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Meet the Experts

Genetic cancer predisposition syndromes among older adults

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ABSTRACT

Earlier age at onset is one characteristic of hereditary cancer syndromes, so most studies of genetic testing have focused on young patients with cancer. However, recent studies of multigene panel tests in unselected cancer populations have detected a considerable proportion of older patients with germline pathogenic variants (PVs) in cancer susceptibility genes. As the number of older patients with cancer continues to rise, clinicians should be aware of genetic/genomic cancer risk assessment (GCRA) criteria in both young and older adults. Identifying individuals with a germline PV in a cancer susceptibility gene may be important for precision therapy of current cancers and screening and prevention of new primary cancers, as well as cascade testing to identify high cancer risks for family members. Typically, hereditary predisposition germline genetic testing has been recommended for patients with early onset cancers and/or a family history of cancer. However, more recently international guidelines recommend testing for potential therapeutic intervention regardless of age for some tumors frequently seen in older patients, such as epithelial ovarian, pancreatic, and metastatic prostate and breast cancers. GCRA in older patients may present challenges including: clonal hematopoiesis (CH) confounding test interpretation, ethical aspects (autonomy, nonmaleficence, beneficence), patient health status, comorbidities, as well as lack of insurance coverage. These factors should be considered during genetic counseling and when considering cancer screening and risk reduction procedures. This manuscript reviews available data on common hereditary cancer syndromes in older patients and provides tools to help providers perform GCRA in this population.

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1. Introduction

Hereditary cancer syndromes are caused by germline mutations (or pathogenic variants - PVs) in a cancer susceptibility gene, leading to an increased risk of developing cancer during an individual's life span. Typical characteristics of hereditary cancer syndromes, which account for around 10% of all cancers, are onset at an early age and multiple affected family members [1]. The most common hereditary cancer syndromes include hereditary breast and ovarian cancer syndrome (HBOC) and Lynch syndrome (LS); however, many rarer yet important to recognize syndromes exist such as polyposis syndromes [1], Li-Fraumeni syndrome, Cowden syndrome, and hereditary diffuse gastric cancer syndrome, among others. Identification of individuals carrying PVs is imperative, as more effective precision therapy may be possible, and risk reduction strategies can be implemented for the patient and their at-risk family members to prevent or detect cancer at an early stage.

Molecular genetic discoveries resulting from the study of syndromic families, rare case presentations, and testing of unselected cancer populations indicate that the spectrum of hereditary cancer syndromes and their penetrance (proportion of individuals carrying a particular genotype who express the disease or phenotype) might vary according to the molecular defect [2–4]. For example, high-penetrance PVs are responsible for most well-known hereditary cancer syndromes (*BRCA1, BRCA2, TP53, PTEN*, Lynch syndrome genes) with relative cancer risk estimates above 5.0, while moderate-penetrance gene variants (in *ATM, CHEK2, BRIP1* and *PALB2*) are less understood and may be unknown to providers, with relative cancer risks generally well under 5.0 [5]. Therefore, not every individual in a hereditary cancer family gets cancer at a young age and it will depend on the type of defect, gene involved as well as other modifiers. This is supported by recent observations of PVs in cancer predisposition genes among women diagnosed with breast cancer after age 60 years which illustrates potential challenges for guideline driven referral for genetic/genomic cancer risk assessment (GCRA) [6,7].

Limited information is available about the burden of hereditary cancers among patients diagnosed at an older age. Environmental factors that modify hereditary cancer risks are also poorly understood [8]. Aging is one of the most important risk factors for cancer, and currently, half of the people with cancer are aged ≥65. Since the population is aging, and more people are living longer, the number of new cancer cases in older individuals is rising. Global life expectancy is currently of 71.6 years, and people aged ≥65 will amount to 1 billion of people by 2030. This will lead to an increase in the number of annual cancer cases diagnosed among older individuals—projected to be approximately 13.7 million by 2035 [9].

The existence of a familial component, including cancers diagnosed at advanced ages, can foreshadow a higher risk of cancers in subsequent generations, and illuminating the fact that genetic risk plays an important part in this process [8]. Thus, it is compelling to understand the role of genomics in older people with cancer. In this review, we examine the role of cancer genomics in older patients, criteria for GCRA, challenges related to interpretation of genetic test results, and ethical aspects of GCRA in older adults. Additionally, we provide recommendations regarding tailoring the implementation of risk-reducing strategies in older patients with hereditary cancer syndromes and highlight the importance of cascade testing to identify at-risk family members and enable precision screening and prevention.

2. Frequency and Spectrum of Pathogenic Variants in Older Adults

Most studies reporting the frequency of PVs have focused on patients that meet traditional GCRA referral criteria, which means predominantly patients with personal and family history of cancer and early age at cancer onset. However, increasingly studies in less selected populations are allowing estimation of the frequency of PVs in older patients (Table 1) [7,10].

3. HBOC Syndromes

About 5–10% of all breast cancer (BC) cases are caused by a PV in a cancer susceptibility gene, with the most frequent being in *BRCA1* or *BRCA2*. Features of HBOC syndromes include early onset of BC, ovarian cancer (OC) at any age, bilateral BC, and male BC, and increased risk for other cancers, such as prostate, pancreas and melanoma [11]. Approximately 6% of older women with BC carry PVs, which is almost double that reported in unselected older women [10,12,7]. In a multicentric study of 10,000 women with BC, *BRCA2* was the most frequently mutated high-risk BC predisposition gene in older carriers (40%), followed by *BRCA1* (29%), and *PALB2* (8.5%). *CHEK2* was the most frequent moderate-risk gene (14%), followed by *ATM* and *NF1* (2.8% each) [7]. Interestingly, the proportion of moderate risk PVs in older women was higher than in their younger counterparts (20 vs. 7%). Moderate-risk PVs have been reported to be enriched among older carriers [13]. For example, a higher frequency of *CHEK2* PVs (9–14%) was found among older Japanese women [7,14]. Additionally, the frequency of high and moderate-risk PVs may vary according to BC subtype; with patients affected by triple-negative breast cancer (TNBC) showing a higher frequency of PVs. Two cohorts found a high frequency of PVs among older women with TNBC, ranging from 13 to 22%, and the most common PVs identified was *BRCA1* [15,16]. Cowden syndrome is caused by germline mutations in *PTEN*; it is considered a high-risk cancer syndrome characterized by the development of hamartomas and carcinomas of the thyroid, breast, endometrium and kidney. In large studies the median age at cancer diagnosis is typically 40 years, however second malignancies can occur late in life [17].

Regarding OC, about a half of women carrying PVs are aged ≥60 [18]. The most common PVs are in *BRCA1* and *BRCA2*, and less frequently mismatch repair genes (MMR), *BRIP1*, *RAD51D*, and *RAD51C* [18,19]. Median age at the time of OC diagnosis seems to be higher among patients with *BRCA2* PVs than among those with PVs in *BRCA1* [20] (59 vs. 52 years). Patients with OC carrying *BRIP1* and *RAD51C* PVs are also older at the time of cancer diagnosis [21] than *BRCA1* and *BRCA2* PV carriers.

Prostatic cancer is also associated with *BRCA2* among the spectrum of genes associated with HBOC syndromes, and 50–60% of patients carrying germline PVs are aged ≥60 [22]. Approximately 12% of patients with metastatic prostatic cancer carry germline PVs, in *BRCA2* (most frequent), *ATM*, *BRCA1*, *CHEK2*, *HOXB13*, *PALB2*, *RAD51D* and *MMR* genes [23]. In patients with localized prostate cancer, rates of germline DNA repair mutations are ~6% in those with high-risk disease [24]. Furthermore, prostate cancer in men with germline *BRCA* mutations has a more aggressive phenotype and there are also possible treatment implications for patients with DNA repair genes. Current guidelines recommend patients with metastatic and high-Gleason grade localized prostatic cancer be considered for genetic testing [25]. Cascade testing of at-risk relatives and cancer screening and prevention leverages germline genetic predisposition information [11].

Finding high-penetrance PVs, such as *BRCA1* or *BRCA2*, might lead to enhanced BC screening or to risk-reducing procedures such as bilateral salpingo-oophorectomy (BSO), which provide survival benefits even among older patients [26,27]. Additionally, the influence of genetic testing on therapeutic decisions should also be considered, patients with *BRCA* PVs and breast, prostate, ovarian, or pancreatic cancer may be candidates for therapy with poly (adenosine diphosphate-ribose) polymerase (PARP) inhibitors [25,28–30].

4. Hereditary Gastrointestinal Cancer Syndromes

Hereditary gastrointestinal cancer syndromes cause 5–10% of all gastrointestinal cancers. The most common is LS, which is caused by germline PVs in DNA MMR genes (*MLH1, MSH2, MSH6, or PMS2*) and, less frequently, familial adenomatous polyposis (FAP) caused by PVs in the APC gene [1]. Although, these syndromes predispose to

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Table 1
Frequency of pathogenic variants in older patients.

Study	Frequency of PVs (%)	Study population	Current General[a] Genetic Testing Criteria [25]
Breast cancer			o BC ≤ 50 y
Chavarri-Guerra et al [7]	5.6	Patients diagnosed with BC ≥65 y	o TNBC ≤60 y
Momozawa et al. [14]	3.2–4.4	Unselected Japanese patients with BC diagnosed ≥60 y	o Two BC primaries o OC OC (any age)
Tung et al [10]	6.4	Patients diagnosed with BC ≥60 y	o Pancreatic cancer (any age)
Kurian et al [77]	7	Women tested clinically for hereditary cancer risk	o High grade or metastatic prostatic cancer
Suszynska et al [78]	12	Meta-analysis (43 studies)	o BC at any age and: • 1 close blood relative with • BC ≤ 50 y; or • Invasive OC; or • Male BC; or • Pancreatic cancer; or • High grade or metastatic prostate cancer • ≥2 close blood relatives with BC at any age • Metastatic BC
Ovarian cancer			
Lilyquistet al [19,18]	13	Women with OC referred to genetic testing	
Norquist et al [20]	15	Patients with OC diagnose (median age 60 y)	
Suszynska et al [78]	21	Meta-analysis (15 studies)	
Colon cancer			CRC or endometrial cancer and any of the following:
Yurgelun et al [38]	10	Unselected patients with CRC (median age at diagnosis 55 y)	o ≤ 50 y o Synchronic or metachronic LS related cancer o ≥1 FDR or SDR with LS related cancer ≤50 ➢ 2 FDR or SDR with LS related cancer any age o CRC with MSI high o CRC or endometrial with MMR deficiency o Confirmed pancreatic adenocarcinoma
Chavarri-Guerra et al [37]	8	Patients diagnosed ≥60 y with CRC.	
Pancreatic cancer			o FDR o SDR with pancreatic adenocarcinoma
Lowery et al [46]	20	Unselected patients with exocrine pancreatic (median age 65 y)	
Shindo et al [48]	4	Patients with pancreatic cancer. (Mean age at diagnosis 65 y)	
Salo-Mullenet al [47]	15	Patients with pancreatic cancer referred fo genetic testing (mean age at diagnosis 63 y)	
Zhenet al [45]	3.5–8	Personal history of pancreatic cancer (with and without family history of pancreatic cancer)	
Dudley et al [79]	18	Patients with exocrine pancreatic cancer (mean age at diagnosis 71.2 y).	
Prostatic cancer			o High or very high-Gleason (≥7) grade prostate cancer
Pritchard et al [23]	12	Patients with metastatic prostatic cancer. (60% were aged ≥60 y at diagnosis)	o Metastatic prostate cancer o Strong family of prostate cancer: brother or father or multiple family members with prostate cancer <60 y or died from prostate cancer
Nicolsoi P, et al [22]	17	Unselected patients with prostate cancer (mean age at diagnosis 60 y)	o Ashkenazi Jewish ancestry o ≥3 cancers on same side family, especially diagnose <50 y

BC: breast cancer; CRC: colorectal cancer; FDR: first degree relative; LS: Lynch syndrome; MMR: mismatch repair; MSI: microsatellite instability; OC: ovarian cancer; SDR: second degree relative; TNBC: Triple negative breast cancer; PVs: pathogenic variants, y: years.
[a] Please see NCCN guideline specifics for a more thorough description of individuals that warrant genetic cancer risk assessment and consideration of testing.

early-onset colorectal cancer (CRC), 30–40% of patients with PVs in MMR genes are identified ≥ age 60 [31,32,33].

Current guidelines recommend universal MMR immunohistochemical or microsatellite instability (MSI) tumor testing in all patients with a personal history of CRC [34]. In tumors deficient in MMR pathway expression, germline genetic testing is recommended. Furthermore, patients with MMR deficiency tumors (either due to a germline defect or somatic mutations) may be candidates for immunotherapy treatment [35,36].

In a community-based high risk screening clinic cohort, we found a considerable frequency of PVs in individuals aged ≥60 years at CRC diagnosis (8%) [37]; The most common PVs were in MMR genes both in younger and older individuals (72 vs 84%) [37]. Another study found that 10% of patients with CRC unselected for high-risk features (early age at diagnosis, personal and family history of cancer) carried PVs (most commonly LS associated genes followed by moderate penetrance genes, and less frequently, in polyposis associated genes) [38].

Most patients with LS are diagnosed with CRC before age 50 [25,40]. However, LS-associated cancers may occur later in life. Cumulative incidence at 75 years for any LS associated cancer varies from 20 to 80% depending on the type of gene mutated. [34] Overwhelmingly, CRC and endometrial cancers are the most common cancers. Most gynecological cancer occur before the age of 60 years [41], however endometrial cancer has been reported in women over 70 years. Regarding other less common LS associated cancers, peak age incidence rates for renal, and brain tumors is 50–69 years, while urothelial, small bowel, gastric, pancreatic and skin cancer can occur after age 70. Age at cancer diagnosis also varies by the gene mutated, e.g. women with *MSH6* PVs present with endometrial cancer at later ages than women with other LS PVs [41,42]. This suggests that cancer risk in LS might be influenced by other factors, including age, and surveillance strategies can be adapted [43].

Individuals with FAP have an earlier CRC onset with an up to 100% lifetime risk in untreated patients by their early forties. In attenuated forms of FAP, CRC is diagnosed later in life with a mean age at diagnosis of 56 years [39]. Moderate penetrance genes (*CHEK2*, monoallelic *MUTYH, POLD1, POLE*) and the APC gene variant p.I1307K are found in approximately 5% of patients with CRC. The age at diagnosis is older when compared to those with LS. However, the data regarding moderate penetrance genes is less robust and the genes involved and cancer spectrum for some of the gene variants remains poorly understood [38].

Another gastrointestinal tumor associated with germline PVs is pancreatic adenocarcinoma (termed pancreatic cancer from here on), which has a mean age at diagnosis of 70 years. It has been estimated

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that 7–10% of individuals with pancreatic cancer carry a hereditary predisposition PV [44,45]. Patients with pathogenic germline alterations tend to be younger than those with sporadic cancer (60 vs 66 years) [44]. However, about 40% of them will have pancreatic cancer after the age of 60 [46]. In fact, age at diagnosis for those carrying a *BRCA2* mutation were equivalent to non-carrier individuals [47]. The most frequent PVs in pancreatic adenocarcinoma are in *BRCA2*, followed by *ATM*, *CDKN2A*, *PALB2*, *MLH1*, *BRCA1,* and *TP53* [48] [49].

Gastric cancer is an infrequent component of several inherited cancer predisposing syndromes, including LS, FAP, and hereditary diffuse gastric cancer (HDGC). HDGC is a rare, autosomal dominant inherited form of gastric cancer caused by germline *CDH1* mutations and cause early onset of diffuse gastric cancer and breast cancer [50]. Mean age at gastric cancer diagnosis is 40 years and relative risk reduces after 50 years of age. However, after 60 to 80 years the relative risk (RR) is still very high (RR 35) for those that have not yet presented with disease; for breast cancer the RR after 50 years is >7 [51].

5. Who Should Have GCRA and Genetic Testing?

Conditions for recommending genetic testing are shown in Table 2. However, patients who do not clearly qualify for testing by traditional criteria might have a significant rate of PVs [52,53]. Additionally, early age of onset and family history are not a requirement for genetic testing among patients with breast, ovarian, pancreatic and prostatic cancer: in part because they may benefit from treatment with recently approved targeted agents. Thus, the use of germline hereditary cancer predisposition genetic testing in older patients may be expanding.

6. Participation of Older Adults in Genetic Testing

Although older adults are underrepresented in genetic testing studies, they have a high willingness to participate. A survey looking at willingness to have genetic testing in women with personal history of breast cancer (mean age at diagnosis 62 years) reported that 60% wanted testing and 30% already had a testing [54]. Another study looking at apolipoprotein E genotype for Alzheimer's disease reported 88% of patients aged ≥65 agreed to participate, with 78% also providing samples for DNA banking. The main reasons for refusing participation were confidentiality concerns, lack of perceived benefits, and feeling uncomfortable [55]. Older adults frequently favor disclosing their genetic results, especially when the health benefit to their relatives is considered.

Inconsistent and complex health insurance coverage policies may limit genetic testing patient participation. For example, Medicare (a common form of health insurance coverage in the United States for older adults) does not routinely cover genetic testing for individuals without personal history of cancer. Coverage is provided only under special circumstances including *BRCA* mutation in a close relative, at least two close blood relatives with a *BRCA*-related cancer or Ashkenazi Jewish ancestry and at least on close blood relative with a *BRCA*-related cancer [56].

7. Genetic Testing Interpretation Challenges

Cancer predisposition germline genetic testing may be performed on either saliva or blood samples, which are considered representative of germline status. However, PVs related to clonal hematopoiesis (CH), which is the clonal expansion of abnormal white blood cells in an individual [57] is common in older adults and increases with age and cytotoxic therapy exposure [58]. Between 9.5 and 18.0% of healthy people aged ≥70 have significant CH, compared to <2% among younger adults [57,59]. CH is associated with the risk for developing leukemia and atherosclerosis, as well as cancer progression and decreased overall survival [59,58].

Importantly, CH can confound genetic testing. In a large commercial laboratory data set of >100,000 tests, 72 of 353 *TP53* cases manifested abnormal next-generation sequencing metrics (e.g., variant allele fraction <30% or abnormal copy number variation metrics) [60]. Of these, most (91.7%) were identified through multi-gene panel testing and did not meet Li-Fraumeni syndrome by phenotypic criteria [61]. Non-germline origins of the PVs were identified for 91% of cases with ancillary material. Some of these were due to overt hematologic neoplasia, but most were likely age-related [60]. Thus, if a *TP53* variant is identified in an older adult, caution must be taken given the high potential for somatic interference due to CH, rather than Li-Fraumeni syndrome. As such, DNA testing of an alternative tissue, such as skin, or cascade testing of family members is often required as part of a comprehensive diagnostic workup.

Among genes typically analyzed as part of GCRA, *TP53*, *ATM*, and *CHEK2* are the ones most often involved in CH [62]. Among those with no reported history of cancer in a large high-risk screening clinic cohort who carried a likely somatic variant, 54.2% carried a variant in one of these three genes. The presence of these variants was associated with increasing age (OR 3.1) and personal history of cancer (OR 3.3) [62]. Their presence was most notable in older individuals with OC (almost 2% of individuals over age 71), likely due to older age at OC diagnosis and prior cytotoxic treatments. The substantial rate of these variants in patients with OC was consistent with previous studies showing an association of CH in OC patients [63].

8. Ethical Considerations

Informed consent is an important aspect of any genetic test due to the sensitive nature of genetic data. Ethical principles (autonomy, nonmaleficence, beneficence) are especially relevant in older adults, making counseling before and after testing essential [64]. For instance, decision-making capacity (autonomy) may be impacted by cognitive impairment, which is more common among older adults. Even among cognitively normal populations, patient understanding of genetic information varies according to educational and cultural background, health literacy, and language. Therefore, informed consent procedures should address these factors by simplifying the amount and type of information, using visual aids, and engaging family members in the process. In cases where decision-making is impaired, legally-designated relatives may make decisions on the patient's behalf in accordance with his/her previously expressed wishes [64].

Approximately a quarter of older patients with cancer have adjustment disorder, anxiety and/or depression [65], and involvement of mental health professionals during disclosure of results might be appropriate in selected cases. In these cases, the principle of non-maleficence (to do no harm) may need to be considered prior to genetic testing, since mood disorders may be worsened by disclosure of results [65].

In older patients with limited life expectancy (due to comorbidities or terminal illness), genetic testing may not inform therapy, particularly in cases with moderate risk PVs. However, the principle of beneficence (for the benefit of others) also needs to be taken into consideration, since even though testing may not benefit the patient, it may benefit their family members. If genetic testing is desired by a severely ill patient, a family delegate may be assigned to receive test results in the case of the patient's demise. DNA baking may also be considered for future update germline genetic testing, [66] as testing platforms also may improve over time [67].

Table 2
Conditions for recommending genetic testing [80].

1. Individual has a personal and/or family history suggestive of a hereditary cancer syndrome
2. Test results can be adequately interpreted
3. Results will influence the medical or therapeutic management of the individual or his/her family members
4. Testing is preceded by informed consent.

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9. Integrating Risk-Reducing Recommendations into the Care of Older Adults

Evidence for risk-reducing recommendations are based on cumulative cancer incidence, which has been calculated up to 80 years. The benefits of enhanced surveillance and risk-reducing strategies for older patients remains largely unknown. A potentially useful strategy to determine the benefit of these interventions is the estimation of life expectancy, which can be obtained using validated tools such as the Lee, Suemoto or Schonberg indices (available online at Eprognosis.org).

When considering risk-reducing surgeries, such as hysterectomy in LS or BSO in HBOC syndromes, it is helpful to balance age-adjusted cancer risk with predicted clinical benefits and life expectancy. For example, the risk of endometrial cancer in some types of LS is approximately 1% per year; therefore, in a patient with a predicted life expectancy of 10 years, the cumulative risk of endometrial cancer during the remaining life-span would be about 10% [68,69]. Despite a modest numerical risk for ovarian cancer, the lack of efficacious screening tools and overwhelming mortality should prompt consideration of risk reduction surgery at any age where treatment of the respective malignancy would be contemplated. A good resource for age-adjusted cancer risks in PV carriers can be found online at https://ask2me.org/ [70]. Fig. 1 shows cancer risk estimates for adults aged 60–85 for selected PVs and tumors.

Surgery has an increased risk of morbidity and mortality among older patients (up to 28% and 2.3%, respectively [71]). This partially depends on the patient's functional status and type of surgery, and thus conducting a geriatric assessment (GA) along with a thorough preoperative evaluation could improve patient selection for risk-reducing surgery. Patients can be screened using simple tools (such as the G8 geriatric screening tool), followed by a full GA, which can lead to the identification psychosocial and functional problems not detected during routine assessments [72]. This strategy may lead to the identification of frail patients with increased risk of surgical morbidity and mortality [73].

Patient preferences should always be considered in the management of their own cancer risk. For instance, potential strategies for reducing the risk of endometrial and OC in LS include routine endometrial biopsy, transvaginal ultrasound, and CA125 testing, or prophylactic hysterectomy with BSO [25], with each option having different risks and benefits. A study evaluating preferences in this setting found that family history of cancer and patient age influenced decision-making, with older patients being more likely to choose surgery [74]. For HBOC, the options for reducing BC risk might include enhanced surveillance with

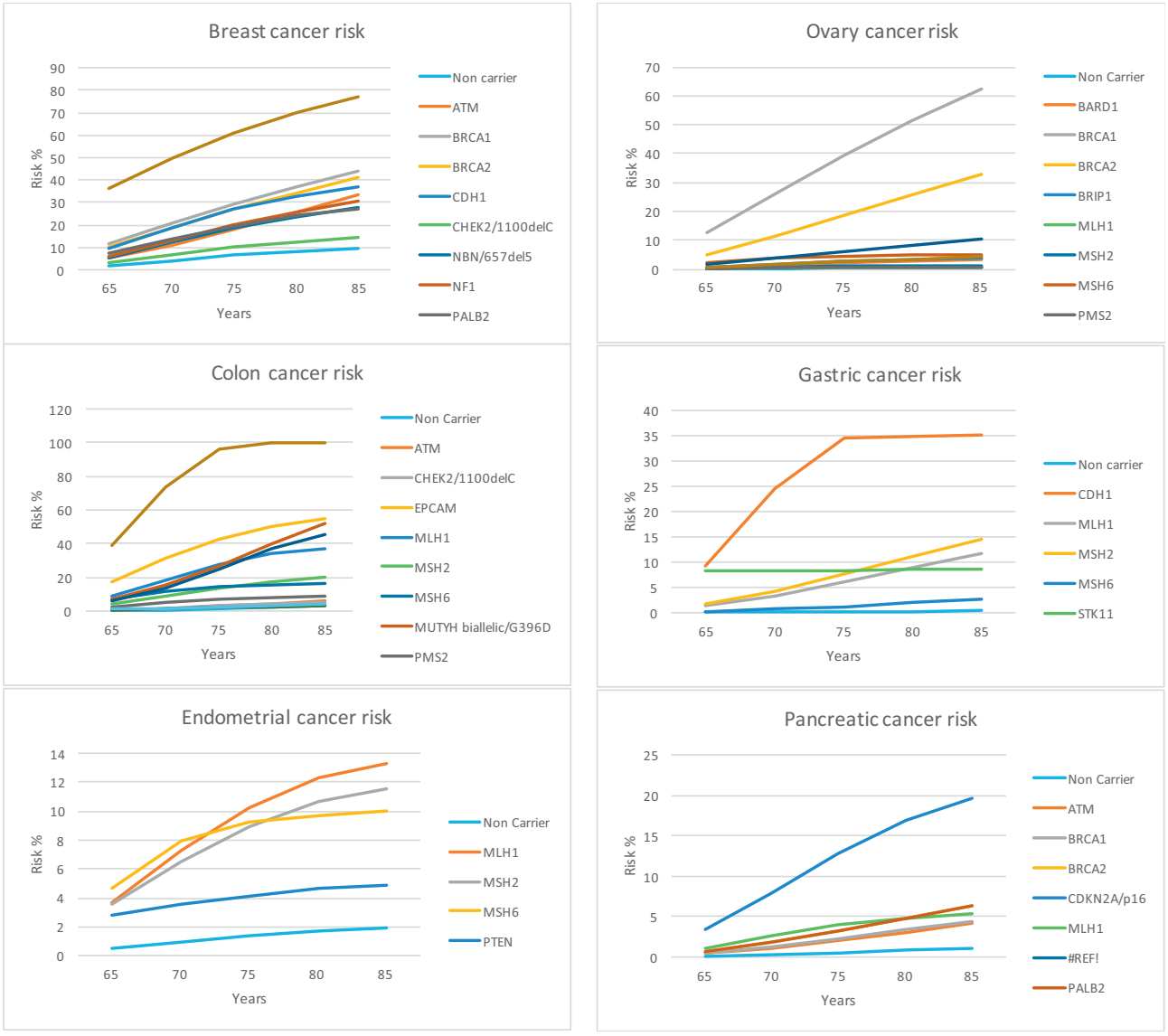


Fig. 1. Cancer Risk estimates for a 60-year adult up to age 85. Data from ask2me calculator [70].

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annual mammogram and breast MRI, or bilateral prophylactic mastectomy [25]. However, the benefit of mastectomy decreases with age (due to the lower age-adjusted residual lifetime cancer risk) and recommending continued surveillance to older women [75] is an acceptable, and often preferable, alternative. Online decision-making tools for women with *BRCA* PVs can help decision making by providing an estimate of the age-adjusted cancer risk, as well as the effect of risk-reducing procedures on survival [76].

10. Conclusions

A considerable number of older patients with cancer may carry a cancer predisposition gene. HBOC syndrome occurs in 6% of older women with BC, and a significant proportion of older patients with OC carry PVs. *BRCA2* and *CHEK2* are the most frequent PVs in older patients with BC, while *BRCA1* and *BRCA2* are more frequently found in older patients with OC. Similarly, approximately 8% of older patients with CRC carry PVs in hereditary cancer genes, with MMR genes being the most frequent. Additionally, many non-CRC LS-related cancers may be diagnosed at older ages.

When genetic testing is recommended for an older patient, it is important to be aware of potentially confounding factors such as CH. In those cases, allele fraction should be taken into account before considering a germline PV, which normally is reported with an allele fraction above 30%. In certain cases, DNA testing of an alternative tissue, such as skin, may be required.

Once an older patient is diagnosed with a hereditary cancer predisposition PV, it is important to consider comorbidities and life expectancy, age-adjusted cancer risks, screening and procedural risks and benefits, and patient preferences. Several tools can help guide decision-making, including life expectancy and genetic risk calculators, and geriatric assessment tools.

Although the role of genetic testing in older adults needs further study, clinicians should refrain from using chronologic age alone to exclude patients from GCRA and be aware of specific challenges when genetic testing is considered in an older adult.

Author Contributions

Study concept and design: Y.C.G., J.N.W.
Data acquisition: Y.C.G. T.P.S., O.L.L.
Data analysis and interpretation: All authors.
Manuscript preparation, editing, and review: All authors.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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