Title
Hereditary Cancer Clinics Improve Adherence to NCCN Germline Testing Guidelines for Pancreatic Cancer.

Journal
Journal of the National Comprehensive Cancer Network, 22(5)

ISSN
1540-1405

Authors
Rosso, Claudia
Marciano, Naomie Devico
Nathan, Deepika
et al.

Publication Date
2024

DOI
10.6004/jnccn.2023.7333

Peer reviewed

HHS Public Access

Author manuscript

J Natl Compr Canc Netw. Author manuscript; available in PMC 2024 October 09.

Published in final edited form as:

J Natl Compr Canc Netw. ; 22(5): 299–305. doi:10.6004/jnccn.2023.7333.

Hereditary Cancer Clinics Improve Adherence to NCCN Germline Testing Guidelines for Pancreatic Cancer

Claudia Rosso, MD[1], **Naomie Devico Marciano, MS**[1], **Deepika Nathan, MS**[2], **Wen-Pin Chen, MS**[3], **Christine E. McLaren, PhD, MS, MA**[3], **Kathryn E. Osann, PhD, OTH**[1], **Pamela L. Flodman, MS**[2], **May T. Cho, MD**[3,4], **Fa-Chyi Lee, MD, MS**[3,4], **Farshid Dayyani, MD, PhD**[3,4], **Jason A. Zell, DO, MPH, MS**[3,4], **Jennifer B. Valerin, MD, PhD**[3,4]

[1]School of Medicine, University of California, Irvine, Irvine, CA

[2]Division of Genetic and Genomic Medicine, Department of Pediatrics, University of California, Irvine, Irvine, CA

[3]Chao Family Comprehensive Cancer Center, University of California, Irvine, Irvine, CA

[4]Division of Hematology/Oncology, Department of Medicine, UCI School of Medicine, Irvine, CA

Abstract

Background: Pancreatic ductal adenocarcinoma (PDAC) has a poor prognosis, with a 5-year overall survival rate of 10%. In November 2018, NCCN recommended that all patients with PDAC receive genetic counseling (GC) and germline testing regardless of family history. We hypothesized that patients with PDAC were more likely to be referred for testing after this change to the guidelines, regardless of presumed predictive factors, and that compliance would be further improved following the implementation of a hereditary cancer clinic (HCC).

Methods: We conducted a single-institution retrospective analysis of patients diagnosed with PDAC from June 2017 through December 2021 at University of California, Irvine. We compared rates of genetics referral among patients in different diagnostic eras: the 18-month period before the NCCN Guideline change (pre-NCCN era: June 2017 through November 2018), 14 months following the change (post-NCCN era: December 2018 through January 2020), and 18 months after the creation of an HCC (HCC era: June 2020 through December 2021). Family and personal

Correspondence: Jennifer B. Valerin, MD, PhD, UCI School of Medicine, Division of Hematology/Oncology, Department of Medicine, 101 The City Drive South, ZOT 4061, Orange, CA 92868. jvalerin@hs.uci.edu.

Author contributions: *Conceptualization:* Rosso, Marciano, Nathan, Valerin. *Data curation:* Rosso, Marciano. *Formal analysis:* Chen, McLaren, Osann, Flodman. *Investigation:* Rosso, Marciano, Nathan, Zell, Valerin. *Methodology:* Rosso, Marciano, Nathan, Chen, Osann, Flodman, Valerin. *Supervision:* Zell, Valerin. *Writing—original draft:* Rosso, Marciano. *Writing— review & editing:* Chen, Cho, Lee, Dayyani, Zell, Valerin.

Disclosures: Dr. Dayyani has disclosed receiving grant/research support from Amgen, AstraZeneca, Bristol Myers Squibb, Exelixis, Genentech, Ipsen, Signatera, and Taiho; serving as a consultant for AstraZeneca, Eisai, Exelixis, Genentech, Foundation Medicine, and Ipsen; receiving honoraria from Amgen, Deciphera, Eisai, Exelixis, Ipsen, Servier, Signatera, and Sirtex; and having a spouse who is employed by Roche Diagnostics US. Dr. Zell has disclosed serving as a consultant for Tempus. Dr. Valerin has disclosed serving as a consultant and on an advisory board for Tempus; and serving on the speakers bureau and as a scientific advisor for AstraZeneca. The remaining authors have disclosed that they have not received any financial consideration from any person or organization to support the preparation, analysis, results, or discussion of this article.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

cancer history, genetics referral patterns, and results of GC were recorded. Data were compared using chi-square, Fisher exact, and multivariate analyses.

Results: A total of 335 patients were treated for PDAC (123 pre-NCCN, 109 post-NCCN, and 103 HCC) at University of California, Irvine. Demographics across groups were comparable. Prior to the guideline changes, 30% were referred to GC compared with 54.7% in the post-NCCN era. After the implementation of the HCC, 77.4% were referred to GC ($P<.0001$). The odds ratio (OR) for referral to GC among patients with a positive family history of cancer progressively decreased following the change (pre-NCCN era: OR, 11.90 [95% CI, 3.00–80.14]; post-NCCN era: OR, 3.39 [95% CI, 1.13–10.76]; HCC era: OR, 3.11 [95% CI, 0.95–10.16]).

Conclusions: The 2018 updates to the NCCN Guidelines for PDAC recommending germline testing for all patients with PDAC significantly increased GC referral rates at our academic medical center. Implementation of an HCC further boosted compliance with guidelines.

Background

Hereditary pancreatic cancer is defined as pancreatic adenocarcinoma (PDAC) due to a specific genetic defect.[1] Research estimates that 10% to 20% of PDAC cases are hereditary, with the treatment approach often differing based on the presence or absence of genetic mutations.[2–4] In particular, *BRCA1*, *BRCA2*, *PALB2*, and *CDKN2A* are among the growing list of genes that have been implicated in PDAC. Mutations leading to deficiency in homologous recombination repair, including *BRCA1*, *BRCA2*, and *PALB2*, are common.[5] Notably, studies show that *BRCA* mutations confer a prognostic benefit.[2] The median overall survival (OS) for patients with a *BRCA1* or *BRCA2* mutation is 14 months compared with approximately 9 months across all patients with PDAC.[6–8] Patients with homologous recombination deficiencies, whose treatment regimens included platinum-based therapies such as oxaliplatin and cisplatin, have demonstrated significant improvements in OS compared with those whose regimens did not (23.8 vs 8.3 months).[9] PARP inhibitors, directed at tumors with germline mutations, have also shown increasing success in treating PDAC.[10,11] These agents are typically used in patients with *BRCA* mutations during the maintenance period following platinum-based therapy.[5,12] These advances have prompted deeper exploration into the molecular genetics of PDAC as a gateway to new therapeutic options.[8] More recently, immunotherapy has shown promise in treating *BRCA*-mutant PDAC as well, but more data are needed.[13]

Contrary to popular belief, clinical factors such as family history of cancer and young age of onset are not reliable predictors of which patients may carry a pathologic germline mutation.[3] Misconceptions surrounding which populations are more likely to have abnormal genetic testing results have been a barrier to both referral to genetic counselor on the provider's behalf and attendance on the patient's part.[14] The literature shows typical rates of genetic testing of patients with PDAC to be quite low; a large study looking at the years 2015 through 2017 found that 32% were referred, and only 19% completed testing.[15] It is worth noting that studies have identified individual-level barriers, which include the perceived cost of genetic testing, misconceptions about the testing process, fear of genetic discrimination, and distrust of the medical system.[16] Furthermore, patients might not always understand the need or benefit of genetic testing. At an institutional level, other barriers,

such as the shortage of genetic counselors, contribute to a prolonged wait time for an appointment, underreferral, and underutilization of genetics services.[17]

On November 8, 2018, NCCN released an update to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Pancreatic Adenocarcinoma stating that all patients with PDAC should receive germline genetic testing regardless of family history.[18] This contrasts with previous guidelines recommending germline testing only for those patients who had a personal or family history of cancer meeting specific criteria.

At University of California, Irvine (UCI), a hereditary cancer clinic (HCC) was implemented in June 2020. The approach of the HCC was multifaceted, with the primary goal to provide a conduit of communication between oncologists and genetic counselors, thereby standardizing the process of referral to their services. UCI's HCC expands on an interdisciplinary approach to testing known as the tandem model[19] (Figure 1). The goal was to increase patient testing by developing standardized protocols for sample collection, genetic testing, and review of results. Prior to being seen at the HCC, charts are sorted based on patient need. At the HCC, the medical oncologist provides initial genetic counseling (GC) to patients based on their family history and presenting cancer. This involves reviewing patients' cancer risk, implications for their relatives, guidelines for testing, and benefits of germline sequencing. Additionally, during this session patients are consented and samples are collected, thereby decreasing the time between the decision to test and subsequent execution. Lastly, results are discussed with the patients, and further counseling regarding need for preventive care or testing for their family is provided when appropriate.

We hypothesized that patients with PDAC were more likely to be referred to a genetic counselor after the change to the NCCN Guidelines regardless of presumed predictive factors, such as personal or family history of relevant cancer, and that this compliance would be further improved following the implementation of the HCC.

Methods

We conducted a single-institution retrospective analysis of patients diagnosed with PDAC from June 2017 through December 2021. Using the retrospective data provided by UCI's cancer registry, 335 patients were identified with a diagnosis of PDAC and having at least one visit with a medical or surgical oncologist in the outpatient setting. Patients who had received only an inpatient consultation were excluded. Patients were divided into time periods based on their date of pathologic diagnosis.

We reviewed the electronic medical records and documented demographic characteristics, including age at presentation, ethnicity/race, family history of any cancer, family history of *BRCA*-related cancers (breast, ovarian, PDAC, and prostate) in first-degree and second-degree relatives, prior personal history of cancer, and referral to GC. Further information on attendance of a counseling session by any health care provider and completion of actual testing was also obtained. Cases in which patients were directly tested by their cancer care provider were included regardless of whether they ultimately saw a licensed genetic counselor. For those who underwent genetic testing, results were noted if available. We

compared rates of genetic referral among patients based on their diagnostic eras, which we determined to be the 18-month period prior to the November 2018 NCCN Guideline change recommending referral to GC for all patients with PDAC (pre-NCCN era: June 2017 through November 2018), 14 months following this guideline change (post-NCCN era: December 2018 through January 2020), or 18 months after the creation of an HCC (HCC era: June 2020 through December 2021).

We used descriptive statistics to analyze the characteristics of these patients. Statistical tests were conducted using a 2-sided Fisher exact test and chi-square test, whichever was appropriate, to compare 2 groups in each of categorical variables using SAS 9.4 (SAS Institute Inc.). This retrospective study was approved by the UCI Institutional Review Board.

Results

Patient Characteristics

We identified 335 patients diagnosed with PDAC at a large academic cancer center. Of these individuals, 123 were diagnosed in the pre-NCCN era, 109 in the post-NCCN era, and 103 in the HCC era. Patient demographics were similar across all 3 time periods (Table 1). The median age at diagnosis for the entire cohort was 69 years. Among those found to have a deleterious germline mutation, the median age at diagnosis was 64 years. Data pertaining to the clinical stage at diagnosis were also obtained. Patients were categorized as either nonmetastatic (resectable, borderline resectable, or locally advanced) or metastatic at presentation. In the pre-NCCN era, 42% of patients had metastatic disease at diagnosis compared with 40.2% in the post-NCCN era. In the HCC era, 29% had evidence of metastasis at presentation (P=.121). In the pre-NCCN, post-NCCN, and HCC eras, respectively, 66.7%, 66.1%, and 78.1% were seen at least once by medical oncology (P=.108) rather than by surgery alone. Of all patients whose genetic testing results were known, 9 (15%) had a mutation in the DNA damage repair pathway (*ATM* or *BRCA1/2*), 2 (3%) possessed hereditary Lynch syndrome mutations (*MLH1*, *MSH2*, *MSH8*, or *PMS2*), and 5 (8%) had “other” known mutations.

Referral Patterns

Overall, 54% of patients were referred to GC, 67% of which attended their initial consultation. Of these, 88% had germline testing and 21% had a deleterious mutation related to PDAC. Of mutation-positive patients in the pre-NCCN and post-NCCN eras, 100% had a known family history of cancer compared with 86% in the HCC era (P= 1.00). There was no significant difference in referral rates among those seen by medical versus surgical oncology (52.5% vs 59.5% referred, respectively; P=.408).

When analyzed in relation to the transition point of the NCCN Guidelines in 2018 (Table 2), data showed that 30% were referred to GC prior to this point, whereas 54.7% were referred to GC in the 14-month post-NCCN era. After implementation of the HCC, 77.4% were referred to GC. The P value comparing all 3 proportions was <.0001, showing that there was a statistically significant increase in the proportion of patients referred following the NCCN changes. The odds of being referred to GC were 2.816 times higher in the

post-NCCN era compared with the earlier pre-NCCN era (95% CI, 1.34–5.66; P <.0001). Moreover, the odds of referral following the HCC intervention were 2.835 times higher than the post-NCCN era (95% CI, 1.406–5.839; P <.0001). Of referred patients in the pre-NCCN, post-NCCN, and HCC eras, attendance rates were 83.3%, 96.3%, and 74.1% (P=.04), respectively.

A similar proportion of those who attended counseling in the pre-NCCN, post-NCCN, and HCC eras proceeded with genetic sequencing (100%, 91.7%, and 92.9%, respectively; P=.841). A decreasing proportion of patients tested were found to possess a deleterious germline mutation related to PDAC; these were 33.3%, 27.3%, and 15.8% in the pre-NCCN, post-NCCN, and HCC eras, respectively. However, this difference was not statistically significant (P=.382).

Referral patterns were also assessed according to each patient's family history. Of 124 patients referred, 93 had a family history of cancer (75%). In the pre-NCCN era, the odds of referral to GC in patients with a positive family history of cancer compared with no family history was 11.90 (95% CI, 3.00–80.14). The odds of being referred based on family history progressively decreased in the eras following the NCCN changes; in the post-NCCN era, the odds ratio (OR) was 3.39 (95% CI, 1.13–10.76), whereas in the HCC era the OR was 3.11 (95% CI, 0.95–10.16), though not statistically significant.

Data on prior personal history of cancer were also collected. Of 124 patients referred, 23% had a personal history of cancer other than PDAC. For these individuals, the OR for referral decreased from the pre-NCCN era (OR, 2.88; 95% CI, 0.86–9.69) to the HCC era (OR, 2.60; 95% CI, 0.64–17.59); however, this was not statistically significant. Focusing on the patients with a family history of *BRCA*-related cancer (PDAC, breast, ovarian, or prostate), the odds of referral in the pre-NCCN era were 6.324 (95% CI, 1.24–47.21) compared with 2.67 (95% CI, 0.83–9.73) in the post-NCCN era and 3.77 (95% CI, 1.08–17.74) in the HCC era.

When assessing GC referral patterns after implementation of the HCC, data showed a significant increase in referrals (40.9% before HCC vs 77.4% after; P<.0001; Table 3).

Survival

Survival analysis showed no difference in OS of patients in the pre-NCCN, post-NCCN, and HCC eras. One-year survival rates were 69%, 79%, and 73%, respectively (P=.14; Figure 2). The probability of dying was 1.33 times higher in the pre-NCCN era compared with post–guideline changes (95% CI, 0.97–1.82; P=.08; data not shown).

Discussion

Recent advancements in molecular sequencing have provided prognostic information about disease biology and led to meaningful opportunities for targeted therapy across a wide variety of cancers. Actionable data on hereditary cancer syndromes associated with PDAC, however, are still desperately needed. Following the 2018 NCCN recommendations for germline testing of all patients with PDAC, there was a marked increase in the proportion of patients referred to GC at our tertiary academic medical center (30.0% vs 54.7% and

77.4% for the pre-NCCN vs post-NCCN and HCC eras, respectively; $P<.0001$), indicating compliance with guidelines. A lesser proportion of patients attended their GC appointments during the HCC era (74.1%) compared with the prior time periods (83.3% pre-NCCN and 96.3% post-NCCN). Given the overlap between the HCC era and COVID-19 pandemic, this significant difference is likely attributable to the patients' ability to mail in their DNA samples without having to "attend" in-person appointments as in prior eras. In the HCC era, approximately 3 of every 4 patients with PDAC received a GC referral. This begs the question of what barriers to physician referral exist and what steps can be taken to facilitate easier access to GC.

Significant barriers to genetic testing have frequently been described in the literature, with many related to the current national shortage of genetic counselors. The National Society of Genetic Counselors recently conducted a study assessing such barriers.[20] Long wait times were cited as an important deterrent to referring patients despite clear clinical indications to do so. Data on national average wait times for initial GC consultations are lacking. At UCI, there was an average wait time of 74 days, with results taking up to 5 weeks to report. A total of 36% of patients presented with metastatic disease, which is consistent with national statistics. This implies that there is a limited window of opportunity for a patient to undergo testing before potentially passing away. Health care providers, regardless of specialty, should therefore start the process of referral to GC early to maximize the patient's opportunity for testing. In our study, the percentage of patients seen at least once by medical oncology in consecutive eras was 66.7%, 66.1%, and 78.1%, with the remaining significant proportion seen by surgery alone. This indicates that many patients are diagnosed with PDAC by non-oncologists. This illustrates the importance of empowering all members of the medical team, including surgeons and gastroenterologists, to refer patients to GC or perform the testing themselves.

Since the NCCN Guidelines changes, multiple institutions have modified their modes of referral from the traditional model to a tandem or triage approach.[19] In 2 recent studies trialing in-clinic testing by non-GC providers, germline testing substantially increased (3.5-fold to 6.5-fold) following intervention when compared with the traditional model.[15,21] Another study highlighted that rates of GC at their institution were steadily increasing every year from June 2019 through June 2021 without the implementation of an automated referral system, yet it remained suboptimal at 61%.[22]

In 2019, faced with the nationwide scarcity of genetic counselors and increased need for GC, our institution implemented an HCC. In this model, a medical oncologist acts as a coordinator between the different teams involved in patient care. Notably, at the HCC, the medical oncologist who treats most patients with PDAC can provide genetic counseling and testing to patients. In doing so, the wait time for genetic testing is significantly reduced because consenting patients are tested in their initial diagnostic appointments. This may also address the barrier of high cost to the patient. Recent data have shown that models requiring genetic counselor input prior to testing create barriers specifically for low-income populations.[23] Bypassing the need for clinician referral has been shown to increase uptake and improve time to testing.[24] Implementation of the HCC increased rates of genetic testing

significantly (Table 3). These data provide a quantitative measure of success in actively implementing important changes to NCCN Guidelines.

Although predominantly only patients with a personal or family history were being referred prior to the guideline changes, this factor became less important in subsequent eras. Based on emerging data showing family history to be a poor predictor of which patients possess a deleterious mutation, it is crucial to consider any patient with PDAC to be a candidate for germline testing.[3]

In a recent prospective, multisite study evaluating the prevalence of pathologic germline variants in patients with PDAC, 15.2% were found to possess a deleterious mutation.[25] This value was significantly lower than that found among the patients in our pre-NCCN and post-NCCN eras, in which 33% and 27% were found to be mutation-positive, respectively. This is likely because the patients being referred in earlier eras were a highly selected population that was more likely to have a positive personal or family history of cancer. Prevalence progressively decreased in consecutive time periods as testing was expanded, eventually resulting in a proportion (16%) closer to the expected rate of approximately 15%.

Although patients possessing a *BRCA* mutation have been shown to respond better to treatments such as PARP inhibitors and platinum agents, our median OS did not improve despite identifying more *BRCA* mutations.[26] This is consistent with the findings of the POLO trial, which demonstrated a better progression-free survival but not OS in patients with hereditary PDAC receiving the PARP inhibitor olaparib.[27] Across all eras, patients presenting with deleterious germline mutations had a younger median age at the time of diagnosis than the general cohort (64 vs 69 years). Importantly, young age at presentation is a positive prognostic indicator for PDAC. A 2020 study found that the 5-year survival of patients with PDAC aged 20 to 40 years was nearly 3 times that of those aged >40 years.[28] A recent retrospective chart review of 133 patients found that patients with pathologic germline variants in DNA mismatch repair genes had a significantly better OS than those without.[29] Most notably, demographics, including patient age, were similar in both groups. This supports a biologically based survival benefit, such as less aggressive tumor characteristics.[2] Furthermore, it is well established that patients with a homologous recombination repair gene mutation have improved survival compared with those without when treated with first-line platinum chemotherapy. Therefore, prompt genetic testing and identification of patients with such mutations helps maximize survival.[9,22,30] These findings warrant concerted efforts to identify patients with germline mutations because their tumor's unique biologic profile may significantly alter their disease course.

One limitation of this study is the lack of data available on patient compliance following their referral to GC. Patients often switched oncology providers or were lost to follow-up. This resulted in a significant proportion of patients with unknown data. Potential confounding factors included differences in insurance coverage for testing across eras. Additionally, costs of genetic testing have generally decreased in recent years.[31] Although data on changes in insurance coverage and the price of genetic testing across our specified time periods are lacking, it is important to consider these factors as potential confounders in this study. Other factors to consider include that patients and physicians at this large

academic cancer center may be better informed about the potential therapeutic implications of discovering deleterious mutations; they may therefore be more willing to use these services than the average institution. Additionally, data on the prevalence of deleterious mutations were limited by a small sample size of germline-tested patients, especially in the earlier eras when testing rates were low. Lastly, in later eras, patients tended to have panels of genes tested rather than individual genes.

Conclusions

The 2018 changes to the NCCN Guidelines recommending germline testing for all patients with PDAC significantly increased GC referral rates at this academic medical center. The implementation of an HCC further boosted compliance with guidelines.

Funding:

This publication was supported by the Chao Family Comprehensive Cancer Center Biostatistics Shared Resource, supported by the National Cancer Institute of the National Institutes of Health under award number P30CA062203.

References

1. Grover S, Syngal S. Hereditary pancreatic cancer. Gastroenterology 2010; 139:1076–1080.e2. [PubMed: 20727885]
2. Goldstein JB, Zhao L, Wang X, et al. Germline DNA sequencing reveals novel mutations predictive of overall survival in a cohort of patients with pancreatic cancer. Clin Cancer Res 2020;26:1385–1394. [PubMed: 31871297]
3. Daly MB, Pal T, AlHilli Z, et al. NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 3.2024. Accessed February 15, 2024. To view the most recent version, visit https://www.nccn.org
4. Tempero MA, Malafa MP, Benson AB III, et al. NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. Version 1.2024. Accessed February 15, 2024. To view the most recent version, visit https://www.nccn.org
5. Petersen JM, Jhala DN. Compliance with the current NCCN Guidelines and its critical role in pancreatic adenocarcinoma. Lab Med 2023;54:e1–9. [PubMed: 35706071]
6. Golan T, Kanji ZS, Epelbaum R, et al. Overall survival and clinical characteristics of pancreatic cancer in BRCA mutation carriers. Br J Cancer 2014;111: 1132–1138. [PubMed: 25072261]
7. Li Q, Feng Z, Miao R, et al. Prognosis and survival analysis of patients with pancreatic cancer: retrospective experience of a single institution. World J Surg Oncol 2022;20:11. [PubMed: 34996486]
8. Pihlak R, Valle JW, McNamara MG. Germline mutations in pancreatic cancer and potential new therapeutic options. Oncotarget 2017;8:73240–73257. [PubMed: 29069866]
9. Pokataev I, Fedyanin M, Polyanskaya E, et al. Efficacy of platinum-based chemotherapy and prognosis of patients with pancreatic cancer with homologous recombination deficiency: comparative analysis of published clinical studies. ESMO Open 2020;5:e000578. [PubMed: 33551067]
10. Golan T, Hammel P, Reni M, et al. Maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer. N Engl J Med 2019;381:317–327. [PubMed: 31157963]
11. de Bono J, Ramanathan RK, Mina L, et al. Phase I, dose-escalation, two-part trial of the PARP inhibitor talazoparib in patients with advanced germline BRCA1/2 mutations and selected sporadic cancers. Cancer Discov 2017;7:620–629. [PubMed: 28242752]
12. Lai E, Ziranu P, Spanu D, et al. BRCA-mutant pancreatic ductal adenocarcinoma. Br J Cancer 2021;125:1321–1332. [PubMed: 34262146]

13. Terrero G, Datta J, Dennison J, et al. Ipilimumab/nivolumab therapy in patients with metastatic pancreatic or biliary cancer with homologous recombination deficiency pathogenic germline variants. JAMA Oncol 2022;8:1–3.
14. Dusic EJ, Theoryn T, Wang C, et al. Barriers, interventions, and recommendations: improving the genetic testing landscape. Front Digit Health 2022;4:961128. [PubMed: 36386046]
15. Walker EJ, Goldberg D, Gordon KM, et al. Implementation of an embedded in-clinic genetic testing station to optimize germline testing for patients with pancreatic adenocarcinoma. Oncologist 2021;26:e1982–1991. [PubMed: 34506673]
16. Guo F, Hirth JM, Fuchs EL, et al. Knowledge, attitudes, willingness to pay, and patient preferences about genetic testing and subsequent risk management for cancer prevention. J Cancer Educ 2022;37:362–369. [PubMed: 32642924]
17. Shindo K, Yu J, Suenaga M, et al. Deleterious germline mutations in patients with apparently sporadic pancreatic adenocarcinoma. J Clin Oncol 2017;35:3382–3390. [PubMed: 28767289]
18. Tempero MA, Malafa MP, Chiorean EG, et al. NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. Version 1.2019. Accessed February 15, 2021. To view the most recent version, visit https://www.nccn.org
19. Cohen SA, Gustafson SL, Marvin ML, et al. Report from the National Society of Genetic Counselors service delivery model task force: a proposal to define models, components, and modes of referral. J Genet Couns 2012;21:645–651. [PubMed: 22566244]
20. Boothe E, Greenberg S, Delaney CL, et al. Genetic counseling service delivery models: a study of genetic counselors' interests, needs, and barriers to implementation. J Genet Couns 2021;30:283–292. [PubMed: 32885542]
21. Ramsey ML, Tomlinson J, Pearlman R, et al. Mainstreaming germline genetic testing for patients with pancreatic cancer increases uptake. Fam Cancer 2023;22:91–97. [PubMed: 35713757]
22. Crowley F, Gandhi S, Rudshteyn M, et al. Adherence to NCCN genetic testing guidelines in pancreatic cancer and impact on treatment. Oncologist 2023;28:486–493. [PubMed: 36933202]
23. Stenehjem DD, Au T, Sainski AM, et al. Impact of a genetic counseling requirement prior to genetic testing. BMC Health Serv Res 2018;18:165. [PubMed: 29514700]
24. Chittenden A, Haraldsdottir S, Ukaegbu C, et al. Implementing systematic genetic counseling and multigene germline testing for individuals with pancreatic cancer. JCO Oncol Pract 2021;17:e236–247. [PubMed: 33439686]
25. Uson PLS Jr, Samadder NJ, Riegert-Johnson D, et al. Clinical impact of pathogenic germline variants in pancreatic cancer: results from a multicenter, prospective, universal genetic testing study. Clin Transl Gastroenterol 2021;12:e00414. [PubMed: 34620795]
26. Martínez-Galán J, Rodriguez I, Caba O. Importance of BRCA mutation for the current treatment of pancreatic cancer beyond maintenance. World J Gastroenterol 2021;27:6515–6521. [PubMed: 34754149]
27. Kindler HL, Hammel P, Reni M, et al. Overall survival results from the POLO trial: a phase III study of active maintenance olaparib versus placebo for germline BRCA-mutated metastatic pancreatic cancer. J Clin Oncol 2022;40:3929–3939. [PubMed: 35834777]
28. Wang H, Liu J, Xia G, et al. Survival of pancreatic cancer patients is negatively correlated with age at diagnosis: a population-based retrospective study. Sci Rep 2020;10:7048. [PubMed: 32341400]
29. Wieme G, Kral J, Rosseel T, et al. Prevalence of germline pathogenic variants in cancer predisposing genes in Czech and Belgian pancreatic cancer patients. Cancers (Basel) 2021;13:4430. [PubMed: 34503238]
30. Park W, Chen J, Chou JF, et al. Genomic methods identify homologous recombination deficiency in pancreas adenocarcinoma and optimize treatment selection. Clin Cancer Res 2020;26:3239–3247. [PubMed: 32444418]
31. Chen Z, Kolor K, Grosse SD, et al. Trends in utilization and costs of BRCA testing among women aged 18–64 years in the United States, 2003–2014. Genet Med 2018;20:428–434. [PubMed: 28933789]

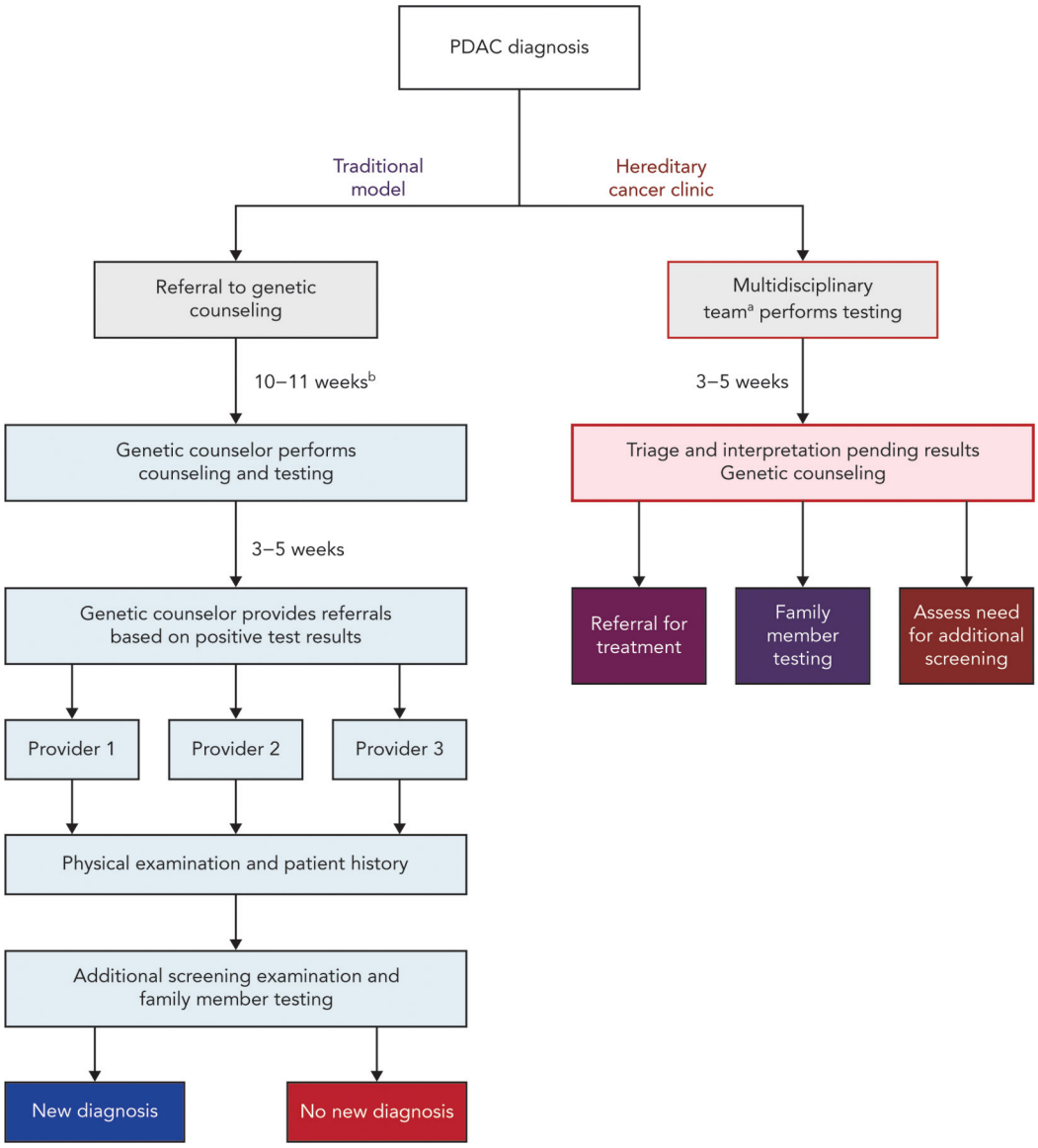


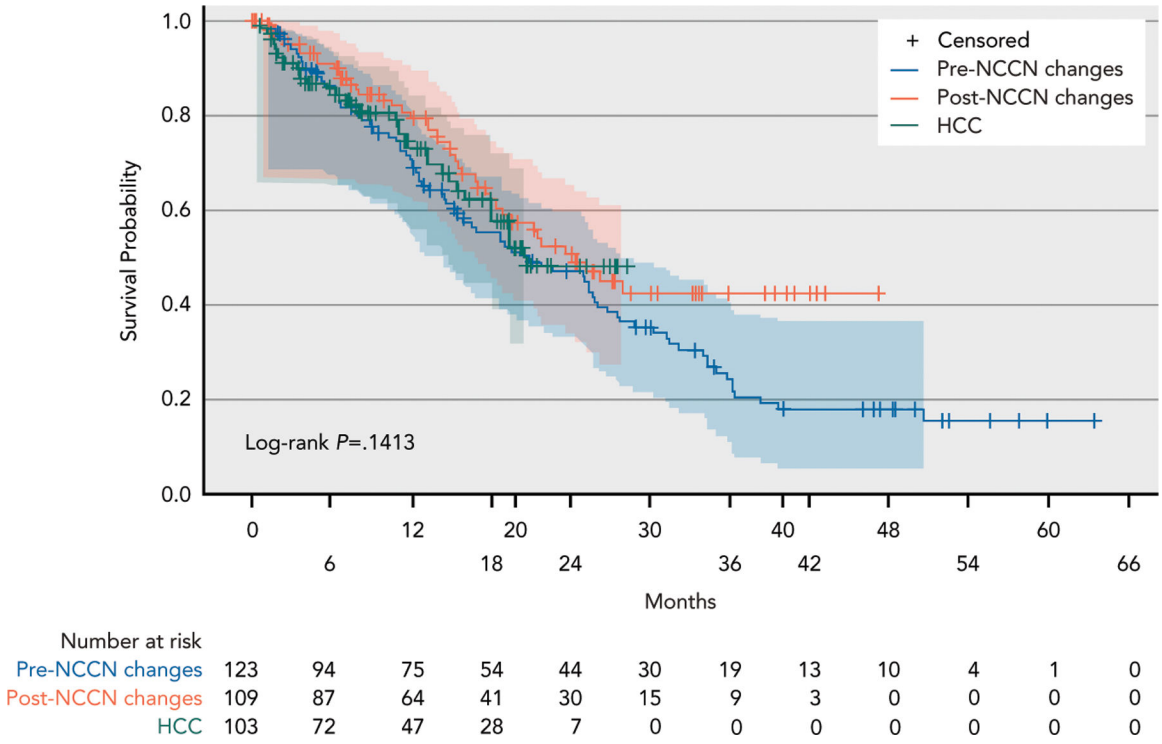
Figure 1.

Genetic testing flowchart showing traditional model versus hereditary cancer clinic model.

Abbreviation: PDAC, pancreatic ductal adenocarcinoma.

[a]Composed of oncologists, surgeons, and genetic counselors.

[b]Average wait time for genetic counseling appointment at the University of California, Irvine from 2019 through 2023.



Number at risk												
Pre-NCCN changes	123	94	75	54	44	30	19	13	10	4	1	0
Post-NCCN changes	109	87	64	41	30	15	9	3	0	0	0	0
HCC	103	72	47	28	7	0	0	0	0	0	0	0

Figure 2.

Kaplan-Meier analysis of overall survival.

Abbreviation: HCC, hereditary cancer clinic.

Table 1.

Patient Demographics

Characteristic	All n (%)	Pre-NCCNa n (%)[a]	Post-NCCNb n (%)[b]	HCC[c] n (%)	P Value
Patients, N	335	123	109	103	
Median age at diagnosis, y	69	68	68	70	.663[d]
Sex					.5553
Male	183 (54.6)	68 (55.3)	63 (57.8)	52 (50.5)	
Female	152 (45.4)	55 (44.7)	46 (42.2)	51 (49.5)	
Race/Ethnicity					.3202
White	198 (59.1)	74 (60.2)	64 (58.7)	60 (60.6)	
Black/African American	8 (2.4)	4 (3.3)	4 (3.7)	0 (0.0)	
Asian	55 (16.4)	20 (16.3)	21 (19.3)	14 (14.1)	
Hispanic	44 (13.1)	17 (13.8)	9 (8.3)	18 (18.2)	
Other[e]	26 (7.8)	8 (6.5)	11 (10.1)	7 (7.1)	
Personal history of cancer					.4756
No	256 (76.4)	96 (83.5)	80 (76.9)	80 (80)	
Yes	63 (18.8)	19 (16.5)	24 (23.1)	20 (20)	
Family history of cancer					.4136
No	109 (32.6)	40 (39.2)	40 (41.2)	29 (32.2)	
Yes	180 (53.7)	62 (60.8)	57 (58.8)	61 (67.8)	
Family history of BRCA cancer					.0001
No	204 (60.9)	89 (89)	60 (69)	55 (63.2)	
Yes	70 (20.9)	11 (11)	27 (31)	32 (36.8)	
Family history of pancreatic cancer					.0081
No	257 (76.7)	98 (98)	83 (95.4)	76 (87.4)	
Yes	17 (5.1)	2 (2)	4 (4.6)	11 (12.6)	
Clinically relevant stage					.1208
Nonmetastatic	184 (54.9)	58 (58)	55 (59.8)	71 (71)	
Metastatic	108 (32.2)	42 (42)	37 (40.2)	29 (29)	

J Natl Compr Canc Netw. Author manuscript; available in PMC 2024 October 09.

Unknowns were excluded for the analysis.

All *P* values of chi-square test except where indicated. The reported *P* values indicate if a statistically significant difference in proportion exists when comparing time periods.

Abbreviation: HCC, hereditary cancer clinic.

[a] Cohort of patients first diagnosed prior to the NCCN Guidelines change.

[b] Cohort of patients first diagnosed following the NCCN Guidelines change.

[c] Patients diagnosed after establishment of the HCC.

[d] *P* value of Fisher exact test.

[e] Other includes Native Hawaiian, American Indian, Alaskan Native, or mixed.

Table 2.

Genetic Counseling Referral Patterns

	All n/N (%)	Pre-NCCN n/N (%)	Post-NCCN n/N (%)	HCC n (%)	P Value
Total, N	**368**	**125**	**140**	**103**	
Referred to genetic counseling	124	24/80 (30.0)	35/64 (54.7)	65/84 (77.4)	<.0001[a]
Attended genetic counseling	84	15/18 (83.3)	26/27 (96.3)	43/58 (74.1)	.0362
Completed testing	74	13/13 (100)	22/24 (91.7)	39/42 (92.9)	.8411
Deleterious mutation–positive	15	3/9 (33.3)	6/22 (27.3)	6/38 (15.8)	.3818

All *P* values of Fisher exact test except where indicated. The reported *P* values indicate if a statistically significant difference in proportion exists when comparing time periods. Unknowns were excluded for the analysis.

Abbreviation: HCC, hereditary cancer clinic.

[a] *P* value of chi-square test.

Table 3.

Genetic Counseling Referral Patterns Era-to-Era Comparison

	Referred to Genetic Counseling					
	Yes		No		Nominal *P* Value	Bonferroni Corrected *P* Value (Significance Level .01)
Pre-NCCN vs post-NCCN	24	35	56	29	.0038	.01
Pre-NCCN vs HCC	24	65	56	19	<.0001	.01
Post-NCCN vs HCC	35	65	29	19	.0035	.01
Pre-NCCN and post-NCCN (combined) vs HCC	59	65	85	19	<.0001	.01
Pre-NCCN vs post-NCCN and HCC (combined)	24	100	56	48	<.0001	.01

Nominal *P* value of chi-square test. After Bonferroni correction method for 5 tests adjusts the multiple comparison value to be *P*<.01 as the significance level. Abbreviation: HCC, hereditary cancer clinic.