ORIGINAL ARTICLE

Financial toxicity in patients followed for branch-duct intraductal papillary mucinous neoplasms: the risk that arises from "too much" for nothing

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Abstract

Background: No data exist about financial toxicity (FT) for branch duct intraductal papillary mucinous neoplasms (BD-IPMNs).

Methods: This prospective study analyzed patients with BD-IPMNs from 2023 to 2024. Demographics, clinical data of interest, and radiological and endoscopic information were recorded for each patient. The "Comprehensive Score for Financial Toxicity" (COST) patient-reported outcome measure was used to assess financial toxicity (FT). Lower COST values indicate greater FT. A multilevel, multivariate mixed-effects model was employed.

Results: One hundred sixteen patients were interviewed during routine outpatient follow-up visits. Eighty patients agreed to complete the survey (68.9 %). The COST score was 18 (15–21, IQR), showing a fairly normal distribution (Shapiro–Wilk $p = 0.054$). The older the age at diagnosis, the greater the perception of FT ($p < 0.001$). As educational status increased, the FT burden also increased (–1.4 ± 0.6; $p = 0.047$). Private/self-employed patients (–3.7 ± 1.3; $p = 0.004$) and unemployed patients (–2.3 ± 1.0; $p = 0.016$) reported a higher perception of FT compared to pensioners or publicly employed individuals. WFs increase FT (–1.9 ± 0.8; $p = 0.014$). The longer the follow-up duration, the greater the FT (–0.3 ± 0.1; $p = 0.043$).

Conclusion: FT can be seen in the BD-IPMN population. The patient's perspective must be taken into account during follow-up.

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Introduction

In recent years, several studies have clarified that the branch-duct intraductal papillary mucinous neoplasms (BD-IPMN) present a low risk of progression.[1–4] Nonetheless, due to the small number of low-risk BD-IPMNs that change during the follow-up,[5] International and European guidelines[6–8] recommended multiple and repeated radiological exams to intercept the signs of changes early. However, the follow-up schedules are very tight as interval time, requiring at least one magnetic resonance (MRI) every eighteen months in the most optimistic scenario. Indeed, with controversial results, several studies[9,10] tried to evaluate the economic sustainability of BD-IPMN active surveillance from the healthcare system's point of view. Nowadays, surveillance seems to be not worldwide sustainable, requiring high costs for a minimal gain in lifespan for the patients.[11]

From the patient's point of view, the impact of active surveillance was less studied. The PACYFIC study[12] recently showed that surveillance could produce both negative and positive effects: the follow-up reduced the concerns of developing pancreatic cancer in most patients, but one-third of them considered the surveillance burdensome and the reason for anxiety. However, no studies have clarified the impact of intensive surveillance on the economic status of the patients.

Financial toxicity (FT) describes the financial burden and distress that can arise for patients due to chronic disease treatment or follow-up.[13] FT has been described for cancer patients in the user-pays healthcare systems and could produce delays in

medical visits or doses of medications.[14–16] FT could also increase the "out-of-pocket" related expenses, which are not covered by insurance or the healthcare system and involve a patient's outlay of money.[14] Finally, FT may be related to worsening health disparities among cancer survivors.[15,16] FT can also be observed in a universal health system[17] and for patients with non-neoplastic chronic disease.[18] The intensive surveillance recommended for BD-IPMN patients and the high costs of MRI could produce FT similar to cancer or chronic disease. However, this point has never been investigated.

The present study aims to evaluate if intensive follow-up according to current guidelines[6–8] leads to FT in patients with BD-IPMN.

Methods

Patients and eligibility criteria

This study was approved by the local review board with the following code PANBO 064/2017/U/Oss and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. The survey followed the Consensus-Based Checklist for Reporting of Survey Studies (CROSS) guidelines.[19] An informed consentwas obtained before each patient's interview. In this pilot study, patients with BD-IPMNs receiving visits for follow-up as outpatients at a tertiary academic IRCCS "Azienda Ospedaliero-Universitaria" of Bologna were invited to participate between May 2023 and May 2024. We included only patients with a suspected BD-IPMN diagnosed with MRI or EUS. The exclusion criteria were: (i) a follow-up inferior to 12 months from diagnosis; (ii) previous pancreatic resection; (iii) cysts highly suspicious for an alternative diagnosis; (iv) presence of high-risk stigmata; (v) indication for surgery; (vi) absence of relevant data for the study.

Data collection, definitions, and end point

At the time of the visit, for each patient, demographics (age and gender) and clinical data of interest (jaundice, acute pancreatitis, new onset, or worsening diabetes) were registered. Radiological and endoscopic characteristics of the cyst, including location, cyst size, and worrisome features (WFs), were also obtained. When multiple cists were present, the larger size was considered for the analysis. Duration of surveillance was defined as the interval from diagnosis to the date of the last follow-up. Surveillance was performed in line with IAP guidelines.[6,20] A dedicated questionnaire was administered to the patients during the annual visit to measure the FT. The Italian version of the "COmprehensive Score for Financial Toxicity" (COST)[21] patient-reported outcome measure was used. This questionnaire, usually used for patients with cancer, was recently validated for chronic diseases, such as diabetes.[18] We used the recent version (2.0) online,[22] reported in **supplementary materials**. The questionnaire contained twelve questions. Each question can obtain a score from 0 to 4, for a total score ranging from 0 to 48: the lower the COST scores, the higher the FT.

Also, the quality of life was evaluated using the Centers for Disease Control's (CDC) Health-Related Quality of Life Scale (HRQOL-14) questionnaire. The questionnaire contained three modules: (i) the Healthy Days Core module (4 questions), indicating general health; (ii) the Activity Limitations module (5 questions), indicating the limitations in daily life; (iii) the Healthy Days Symptoms module, (5 questions), indicating the weight of symptoms in daily life. The original questionnaire divided the results into excellent, very good, good, fair, and poor. For analytical purposes, we divided the results of patients with poor general and non-poor general health.

The survey took about 10 min, and patients could complete the survey only once. Two coders (VDA and CG) entered survey responses into a study database, and 20 consecutive surveys were double-coded to assess internal validity. We consider the patients at risk for FT when COST is inferior to 26 points.[23]

Statistical analysis

The analysis was completed on a de-identified dataset. The characteristics of patients were described as numbers and percentages or as medians, means, interquartile ranges (IQR), ranges, or standard deviation (SD). The distribution of COST and HRQOL-14 scores was evaluated for normality using the Shapiro–Wilk test. Correlations between patients' characteristics and COST scores were analyzed using a multilevel multivariate mixed-effects model to adjust for non-representative sampling. This model is also known as a multilevel or hierarchical linear model. The overall error distribution of the linear mixed-effects model is assumed to be Gaussian, and heteroskedasticity and correlations within the lowest-level groups also may be modeled. The effect of covariates was measured, and the coefficient and SE were reported. LASSO preselection of covariates was used to avoid overfitting. To explore the potential variability of financial toxicity (FT) across different healthcare settings, we conducted a Monte Carlo simulation assuming plausible variations in the COST score based on prior literature. For the "universal" system (*e.g.*, Italy), we used the observed mean and standard deviation of COST. For "user-pays" systems (*e.g.*, USA), we assumed a mean of 18 (±6), reflecting previously published findings in insured cancer patients.[18] The simulation modeled the distribution of FT under these assumptions to test the robustness and transferability of our findings. We computed Cohen's d effect sizes to quantify healthcare model differences. According to standard interpretation of Cohen's d, a value between 0 and 0.2 indicates a small effect (corresponding to $\leq$15 % non-overlapping population between groups); values between >0.2 and 0.5 indicate a medium effect ($\leq$33 % non-overlap); values between >0.5 and 0.8 correspond to a large effect ($\leq$50 % non-overlap); and values above 0.8 suggest a very large effect, with >50 % of the distributions not overlapping. To further explore the impact of individual predictors on financial toxicity, we performed a threshold analysis based on Monte Carlo

simulation. Using the effect sizes derived from our multivariable regression model, we simulated adjusted COST score distributions for each significant covariate. The proportion of patients falling below the observed median COST value (COST < 18) was computed for both a universal and a user-pays healthcare system scenario. This allowed for a comparative assessment of financial vulnerability across systems and risk profiles.

All statistical analysis was performed using STATA (Statistical software for data science, release 18, Stata Corp, College Station, TX), and R-project (R version 4.2.2; R Foundation for Statistical Computing, Vienna, Austria. A P value < 0.05 was considered statistically significant. The simulation was performed using Python 3.10 with numpy for data generation, scipy.stats for effect size calculation (Cohen's d), and matplotlib for visualization.

Results

STROBE and CROSS checklists were reported as supplementary materials. Fig. 1 summarizes the flowchart selection of patients. One hundred and sixteen patients were told about this study during routine outpatient follow-up visits, and 80 (68.9 %) individuals agreed to participate and complete the survey. Two authors (VD and CG) coded the responses with a high "inter-coder" agreement (overall agreement of 98.8 %). Doubts were resolved by discussing them with the senior authors (RC).

Characteristics of patients

Table 1 summarizes the characteristics of 80 patients who accepted to participate in the survey. The median age at the diagnosis was 60 (53–66, IQR) years, with the prevalence of female gender (63.8 %). Most patients (68.7 %) presented a high educational status (graduate or bachelor's degree). At the time of the interview, most patients were pensioners (62.5 %), public employed (20 %), or private/self-employed (10 %). Only a minority (7.5 %) declared to be unemployed. Only 30 % of interviewees declared to have one or more dependent children. As expected in a public health care system, the minority of patients (5 %) have medical insurance. The general condition of patients was quite good, with a median Comorbidity Charlson Index (CCI) of 2 (1–2). Only 12.5 % of patients were symptomatic. The median size of larger cysts was 10 mm (7.5–10.5). The cysts were nearly equally located in the head (33.8 %), body (40 %), or tail (26.2 %). Multifocal lesions were observed in 38.7 % of patients. WFs were present at the diagnosis only in 23.7 % of patients; 18 (22.5 %) patients had only one WF, while 1 (1.3 %) presented two WFs. Ten patients presented cysts larger than 30 mm in size, four thickened septa, and one thickened septa and main duct between 5 and 9 mm. The median follow-up was 66 months (46–100, IQR). Most patients were followed with an MRI or CT scan (81.3 %), while 18.7 % had US. Most patients had a follow-up every 12 months (82.5 %), while 17.5 % had a follow-up every 6 months. Only 18.7 % of patients developed

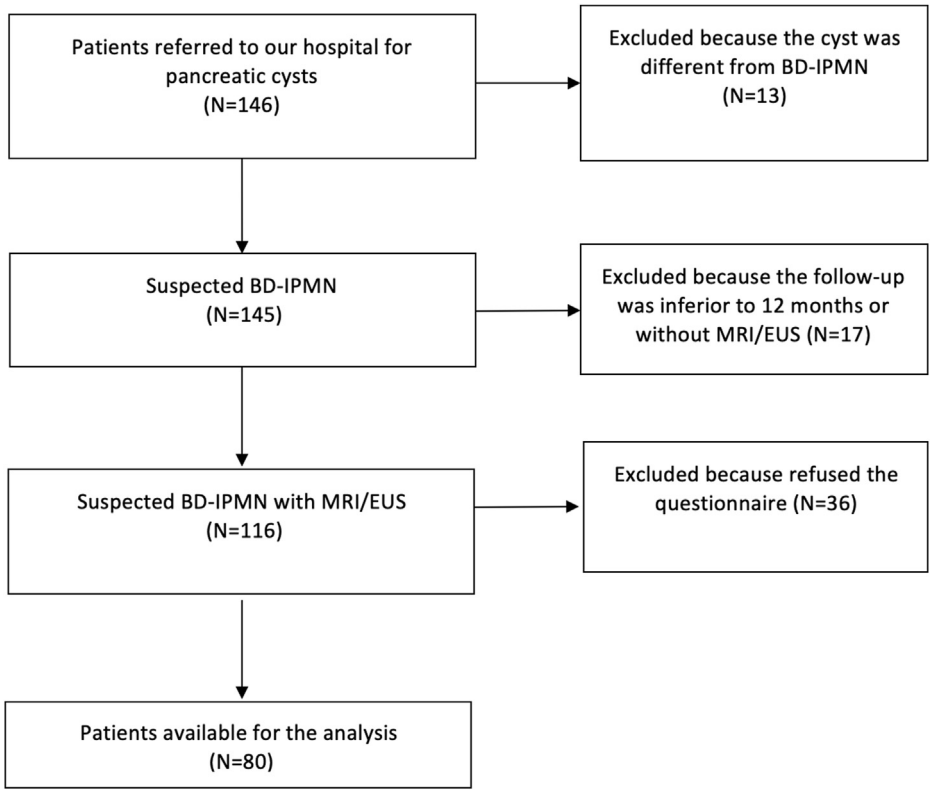

Figure 1 **Flowchart selection. Legend:** BD-IPMN = branch duct intraductal papillary mucinous neoplasms

significant changes during follow-up, requiring EUS + FNB or follow-up modification. At the end of the follow-up, 41.2 % of patients had at least one WF, and the patients with two WFs were two (2.5 %). None of the patients required surgery or developed pancreatic adenocarcinoma (PDAC).

Survey

Table 2 shows the results of the survey. The patients who reported poor general health (GH) were 72.5 %. The median mental unhealthy days were 10 (0–22.5, IQR); the median physical unhealthy days were 15.5 (0–30, IQR); and the median overall unhealthy days were 24.5 (0–30). HRQOL-14 scores have a normal distribution (Shapiro–Wilk $p > 0.05$). The median COST score was 18 (15–21, IQR), having a quite normal distribution (Shapiro–Wilk $p = 0.054$).

Table 3 and Fig. 2 show the factors related to COST. LASSO preselection identified the following variables as informative: age, gender, educational status, employment, symptoms, size of larger cysts, WFs, the diagnosis, years in follow-up, type of examination, and QoL. Based on the LASSO analysis, the presence of dependent children, medical insurance, site, multifocal, number of WFs, changes during the follow-up, and WF at the end of follow-up were irrelevant to the analysis. Older age at diagnosis was associated with lower COST scores ($p < 0.001$), with a decrease of 3 points for each decade. Increasing the educational status, the COST score decreased (-1.4 ± 0.6; $p = 0.047$). Private/self-employed (-3.7 ± 1.3; $p = 0.004$) and unemployed (-2.3 ± 1.0; $p = 0.016$) patients had lower COST score when compared with pensioners or publicly employed people. WFs at the diagnosis reduced the COST score (-1.9 ± 0.8; $p = 0.014$). The higher the follow-up duration, the lower the COST score (-0.3 ± 0.1; $p = 0.043$). Age, gender, symptoms, size of larger cysts, type of examination, and follow-up schedule did not significantly influence the COST scores. The multivariable model also showed that poor quality of life was not significantly associated with FT (effect 1.1 ± 0.8, $p = 0.182$) and did not meet criteria for retention in the final multivariable model.

Montecarlo simulation

Fig. 3 reports the Monte Carlo simulation of 20,000 in-silico patients (10,000 per healthcare system) comparing a universal and a user-pays model. While both scenarios showed the same mean COST score of 18, the distribution was noticeably wider in the user-pays system (SD 6 vs. SD 4), indicating greater variability in perceived financial toxicity. The threshold analysis with 95 % confidence intervals (Fig. 4) showed that the proportion of patients with COST scores below the observed median (COST <18) was similar in the universal healthcare system compared to the user-pays system across all covariates. Threshold analysis identified three conditions associated with a difference in the proportion of patients with COST <18 between the universal and user-pays systems, with a Cohen's d greater than 0.200 (non-small difference). These were: age +20 years from baseline ($d = 0.26$; 87.2 % universal vs. 78.1 % user-pays), age +30 years ($d = 0.30$; 94.1 % vs. 85.2 %), and self-employed status ($d = 0.25$; 83.3 % vs. 73.0 %). In all cases, the proportion of patients falling below the threshold was higher in the universal system.

Discussion

The results of the present pilot study demonstrated that FT could be experienced by patients with BD-IPMN who underwent intensive surveillance (every 6 or 12 months). FT has recently been described in the US as an undervalued and extended problem involving more than 137 million patients annually.[24] FT represents the negative impact of the high cancer treatment and follow-up costs.[13] FT could significantly reduce follow-up and therapy compliance. FT also could increase anxiety, depression, and stress, reducing spending on food, clothing, or social activity.[13] Interestingly, FT is not limited to oncological disease but could be observed in multiple chronic conditions.[18,25] According to the National Cancer Institute (NHI) definition,[26] the BD-IPMN can be assimilated to a chronic disease: (i) it is a disease that usually lasts for 3 months or longer and may get worse over time; (ii) it occurs in older adults; (iii) it requires period control but rarely could be cured. Moreover, BD-IPMN requires an extensive follow-up,[6–8] even if the risk of malignant occurrence is very low.[27,28]

The present cohort accurately represented the typical low-risk BD-IPMN population for several reasons: (i) the extended follow-up period, lasting more than 5 years; (ii) the high cost of radiological exams, as patients were monitored primarily with MRI or CT scans; (iii) the low cancer risk. Indeed, only 18.7 % of patients exhibited significant changes during follow-up, and none developed pancreatic adenocarcinoma (PDAC). This observation is particularly noteworthy because it arises from a universal healthcare system in which most individuals analyzed did not have private insurance. In the Italian system, the regional healthcare system primarily covered MRI or EUS costs, with a minor contribution from patients based on their salary range. The IAP guidelines recommend extensive follow-up with MRI every 6–18 months, irrespective of the type of healthcare system. However, the accessibility of MRIs poses a challenge in universal healthcare systems, as patients with BD-IPMN compete for MRI scans with those suffering from aggressive cancers or severe cardiovascular diseases. For instance, in the Canadian healthcare system, the number of MRIs performed at private facilities has risen in recent years, with payment through private insurance or out-of-pocket expenses being the primary funding source for MRI scans in private settings. The current study demonstrated, for the first time in our knowledge, that an intensive follow-up for BD-IPMN could produce adverse financial effects from the healthcare system's and the patient's point of view. The median COST score observed in the present population was 18, and the financial burden was unexpectedly relevant and very similar to those observed in the user-pays healthcare system.[21,29–31] In other words, despite a well-developed social welfare system

Table 1 Characteristics of 80 patients with BD-IPMN

Characteristics	N(%) or median (IQR)
Age at diagnosis (years)	60 (53–66)
Gender	
Male	29 (36.2)
Female	51 (63.8)
Education status	
Primary/Middle School	25 (31.3)
High School/University	55 (68.7)
Employment status	
Pensioner	50 (62.5)
Public employed	16 (20)
Private or self employed	8 (10)
Unemployed	7 (7.5)
Dependent children	
No	56 (70)
Yes	24 (30)
Medical insurance	
No	76 (95)
Yes	4 (5)
CCI	2 (1–2)
Symptoms	
No	70 (87.5)
Yes	10 (12.5)
Size of largest lesion	10 (7.5–10.5)
Site	
Head	27 (33.8)
Body	32 (40)
Tail	21 (26.2)
Multifocal	
No	49 (61.3)
Yes	31 (38.7)
WF at diagnosis	
No	61 (76.2)
Yes	19 (23.7)
Number of WF at diagnosis	
0	61 (76.2)
1	18 (22.5)
2	1 (1.3)
Follow-up (years)	66 (46–100)
Imaging for follow-up	
MRI or CT	65 (81.3)
US	15 (18.7)
Interval time	
<12 months	66 (82.5)
>=12 months	14 (17.5)
Changing in follow-up	
No	65 (81.3)
Yes	15 (18.7)
WF at enrollemnt	
No	47 (58.8)
Yes	33 (41.2)

(*continued on next column*)

Table 1 (*continued*)

Legend: **IQR**=Interquartile range; **CCI**= Charlson Comorbidity Index; **WF**= Worrisome features; **MRI** = Magnetic resonance; **CT**=Computed tomography; **EUS** = Endoscopic Ultrasound; **US**= Ultrasonography.

Table 2 Financial Toxicity and quality of life in patients with BD-IPMN

Parameters	Median (IQR) or N(%)	Shapiro–Wilk (*p*-value)
HRQOL-14 scores		
Patients with poor GH	72.5 %	-*
Mental unhealthy days	10 (0–22.5)	0.092
Physical unhealthy days	15.5 (0–30)	0.598
Mental and physical unhealthy days	24.5 (0–30)	0.130
FT		
COST score	18 (15–21)	0.054

Legend: GH = general health; IQR= Interquartile range; FT=Financial toxicity; HRQOL= Health-Related Quality of Life Scale; * = not applicable to dichotomic variables.

Table 3 Factor influencing financial toxicity

Factors	Effect (95 CI) on COST scores	*p*-value
Age at diagnosis (for each decade)	–3 ± 1	<0.001
Male gender	0.7 ± 0.7	0.409
High school/University	–1.4 ± 0.6	0.047
Pensioner	*Referent*	
Public employed	–1.0 ± 1.2	0.369
Private/Self employed	–3.7 ± 1.3	0.004
Un-employed	–2.3 ± 1.0	0.016
Symptoms	1.1 ± 1.1	0.331
Larger cysts (for each mm)	–0.1 ± 0.1	0.355
WFs at the diagnosis	–1.9 ± 0.8	0.014
Follow-up duration (for each year)	–0.3 ± 0.1	0.043
MRI/CT use	0.7 ± 0.7	0.345
GH no-good	1.1 ± 0.8	0.182
Mental and physical unhealthy days	0.1 ± 0.1	0.123

FT = financial toxicity; MRI = Magnetic resonance imaging; CT = Computed tomography.

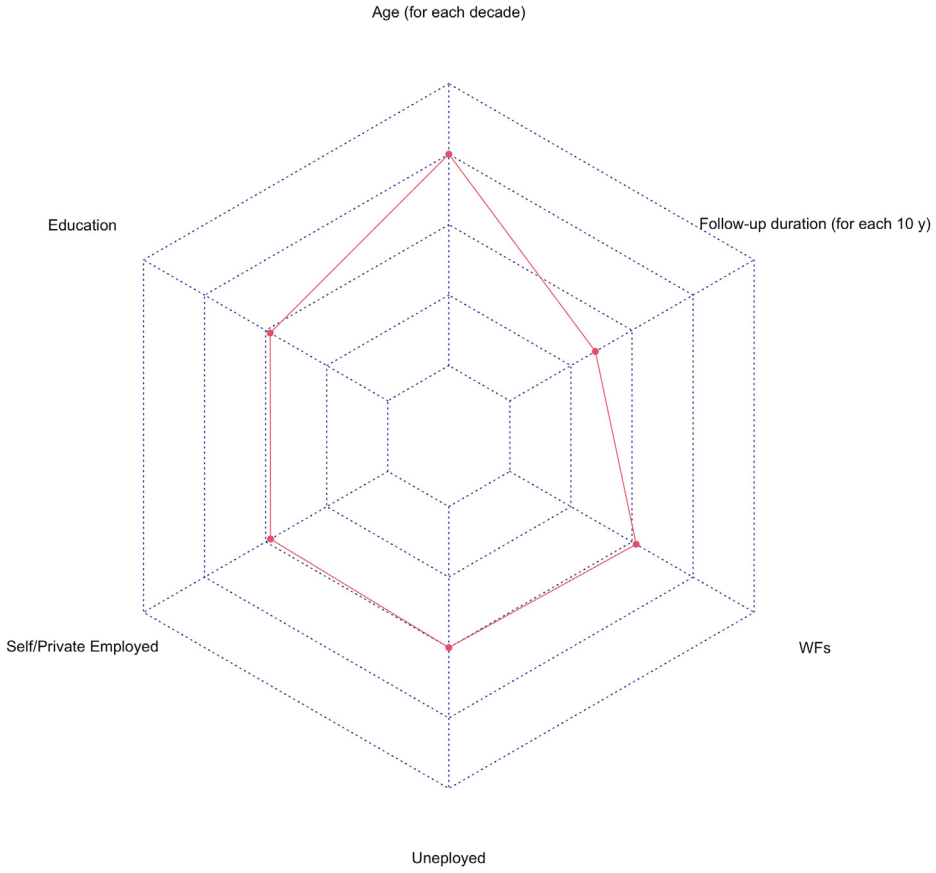

Figure 2 **Radar chart representing factors related to financial toxicity. Legend:** the blue line represents the mean average effect on the COST score

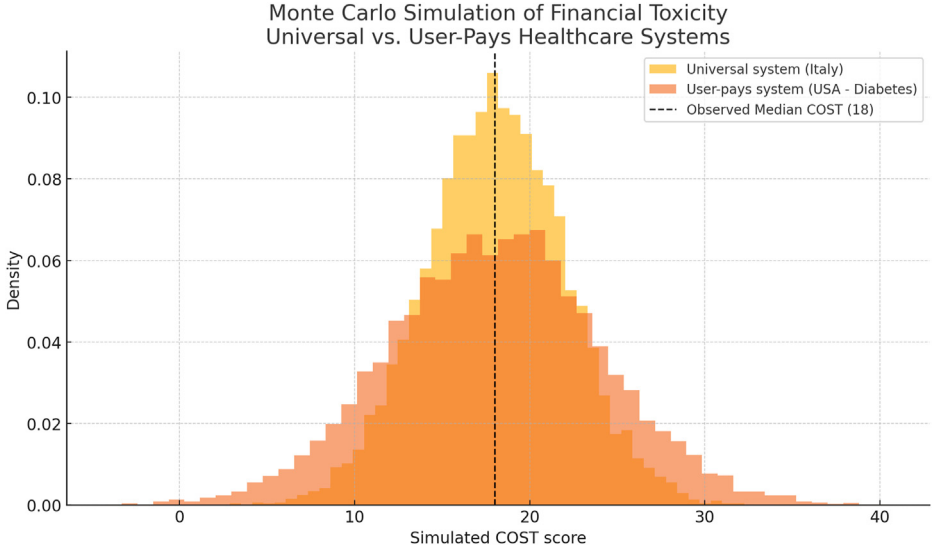

Figure 3 **Monte Carlo simulation of the COST scores distribution in three healthcare system models.** The simulation modeled 10,000 virtual patients per system using normally distributed COST scores: universal healthcare and user-pays models. The vertical dashed line indicates our real-world dataset's observed median COST score

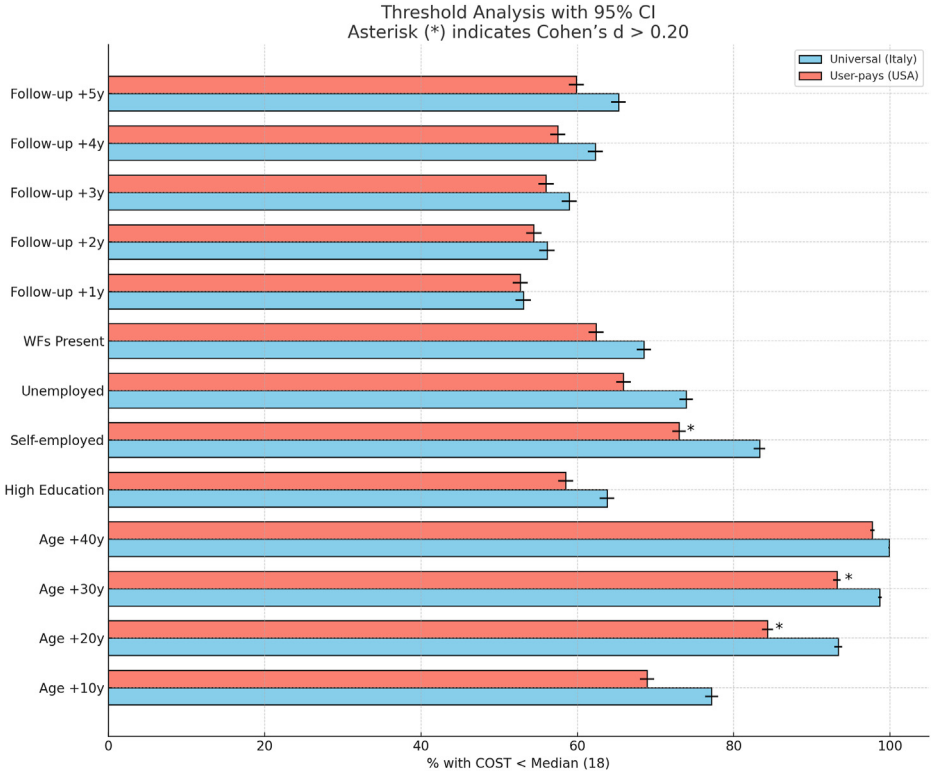

Figure 4 Threshold analysis based on Monte Carlo simulation. Each horizontal bar represents the proportion of simulated patients with a COST score below the observed median value (COST <18), indicating financial difficulty greater than the median. Using effect estimates from the multivariable model, simulations were conducted separately for two healthcare system models: a universal system and a user-pays system. Covariates include age (+10 years), education level (high vs. low), employment status (self-employed or unemployed vs. pensioner/public), presence of worrisome features (WFs), and follow-up duration (+5 years). Black horizontal lines represent 95 % confidence intervals derived from Monte Carlo sampling (n = 10,000)

designed to provide payments for those unable to work due to unemployment, illness, or disability, the financial burden could be observed. Our reports agreed with the results of Perrone *et al.*,[17] who registered FT for 16 different types of cancer. However, what is surprising is that a financial burden was present here for a precancerous disease, probably related to intense follow-up. Two factors are associated with FT: patient-related, which was also observed for other conditions, and disease-related, which was specific for BD-IPMN. Age decreases the COST score, increasing the perception of FT. This was probably because increasing age increased the probability of patients being frailer and more exposed to financial difficulty. Also, the type of employment was related to the FT degree. Pensioners and public employees have higher COST scores and lower FT than self-employed, private, or unemployed employees. Also, this observation is reasonable and in line with previous data about the financial burden.[22,31] Finally, the perception could also be conditioned by the educational level: a higher academic level corresponds to a better perception of financial difficulty related to BD-IPMN follow-up. The disease-related factors were the presence of WF features, which increased the probability of a financial burden. This is obvious because, as guidelines[6–8] recommend, follow-up should be more intense than for patients with an increased risk.[1] On the contrary, the absolute value of the cyst in size, even if correlated to the risk of malignancy and follow-up schedule, is less critical to WFs' presence who imposed an intensive follow-up (<12 months). Equally obvious, the longer the follow-up duration, the lower the COST score, and the higher the FT. However, this data is fascinating and emphasizes the need for follow-up discontinuation in patients with stable BD-IPMN after five years of follow-up.[5,20] It should be noted that the interviewee's preexisting quality of life was not influenced by BD-IPMN presence. However, the quality of life could represent a very important confounding factor in this study. Indeed, several predictors of FT, such as age, educational status, and employment, are well-known predictors of poor quality of life.[32–34] So, poor quality of life could be associated with but unrelated to FT. To avoid this bias, we registered and analyzed the QoL. The multivariate model has excluded the confounding effect of quality of life on FT. Finally, an exploratory Monte Carlo simulation supported the potential transferability of our findings across different healthcare settings. By assuming realistic

variations in the average COST score based on previous literature,[17,18] the simulation showed that FT remains significant also in universal and user-pays models. This reinforces the relevance of our observations even outside of a universal healthcare context. Our median COST score of 18, observed in a publicly funded system, overlaps with estimates reported in insurance-based systems. Moreover, threshold analysis suggests that financial vulnerability is not uniformly mitigated even within a universal healthcare system.[35] Subgroups such as older patients and self-employed individuals remain disproportionately exposed to financial toxicity, as shown by the higher proportion of patients falling below the median COST score and the moderate effect sizes observed. On the other hand, the broader distribution of the COST score in the user-pays setting compared to the universal system (SD 4 vs SD 6) suggests that in the user-pays setting, out-of-pocket expenses and indirect costs may contribute to a more unequal distribution of financial stress. Demonstrating the presence of FT is particularly relevant, as it may support more individualized surveillance strategies. In clinically stable and elderly patients, who may experience greater economic vulnerability, adopting less intensive follow-up schedules, or even surveillance discontinuation, could be proposed.[36,37]

The study has strengths and limitations. It utilized a validated tool to measure FT and documented this phenomenon for the first time. However, patients were recruited from a single high-volume center and the same pancreatic team. A primary limitation is the small sample size, which reflects the difficulty in capturing information about the economic status of patients in high-volume centers. Nonetheless, the LASSO approach allows for data analysis using a multivariate method. Third, although we aimed to understand the factors related to FT, other unmeasurable factors, such as varying local social welfare programs, unknown or unreported family situations, or acute financial hardships within families, may have influenced the survey. For instance, the out-of-pocket expenses for travel, parking, or one-night accommodations are challenging to track and are not always disclosed. Fourth, the study's setting may limit the results' external validity. We tried to limit this bias using a Monte Carlo simulation to simulate our results in a user-pays system. Therefore, some insights, with caution, may be transferred from universal care systems to insurance-based ones. Finally, an increasing body of evidence links the quality of care to the universal care system, particularly in governance and the efficiency of healthcare services and systems. All these limitations diminish the inference and the potential for generalization, necessitating further quantitative research to validate the current findings.

In conclusion, the importance of this study was doubled. On the one hand, it represents the first investigation of FT in BD-IPMN patients, who should be considered a potentially vulnerable group due to the intensive and lengthy surveillance. The economic sustainability of follow-up should be addressed from the health care system and the patient's point of view. Several reports[5,20] recently suggested that prolonged or intensive follow-up could not be necessary for patients with low-risk BD-IPMN, and the FT could represent a further reason to discontinue the follow-up in stable BD-IPMN or prolong the interval time in those who required surveillance. Further multicentric and prospective studies are needed to unravel the complexity behind the observed financial burden.

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Conflicts of interest

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hpb.2025.06.007.

