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Title: Absenteeism and indirect costs during the year following the diagnosis of an operable breast cancer: a prospective multicentric cohort study.

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Declarations of interest: none

1 **Abstract:**

2 Background: Diseases consequence on individual work as much as consequences of being
3 absent from work are matters of interest for decision makers.

4 Methods: We analyzed lengths of absenteeism and related indirect costs for patients with a
5 paid activity in the year following the diagnosis of early stage breast cancer, in the
6 prospective OPTISOINS01 cohort. Both human capital and friction costs approach were
7 considered for the valuation of lost working days (LWD). For the analysis, the friction period
8 was estimated from recent French data. The statistical analysis included simple and multiple
9 linear regression to search for the determinants of absenteeism and indirect costs.

10 Results: 93% of the patients had at least one period of sick leave, with on average 2 period
11 and 186 days of sick leave. 24% of the patients had a part-time resumption after their sick
12 leave periods, during 114 days on average (i.e. 41 LWD). Estimated indirect costs were
13 22,722.00 € and 7,724.00 € per patient, respectively for the human capital and the friction cost
14 approach. In the multiple linear regression model, factors associated with absenteeism were:
15 the invasive nature of the tumor ($p=.043$), a mastectomy ($p=.038$), a surgery revision
16 ($p=.002$), a chemotherapy ($p=.027$), being a manager ($p=.025$) or a craftsman ($p=.005$).

17 Conclusion: Breast cancer lead to important lengths of absenteeism in the year following the
18 diagnosis, but almost all patients were able to return to work. Using the friction cost or the
19 human capital approach in the analysis led to an important gap in the results, highlighting the
20 importance of considering both for such studies.

21

22 Keywords: Health economics; Breast cancer; Indirect costs; Absenteeism; Economic burden

23

24	List of abbreviations
25	BC: Breast Cancer
26	FC: Friction costs
27	HAS: French Health Authority
28	HC: Human Capital
29	HTA: Health Technology Assessment
30	LWD: Lost Working Days
31	

32 **Introduction**

33 Breast cancer (BC) is the most common cancer in French women with an estimated
34 incidence of 54,062 new cases in 2015 (standardize incidence rate of 97.4 cases per 100,000
35 women per year). Usually, costs associated with health care interventions are split between
36 direct costs referring to the resource utilization and indirect costs which represent the
37 productivity lost or time cost due to illness. Different Health Technology Assessment (HTA)
38 agencies developed guidelines including cost components to be included in economic
39 evaluation, generally recommending exclusion of indirect costs for various reasons. The
40 French Health Authority (HAS) alternatively suggested to consider production costs of health
41 care interventions including the standard direct costs and time cost of patients for the delivery
42 of care but excluding time cost due to the underlying condition (1).

43 BC generates important direct costs for health care systems. A study conducted in
44 France on the national public health insurance database concluded that BC was the most
45 expensive, representing 18.5% of all the cancer expenditures (2). In the US, the estimated
46 lifetime treatment costs ranged from \$20,000 to \$100,000 (3). Moreover, since BC is mostly
47 prevalent in women of working age, it induces important indirect costs which should be
48 consider to allow a more comprehensive approach of this disease in a societal perspective.

49 Methodology of indirect costs measurement raise several issues, especially the
50 valuation of lost productivity related to the time lost due to illness. Defined by Rice, the
51 human capital (HC) approach values the entire time lost, regardless of the duration of absence
52 (4). To the contrary, in the friction costs (FC) approach, it is assumed that indirect costs only
53 occur during the limited period before adjustment of firms to the workers absence defining a
54 friction period (5). Even though both may provide useful information, using one approach or
55 the other leads to estimates which may differ dramatically especially when considering a
56 lifetime horizon (6–8).

57 Data over absenteeism and indirect costs are useful for decision makers when
58 considering cost-of-illness studies or model-based economic evaluations on innovative
59 treatments or screening strategies. Few studies in the literature focus on indirect costs of BC
60 and absenteeism with estimates ranging from \$8,068 (9) to \$21,086 per patient (10),
61 highlighting the importance of the methodology used and country of interest. In France, only
62 one study reported indirect costs associated with adjuvant chemotherapy in BC (11). There is
63 also few information over individual characteristics driving the level of indirect costs. To
64 maintain employment or early return at work could be justified in order to decrease economic
65 burden of the disease from a societal perspective but also to limit its impact on patient's
66 personal life (social environment, long term professional goals, etc.). In some countries, like
67 France, it is considered as a public health priority (12,13). It could be promoted with
68 multidisciplinary interventions and innovative treatments associated with less toxicity (14).

69 The objective of this study was to describe the indirect costs of absenteeism and their
70 determinants in the first year following the diagnosis of early BC in a French population-
71 based prospective cohort study, using both the HC and the FC approach.

72

73

74 **Material and methods**

75 *Population*

76 We analyzed indirect costs in early BC, during the year following diagnosis. This
77 study is part of a global research on BC pathways and burden of disease of the French
78 prospective and multicentric study OPTISOINS01. The design of this prospective trial was
79 previously described (15). Patients were included in this cohort by 8 centers (three University
80 hospitals, four local hospitals, one comprehensive cancer center) in three departments of the
81 Ile-de-France region between 2014 and 2016. Patients included were female with a
82 histologically confirmed, previously untreated and firstly operable BC (exclusion of
83 metastatic, locally advanced or inflammatory BC as defined by the AJCC). Patients were
84 prospectively followed during a year with a collection of information over three work
85 packages: 1/resource utilization and costs of pathways, 2/patient satisfaction and work
86 reintegration, 3/quality, coordination and access to innovation. Individual social and economic
87 characteristics were also recorded at the beginning of the study.

88 From the initial cohort of OPTISOINS01, we included all patients reporting a paid
89 activity at the moment of diagnosis. They were excluded if the data on wage or absenteeism
90 were missing.

91 All components of absenteeism were included as part of indirect costs: sick days, part-
92 time resumption, early retirement, mortality. Indirect costs related to presenteeism and unpaid
93 work were excluded from the field of this study. A specific questioner in the second work
94 package was used to assess time lost due to the disease during the year of survey: dates of
95 work and absence from work during treatment, work arrangements, on-shift status (e.g., the
96 recognition of disability at work, applications for disability allowance, retirement, and layoff).
97 We did not consider indirect costs of relatives.

98 *Calculations methods for indirect costs*

99 Periods of absenteeism were considered using both HC and FC approach, addressed
100 separately. In the HC approach, we assumed that indirect costs were generated during the
101 entire period of absenteeism (4). According to the FC approach (6), after a friction period, the
102 level of productivity is restored because of the replacement of the sick individual and no
103 indirect costs occurs. However, medium-term global macroeconomic consequences may arise
104 in an international competitive labor market with an impact on macroeconomic indicators.
105 During the friction period and because of various parameters (diminishing returns to labour,
106 internal labour reserve within firms, and delaying work after the absence period) the
107 production losses are lower than estimates based on the HC approach. With the FC approach,
108 we restricted indirect costs to the friction period and used a friction coefficient to reduce the
109 value of lost production. We assumed insignificant medium-term macro-economic
110 consequences for this cohort.

111 According to Koopmanschap's method, job vacancy duration estimates (i.e. length of
112 recruitment processes) increased with 30 days of time lag (for the decision to recruit and the
113 time between the recruitment and the first working day) were used as a proxy for the friction
114 period's length (6). As job vacancy duration depends on professional categories, we stratified
115 the estimation on this factor (managers vs. others). Data over jobs vacancy durations were
116 scarce in the French literature (including the grey literature). The *ofer* survey conducted in
117 2005 by the labor department reported means of 56 days for managers and 28 days for other
118 professional categories (16). In 2017, *Pole-emploi* job offers were filled in 56 days for
119 managers and 36 days for other categories (17). Consequently, we assumed a friction period
120 of 86 days for managers and 62 days for other professional categories. For the friction
121 coefficient, we used a value of 0.8, initially computed by Koopmanschap et al. (using the

122 estimated elasticity for annual labor time versus labor productivity) and never updated
123 afterwards (6).

124 Periods of absenteeism were recorded including days off (week end) in the patient's
125 questioner and converted into Lost Working Days (LWD) for the analysis: five LWD for 7
126 sick days, 2.5 LWD for 7 days of part-time resumption, 251 LWD for a death or an early
127 retirement (considering 5 working days per week during a year). Representing lost
128 productivity, LWD were valued in euros by daily individual wages supplemented with
129 employers and employee social contributions (computed with an online tool (18)). Wages
130 were self-reported by the patients as their monthly net income. In the FC approach, if multiple
131 periods of absenteeism were recorded, interspersed by work period, we assumed a new entire
132 friction period for each period of absenteeism.

133 *Statistical analysis*

134 We performed different models of simple and multiple linear regressions using the
135 Stata\IC 14.0 software (StataCorp, College Station, Texas). In the first model, the independent
136 variable was the estimate number of LWD, with the HC approach. In the second model, the
137 independent variable was the amount of indirect costs. As HC and FC approaches lead to
138 different values, we performed two different statistical analyses. Dependent variables
139 integrated in a simple linear regression were: marital status, professional category, cancer
140 histology, surgical treatment, adjuvant treatment in the BC treatment. Factors correlated with
141 the independent variable (with a p-value<.1) were integrated in the multiple linear regression.
142 A p-value < .05 was considered significant.

143 We conducted a univariate sensitivity analysis on estimated parameters of the FC
144 approach (friction period length, friction coefficient) by applying them $\pm 20\%$ variation and
145 constructed a Tornado diagram to illustrate the effect on indirect costs. This analysis was also
146 conducted for subgroups: managers and other professional categories.

147 To facilitate the use of our data in other medico-economic analysis, we estimated
148 average indirect costs in subgroups, according to the care pathway and the occupational
149 activity.

150 This study was approved by the French National ethics committee (CCTIRS
151 Authorization n°14.602 and CNIL DR-2014-167) and covers research at all participating
152 hospitals. This study was registered with ClinicalTrials.gov (Identifier: NCT02813317).

153

154

155 **Results**

156 On the 617 screened patients, 604 were included in the OPTISOINS01 cohort. Some
157 patients were excluded from our study either due to the absence of paid activity during the
158 study period (n=307) or due to missing data (wages for 42 patients and length of absenteeism
159 for 87 patients). Finally, 168 patients were included in the analysis (figure 1). Patients
160 characteristics are presented in table 1.

161 Eleven patients did not have any period of absenteeism. One hundred fifty six patients
162 (93%) had at least one period of sick leave, with on average 2 period and 186 days of sick
163 leave (i.e. 133 LWD). Forty patients (24%) had a part-time resumption after their sick leave
164 periods, during 114 days on average (i.e. 41 LWD). Five patients did request for early
165 retirement but procedures were still pending at the end of the follow-up. No death was
166 declared during the study period. On average, managers declared less sick leave days than
167 other professional categories (146 and 172, respectively) but longer period of part time
168 recovery (33 and 24, respectively). Using the HC approach, we recorded a total of 20 973
169 LWD (mean: 125 LWD per patient). Then, using the FC approach, we computed a total of
170 8 297 LWD (mean: 49 LWD per patient). For 66 patients (38%), there were no differences in
171 the computed number of LWD using on approach or the other. Patients in this subgroup had
172 significantly less mastectomy (11%), less axillary lymph node dissection (5%) and less
173 chemotherapy (27%) than the whole sample.

174 As a consequence, using the HC approach, the total estimated indirect costs in the
175 cohort were three times those estimated with the FC approach : 3,817,000.00 € vs.
176 1,298,000.00 €. Respectively, this represented 22,722.00 € and 7,724.00 € of indirect costs,
177 per patient, during the first year after diagnosis. In both approaches, the main driver of lost
178 productivity and indirect costs was sick leave days, representing 90% of the total amount.
179 Part-time resumption only accounted for 10% of the total of these costs (figure 2). Indirect

180 costs were higher for managers than other professional categories: 11,044 €/patient vs. 5,353
181 €/patient with the FC approach, despite less sick leave days in this group. This result is
182 explained by highest incomes.

183 In the multiple linear regression model, factors associated with the number of LWD
184 were: the invasive nature of the tumor (+65 LWD, $p=.043$), a mastectomy (+40 LWD,
185 $p=.038$), a surgery revision (+48LWD, $p=.002$), a chemotherapy (+35 LWD, $p=.027$), being a
186 manager (-33LWD, $p=.025$) or a craftsman (-113LWD, $p=.005$) (compared to being a paid
187 employee). With both approaches, in the simple linear regression model, individual indirect
188 costs were correlated with the invasive nature of the tumor, characteristics of the treatment
189 (mastectomy, axillary lymph node dissection, chemotherapy) and socio-economic
190 characteristics (high educated vs. low educated, being manager vs. being a paid employee)
191 (see Table 2. For details and differences between HC and FC approach). In the HC approach,
192 factors significantly associated with indirect costs in the multiple linear regression model
193 were: a mastectomy ($p=.046$), a revision surgery ($p=.003$) and being a craftsman ($p=.023$).
194 Being a manager, the invasive nature of the tumor or receiving a chemotherapy increased
195 indirect costs in the model but with less degree of statistical signification. In the FC approach,
196 being a manager was the only significant factor associated with indirect costs in the multiple
197 linear regression model ($p<.001$) (Table 2).

198 In the univariate sensitivity analysis for the FC approach, the variation of friction
199 coefficient (benchmark: 0.8; +/-20%) impacted the most the amount of indirect costs from
200 6,179 €/patient to 9269 €/patient (basis: 7,724€/patient) (Figure 3). In the subgroup analysis,
201 indirect costs for managers were much more sensitive to a variation on estimated parameters
202 than other professional categories.

203 Tables with estimated average indirect costs by care pathway and occupational
204 activities are published in the supplementary data.

205 **Discussion**

206 Breast cancer associated direct costs are already well-documented in the literature.
207 Determinants of the indirect costs are less known. Studying the OPTISOINS cohort, Arfi et al.
208 (19) estimated the average daily allowances for sick leave costs (i.e. indirect medical costs)
209 around 8 841 € per patients for the first year from diagnosis. In the same cohort, we showed
210 that BC often cause sick leave periods and part-times recoveries in the year following
211 diagnosis leading to important indirect costs even in the absence of mortality. However, the
212 utilization of two different approaches conducted to a gap in the estimated indirect costs per
213 patient: 22,722.00 € for the HC approach and 7,724.00 € for the FC approach. Factors were
214 correlated to the number of LWD and the amount of indirect costs in the HC approach: the
215 invasive nature of the tumor, receiving a mastectomy, a revised surgery, a chemotherapy,
216 being a manager or a craftsman. Estimated indirect costs in the FC approach were mostly led
217 by the occupational status since managers present higher wages and higher friction periods.

218 BC mean age of diagnosis matches with the mean age of retirement in industrialized
219 countries (62 years old in France) (20). Moreover the age of retirement is nowadays being
220 delayed in many countries, following the increase of life expectancy (21). Thus, absenteeism,
221 indirect costs and more generally work consequences associated with this disease are
222 concerns for decision makers. In the OPTISOINS01 initial cohort, half of the patients had a
223 paid activity during the study period. On average, these patients spent almost half the year
224 after diagnosis in sick leave and 24% of the patients returned to work in part-time resumption
225 for a mean period of 114 days. A mean of 125 LWD was recorded for each patient and 26
226 patients were absent from work during the entire year of analysis, highlighting the impact of
227 BC on paid work. Only few studies report such data. Two US retrospective cohort studies
228 found that working patients with BC had significantly higher length of absenteeism in
229 comparison with "control" patients (without BC) (9,22). However, using a HC approach in the

230 year following diagnosis, they found shorter period of absenteeism: about 10 days of sick
231 leave and between 25 and 45 days of short-term disability (according to the severity of the
232 disease). In Sweden, patients in the first year after a primary BC declared on average 271
233 working hours lost in the last 3 months before their interview (10). In accordance with our
234 results, mortality and early retirement were rare in the first year following diagnosis.

235 We conducted the first prospective cohort study focusing on cost of absenteeism
236 related to BC. The large initial sample size of OPTISOINS01 allowed us to exclude working
237 patients with missing data which could have affected the quality of the analysis. Due to the
238 geographical design of the study, most patient in this cohort reside near Paris and may have
239 different socio-economic characteristics than the national population. Indeed, we noticed that
240 the proportion of managers in our sample was larger than in the French active population
241 (41.6% vs. 17.1%), as well as the average wage (2,214€ vs.1,926€) (governmental data) (23).
242 The time frame was limited to one year after diagnosis but most indirect costs related to BC
243 occurs during this first year, except when the disease progresses to a metastatic stage or a
244 recurrence (10,24).

245 We only considered in this study indirect costs due to absenteeism. There is a growing
246 interest for presenteeism, i.e. workers being at job with reduced capacity and productivity due
247 to illness, and unpaid work, which generate indirect costs (25). Exploring those phenomena
248 require suitable tools (iMTA Productivity Cost Questionnaire (26), Valuation of Lost
249 Productivity (27)) which weren't used on our cohort. As a consequence, this component was
250 excluded from our analysis. Even though few studies suggest substantial indirect costs
251 associated with presenteeism and unpaid work (24,28,29), there is no recommendation on
252 their integration.

253 Usually, authors refer to unique method for the calculation of the lost productivity
254 value, the HC approach being the most commonly employed. For the FC approach, authors

255 use friction periods initially estimated by Koopmanschap et al. (2.8-3.2 months (6)), or other
256 values but without justification on their sources (30). Nevertheless, Koopmanschap's
257 estimation is based on outdated data (1988-1990) and restricted to the Dutch labor market.
258 The time to fill job vacancies (i.e. the length of recruitment processes) increased by four
259 weeks of time lag (decision to recruit and time between the recruitment and the first working
260 day) was used to approximate the friction period. Therefore, the friction period's length is
261 strongly correlated with the unemployment rate and the economic environment. It varies over
262 time and across countries. It also has to be stratified on the socio professional category, since
263 the recruitment process is longer for managers than for employees (31). In the absence of
264 guidelines, we preferred to use both approaches and used French grey literature sources to
265 estimate friction periods length, following the Koopmanschap's method. Compared to his
266 results, our estimation was similar for managers but much shorter for other socio professional
267 categories (62 vs. 86 days), highlighting the importance of using proper data for the FC
268 approach. Nevertheless, our sensitivity analysis focused on the importance of the friction
269 coefficient estimate on the amount of indirect costs. In order to improve the robustness of our
270 results, we would need to proceed on our own estimation for France, which unfortunately was
271 not possible here as it requires unavailable micro economic data at the firm level. Friction
272 period duration and friction coefficient values should then be regularly estimated and updated
273 to facilitate the application of the FC approach.

274 As mentioned above, the necessity to account for indirect costs related to productivity losses
275 in economic studies is not clearly established. Health Technology Assessment agencies
276 provide different guidelines. Those focusing on payer perspective recommend to exclude
277 those costs from the evaluation (32,33). By contrast, other agencies adopting a collective or
278 societal perspective, including the World Health Organization, propose to include indirect
279 costs, sometimes in a separate analysis (34–36). Besides the methodological challenge to

280 measure indirect costs, ethical objection are often mentioned (37). Indeed, if decision makers
281 use those studies to plan resource allocations, working age people would be favored over
282 young or elderly, and any other unemployed population. Moreover, authors discuss the risk of
283 double counting in cost-effectiveness evaluation when including productivity loss. The
284 question is to determine whether individuals take into account the impact of disease would
285 have on their income and career when they assess its impact on quality of life, which is
286 included in the denominator of the incremental cost-effectiveness ratio (ICER) (38,39). By
287 presenting direct and indirect costs in separate analysis, authors allow decision-makers to take
288 a stand regarding these scientific and equity issues in healthcare resource utilization.

289 Furthermore, the relationship between disease and work should be more precisely
290 studied to limit the consequences of being sick on occupational activity. The low proportion
291 of early retirement procedures and the absence of dismissal in our cohort will reassure BC
292 patients on their future capacity to work and motivate them to use part time recovery when
293 needed. Another study showed a good readjustment to the workplace for patient after a BC
294 (40).

295

296 **Conclusion**

297 We believe crucial to report absenteeism, productivity losses and indirect costs.
298 Moreover, accurate data on type and length of absenteeism are fundamental, particularly for
299 economic studies based on simulated models and using a societal perspective.

300

301

302 **Declarations**

303 **Ethics approval**

304 This study was approved by the French National ethics committee (CCTIRS Authorization
305 n°14.602 and CNIL DR-2014-167) and covers research at all participating hospitals. This
306 study was registered with ClinicalTrials.gov (Identifier: NCT02813317).

307 **Ethics, consent to participate**

308 All individuals included in this study consented to participate after a complete information.

309 **Consent for publication**

310 A written consent for publication was obtained from all individuals included in this study.

311 **Availability of data and materials**

312 The datasets used and/or analysed during the current study are available from the
313 corresponding author on reasonable request.

314 **Competing interests**

315 The authors declare that they have no competing interests.

316 **Funding**

317 This study was supported by a grant from the French National Cancer Institute, dedicated to
318 economic studies of innovative techniques (PRME-K-2013). The funder had no role in the
319 study design; in the collection, analysis, and interpretation of data; in the writing of the report;
320 and in the decision to submit the paper for publication.

321 **Authors' contributions**

322 CF, RR and DH contributed to the acquisition of data. CF, CT, PL, SB, BA, RR and DH
323 contributed in (1) the conception and design of the study, or acquisition of data, or analysis

324 and interpretation of data, (2) drafting the article or revising it critically for important
325 intellectual content, (3) final approval of the version to be submitted.

326 **Acknowledgements**

327 The authors acknowledge the French National Cancer Institute.

328 **Figure Title:**

329 Figure 1. Flow-chart.

330 Figure 2. Indirect costs per patient.

331 Figure 3. Tornado diagram for the univariate sensitivity analysis.

332 **Figure legends:**

333 Figure 2: Tch: Human Capital Approach. Tcf: Friction Costs Approach.

334 Figure 3: Horizontal axis: cost (€) / patient. SPC: socio professional category. For the
335 subgroup analysis, the variation is applied only for the patients in the subgroup.

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338

339

Table 1. Characteristics of the sample (n=168).

Age¹ (years)	50,1 (±7.4)
Marital status	
-Single	31 (18.5%)
-Married	106 (63.1%)
-Divorced	28 (16.7%)
-Widow	1 (0.6%)
-Missing data	2 (1.2%)
Educational attainment	
-Elementary	10 (6%)
-Middle school	36 (21.4%)
-High school	24 (14.3%)
-Post High school	98 (58.3%)
Socio professional group	
-Employee	70 (41.7%)
-Manager	70 (41.7%)
-Temporary worker	20 (11.9%)
-Craftsman	5 (3%)
-Missing data	3 (1.8%)
Monthly wage¹ (€)	2 214 (±761)
Diagnostic modality	
-Screening	69 (41.1%)
-Other	99 (58.9%)
Histology	
-In situ	21 (12.5%)
-Invasive	146 (86.9%)
-Missing data	1 (0.6%)
Surgery	
-Lumpectomy	129 (76.8%)
-Mastectomy	39 (23.2%)
-Sentinel lymph node	121 (72%)
-Axillary lymph node dissection	33 (19.7%)
-No lymph node surgery	14 (8.3%)
Number of surgical procedures	
-1	129 (76.8%)
-2	36 (21.4%)
-3	3 (1.8%)
Adjuvant radiation therapy	153 (91.1%)
Adjuvant chemotherapy	80 (47.6%)
Adjuvant endocrine therapy	121 (72%)
Sick leave	
-Proportion with at least one period	156 (92.9%)
-Number of period ¹	2
-Number of days ¹	173 (±155)
-Number of days if at least one period ¹	186 (±153)
Part-time resumption	
-Proportion	40 (23.8%)
-Number of period ¹	1
-Number of days ¹	27 (±63)

-Number of days if part-time resumption¹ 114 (±83)

341

1: mean (+/-standart deviation).

342

343

Tableau 2. Regression models on indirect costs.

	HC approach-SLR		HC approach-MLR		FC approach-SLR		FC approach-MLR	
	Coef. [95%IC]	p-value	Coef. [95%IC]	p-value	Coef. [95%IC]	p-value	Coef. [95%IC]	p-value
Age	-18.7	.928	-	-	21.4	.32	-	-
Marital status			-	-			-	-
-Single								
-Married	1515	.71			1152	.384		
-Divorced	3770	.471			1076	.524		
Educational attainment			-	-			-	-
-post high school								
-elementary	-4867	.462			-5458	.08		
-middle school	-6785	.082			-4160	.001		
-high school	1462	.747			-1029	.464		
Socio professional group								
-Paid employee								
-Manager	55 73	.096	4838	.117	5694	<.001	5688	<.001
-Temporary	-1726	.73	-618	.894	1505	.305	1838	.212
-craftsman	-15819	.085	-19231	.023	-3760	.161	-4248	.111
Diagnose by screening	-898,7	.775	-	-	-858	.394	-	-
Inavasive nature	13849	.003	11676	.086	2743	.067	1573	.462
Breast surgery								
-tumorectomy								
-mastectomy	13549	<.001	8183	.046	2489	.033	859	.505
Axillary surgery								
-sentinal lymph node								
-no gesture	-6692	.216	3152	.676	-1591	.371	458	.847
-complete dissection	14023	<.001	5271	.215	3122	.012	2297	.088
Number of surgical procedures	7710	.018	9624	.003	1465	.162	1652	.102
Chemotherapy	11300	<.001	5245	.113	1760	.075	420	.687
Radiotherapy	-9240	.087	-4003	.465	-1756	.312	-1282	.459
Hormonotherapy	5743	.094	1837	.624	1135	.303	732	.537

345

SLR: Simple Linear Regression. MLR: Multiple Linear Regression. HC: Human Capital. FC: Friction costs.

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353 **References**

- 354 1. Haute Autorité de Santé. (2011). Choix méthodologiques pour l'évaluation
355 économique à la HAS. Disponible sur : <www.has-santé.fr>.
- 356 2. Tuppin P, Pestel L, Samson S, Cuerq A, Rivière S, Tala S, et al. [The human
357 and economic burden of cancer in France in 2014, based on the Sniiram
358 national database]. *Bull Cancer (Paris)*. juin 2017;104(6):524-37.
- 359 3. Campbell JD, Ramsey SD. The costs of treating breast cancer in the US: a
360 synthesis of published evidence. *PharmacoEconomics*. 2009;27(3):199-209.
- 361 4. Rice DP, Hodgson TA, Kopstein AN. The economic costs of illness: A
362 replication and update. *Health Care Financ Rev*. 1985;7(1):61-80.
- 363 5. Koopmanschap MA, van Ineveld BM. Towards a new approach for
364 estimating indirect costs of disease. *Soc Sci Med*. 1992;34(9):1005-10.
- 365 6. Koopmanschap MA, Rutten FF, van Ineveld BM, van Roijen L. The friction
366 cost method for measuring indirect costs of disease. *J Health Econ*. juin
367 1995;14(2):171-89.
- 368 7. Krol M, Brouwer W. How to estimate productivity costs in economic
369 evaluations. *PharmacoEconomics*. avr 2014;32(4):335-44.
- 370 8. Marcotte DE, Wilcox-Gök V. Estimating the employment and earnings costs
371 of mental illness: recent developments in the United States. *Soc Sci Med*
372 1982. juill 2001;53(1):21-7.
- 373 9. Fu AZ, Chen L, Sullivan SD, Christiansen NP. Absenteeism and short-term
374 disability associated with breast cancer. *Breast Cancer Res Treat*. nov
375 2011;130(1):235-42.
- 376 10. Lidgren M, Wilking N, Jönsson B, Rehnberg C. Resource use and costs
377 associated with different states of breast cancer. *Int J Technol Assess*
378 *Health Care*. 2007;23(2):223-31.
- 379 11. Laas E, Vataire A-L, Aballea S, Valentine W, Gligorov J, Chereau E, et al.
380 Evaluation of the costs and resource use associated with adjuvant
381 chemotherapy for breast cancer in France. *J Med Econ*.
382 2012;15(6):1167-75.
- 383 12. Institut National du CAnCer. (2015). Plan cancer 2014 - 2019. Disponible
384 sur : <www.e-cancer.fr>.

- 385 13. Institut National du CAncer. (2017). Charte des 11 engagements « cancer
386 et emploi ». Disponible sur : <www.e-cancer.fr>.
- 387 14. de Boer AGEM, Taskila TK, Tamminga SJ, Feuerstein M, Frings-Dresen
388 MHW, Verbeek JH. Interventions to enhance return-to-work for cancer
389 patients. *Cochrane Database Syst Rev.* 25 sept 2015;(9):CD007569.
- 390 15. Baffert S, Hoang HL, Brédart A, Asselain B, Alran S, Berseneff H, et al. The
391 patient-breast cancer care pathway: how could it be optimized? *BMC*
392 *Cancer.* 12 mai 2015;15:394.
- 393 16. Offre d'emploi et recrutement (OFER) - 2005, DARES - Ministère du travail
394 (producteur), ADISP-CMH (diffuseur).
- 395 17. Pole-emploi. Statistiques, études et évaluations. Enquête « besoin en
396 main- d'oeuvre ». Avril 2017.
- 397 18. <https://embauche.beta.gouv.fr/>.
- 398 19. Arfi A, Baffert S, Soilly A-L, Huchon C, Reyal F, Asselain B, et al.
399 Determinants of return at work of breast cancer patients: results from the
400 OPTISOINS01 French prospective study. *BMJ Open.* 18 mai
401 2018;8(5):e020276.
- 402 20. Institut National du CAncer. (2016). Les cancers en France. Disponible sur :
403 <www.e-cancer.fr>.
- 404 21. Mutual Information System on Social Protection. MISSOC database.
405 Comparative tables. Disponible sur : <www.missoc.org>.
- 406 22. Wan Y, Gao X, Mehta S, Wang Z, Faria C, Schwartzberg L. Indirect costs
407 associated with metastatic breast cancer. *J Med Econ.* oct
408 2013;16(10):1169-78.
- 409 23. Source: internet. Available on: <https://www.insee.fr/fr/accueil>.
- 410 24. Gordon L, Scuffham P, Hayes S, Newman B. Exploring the economic impact
411 of breast cancers during the 18 months following diagnosis.
412 *Psychooncology.* déc 2007;16(12):1130-9.
- 413 25. Hemp P. Presenteeism: at work--but out of it. *Harv Bus Rev.* oct
414 2004;82(10):49-58, 155.

- 415 26. Bouwmans C, Krol M, Severens H, Koopmanschap M, Brouwer W,
416 Hakkaart-van Roijen L. The iMTA Productivity Cost Questionnaire: A
417 Standardized Instrument for Measuring and Valuing Health-Related
418 Productivity Losses. *Value Health J Int Soc Pharmacoeconomics Outcomes*
419 *Res.* sept 2015;18(6):753-8.
- 420 27. Zhang W, Bansback N, Boonen A, Severens JL, Anis AH. Development of a
421 composite questionnaire, the valuation of lost productivity, to value
422 productivity losses: application in rheumatoid arthritis. *Value Health J Int*
423 *Soc Pharmacoeconomics Outcomes Res.* janv 2012;15(1):46-54.
- 424 28. Łyszczarz B, Nojszewska E. Productivity losses and public finance burden
425 attributable to breast cancer in Poland, 2010-2014. *BMC Cancer.* 10 oct
426 2017;17(1):676.
- 427 29. Tachi T, Teramachi H, Tanaka K, Asano S, Osawa T, Kawashima A, et al. The
428 impact of side effects from outpatient chemotherapy on presenteeism in
429 breast cancer patients: a prospective analysis. *SpringerPlus.* 2016;5:327.
- 430 30. Kigozi J, Jowett S, Lewis M, Barton P, Coast J. Estimating productivity costs
431 using the friction cost approach in practice: a systematic review. *Eur J*
432 *Health Econ HEPAC Health Econ Prev Care.* janv 2016;17(1):31-44.
- 433 31. Kigozi J, Jowett S, Lewis M, Barton P, Coast J. Valuing productivity costs
434 using the friction-cost approach: Estimating friction-period estimates by
435 occupational classifications for the UK. *Health Econ.* déc
436 2017;26(12):1862-8.
- 437 32. NICE. Guide to the methods of technology appraisal 2013.
- 438 33. Academy of managed care pharmacy. A format for submission of clinical
439 and economic evidence in support of formulary consideration. 2016.
- 440 34. WHO. Guide for standardization of economic evaluations of immunization
441 programmes. 2008.
- 442 35. CES. Actualisation partielle du guide méthodologique pour l'évaluation
443 économique des stratégies de santé.
- 444 36. Wellpoint. Health technology assessment guidelines. Drug submission
445 guidelines for new products, new indications, and new formulations.
446 September 2008.

- 447 37. Drummond M. Cost-of-illness studies: a major headache?
448 PharmacoEconomics. juill 1992;2(1):1-4.
- 449 38. Tilling C, Krol M, Tsuchiya A, Brazier J, van Exel J, Brouwer W. The impact of
450 losses in income due to ill health: does the EQ-5D reflect lost earnings?
451 [Internet]. 2009 [cité 23 mai 2018]. Disponible sur: [https://mpra.ub.uni-](https://mpra.ub.uni-muenchen.de/29837/)
452 [muenchen.de/29837/](https://mpra.ub.uni-muenchen.de/29837/)
- 453 39. Lensberg BR, Drummond MF, Danchenko N, Despiégel N, François C.
454 Challenges in measuring and valuing productivity costs, and their relevance
455 in mood disorders. Clin Outcomes Res CEOR. 2013;5:565-73.
- 456 40. Maunsell E, Drolet M, Brisson J, Brisson C, Mâsse B, Deschênes L. Work
457 situation after breast cancer: results from a population-based study. J Natl
458 Cancer Inst. 15 déc 2004;96(24):1813-22.

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