison between the 2 groups.



**Figure 1.** Progression-free survival (PFS) of the entire cohort (n=81)





**Figure 2.** Mean (+SD) of CHQ global scale and subscales scores for 52 patients treated for DTF during childhood for parent form (Top) and child form (Bottom) in black for cohort study and grey for US healthy population. Numbers are p-values of Wilcoxon tests of comparison between the 2 groups.

**Abbreviations:** GGH = General Health perceptions; PF = physical Functioning; REB = Role/social limitation emotional behavior; RE = Role/social Emotional; RB = Role/social Behaviour; RP = Role/Social limitations physical ; BP = Bodily pain; BE= General behaviour; GBE = Global behaviour item; MH = Mental health; SE= Self Esteem ; GH = General health; PE = Parental impact-emotional; PT = Parental impact-time; FA = Family – limitation in activity FC = Family cohesion; PhS = Physical summary score; PsS = Psychosocial summary score; SD= standard deviations.