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Evaluation of a Telehealth Service to Support the Uptake of Breast Cancer Prevention Medications: A Process Evaluation

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Master of Philosophy – MDHS (Medicine)

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Faculty of Medicine, Dentistry and Health Sciences

The University of Melbourne

The Sir Peter MacCallum Department of Oncology

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Master of Philosophy

Abstract

Background

Despite evidence that risk-reducing medications (RRMeds) can reduce the incidence of estrogen receptor-positive breast cancer by up to 50%, uptake in routine care remains low. In Australia, barriers include limited awareness among women and clinicians, concerns regarding adverse effects, and low clinician confidence in discussing and prescribing these medications in primary care. Conversely, access to specialist support and clear prescribing guidance have been identified as key facilitators of RRMed use. To address this evidence–implementation gap, the Preventing Cancer with Medications (PCMed) Telehealth Service was implemented to support informed decision-making and appropriate RRMed use among women at increased risk of breast cancer.

Methods

This mixed-methods evaluation of the PCMed Service was conducted, informed by the Knowledge to Action Framework. The evaluation examined baseline RRMed use prior to service implementation, RRMed uptake among women attending the service, feasibility of the service in routine clinical practice, fidelity to the planned PCMed intervention, and implementation challenges and adaptations. Baseline RRMed use was assessed through a retrospective chart review of 100 eligible women attending specialised clinics before service implementation. RRMed uptake was assessed among 37 women attending the PCMed Service without contraindications to RRMed use. Feasibility and fidelity were evaluated using prospectively collected service-delivery data from 73 participants over an 18-month period. A record of implementation challenges, adaptations, and reflections was maintained throughout the study period.

Results

Prior to implementation, documented discussion of RRMeds was uncommon (4%), and prescribing within 12 months was rare (1%). Among women attending the PCMed Service without contraindications, 20 of 37 (54.1%) commenced a RRMed within 6 months. Fidelity to the planned service model was high, with video-based telehealth used for 92.8% of consultations and 93.1% of participants reaching a decision regarding RRMed uptake within two consultations. Attendance at planned follow-up appointments was high (93.1%), while the need for additional unplanned consultations was low (n=9), supporting service feasibility. Implementation adaptations included greater use of participant self-completed risk

assessments to reduce clinician workload, and modified discharge processes that allowed women commencing a RRMed to remain linked with the PCMed Service for re-entry if required.

Conclusion

RRMed uptake among service attendees was high, fidelity to the planned intervention was maintained, and only minor adaptations to service delivery were necessary, supporting PCMed as a practical strategy for addressing the evidence–implementation gap in primary breast cancer prevention.

Declaration

This is to certify that:

a) The thesis comprises only my original work towards the Master of Philosophy – MDHS (Medicine), except where indicated in the Preface;
b) Due acknowledgement has been made in the text to all other material used;
c) The thesis is no longer than the maximum word limit in length, exclusive of tables, bibliographies, and appendices.

Katrina West RN, Grad Dip, MN (Nurse Pract)

Preface

This thesis incorporates material from the following peer-reviewed publication:

West KL, Spelman T, Cui W, Latham S, Deij S, Minck S, Mason S, Saunders C, Poliness C, James PA, Wheeler G, Keogh L, Best S, Phillips KA. Evaluation of a Telehealth Service to Support Breast Cancer Prevention Medication Uptake: A Protocol of a Mixed Methods Study. BMJ Open. 2025;15(6):e098198. Published 18 June 2025.

Candidate Contribution

As first author, I led the writing of this publication, contributing an estimated 75% overall. I produced all drafts, coordinated and responded to co-author feedback and peer reviewer comments, and prepared the final manuscript for submission. I co-designed the study with Kelly Anne Phillips and Stephanie Best, and contributed to the development of the study protocol, including the specification of objectives and the data collection and analysis plans, under the guidance of the supervisory team. I also collaborated with Tim Spelman on the statistical design and analysis plan.

The components I regard as my sole or primary work are the literature review, drafting of the manuscript, coordination of manuscript revisions, responding to peer reviewers, and preparation of the final submitted manuscript. My primary contributions also included development of the study protocol and contribution to the study design, objectives, data collection and analysis plans.

Incorporation of Publication Material

The published protocol is presented in Chapter 2. Selected material from this publication has also been incorporated or adapted for inclusion elsewhere in this thesis as detailed below.

Thesis location	Material Incorporated	Nature of use
Chapter 1, Section 1.1.1 Table 1.1, pages 17-18.	The primary aim and secondary aims.	Taken from publication.
Chapter 1, Section 1.10.2, page 34.	Aim 1, 2 and 3.	Adapted from publication.
Chapter 2, Section 2.3, page 39.	Figure 2.2: Adaptation of the Knowledge to Action (KTA) Framework for risk-reducing medications (RRMeds).	Adapted from publication.
Chapter 5, Section 5.2, page 66.	Figure 5.1: PCMed Service Pathway.	Adapted from publication.

Note:
Taken from publication: material replicated verbatim from the published protocol.
Adapted from publication: material modified from the published protocol to align with the scope and context of this thesis, which presents an interim analysis with a defined subset of the published study aims.

In accordance with university regulations regarding self-citation, this publication is not included in the thesis bibliography. Throughout this thesis, where reference to the published protocol is required, readers are directed to this Preface for full publication details.

Additional Material

The full study protocol (Appendix 1) contains additional methodological detail beyond the published protocol due to journal word limits. This unpublished material is included for transparency and methodological completeness.

Other Declarations

No work included in this thesis has been submitted for any other qualification.

Work carried out prior to enrolment in the MPhil program included the full study protocol (versions 1 and 2). Subsequent protocol amendments (versions 3, 4, and 5) were undertaken after enrolment. The full study protocol with amendments is included in Appendix 1.

No digital editorial assistance or generative AI tools were used in preparing the thesis. No third-party human editorial assistance was provided in preparing this thesis, other than feedback from my thesis supervisors.

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This study was also supported by Tour de Cure Grant (RSP-307-2024) and the Peter MacCallum Cancer Centre.

Principal Investigator and Thesis Supervisor, Kelly-Anne Phillips is an Australian National Health and Medical Research Council Leadership Fellow (1195294).

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A very special thank you to my mentor, Associate Professor Laura Forrest. Our coffee catchups were a lifeline, particularly during the most overwhelming moments. Laura, your wisdom, patience, and ability to help me regain perspective and find my way forward were invaluable.

I am grateful to the members of my Student Advisory Committee for their guidance: Professor Ben Teh, Chair; Associate Professor Louise Cheng, Co-Chair; Dr Kevin Sek; Associate Professor Annette Lim; Dr Laura MacPherson; and Dr Dane Cheasley. Thank you also to content experts Professor Roger Milne and Professor Sanchia Aranda for their valuable insights.

Thank you to Professor Phillips's research team, including Lucy Stanhope (formerly of the team), Jana Reed, Sarah Mason, Sarah Latham, and Steph Nesci, for the invaluable support in service development and for their contribution to this research journey.

To my dear friend Jacinta Elks, thank you for that fateful phone call about a job at Peter Mac, and for your continued belief in me and the support you provided through my nurse practitioner training and beyond. I would not be here without your encouragement.

Finally, to my family - my husband, Greg and my children, Emily and Tom – thank you for your unwavering love, patience, and encouragement, and support throughout this journey. The countless hours away from home were only made possible by your understanding and belief in me. Emily, your commitment to empowering other women continues to inspire me daily. To all three of you – I am profoundly grateful and blessed beyond measure.

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Abbreviations

AI	Aromatase inhibitor
ADH	Atypical ductal hyperplasia
AH	Atypical hyperplasia
ALH	Atypical lobular hyperplasia
ASCO	American Society of Clinical Oncology
BOADICEA	Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm
CI	Confidence interval
DCIS	Ductal carcinoma in situ
ER	Estrogen receptor
GBCI	Global Breast Cancer Initiative
GP	General practitioner
HDI	Human Development Index
HL	Hodgkin lymphoma
HR	Hazard ratio
HRT	Hormone replacement therapy
IBIS	International Breast Cancer Intervention Study
kConFab	Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer cohort study
KTA	Knowledge to Action Framework
LCIS	Lobular carcinoma in situ
NCCN	National Comprehensive Cancer Network
NICE	National Institute for Health and Care Excellence
NP	Nurse practitioner
PBS	Pharmaceutical Benefits Scheme
PCMed	Preventing Cancer with Medications Telehealth Service

PMCC	Peter MacCallum Cancer Centre
RACPG	Royal Australian College of General Practitioners
RMH	Royal Melbourne Hospital
RRMeds	Risk-reducing medications
SERMs	Selective estrogen receptor modulators
TGA	Therapeutic Goods Administration
WHO	World Health Organisation

Glossary

Catchment Clinics	The participating specialist clinics from which women were identified as potentially eligible for referral to the PCMed Service. These clinics provide care to women at increased risk of breast cancer and include: • The Royal Melbourne Hospital Familial Cancer Clinic. • Peter MacCallum Cancer Centre Familial Cancer Centre. • Peter MacCallum Cancer Centre Breast Surgical Oncology Clinic. • Peter MacCallum Cancer Centre Late Effects Clinic.
Decision Consultation	The consultation in which a woman decides whether to commence a risk-reducing medication. This may occur at either the Initial Consultation or a Repeat Consultation.
General Practitioner (GP)	A medical practitioner who provides primary care in the community.
Human Development Index	A measure of a nation's longevity (life expectancy at birth), education (mean years of schooling), and gross national income per capita.
Initial Consultation	The first consultation in the PCMed Service in which the woman received personalised information on her breast cancer risk, and the benefits and disadvantages of taking risk-reducing medications.
Post-Prescription Consultation	A planned consultation 8-10 weeks after initiation of a risk-reducing medication.
Post-Prescription Consultations Ad hoc	Unplanned consultations requested by the woman, her referring clinician, or her GP to address concerns usually following initiation of risk-reducing medications.
Repeat Consultation	A subsequent consultation for women who require more time to decide on whether to take a risk-reducing medication.
Risk-reducing medications	Medications used in the primary prevention of breast cancer. These medications are commonly referred to as chemoprevention and include tamoxifen, raloxifene, anastrozole, and exemestane.

PART I: INTRODUCTION AND METHODS

Chapter 1: Introduction

1.1 Thesis Overview

This thesis presents an interim analysis of a larger mixed-methods evaluation of the Preventing Cancer with Medications (PCMed) Telehealth Service. A description of the study protocol has been published in a peer-reviewed journal (as detailed in the Preface) and is presented in Chapter 2. The full study protocol including additional methodological detail beyond the published version, is provided in Appendix 1.

While the thesis title refers to "breast cancer prevention medications", the term "risk-reducing medication/s" (RRMed/s) is used throughout this thesis. This terminology more accurately reflects that these medications reduce risk rather than provide absolute prevention, with nomenclature consistent with current Australian guidelines.[1, 2]

Given the time constraints of the Master of Philosophy degree, this thesis addresses a defined subset of outcomes from the published study protocol, using data available to 30 June 2025. This approach was endorsed by the Graduate Student Committee.

Evidence from Phase III clinical trials has shown RRMeds to be efficacious in reducing breast cancer risk.[3-15] Despite endorsement by Australian and international clinical guidelines uptake remains low, with only 2.4% of Australian women aware of their increased breast cancer risk having used these medications.[16] Key barriers include limited awareness among women and clinicians about RRMeds, with very few general practitioners (GPs) confident in discussing or prescribing them.[17] Importantly, specialist support and clear guidance were identified as key facilitators to prescribing RRMeds.[17]

The Preventing Cancer with Medications Telehealth Service (PCMed Service) was established at Peter MacCallum Cancer Centre (PMCC) to address this evidence-implementation gap. This service accepts referrals from specialist clinics managing women at increased risk of breast cancer, including participating study sites at PMCC and the Royal Melbourne Hospital (RMH). The clinics from participating study sites are collectively termed "Catchment Clinics" in this thesis. These comprise: The RMH Familial Cancer Clinic; PMCC Familial Cancer Centre; PMCC Breast Surgical Oncology Clinic; and PMCC Late Effects Clinic. To the authors' knowledge, it represents the first Australian service, and among the first internationally, dedicated to

specialist-supported RRMed initiation through video-delivered telehealth consultations with planned transfer to ongoing GP-led care.

1.1.1 Scope of this thesis

This thesis reports on a defined subset of outcomes from the larger mixed-methods evaluation of the PCMed Service. Specifically, this thesis reports:

1. Baseline RRMed use prior to PCMed Service implementation, assessed through retrospective chart review of women attending Catchment Clinics* (Chapter 3).
2. RRMed uptake at 6 months among women who attended the PCMed Service, and had no contraindications to RRMed use, and characteristics associated with uptake (Chapter 4).
3. Process evaluation findings, including service feasibility, fidelity to the planned PCMed Service intervention, and implementation adaptations (Chapter 5).

Table 1.1 maps the aims of the published study protocol (see Preface for publication details) against those addressed in this thesis.

Table 1.1 Aims for the larger PCMed Service mixed-methods evaluation versus a subset of aims addressed in this thesis

Aims (as per published study protocol)	**Addressed in this thesis?**	**Chapter**
The primary aim is: To determine whether the PCMed Service is associated with an increased use of RRMeds by women who attended Catchment Clinics, compared with use by similar women who attended Catchment Clinics before the implementation of the PCMed Service.	Yes (modified aim) To determine the use of RRMeds by women who attended Catchment Clinics before the implementation of the PCMed Service.	Chapter 3
Secondary aims include: To describe the adoption of the PCMed Service by women who attend Catchment Clinics. Specifically, the proportion of eligible women who attend the PCMed Service following a Catchment Clinic appointment where the PCMed Service is discussed.	No	n/a
To determine the uptake of RRMeds for all clients who attend the PCMed Service and the associated characteristics.	Yes (modified) To determine the uptake of RRMeds among women attending the PCMed Service to December 2024, who have no contraindications to use, and describe associated characteristics.	Chapter 4

To explore the reasons for not taking up RRMeds and the associated characteristics.	No	n/a
To explore the acceptability of the PCMed Service to clients.	No	n/a
To explore the acceptability of the PCMed Service to clinicians.	No	n/a
To determine the feasibility and fidelity of the PCMed Service intervention and any adaptations required.	Yes (modified) To determine the feasibility and fidelity of the PCMed Service intervention at 30 June 2025, and to determine any adaptations required.	Chapter 5
To evaluate the cost of delivering the PCMed Service from the perspective of the healthcare provider.	No	n/a
Footnote: n/a = not applicable.		

Findings from the complete evaluation, including outcomes not reported here, will be disseminated through peer-reviewed publications following completion of data collection and analysis.

1.2 Breast Cancer

Breast cancer is the most diagnosed cancer and the leading cause of cancer-related death in women worldwide. In 2020, an estimated 2.3 million new breast cancer cases, and 685 000 deaths occurred globally, with approximately 7.8 million women living with a history of breast cancer. The global burden of breast cancer continues to rise with projections estimating 3.2 million new cases annually and 1.1 million breast cancer related deaths by 2050.[18]

The increasing incidence rates of breast cancer are influenced by various underlying factors that differ across settings. In countries with a high Human Development Index (HDI), the rise in breast cancer cases is associated with the prevalence of established risk factors, including a reduced number of pregnancies, increased maternal age at first birth, decreased breastfeeding rates, obesity, physical inactivity, higher alcohol consumption, and the use of exogenous hormones.[18] To a lesser extent, population-based screening programs enhance detection rates, contributing to the observed increase in incidence in these high-HDI regions.[18] In contrast, breast cancer incidence rates in low-HDI and middle-HDI countries remain relatively low; however, they are accompanied by high mortality rates largely due to inequities in early detection, effective treatment and a range of systemic, economic, and social challenges.[18] The projected increase in breast cancer cases in the coming decades is expected to be greater in

these countries due to economic advances, which in turn lead to increased life expectancy and a higher prevalence of lifestyle and reproductive risk factors.[18]

In Australia, breast cancer represents a significant public health burden. In 2025, it is estimated that 20,000 women will be diagnosed with breast cancer and greater than 3000 deaths will occur from the disease.[18] Although mortality rates have declined; largely due to advances in treatment and early detection through population-based screening, breast cancer was the leading cause of death among Australian women aged 45 to 74 years in 2023.[19] In terms of healthcare expenditure for females, cancer and other neoplasms represented the second-highest cost burden for 2022 to 2023, totalling $8.5 billion, of which breast cancer accounted for the largest proportion ($1.7 billion).[20] Beyond healthcare costs, breast cancer carries substantial societal burden, with post-diagnosis productivity losses estimated at $1.4 million in lost wages and earnings in Australia.[21] In 2015, metastatic breast cancer was associated with $6.6 million in productivity losses in the United States of America (USA). Families also face hidden costs related to travel for treatment, and specialised clothing, such as bras and wigs.[22] In low-income to middle-income countries, families often find themselves impoverished due to the costs related to cancer care, perpetuating cycles of poverty for future generations.[22] In 2020, over 1 million children globally became orphans due to cancer, with 25% of these orphans losing their parent to breast cancer. These maternal orphans are less likely to complete their education, further exacerbating the cycle of poverty.[22]

Beyond the financial devastation and productivity loss, breast cancer treatment inflicts a personal cost, with women facing a multitude of challenges across emotional, physical, and cognitive domains, extending beyond cancer care. Approximately one-third of women experience anxiety or depressions following a breast cancer diagnosis,[23] with many living in a persistent fear of recurrence, often described as “waiting for the other shoe to drop”.[24] These psychological burdens can be exacerbated by concerns about body image, sexuality and the impact disease has on their roles as mothers and partners.[25] Physical sequalae of breast cancer treatment include pain, lymphoedema, and fatigue.[26] Cognitive dysfunction, often referred to as “chemo brain” is common, manifesting as difficulties with memory, attention and executive function.[23] These physical and cognitive changes can impact daily functioning, quality of life, and erode self-confidence.[25]

Importantly, many breast cancers are preventable, highlighting the need for effective and scalable prevention strategies.[22]

1.3 Breast Cancer Risk Factors

Susceptibility to breast cancer is multifactorial, with many factors influencing an individual's likelihood of developing the disease. These risk factors are typically classified into two groups: modifiable and non-modifiable. Modifiable factors can be changed through lifestyle adjustments or medical interventions, while non-modifiable factors, such as age or genetics, are inherent and cannot be changed.[22]

1.3.1 Potentially modifiable breast cancer risk factors

Modifiable factors associated with increased breast cancer risk include excess weight (in postmenopausal women),[27] alcohol consumption,[28] physical inactivity,[29] not breastfeeding,[27] the use of hormonal contraceptives[30, 31] or combined hormone replacement therapy (HRT),[32] especially when used for greater than five years,[30-32] and dense breast tissue.[33] In high-income countries, the proportion of breast cancer cases attributed to these modifiable factors is estimated at 8-13% for obesity, and up to 28% in postmenopausal Black women in the USA, 4-16% for alcohol consumption, 2-10% for physical inactivity, 4% for not breast feeding, 2.1% for HRT use, and 0.8% for hormonal contraceptive use.[22]

1.3.2 Non-modifiable factors

Being female is a key risk factor, largely due to the influence of circulating estrogens.[27] Reproductive history also influences risk, as it impacts lifetime exposure to endogenous hormones.[27] Key reproductive factors associated with an increased breast cancer risk include early menarche, late menopause, and having a first full-term pregnancy in the late twenties or later.[27] Conversely, early menopause, childbirth in the early twenties, multiple live births, and extended breastfeeding durations have been shown to provide a protective effect against breast cancer.[27]

Age is another major determinant of breast cancer risk, with most breast cancers occurring in women over 50 years.[27] Ethnicity further influences incidence rates, as white non-Hispanic women exhibit the highest rates of breast cancer.[27] Additionally, benign breast disease, including lobular carcinoma in situ (LCIS), and atypical hyperplasia (AH), which includes atypical lobular hyperplasia (ALH) and/or atypical ductal hyperplasia (ADH), are associated with an increased breast cancer risk.[34] The 10-year cumulative incidence is estimated at 11.8% for LCIS, 15.4% for ALH, 13.9% for ADH, and up to 17% for combined LCIS and ALH, though individual risk will vary by age at diagnosis.[34]

Women who have had previous radiation therapy to the chest prior to age 35 years of age, are at a heightened risk of developing a secondary breast cancer, with the risk rising above that of the population eight years post-radiotherapy.[35-38]

Germline pathogenic mutations in breast cancer predisposition genes account for approximately 5% of breast cancer cases.[39, 40] These include high-penetrance genes, such as *BRCA1, BRCA2, PALB 2, TP53, CDH1, PTEN* and *STK11*, as well as moderate-penetrance genes, *ATM, BARD1, CHEK2, RAD51C and RAD51D*, which contribute to risk to a lesser extent.[39]

A family history of breast cancer is another important risk factor, with approximately 20% of women diagnosed with breast cancer reporting to have a first-degree relative, such as a mother or sister who was also affected. This underscores the importance of familial links in risk assessment.[27]

1.4 Breast Cancer Risk Assessment

The culmination of genetic and non-genetic risk factors contributes to an individual's unique breast cancer risk profile. Breast cancer risk assessment is the process of using these risk factors to estimate a woman's probability of developing the disease within a specific timeframe, such as 10-year, or residual lifetime risk,[41] and can be estimated using risk prediction models, also known as risk assessment tools.[42]

Definitions of "increased risk of breast cancer" vary across clinical guidelines. International guidelines use thresholds ranging from ≥1.66% 5-year risk[43] to ≥20% lifetime risk,[44] while Australian guidelines define increased risk as at least 1.5 times the age-specific population risk.[45] For this thesis, women were considered at increased risk if they had a 10-year risk of at least 5% or a residual lifetime risk of at least 20%, consistent with PCMed Service eligibility criteria and clinical practice thresholds for considering risk-reducing medications.[43] Risk assessment tools can help identify women who meet these criteria, enabling clinicians to offer targeted prevention strategies relevant to an individual's risk.

In Australia, three commonly used and validated prediction tools include the International Breast Cancer Intervention Study (IBIS), or Tyrer-Cuzick Model,[46, 47] the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) model,[48, 49] and iPrevent.[50] The IBIS (Tyrer-Cuzick Model, version 8) combines a genetic segregation model for familial risk with a regression model for personal factors.[41] It incorporates detailed family history (first-degree and second-degree relatives), accounting for high-penetrance gene mutations (BRCA1, BRCA2), reproductive history (menarche, menopause, parity, hormone

replacement therapy), height, weight, benign breast disease (atypical hyperplasia (AH) and lobular carcinoma in situ (LCIS)), and mammographic density.[41, 46] BOADICEA is similar to IBIS but does not incorporate benign breast disease. However, it does accounts for moderate-risk genes (PALB2, CHEK2, ATM), and a polygenic component representing numerous low-effect genes, in addition to high penetrance gene mutations. Another unique feature is its ability to integrate the tumour pathology (e.g., estrogen receptor status) of affected relatives and pedigrees of arbitrary complexity.[41, 48, 49] Developed in Australia, iPrevent[51] is a web-based decision support tool rather than a standalone mathematical model.[50] It uses a specific algorithm to select either IBIS or BOADICEA based on the risk factors entered by the user.[50] It then translates these estimates into simple language and provides risk-stratified management options (such as lifestyle advice, screening, or medication) based on Australian guidelines.[50]

Accurate risk estimation is critical for informing clinical decision-making, facilitating personalised discussions between clinicians and individuals at increased risk, and guiding the appropriate use of prevention strategies.[22] While validated risk prediction tools are essential in estimating breast cancer risk and ensuring preventative strategies are appropriately offered to those who stand to benefit the most,[22] it is important to recognise their limitations and the considerations that need to be made when selecting the most appropriate tool.[22] IBIS and BOADICEA were developed using data primarily from women of European ancestry, potentially leading to inaccuracies for other ethnic groups.[52, 53] Other factors also influence tool selection. IBIS is typically selected when there is a personal history of LCIS or AH,[46] and BOADICEA is preferred when there is a known or suspected genetic mutation in the family, when detailed pathology information is known, or when a woman has a complex family tree.[41] iPrevent may be particularly useful when the aim is to integrate risk estimation with personalised management advice and to support shared decision-making, as it can be completed by women outside the clinical setting and generates a personalised report that can subsequently be reviewed with their healthcare provider.[50, 51]

Estimating breast cancer risk for women with a history of chest irradiation, such as survivors of Hodgkin Lymphoma (HL), presents additional challenges. Existing risk frameworks[38] were developed using historical radiotherapy techniques and may not accurately reflect risk in patients treated with modern protocols.[54] While refined prediction models have been developed,[55, 56] these have limitations including age restrictions or requirements for detailed dosimetry data not routinely available outside specialist radiation oncology units.[55, 56]

These limitations underscore the importance of carefully selecting a risk model that is relevant to the individual's specific risk profile, the information available, and the context in which the

assessment will be performed. Ultimately, breast cancer risk assessment is not a one-size-fits-all approach, but rather a dynamic and evolving process. It requires clinicians to critically evaluate available tools, consider individual patient characteristics and treatment histories, and communicate uncertainties effectively, while also recognising that some tools, such as iPrevent, may support shared decision-making and reduce clinician burden by allowing women to complete the assessment outside the clinical setting before review with their healthcare provider. By acknowledging both the strengths and limitations of existing risk assessment methods, clinicians can better inform women and empower them to make informed decisions about preventative strategies.

1.5 Breast Cancer Prevention

Beyond mortality, breast cancer has an extensive and widespread impact on individuals, families, communities, and society, highlighting the importance of robust and multifaceted prevention efforts.[22] Notably, it is estimated that about 50% of breast cancers occur in the approximately 20% of women who could be identified at increased risk of the disease, based on their risk factor profiles.[52] The Lancet Breast Cancer Commission calls for interventions to systematically identify these women so tailored, evidence-based strategies can be offered.[22]

Currently, breast cancer prevention largely centres around secondary breast cancer prevention which focuses on early detection and prompt treatment to reduce morbidity and mortality. This includes screening programs such as mammography and clinical breast examinations. The World Health Organisation's (WHO) Global Breast Cancer Initiative (GBCI) aims to increase early stage (stage 1 or 2) diagnoses and ensure timely access to services.[57] While important, early detection does not reduce the risk of a breast cancer occurring, and its associated sequelae.

Primary prevention aims to reduce the risk of developing breast cancer through lifestyle and environmental modifications. This includes public health initiatives, promoting healthy diets, physical activity, reduced alcohol consumption, and avoiding tobacco. While valuable, these approaches are insufficient in isolation.[22] The WHO has developed a Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020, which includes strategies to address modifiable lifestyle factors.[58] However, despite these efforts and the WHO's GBCI to reduce cancer mortality, increasing incidence rates suggest current prevention efforts are inadequate.[59] Population-wide interventions to achieve sustained risk factor reduction faces challenges including inadequate funding,[60] limited institutional capacity,[61] resistance from commercial industries,[62, 63] cultural and systemic barriers,[64] and a lack of standardised monitoring and evaluation.[60]

Weight management is an important component of breast cancer prevention in postmenopausal women. Adherence to combined lifestyle recommendations on weight control, physical activity, alcohol intake, and diet has been associated with a 22% to 31% lower breast cancer risk.[22] In postmenopausal women, the Women's Health Initiative observational study found that weight loss of ≥5% was associated with a 12% lower breast cancer risk compared with stable weight.[65] Tailored prevention strategies should address prevention of weight gain and support sustainable weight loss for women who are overweight or obese.[66]

Therefore, to optimally influence breast cancer incidence, strategies must combine minimising exposure to modifiable lifestyle factors with intensified and personalised risk-stratified interventions.[22] These interventions are tailored to an individual's risk profile and include risk-reducing surgery (bilateral mastectomy) and RRMeds.[22]

Risk-reducing surgery is generally reserved for a small subset of women at very high risk of breast cancer, such as women with *BRCA1* or *BRCA2* gene mutations. In contrast, RRMeds are applicable to a broader group of women at increased risk.[22] These medications can benefit women at moderate risk of breast cancer and those women at high risk who may not be suitable candidates for surgery, or for high-risk women who wish to delay or avoid risk-reducing surgery altogether.

1.6 Breast Cancer Prevention Medications

1.6.1 Evidence of Efficacy

Evidence from landmark clinical trials and meta-analyses demonstrates that RRMeds significantly lower the incidence of primary invasive estrogen receptor (ER) positive breast cancer in women at increased risk, with a relative risk reduction ranging from 30%-60%, if taken for 3-5 years.[3, 4, 7, 8, 10, 11] These medications include the selective estrogen receptor modulators (SERMs), tamoxifen and raloxifene, and the aromatase inhibitors (AIs), anastrozole and exemestane.

Selective Estrogen Receptor Modulators (SERMS):

The National Surgical Adjuvant Breast and Bowel Project (NSABP) P-1 trial, involving 13,388 women ≥ 35 years, with a 5-year predicted risk of ≥1.66% (assessed using the Gail Model, also known as the Breast Cancer Risk Assessment Tool -BCRAT),[67] or a history of LCIS or AH, demonstrated a 49% reduction in invasive breast cancers ($p<0.001$) with tamoxifen (20 mg daily for 5 years) compared to placebo,[10] with the benefit primarily seen for ER-positive tumours.[10] An updated analysis at 7-years showed this preventative effect remained, despite

the potential bias introduced by early unblinding due to the positive results.[9] Findings also demonstrated that tamoxifen reduced the incidence of invasive cancer in women with AH and LCIS. In women with AH, the incidence rates of invasive breast cancer were 10.42 and 2.55 per 1,000 person-years in the placebo and tamoxifen groups, respectively (RR 0.25, 95% CI 0.10–0.52).[9] Similarly, in women with LCIS, the corresponding incidence rates of invasive breast cancer were 11.70 and 6.27 per 1,000 person-years in the placebo and tamoxifen groups (RR 0.54, 95% CI 0.27 to 1.02).[9]

The IBIS-I trial (7,154 women with increased risk of breast cancer) demonstrated a reduction in all breast cancers after a median follow-up of 16 years, but importantly the magnitude of benefit differed by menopausal hormone therapy (MHT) use during the active treatment period. Women who never used MHT derived the greatest preventative benefit with a 38% reduction in all breast cancers with a hazard ratio (HR) of 62 (95% CI, 0.48- 0.79), whereas women who used concurrent MHT during the trial experienced a smaller reduction of 12% (95% CI, 0.68-1.13). These findings support that concurrent MHT may attenuate tamoxifen's efficacy and are relevant to clinical decision-making in the prevention setting.[5] Notably, the preventive effect of tamoxifen persisted throughout the 20-year follow-up period, demonstrating long-term risk reduction, extending 15 years beyond the initial 5-years of treatment.[5]

The Study of Tamoxifen and Raloxifene (STAR) P-2 trial involving 19,747 high-risk postmenopausal women, comparing tamoxifen (20 mg/day) vs Raloxifene (60 mg/day) for 5 years, showed that raloxifene was initially equivalent to tamoxifen,[14] but at 81 months raloxifene was less effective than tamoxifen in preventing invasive disease, retaining 76% of tamoxifen's effectiveness (RR 1.24; 95% CI, 1.05–1.47).[15]

In addition to standard-dose tamoxifen regimens evaluated in landmark prevention trials, lower-dose tamoxifen has been investigated in selected higher-risk populations with breast intraepithelial neoplasia. More recently, the randomised placebo controlled trial of low-dose tamoxifen to prevent recurrence in breast non-invasive neoplasia (TAM-01 study), demonstrated that low-dose tamoxifen (5mg/day for 3 years) reduced breast cancer by 42% (HR 0.58; 95% CI, 0.35–0.95) and contralateral breast cancer by 64% (HR 0.36) in women with breast intraepithelial neoplasia (ADH, LCIS, or DCIS) over 10 years.[8, 12] At a median follow-up of 9.7 years, women experienced a durable reduction in breast cancer incidence (HR 0.58), illustrating a preventative effect 7 years after ceasing the medication.[12]

In exploratory subgroup analyses of the TAM-01 study, the estimated benefit of low-dose tamoxifen (5 mg daily) was smaller in the premenopausal than postmenopausal women, and did not reach statistical significance in the premenopausal subgroup (HR 0.67, 95% CI 0.31-1.43). However, there was no statistically significant interaction by menopausal status (p=0.43).[12] In contrast the KARISMA phase II trial demonstrated that reductions in mammographic density with low-dose tamoxifen were predominantly observed in premenopausal women.[68] These findings support biological activity in premenopausal women, but mammographic density reduction is a surrogate biomarker and does not directly establish a reduction in clinical breast cancer events.

A meta-analysis by Cuzick et al. (2013), incorporating individual data from 9 trials with 83,399 women, found that SERMs reduced overall breast cancer incidence by 38% (HR 0.62; 95% CI, 0.56–0.69), with a 51% reduction in invasive ER-positive cancers.[4]

Aromatase Inhibitors:

Aromatase Inhibitors (AIs), anastrozole and exemestane, have also demonstrated significant efficacy in reducing breast cancer risk in postmenopausal women. The IBIS-II trial demonstrated that anastrozole (1mg/day for 5 years) reduced all breast cancers by 53% (HR 0.47; 95% CI, 0.32–0.68)[7] and this reduction remained significant at 49% (HR 0.51; 95% CI, 0.39–0.66) after approximately 11 years of median follow-up, with a 54% reduction in ER-positive invasive cancer.[6] The preventive effect of anastrozole persisted beyond the 5-year treatment period, with follow-up extending to 12 years from treatment initiation.[6]

The MAP.3 trial involving 4,560 postmenopausal women with increased risk, demonstrated that exemestane (25mg/day for 5 years) reduced the breast cancer incidence of invasive breast cancer by 65% (HR 0.35; 95% CI, 0.18–0.70) and all cancers by 53% (HR 0.47; 95% CI, 0.27 to 0.79) after a median follow-up of 35 months.[11] Due to the trial being unblinded following publication, uncertainty remains regarding the potential for extended benefits beyond the 5-year treatment duration.[11]

A Cochrane network meta-analysis, comparing SERMs and AIs across six studies, found that AIs reduced breast cancer risk by 53% (RR 0.47; 95% CI, 0.35–0.63), with an indirect comparison suggesting AIs may be slightly more effective than tamoxifen.[69] However, SERMs and AIs have not been compared directly within a single randomised head-to-head trial, which remains the most robust design for determining their relative efficacy. As such, any comparison between these drug classes relies on indirect comparison and should be interpreted with caution.

The robust evidence from clinical trials and meta-analyses supports the use of RRMeds as an effective strategy for reducing the risk of breast cancer in women at increased risk, and the long-term follow-up shows the protective effects persist for many years after ceasing treatment.

1.6.2 Considerations, Contraindications and Potential Side Effects

While clinical trials have established the efficacy of RRMeds, the benefit of initiating a RRMeds for an individual, must be weighed against any potential harm.

SERMs act by selectively blocking estrogen receptors in breast tissue, thereby inhibiting estrogen-mediated proliferative effects; consequently, they are classified as estrogen antagonist in breast tissue.[70] However, SERMs exert estrogen-like (agonist) effects in other tissues, such as the uterus and bone.[70] These tissue-specific effects, determine therapeutic benefits and potential side effects and are therefore an important consideration in the use of SERMs. For example, SERMs act as agonists in bone tissue leading to increased bone density and reduced risk of osteoporotic fractures in postmenopausal women. Tamoxifen exhibits agonist effect in uterine tissue, which may result in adverse effects affecting the uterus, such as endometrial cancer in postmenopausal women. In contrast raloxifene, acts as an antagonist in uterine tissue and therefore does not increase the risk of endometrial cancer.[70]

AIs work by inhibiting the aromatase enzyme, which is responsible for the peripheral conversion of androgens into estrogen, thereby reducing circulating estrogen levels.[69] As estrogen production in postmenopausal women occurs predominantly in the peripheral tissues rather than the ovaries, AIs are effective only in the postmenopausal population.

Guidelines recommend consideration of RRMeds for women who have been unaffected by breast cancer and have an estimated 5-year risk of at least 3% (Gail Model), a 10-year risk of at least 5% (IBIS), or a diagnosis of AH, or LCIS and who do not have a contraindication for use.[43] Contraindications include pregnancy, breastfeeding, planning pregnancy in the next 3 years, prior bilateral mastectomy, or current use of hormone therapy. Additional contraindications include prior thromboembolic events (for SERMs), endometrial cancer (for tamoxifen), smoking, taking anticoagulants or a strong CYP2D inhibitor (for SERMs) and premenopausal status or osteoporosis (for AIs).[1, 43] Women who are suitable to use a RRMed, should be informed of the potential side effects.[43]

Common side effects include gynaecological and vasomotor symptoms (with SERMs and AIs) and musculoskeletal symptoms (with AIs). These are summarised in Table 1.2.[1] Less common, but more serious effects of RRMeds are summarised in Table 1.3 and include: thromboembolic

events, such as deep vein thrombosis, pulmonary emboli, and stroke (with SERMs), endometrial cancer in postmenopausal women (with tamoxifen), or bone loss (with AIs).[1]

Table 1.2: Common side effects and less serious side effects of risk-reducing medications

Side Effect Category	tamoxifen	raloxifene	exemestane	anastrozole
Vasomotor				
Hot flashes & night sweats)	Extra 1 in 10	Extra 1 in 14	Extra 1 in 12	Extra 1 in 12
Gynaecological				
Vaginal discharge	Extra 1 in 8	Extra 1 in 33	NR	NR
Vaginal dryness	Extra 1 in 50	Extra 1 in 100	Extra 1 in 9	Extra 1 in 9
Musculoskeletal				
Joint & muscle pain	NR	NR	Extra 1 in 30	Extra 1 in 15
General				
Nausea & diarrhoea	NR	NR	Extra 1 in 25	NR
Footnote: Data sourced from the Clinical Oncological Society of Australia (COSA) guideline (2024).[1] Values represent the number of additional women experiencing the side-effect over a 5-year treatment period. For example, "extra 1 in 10" corresponds to an additional 10 cases per 100 women. NR = Not reported.				

Table 1.3: Serious side effects of risk-reducing medications

Serious Side Effect	tamoxifen	raloxifene	exemestane	anastrozole
Thromboembolic & Vascular				
Venous thromboembolism	Extra 1 in 250	Extra 1 in 330	NA	NA
Endometrial Cancer	Extra 1 in 250	No increase	NA	NA
Reduction in bone density	*	*	Increased risk+	Increased risk+
Fractures	*	*	No increase	No increase
Carpal tunnel syndrome	NR	NR	Extra 1 in 100	NR
Cataracts	Extra1 in 250	Fewer than tamoxifen+	NR	NR
Footnote: Data sourced from the COSA guideline (2024).[1] Values represent the number of additional women experiencing the side-effect over a 5-year treatment period. NA = Not applicable; NR = not reported; *indicates a protective effect (as both tamoxifen and raloxifene lower the risk of fracture in postmenopausal women; + indicates the source document did not quantify rates.				

1.6.3 Current Use of Risk-Reducing Medications

Despite evidence and guidelines supporting the use of RRMeds, only 2% of Australian women, who know they are at increased risk for breast cancer, have used prevention medications.[16] A metanalysis by Smith et al. (2016), encompassing 26 studies on RRMeds uptake, reported an overall uptake of 16.3% (25.2% uptake in clinical trials, and 8.7% in the non-trial setting).[71] An

updated systematic review published in 2019 reports global uptake in non-trial settings of approximately 15 to 20%,[72] broadly aligning with the review by Smith et al.[71] Notably, there was considerable heterogeneity with the studies with uptake ranging from 0% to 54.9%.[71] The highest uptake was reported in a small mixed-methods study (n=51) requiring interview participation[73] which may have inflated the results.

Factors associated with improved uptake include increasing age, being on a clinical trial, not having a BRCA 1 or BRCA 2 mutation for premenopausal women, physician's recommendation to use RRMeds, and a heightened personal risk of breast cancer.[71]

For women who use preventative medications, long-term persistence is an important factor to ensure women experience the full preventative effect of the medication. A meta-analysis examining data on persistence found low long-term persistence declines over time.[71] For example, in the IBIS-I tamoxifen trial, persistence dropped from 90% at 1 year to 74% at 4 years.[74] Similarly, Italian data from the IBIS-II anastrozole trial showed a decline from 61.3% at 1 year to 41.6% at 2 years.[75]

Across clinical trials with 5-year follow up data, long-term persistence with tamoxifen ranged from 61% to 81%.[13, 15] Several studies reporting lower persistence in the tamoxifen arm compared with placebo and raloxifene arms,[71] suggesting side effects and tolerability influence use. Some studies suggested persistence with RRMeds was higher in woman with lower depressive symptoms, whereas no sociodemographic characteristics (such as ethnicity, employment, income or living alone) were associated with persistent use.[71] Providing women with opportunities for personalised discussions around the potential side effects and benefits of RRMeds, as well as access to specialist support while taking a RRMed may improve persistence and support sustained use.[71]

1.7 Barriers to Using Risk-Reducing Medications

The underutilisation of RRMeds stems from barriers affecting both women and clinicians. These barriers are multifactorial, ranging from a lack of awareness, misinformation, and concern for side effects to broader systemic failures.

1.7.1 Patient-Related Barriers

Lack of awareness:

In an Australian survey of women (n = 725) at increased risk of breast cancer, who were enrolled in the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer (kConFab), 52% were unaware of the existence of RRMeds.[17] Even among women who

are aware of RRMeds, 23% reported insufficient information as a barrier to making an informed decision about their use.[17] Additionally, available information may be difficult for some women to interpret and apply to their personal circumstances.[76]

Misunderstanding of potential harms may further reduce willingness to consider RRMeds, particularly where risks are not clearly contextualised. In the kConFab survey for example, 62% of pre-menopausal women identified endometrial cancer as their primary concern[17] despite tamoxifen not being associated with an increased risk of endometrial cancer in pre-menopausal women.[15] These findings suggest that misinformation or misunderstanding about potential harms and benefits of RRMeds may influence decision-making and highlight the importance of providing clear, tailored information about RRMeds as a preventive strategy, including expected side effects and absolute risks.

Fear of side effects:

Concern for side effects is consistently reported as a significant barrier to RRMed uptake.[17, 71, 77-81] In the Australian survey, women identified endometrial cancer (45%) and thromboembolic events (45%) as the most concerning potential adverse effects.[17] In addition, symptoms that clinicians may classify as less serious, such as hot flashes, night sweats, and vaginal dryness can still be highly relevant to women as they may interfere with day-to-day functioning and quality of life.[81] For some women, concerns also relate to role functioning, for example, mothers may worry that side effects could reduce their ability to care for their young family.[77]

Psychological and social barriers:

Women's decision about RRMeds are also influenced by psychological and social factors. Negative experiences shared by family members or friends can shape perceptions of medications and deter use.[17, 77, 80] Some women view RRMeds as cancer treatments, leading to confusion with chemotherapy and fear of associated toxicities.[77, 78] For others, taking a daily tablet over several years can act as a reminder of future cancer risk or perceived state of "unwellness".[71, 77] Some women also express a preference of lifestyle modification over medication-based prevention.[17, 79]

Collectively, these patient-related barriers may, in part, be consequences of limited clinician knowledge, which can constrain clinician's ability to provide tailored and accurate information to woman.

1.7.2 Clinician-Related Barriers to Discussing and Prescribing Risk-Reducing Medications

Significant knowledge gaps among clinicians represent a major barrier to RRMed use in Australia. An Australian survey of 74 breast surgeons and 147 GPs revealed that a significant proportion of GPs (35%) are unaware that RRMeds exist.[17] Among GPs who were aware, many felt they lacked the necessary knowledge to initiate prescribing, with only 3% reported feeling "very confident" in providing information, and only 31% believing it was their role to write an initial prescription.[17] Lack of knowledge (45%) was identified as the strongest barrier to prescribing for GPs.[17] A systematic review reinforces these findings, noting that while primary care providers are comfortable with reactive risk assessment, that is taking a family history when required, they report discomfort and low confidence in prescribing RRMeds.[66]

In contrast, breast surgeons demonstrated greater awareness and confidence regarding RRMeds. Only 3% were unaware of RRMeds, and 56% felt "very confident" in providing information to women about these medications.[17] While most (81%) were willing to initiate prescription, only 43% felt it was their role to write ongoing prescriptions.[17] The most frequently reported barrier to prescribing for breast surgeons was concern about the side effects (40%), followed by lack of knowledge or training (15%).[17] A number of breast surgeons (14%) identified lack of time in a consultation as the strongest barrier.[17]

These knowledge deficits and role uncertainties have created a workforce capacity gap, particularly affecting women at moderate risk of breast cancer.[17] Research indicates that breast surgeons and family cancer clinicians are at capacity managing women with existing breast cancer or those at high genetic risk respectively,[76] and consequently may decline referrals for moderate-risk women. Yet GPs often lack the tools, knowledge and confidence to manage these cases in primary care.[17] As a result, many moderate-risk women are not offered RRMeds despite their eligibility. This represents a major unmet need in breast cancer control.

1.7.3 System-Related Barriers

While family cancer clinicians (including geneticists and genetic counsellors) play a crucial role in assessing risk and discussing prevention strategies, many do not have prescribing authority for RRMeds. In the Australian survey, only 20% of genetic health professionals reported having prescribing authority.[82] In addition, even when prescribing authority exists, these clinicians may not perceive RRMed prescribing as part of their professional role.[82] In the same survey, medical oncologists (83%) and breast surgeons (71%) were perceived as the most appropriate clinicians to initiate RRMeds.[82] This division of roles can create discontinuity between risk identification

and treatment initiation, whereby clinicians most central to identifying and counselling eligible women are not positioned to initiate prescribing, while clinicians perceived as most appropriate to prescribe may see fewer unaffected women in routine practice and be less familiar with quantitative risk-assessment tools than clinicians working routinely in risk assessment settings.[82]

Regulatory, medico-legal and funding factors can also impede initiation of RRMeds. Clinician's reluctance to prescribe medications "off-label" has been identified as an additional barrier,[66] with concerns about medico-legal risk potentially reducing willingness to initiate RRMeds.[76, 83] A systematic review reported 58.1% of surveyed primary care physicians in Canada were concerned about prescribing "off-label" medications; conversely, 54% indicated they would be more likely to prescribe if the medications were subsidised.[66] In Australia, SERMs (tamoxifen and raloxifene) are approved by the Therapeutic Goods Administration (TGA),[1] and tamoxifen (20mg daily for 5 years) was listed on the Pharmaceutical Benefits Scheme (PBS) in 2016 for primary breast cancer risk reduction.[1] Prior to PBS listing, cost was identified as a barrier for physicians recommending a RRMed.[76] In Australia, AIs are used "off-label" for breast cancer risk reduction and not PBS listed for primary breast cancer risk reduction[1], which may further constrain routine prescribing.

Finally, system constraints within primary care may limit uptake even when RRMeds may be clinically appropriate. The literature identifies clinician difficulty in performing risk assessment, and lack of confidence in using quantitative tools, as fundamental barriers to RRMed prescribing.[66, 84] Time constraints in primary care consultations also pose a barrier, as clinicians prioritise immediate health concerns and may have insufficient time to counsel women about preventative strategies.[85]

1.7.4 Facilitators to Uptake of Breast Cancer Prevention Medications

The ability to access specialist support and clear guidance was identified by 59% of Australian GPs and 27% of Australian breast surgeons as the strongest potential facilitator for prescribing RRMeds.[17] Findings from a national survey of GPs practicing in the United Kingdom showed GPs were more likely to discuss the risk and benefits of tamoxifen in the setting of prevention, if a specialist clinician would write the first prescription and provides clear ongoing management guidelines.[86]

1.8 The Evidence-Implementation Gap

There remains a large evidence-implementation gap in primary breast cancer prevention. In routine clinical practice, few women are offered RRMeds as an option, despite clear efficacy and guidelines that suggest RRMeds are a standard of care option. A key driver is the limited workforce capacity and systems capability to counsel women on RRMeds and initiate prescription, including clinician time constraints, role perceptions, and prescribing authority, which collectively may reduce the likelihood that RRMeds are discussed and initiated in routine clinical practice.[17, 86] "Uptake" of a RRMed, cannot occur without an offer; women can only consider RRMeds as a preventative option if they are provided information to make an informed decision, and if this option is made accessible through a prescribing and follow-up pathway.

Where women do receive a structured risk consultation in which RRMeds are discussed and offered, initiation (uptake) remains variable,[71, 77] suggesting that access to discussion is necessary but may not be sufficient for uptake. A UK study revealed no socio-demographic characteristics were associated with uptake among women who attended a clinic to discuss their breast cancer risk.[87] This highlights the importance of distinguishing between low overall use of RRMeds due to limited offering in routine clinical practice, and low RRMed initiation among women who have been offered treatment.

1.9 Responding to the Evidence-Implementation Gap

In response to research showing that the evidence-implementation gap is driven by interacting constraints in workforce capacity, variable clinician willingness, and gaps in knowledge and confidence, the PMCC has established the PCMed Service following extensive stakeholder consultation. PMCC, located in Melbourne, is a public hospital dedicated exclusively to cancer treatment, research and education. In this thesis, references to telehealth consultations refer to video-based consultations.

The PCMed Service, which is a first of its kind in Australia, is a consultative telehealth initiative aimed at optimising the uptake of evidence-based RRMeds for women at increased risk of breast cancer. The service is delivered through a collaborative nurse practitioner (NP)-medical oncologist model with structured triage and provides personalised information to empower women to make informed decisions about using RRMeds. For those women who are suitable and wish to use a RRMed, an initial prescription is provided, with care being transferred to their GP once stable on the medication. Additionally, ongoing access to specialist advice is

available for both women and their referring clinicians and GPs to support the sustained use of a RRMed. Further details of the PCMed Service are outlined in the published study protocol presented in Chapter 2.

1.10 Focus and Structure of the Thesis

The focus of this thesis is the presentation of the interim analysis findings of the evaluation of this innovative and complex intervention: the PCMed Service. The study described sits within the field of health services research, which aims to improve the quality, effectiveness, and delivery of healthcare by studying how interventions are implemented and function in real-world settings.

1.10.1 Hypotheses

The overarching hypothesis is that the PCMed Service will support uptake of RRMeds among women attending this Service. The PCMed Service will be feasible to deliver with fidelity to the intended PCMed Service intervention.

1.10.2 Aims

The aims of this thesis are:

1. To determine the use of RRMeds by women (historical controls), who attended Catchment Clinics before the implementation of the PCMed Service.
2. To determine the uptake of RRMeds among women attending the PCMed Service to 31 December 2024, who have no contraindications to use, and describe associated characteristics.
3. To determine the feasibility and fidelity of the PCMed Service intervention, based on Service delivery at 30 June 2025, and to determine any adaptations required.

1.10.3 Thesis structure

This thesis comprises three parts and six chapters.

Part I: Introduction and Methods

Chapter 1: Introduction

This chapter introduced the thesis, contextualising it within existing literature on breast cancer risk, prevention, and the evidence-implementation gap for RRMeds. It outlined the challenges associated with translating the efficacy of RRMeds into widespread clinical practice and introduces the PCMed Service as an implementation strategy to address this gap. The chapter

established the central focus of the thesis: evaluation of the PCMed Service as a complex intervention.

Chapter 2: Methods

This chapter describes the methodological approach used in this thesis. It includes the published study protocol, titled *"Evaluation of a telehealth service to support breast cancer prevention medication uptake: a protocol of a mixed methods study"* (see Preface) which describes the mixed-methods evaluation of the PCMed Service. This thesis focuses on a subset of the protocol aims, specifically pre-implementation RRMed uptake among PCMed Service attendees, and process evaluation outcomes including feasibility, fidelity, and adaptations. Additional methodological detail relevant to these analyses is provided, with the full research protocol included in Appendix 1.

Part II: Results

Chapter 3: Aim 1 – Pre-Implementation Uptake of RRMeds

This chapter presents findings from a retrospective chart review of 100 women (historical controls) who attended Catchment Clinics prior to the implementation of the PCMed Service. It quantifies baseline RRMed uptake in this population, providing context for evaluating the impact of the PCMed Service.

Chapter 4: Aim 2 – Risk-Reducing Medication Uptake Among PCMed Service Attendees

This chapter presents the findings of an interim analysis, undertaken to determine RRMed uptake at 6 months among women who attended the PCMed Service before 31 December 2024 and who had no contraindications to use. It also examines characteristics associated with uptake.

Chapter 5: Aim 3 – Delivery of the PCMed Service: Findings on Feasibility, Fidelity and Adaptations

This chapter presents findings from the interim process evaluation of the PCMed Service. Based on PCMed Service delivery data to the 30 June 2025, it examines the delivery of the Service intervention within a real-world clinical setting, including feasibility of the service model, fidelity to the planned PCMed Service intervention (Appendix 2), implementation challenges, and adaptations made.

Part III: Discussion and Conclusion

Chapter 6: Discussion and Conclusion

This chapter synthesises the findings of the thesis and interprets results in the context of existing literature. It discusses the strengths and limitations of the study and outlines implications for clinical practice, considerations for scale-up and sustainability, and directions for future research.

Chapter 2: Methods

2.1 Overview

Given the time constraints of the Master of Philosophy degree, this thesis reports an interim analysis of a mixed-methods study evaluating the Preventing Cancer with Medications (PCMed) Telehealth Service intervention. It addresses a defined subset of outcomes from the published study protocol (see Preface), using data available to 30 June 2025. This approach was endorsed by the Graduate Student Committee.

An abbreviated study protocol, titled "*Evaluation of a telehealth service to support breast cancer prevention medication uptake: a protocol of a mixed methods study*", was published in the BMJ Open and is included within this chapter. Due to journal word limits, this published protocol provides a condensed description of the study methods. Expanded methods are available in the full research protocol provided in Appendix 1. Additional methodological detail relevant to specific analyses is presented within the relevant results chapters where required.

For clarity, the aims addressed in this thesis are restated below:

1. Determine RRMed use by women (historical controls), who attended Catchment Clinics prior to PCMed Service implementation.
2. Determine RRMed uptake among women attending the PCMed Service at 31 December 2024 who had no contraindications to use and describe associated characteristics.
3. Evaluate the feasibility and fidelity of the PCMed Service delivery at 30 June 2025 and identify implementation challenges and adaptations required.

2.2 Study Design

The study, including the elements presented in this thesis, uses a mixed-methods approach. Quantitative methodology was appropriate because it allows structured measurements of pre-defined outcomes and objective measurements of changes in clinical practice associated with service implementation.[88, 89] This was complemented by qualitative data from the PCMed research journal (Appendix 4), which is valuable in implementation research because it provides insight into contextual factors that may influence intervention delivery.[90] Mixed-methods approaches are particularly suited to complex interventions because they combine quantitative assessment of outcomes with qualitative examination of the processes and conditions that may help explain those outcomes.[91, 92] The research journal provided a record

of implementation challenges and adaptations, thereby supporting transparency in the interpretation of findings.[93]

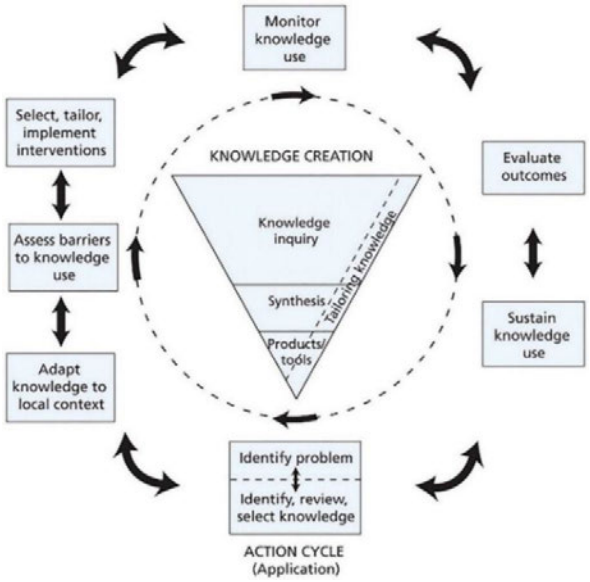
This study adopts a realist ontological position, assuming the PCMed Service and its implementation, including feasibility and fidelity, are real features of clinical practice that exist independently of the researcher but can be examined indirectly through measurable indicators derived from routine clinical data.[88, 89, 94, 95]

Epistemologically, the study is informed by a post-positivist perspective, whereby knowledge is generated through systematic measurement and quantitative analysis, while recognising that findings remain provisional and subject to uncertainty.[91] Findings are therefore interpreted as estimates and considered in light of the observational design and limitations of routinely collected data, including variable data quality.[96-98]

2.3 Theoretical Framework

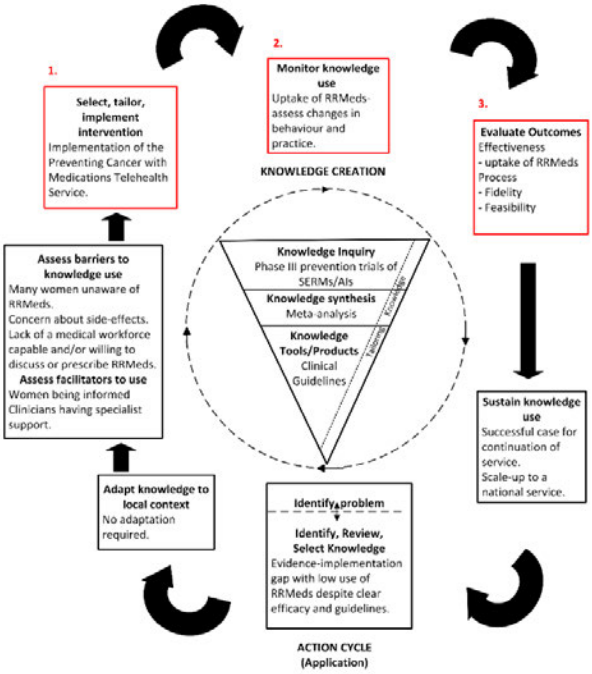
The Knowledge to Action (KTA) Framework (Figure 2.1), was chosen to guide this study as it provides a pragmatic, action-oriented approach to translating evidence into clinical practice, which is essential to the implementation of RRMeds.[99] Unlike more linear implementation models, the KTA framework explicitly integrates knowledge creation with an iterative action cycle, enabling adaptation to local context and responsiveness to emerging barriers and facilitators. This makes it well suited to evaluating complex health service interventions within dynamic clinical environments.

Figure 2.1: The Knowledge to Action Framework illustrating the relationship between knowledge creation and the action cycle, which supports translation of evidence into clinical practice. Adapted from Graham et al. (2006)[99]



In the context of RRMeds, the knowledge creation component is largely complete (Figure 2.2). Evidence from phase III clinical trials[3, 5-15] supported by meta-analyses,[4, 100] has established efficacy, while clinical guidelines[2, 43-45, 101-104] provide a strong foundation for implementation. The persisting challenge lies in translating this existing knowledge into routine clinical practice.

Figure 2.2: Adaptation of the Knowledge to Action Framework for risk-reducing medications



The KTA framework therefore provides a structured approach to addressing this evidence–implementation gap. Within the action cycle, the problem is clearly defined, with low uptake of RRMeds despite strong evidence of benefit. Prior Australian research has identified key barriers and facilitators to their use.[17] This thesis focuses on selected phases of the action cycle (Figure 2.2), specifically implementation of the PCMed Service (Box 1); monitoring knowledge use through assessment of medication uptake (Box 2), and evaluation of outcomes including effectiveness though uptake of RRMeds, feasibility, and fidelity (Box 3).

2.4 Study Setting

This study was conducted within the Parkville Medical Precinct in Melbourne, Victoria, Australia. The precinct includes PMCC, the RMH, and The Royal Women's Hospital. However, participating study sites were limited to PMCC and the RMH.

PMCC is a specialist cancer centre focused on cancer treatment, research, and education, while RMH is a tertiary general hospital providing a broad range of specialist services. Within these

institutions, the participating Catchment Clinics were The Royal Melbourne Hospital Familial Cancer Clinic, Peter MacCallum Cancer Centre Familial Cancer Centre, Peter MacCallum Cancer Centre Breast Surgical Oncology Clinic, and Peter MacCallum Cancer Centre Late Effects Clinic. In this thesis, Catchment Clinics refers to the participating specialist clinics from which women were identified as potentially eligible for referral to the PCMed Service and from which the historical comparison group was drawn. The selection of these clinics was pragmatic, as they were routine clinical settings in which women at increased risk of breast cancer were assessed and managed, and from which potentially eligible women could be identified for referral to the PCMed Service.

2.5 Participants and Recruitment

Participants include women attending Catchment Clinics and all consenting women attending the PCMed Service. Inclusion and exclusion criteria are summarised in the published protocol in section 2.8, with full eligibility criteria and recruitment procedures detailed in the full study protocol (Appendix 1).

2.6 Data Sources and Measures

This thesis draws on three key data sources:

- Retrospective data from consecutive eligible women attending Catchment Clinics before implementation of the PCMed Service (historical controls), were used to determine baseline RRMed use. These women were aged 20 to 70 years, had no personal history of invasive breast cancer of DCIS, and met the study criteria for increased breast cancer risk.
- Prospective data from women attending the PCMed Service, used to assess RRMed uptake and associated characteristics.
- Prospective, process evaluation data, used to assess feasibility, fidelity, and implementation adaptations.
- A record was maintained by the thesis author, who was the nurse practitioner delivering the PC Med Service, to document challenges, pragmatic adaptations, and reflections relevant to service delivery and interpretation of the process evaluation findings. This record is presented as the PCMed research journal in Appendix 4.

Data collection procedures are provided in the published study protocol in section 2.8.

2.7 Data Analysis

Analyses undertaken in this thesis are aligned with the pre-specified study protocols but limited to outcomes relevant to the planned interim analysis. Any deviations from the pre-specified protocols will be described within the relevant results chapters.

2.8 Published Study Protocol

The protocol for the PCMed evaluation study has been published in BMJ Open (see Preface) and is reproduced below. Due to journal word limits, the published protocol provides a condensed description of the study methods; additional detail is available in the full research protocol (Appendix 1).

2.8.1 Published manuscript: Evaluation of a telehealth service to support breast cancer prevention medication uptake: a protocol of a mixed methods study

Open access Protocol

BMJ Open

Evaluation of a telehealth service to support breast cancer prevention medication uptake: a protocol of a mixed methods study

Katrina Louise West ,[1,2] Tim Spelman,[3,4,5,6] Wanda Cui,[1,2] Sarah Latham,[1,2] Sabine Deij,[2,3,7] Sandy Minck ,[8] Sarah Mason,[1,2] Christobel Saunders,[6,9,10] Catherine Poliness,[2,10] Paul A James ,[2,11] Greg Wheeler,[2,12] Louise A Keogh,[13] Stephanie Best,[3,14,15] Kelly Anne Phillips [1,2,16]

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ABSTRACT

Introduction Breast cancer risk can be substantially reduced with risk-reducing medications (RRMeds). Despite their efficacy, and guidelines which support their use for women at substantially increased risk of breast cancer, they are underused. Barriers to their use in Australia include a lack of awareness of RRMeds by women and clinicians, and a primary care workforce that reports a lack of knowledge and confidence in discussing and/or prescribing these medications. In contrast, Australian clinicians have reported specialist support and guidance as a key facilitator. The Preventing Cancer with Medications (PCMed) Telehealth Service was therefore developed to provide this specialist support and to bridge the evidence–implementation gap. The PCMed Service endeavours to increase the appropriate use of RRMeds and support women and their doctors throughout treatment. The aim of this research is to evaluate the effectiveness, adoption, acceptability, feasibility, fidelity and cost of this new Service, and to determine any adaptations that might be required.

Methods and analysis The research uses a mixed methods approach. Effectiveness of the PCMed Service will be evaluated by determining whether the PCMed Service is associated with increased uptake of RRMeds compared with historical data. Secondary outcomes include: adoption of the Service, specifically, the proportion of women who attend a PCMed Service consultation; acceptability of the Service for clients and referring clinicians (using a brief survey and semistructured interviews); feasibility and fidelity by evaluating the adherence to the planned Service processes; and the cost, by reporting the difference between funding received per woman and the cost for service delivery.

Ethics and dissemination This study was approved by the institutional Human Research Ethics Committee (EC00235): HREC/101142/PMCC. The findings will inform future iterations of the Service prior to scaling up. Research findings will be disseminated at scientific meetings and in peer-reviewed journals.

Trial registration number ISRCTN15718519.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A key strength is the theory-informed implementation data collected from participants (clients and clinicians) and the inclusion of cost analyses to aid the future development of the Preventing Cancer with Medications (PCMed) Service.
⇒ The inclusion of a historical cohort from the same clinics as the prospective cohort (for the primary aim), rather than relying on published data for the preimplementation comparator rates of RRMed uptake is also an important strength.
⇒ Implementation of the PCMed Service and evaluation are taking place in one large Australian Cancer Centre, thus potentially limiting the generalisability of the findings.

INTRODUCTION

Globally, breast cancer is the most common cancer in women. In 2020, 2.3 million women were diagnosed with breast cancer and 685 000 women died of the disease.[1] If the current global trends continue, it is expected that there will be 3 million new cases of breast cancer occurring each year by 2040.[2] Importantly, this upward trend is not inevitable, as many of these breast cancers are preventable.[3]

Optimal implementation of proven, intensified prevention strategies for women at substantially increased risk of breast cancer, combined with minimising women's exposure to modifiable risk factors (eg, obesity, alcohol and sedentary lifestyle), will be crucial to lower breast cancer incidence.[3 4] Approximately 50% of breast cancers occur in the 20% of women who are at increased risk.[5]

Several medications reduce the risk of oestrogen receptor-positive breast cancer.[6–17] These medications include the selective oestrogen receptor modulators (SERMs), tamoxifen and raloxifene, and the aromatase

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inhibitors (AIs), anastrozole and exemestane (all hereafter referred to as risk-reducing medications (RRMeds)). Guidelines recommend their consideration in individuals who are at moderate to high risk of developing a future breast cancer,[18–23] excluding those with contraindications such as pregnancy, planning pregnancy in the next 3 years, breastfeeding, prior bilateral mastectomy or use of hormone therapy. Additional contraindications include prior thromboembolic events, endometrial cancer (for tamoxifen), smoking, taking anticoagulants or a strong inhibitor of the CYP2D6 enzyme (for SERMs) and premenopausal status or osteoporosis (for AIs).[24] A single tablet, taken daily for 3–5 years, can reduce the relative risk of breast cancer by between 30% and 60%,[6–17] and the risk reduction persists long after the prescribed treatment period.[8 13 14 16] Despite strong evidence of efficacy and endorsement in national guidelines,[21–23] the use of RRMeds in Australia is low.[25] A major barrier to the use of RRMeds is the concern for side effects.[26 27] Common adverse effects include gynaecological and vasomotor symptoms, menstrual changes, and less commonly, more serious events such as thromboembolism (with SERMs) or endometrial cancer in postmenopausal women (with tamoxifen),[6] or bone loss (with AIs).[10] Confusion between RRMeds and chemotherapy,[26 27] and insufficient information for women to make an informed decision regarding their use,[26–30] suggest that expert medical advice is important for women to weigh the potential benefits and harms in the context of individual risk. Many Australian women at increased risk of breast cancer, and approximately one-third of their primary care physicians (PCPs), are unaware of RRMeds.[27] Another driver of this evidence–implementation gap in Australia is the lack of a medical workforce capable of, and willing to discuss and prescribe RRMeds.[27] In one study, among PCPs who were aware of RRMeds, only 3% were very confident in discussing them, and 31% considered it their role to initiate prescribing, although 98% of PCPs would write ongoing prescriptions.[27] Specialist support has been identified as a key facilitator for PCPs to discuss and prescribe RRMeds.[27] In response to this, the Preventing Cancer with Medications (PCMed) Telehealth Service has been developed to provide specialist support to PCPs. The 'knowledge to action' framework[31] (figure 1) was adapted to guide the development and implementation of the PCMed Service and its concurrent evaluation.

We hypothesise that the implementation of the PCMed Service will be associated with greater use of RRMeds compared with historical controls, and the PCMed Service will be feasible, well-adopted, delivered with fidelity and acceptable to both clients who attend the PCMed Service and to clinicians.

Intervention—novel PCMed Service

The PCMed Telehealth Service at the Peter MacCallum Cancer Centre (PMCC) in Melbourne is the first of its kind in Australia. It is co-led by a medical oncologist (KAP) and a nurse practitioner (KLW). It is the only specialist service in Australia solely dedicated to delivering comprehensive, personalised information to women to facilitate their informed decision-making about using RRMeds. For women who are suitable and choose to take RRMeds, an initial prescription is provided. The woman, her referring clinician and PCP are offered access to ongoing support to promote sustained use of RRMeds. The PCMed Service intervention is detailed in figure 2.

Delivered by telehealth, the PCMed Service is intended for women at substantially increased risk of a first breast cancer who are interested in considering taking medications to reduce their risk. Referrals are accepted from clinicians from the PMCC and surrounding services who routinely see women at increased risk of breast cancer. These referring clinics will henceforth be referred to as 'catchment clinics'; they include Late Effects, Breast Surgical and Familial Cancer Clinics at PMCC and the Familial Cancer Clinic at the Royal Melbourne Hospital. Referrals are also accepted from clinics external to the catchment clinics and from PCPs. Women who attend the PCMed Service are referred to as clients.

Aims

The overarching aim is to evaluate the effectiveness and process of implementing this new clinical service.

The primary aim is:

- To determine whether the PCMed Service is associated with an increased use of RRMeds by women who attend catchment clinics, compared with use by similar women who attended catchment clinics before the implementation of the PCMed Service.

Secondary aims include:

- To describe the adoption of the PCMed Service by women who attend catchment clinics. Specifically, the proportion of eligible women who attend the PCMed Service following a catchment clinic appointment where the PCMed Service is discussed.
- To determine the uptake of RRMeds for all clients who attend the PCMed Service and the associated characteristics.
- To explore the reasons for not taking up RRMeds and the associated characteristics.
- To explore the acceptability of the PCMed Service to clients.
- To explore the acceptability of the PCMed Service to clinicians.
- To determine the feasibility and fidelity of the PCMed Service intervention and any adaptations required.
- To evaluate the cost of delivering the PCMed Service from the perspective of the healthcare provider.

METHODS AND ANALYSIS

Study design

The process evaluation described here is evaluating this new complex intervention (the PCMed Service) using a mixed methods (qualitative and quantitative) approach. The study has prospective and retrospective components.

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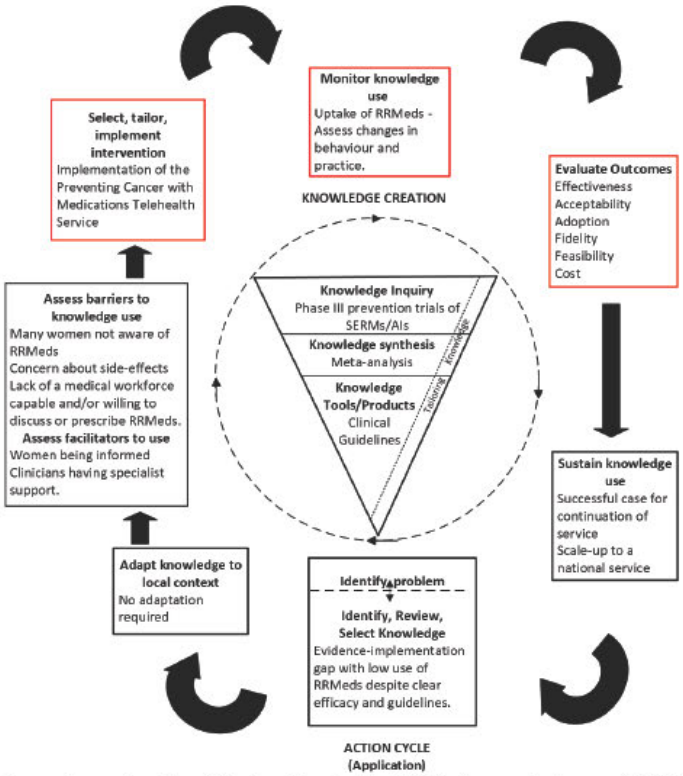

Figure 1 Knowledge creation, as it pertains to the benefits and risks of RRMeds, supports the use of RRMeds as a standard of care. Barriers and facilitators to the uptake of RRMeds have been identified. This research focuses on the steps highlighted in red. AIs, aromatase inhibitors; RRMeds, risk-reducing medications; SERMs, selective oestrogen receptor modulators.

Recruitment to the PCMed Service and study

Prior to the commencement of the PCMed Service, clinicians working in the catchment clinics, including breast care nurses, were informed of the PCMed Service and its concurrent evaluation. Resources were developed and placed in the catchment clinics. These include a client brochure and a clinician fact sheet that describes the Service, eligibility criteria and the referral process.

Eligible women are actively recruited for the PCMed Service from catchment clinics by the nurse practitioner (KLW), who reviews the electronic medical records of women in advance of their catchment clinic appointment and identifies those who are potentially eligible for the PCMed Service. Clinicians seeing these women are reminded by KLW of the PCMed Service and asked to provide eligible women with a client brochure and to refer them to the PCMed Service if appropriate.

Inclusion criteria for the study population

Women are eligible if they have no personal history of invasive breast cancer or ductal carcinoma in situ, are aged between 20 and 70 years, and are at substantially increased risk for future breast cancer. Substantially increased risk, for the purpose of this study, is defined as a remaining lifetime risk of at least 20%, or risk in the next 10 years of at least 5%[18] using any of the three validated risk prediction models commonly used in Australia (ie, iPrevent,[32] Tyrer Cuzick[33 34] or the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA),[35 36]) or a personal history of lobular carcinoma or atypical hyperplasia, or previous thoracic irradiation before age 35 years (and given at least 5 years prior).[37]

Clinicians who see eligible women in the catchment clinics and/or refer to the PCMed Service during the study period will also be recruited to the study to assess the acceptability of the PCMed Service intervention.

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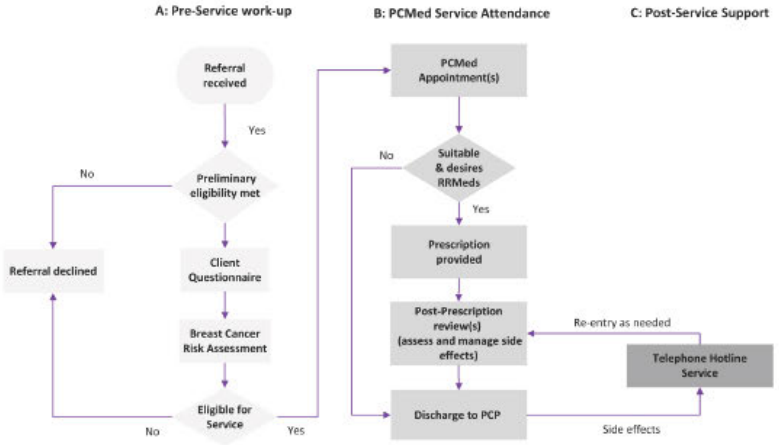

Figure 2 (A) Preservice work-up: referrals are reviewed by the nurse practitioner (KLW). Women who meet preliminary eligibility criteria are sent a questionnaire (regarding demographics, social and medical history, breast cancer risk factors and willingness to consider RRMeds). Breast cancer risk is determined using validated risk prediction models/tools such as iPrevent,[32] Tyrer Cuzick,[33 34] or the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA)[35 36],unless there is a history of thoracic radiotherapy, in which case risk is estimated using published data.[37] For women referred from services external to catchment clinics, the iPrevent[32] prediction model is applied. Eligible women are offered an appointment in the Service. (B) PCMed Service attendance: in the initial telehealth appointment, clients receive a discussion of their personalised breast cancer risk. If a client desires, their 10-year, 20-year or remaining lifetime risk is conveyed as a numerical value. The names and mechanism of action of potentially appropriate RRMeds, the absolute risk reduction that could be achieved with RRMeds, and other benefits and any potential adverse effects of RRMeds are discussed. Client understanding of the information received is assessed. A second consultation is offered for clients requiring more time to decide on whether to take RRMeds. Clients who desire RRMeds receive a prescription and are booked for review in 8–10 weeks to assess and manage any side effects. If tolerating the RRMed, care is transferred to the PCP with additional information and instructions to continue management. (C) Postservice support: a hotline telephone service is provided for clinicians and clients to address any concerns relating to side effects, and additional appointments are made if required. PCMed, Preventing Cancer with Medications; PCP, primary care physician; RRMeds, risk-reducing medications.

Exclusion criteria for the study population

Women who have ever taken RRMeds for breast cancer prevention, or who have had a bilateral mastectomy, are ineligible. The PMCC has an established, highly specialised, multidisciplinary Risk Management Clinic[38] for women who carry (or who are at 50% risk of carrying) a pathogenic variant in a high-risk breast cancer predisposition gene (such as *BRCA1*, *BRCA2*, *PALB2* or *TP53*). Women who are eligible for the PMCC Risk Management Clinic are thus not eligible to attend the PCMed Service (or for this study). Some women with pathogenic variants in moderate-risk genes such as *CHEK2* and *ATM* are eligible for referral to the PCMed Service if they are deemed not eligible for the PMCC Risk Management Clinic.

Clinicians from catchment clinics will be excluded from the study if they are no longer working in the clinic at the end of the study period.

Outcome measures and data collection

Effectiveness of the PCMed Service intervention (primary aim)

The use of RRMeds by similar women before and after the implementation of the PCMed Service will be assessed 12 months after attendance at a catchment clinic. To determine the use of RRMeds prior to the implementation of the PCMed Service, a retrospective chart review is collecting data on consecutive eligible women (historical controls) who attended catchment clinics prior to the commencement of the PCMed Service. For women who attended familial cancer centre catchment clinics, the BOADICEA risk prediction model[35 36] is routinely applied, and each individual's risk is documented in their medical record. Other catchment clinics did not consistently apply risk prediction models. Therefore, the first author (KLW) applies one of the three prediction models at the time of data collection (with the choice of prediction model dependent on which is most appropriate based on the available data). First author (KLW) extracts the following data from the medical record for each woman: date of birth, indigenous status, country of birth, socioeconomic status, marital status, parity, education level, whether an interpreter was required, catchment clinic attended, type of clinician seen in the catchment clinic (eg, geneticist, medical oncologist), date of last

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catchment clinic consultation, whether RRMeds were discussed at that consultation and whether the client had commenced RRMeds within 12 months after the last consultation in the catchment clinic. Comparable data are being collected for the prospective group of women who attend the catchment clinics after commencement of the PCMed Service, regardless of whether they attend the new PCMed Service. For historical controls and those in the prospective cohort, if the first author, KLW, is unable to find evidence of a discussion about RRMeds in the woman's electronic medical record (clinic notes and correspondence), it is presumed that RRMeds were not commenced. It is noted that not all clinicians might routinely document everything discussed in a consultation. Therefore, the prescription history in the medical record is also reviewed. If a discussion about RRMeds is documented, or the prescription history indicates that a RRMed was prescribed, women are contacted to ascertain if RRMeds were commenced within 12 months of that consultation.

Effectiveness of the PCMed Service (secondary aims)

Secondary outcomes include the self-reported use of RRMeds by clients and the reason for not using RRMeds at 6 months after the PCMed Service consultation, where a decision was made regarding whether or not to take RRMeds. These data are obtained through a follow-up telephone call and include (where relevant) whether RRMeds were commenced, the medication commenced, the date of commencement, whether RRMeds were ceased and the reason for ceasing. For women who did not commence RRMeds, data are collected on the reason(s) for not using RRMeds, their intent to use RRMeds in the future, the reason for not intending to use RRMeds (if relevant) and factors that would facilitate use of RRMeds.

Adoption of the PCMed Service

To what extent the PCMed Service intervention is adopted will be measured by the attendance of clients at the Service within 6 months following a documented discussion about the Service at the relevant catchment clinic.

Acceptability of the Service

Quantitative and qualitative data are collected to explore acceptability for both clients and clinicians. Acceptability of the Service to clients is measured using a brief survey based on the theoretical framework of acceptability (TFA).[39] This comprises seven constructs (affective attitude, self-efficacy, burden, intervention coherence, perceived effectiveness, ethicality and opportunity cost) that guide the assessment of a client's perception of acceptability.[39] The survey is sent to clients 2–3 weeks after the PCMed Service consultation where a decision was made on whether to take RRMeds or not. If no response is received, two reminders are sent out at 1–2 weeks, and then 3–4 weeks after the initial invitation was sent.

A subset of clients are invited to participate in semistructured phone interviews after their last consultation in the PCMed Service. The purpose is to interrogate the acceptability survey findings of the PCMed Service for the study sample. An interview guide was developed based on the constructs of the TFA[39] thought to be most relevant to the PCMed Service intervention (ie, affective attitude, self-efficacy, burden, intervention coherence and perceived effectiveness). The interview guide was pilot tested on the first two clients, with questions subsequently refined.

A purposive sampling framework, using quota sampling,[40] will be used to ensure a representative cross-section of the sample population based on age (20–39 years, 40–55 years and >55 years), residence (defined using the Accessibility/Remoteness Index of Australia[41]) and referring clinic. To achieve 'theoretical saturation', it is estimated that a sample size of 15–20 clients is needed. However, saturation will be assessed through preliminary analysis, and data collection will continue until saturation is reached.[42 43]

Acceptability of the Service to clinicians will also be measured using a brief survey based on the TFA.[39] A subset of clinicians will be invited to participate in a semistructured telephone interview. A separate interview guide for clinicians, based on the constructs of the TFA,[39] has been developed which will further explore clinicians' experiences and the acceptability of the PCMed Service, including the referral process and any interactions with the Service. The interview guide will be piloted with the first clinician and refined as required. A purposive sampling framework has been devised, using quota sampling[40] to ensure a representative cross-section of clinicians based on clinic type, specialty and sex (male/female). Clinicians will be recruited until saturation of themes is reached, and it is estimated that a sample size of 15–20 clinicians is needed.[42 43]

Feasibility and fidelity of the PCMed Service

Data are being collected on the number of consultations delivered by telehealth versus face-to-face versus telephone; the type of clinician leading the consultation (nurse practitioner versus medical oncologist); the duration of each consultation; how many consultations were required before a prescription was written for RRMeds or the client was discharged from the Service; the number of clients who failed to attend the planned postprescription consultation and the self-reported reason; the number of additional postprescription reviews required. Utilisation of the telephone hotline service is also being recorded, including the number of calls received, the duration of each phone call, the caller type (eg, client, referring clinician and PCP) and the self-reported reason for the call. Any unintended consequences or deviations from the planned processes in the delivery of the PCMed Service are being documented by the nurse practitioner in a research journal as the events occur.

Cost of the PCMed Service

The cost to deliver the PCMed Service will be evaluated by comparing the average funding received per client who

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attended the PCMed Service with the average cost per client of providing the Service.

Services provided in Australian public hospitals, including PMCC, are funded using an activity-based funding model,[44] with payment based on service activity (ie, the number and type of service provided).[44] It uses national classifications for services and prices, all set in Australia by the Independent Health and Aged Care Pricing Authority.[45] The PCMed Service activity is captured in the PMCC database management systems. The Service activity will be extracted at the end of the study period, and a monetary figure allocated to the activity so the funding received can be calculated.

Data used to calculate the cost of service delivery will include the number and duration of all consultations (including calls to the hotline telephone service) and the attending clinician (nurse practitioner or medical oncologist). Cost per client consultation is calculated by multiplying the duration of the consultation by the hourly cost of the nurse practitioner or medical oncologist, respectively. A reasonable estimate of time spent by an administration officer per client (eg, making appointments, sending notifications) will be used. If an interpreter was used, the cost of the interpreter service will be added. Consultation cost, administration officer cost and interpreter cost will be summed into a total cost per patient.

Statistical considerations and analyses

Sample size considerations

The prospective sample size required for the primary outcome will depend on the uptake of RRMeds in the historical cohort. We will identify 100 consecutive historical controls. Based on Australian data,[25] we expect the uptake of RRMeds in the historical cohort to be 2%. Based on the clinical judgement of the investigators, we consider an increase from a baseline of 2%, prior to the commencement of the PCMed Service, to 20% after its implementation to be clinically significant enough to warrant implementation of this complex intervention. A prospective sample size of 57 clients who attend the PCMed Service from catchment clinics will be required to provide 80% power to detect a minimum change from 2% to 20% at a 5% significance level. To account for a possible 10% loss to follow-up, we will recruit a sample of 63 consenting clients from catchment clinics as they attend the PCMed Service. If the uptake of RRMeds (in the historical cohort) is substantially different from 2%, the prospective sample size will be adjusted.

Recruitment to the Service and the study commenced on 14 November 2023. To date, 100 women (historical controls) have been recruited to the retrospective component of the study and 278 women to the prospective component of the study. Thirty-five of the prospectively recruited women are eligible for the analysis of the primary outcome; the remainder are eligible for other outcome analyses.

Descriptive statistics

Categorical variables will be summarised using frequency and percentage. Continuous variables will be summarised using mean, SD and/or SE and range; or median, IQR and range as appropriate. Event data will be presented as point estimates with associated 95% CI presuming an underlying Poisson, negative binomial or zero-inflated distribution as appropriate.

Inferential statistics

Comparisons of event proportions between the prospective cohort and historical controls will be conducted using a χ^2 test, Fisher's exact test or linear mixed modelling as appropriate. Associations between participant characteristics and study outcomes will be explored using univariable and multivariable logistic, Poisson and/or negative binomial regression and/or linear mixed modelling as indicated. Multivariable models will be assessed for collinearity and interactions between explanatory covariates. Adjustment for clinic effects will be conducted by including the clinic identifier as a random effect in the aforementioned models. The final selection of test or model type will be confirmed on initial review of the collected data, with consideration given to the number of available events for each outcome. For all analyses, $p<0.05$ will be considered significant. All analyses will be undertaken using R statistical computing software, V.4.4.2[46] and/or Stata, statistical software, V.18.[47]

Analysis sets

The analysis for the primary outcome will include all clients from catchment clinics who attend the PCMed Service and historical controls. A sensitivity analysis will consist of all eligible women attending catchment clinics from the commencement of the study period, regardless of whether they attended the PCMed Service, and historical controls.

Analysis of the primary outcome

Effectiveness of the PCMed Service intervention

The proportion of women who start RRMeds within 12 months of a catchment clinic consultation will be summarised preimplementation and postimplementation of the PCMed Service using descriptive statistics. Event proportions will be compared using a χ^2, Fisher's exact test or linear mixed modelling as indicated. Differences in the distribution of confounders between the historical and prospective cohorts will be managed using univariable and multivariable logistic, Poisson and/or negative binomial regression and/or linear mixed modelling as indicated.

Analysis of secondary outcomes

Effectiveness of the PCMed Service

Descriptive statistics will be used to summarise the proportion of women (without contraindications[24]) who used RRMeds within 6 months of their PCMed Service consultation and the reason for non-use of RRMeds at 6 months

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after the initial consultation at PCMed Service, where a decision was made whether to take RRMeds.

Adoption of the PCMed Service

The proportion of women who attended each catchment clinic and who subsequently attended the PCMed Service within 6 months of a catchment clinic consultation will be summarised using descriptive statistics. Associations between participant characteristics and the likelihood of adoption will be analysed using logistic regression. This analysis will use the sensitivity analysis. Descriptive statistics will be used to summarise the reason(s) for declining a referral to the PCMed Service as an exploratory endpoint.

Acceptability of the Service

TFA metrics will be summarised using descriptive statistics. Interview recordings will be transcribed professionally, and transcripts checked against audio recording for accuracy and deidentification prior to analysis. Deidentified transcript data will be managed using NVivo[48] software. The lead analyst will familiarise themselves with the data by reading each transcript multiple times. Interview data will be analysed using an inductive approach informed by the TFA constructs. It is anticipated that the majority of the inductive codes will align with the TFA constructs, however, we will prioritise capturing women's experience with the service by starting with inductive coding. We will then map codes to the concepts of the TFA. To ensure academic rigour, two investigators will independently code the first six interviews and determine the level of agreement on coding the data. After interview 15, new interviews will be reviewed in light of the coding framework to determine when saturation of the main themes is achieved. The final coding framework will be reviewed by all investigators.

Feasibility and fidelity of the PCMed Service

Evaluation of service delivery will be summarised using descriptive statistics. The research journal will be analysed using the framework for reporting adaptations and modifications-expanded.[49]

Cost of the PCMed Service

The cost will be evaluated by determining the difference between the funding received and the cost of service delivery for clients attending the PCMed Service. A sensitivity analysis will consist of calculating the difference between funding received and the cost of service delivery for two client subgroups: clients attending the PCMed Service for consultation but who decline RRMeds, and clients attending the PCMed Service who take up RRMeds. Funding received and the cost of service delivery will be summarised using descriptive statistics.

DISCUSSION

The findings of this process evaluation will provide valuable insights into the effectiveness of the novel PCMed Service in initiating the appropriate use of RRMeds for women at increased risk of a first breast cancer. If successful, the intervention could ultimately have a substantial impact on increasing RRMeds usage, which has been shown to reduce the incidence of oestrogen receptor-positive breast cancer by up to 60%.

Our study will also explore the factors influencing the adoption and acceptability of the PCMed Service for both clients who attend the Service and clinicians. This is crucial for understanding the barriers to service engagement. Previous research has highlighted the lack of confidence among primary care providers in discussing and prescribing RRMeds, suggesting that a telehealth service with specialist support may be an effective solution. By assessing both qualitative and quantitative data on acceptability, we aim to identify strategies to improve uptake of the PCMed Service and to refine its delivery.

Furthermore, evaluating the feasibility, fidelity and cost of the PCMed Service is vital to ensure its sustainability and to inform future implementation strategies and future economic evaluations. We expect that the PCMed Service, if successful, could be replicated in other regions, offering an accessible and scalable model for breast cancer prevention.

In conclusion, this evaluation of the PCMed Service will contribute to closing an important evidence–implementation gap in breast cancer prevention and could inform future public health strategies for women at increased risk of the disease.

PATIENT AND PUBLIC INVOLVEMENT

We are grateful for the contribution of our consumer representative (SMi) and representatives from the local Primary Health Network. SMi assisted in the design of the intervention (PCMed service), development of the research protocol, review of study materials for participants, (including a patient information consent form, the TFA surveys for women and clinicians, correspondence with clients, and client resources) and testing of all processes for clients following receipt of referral to the PCMed Service. The Service and planned concurrent evaluation were presented to the Primary Care and Population Health Committee at PMCC, and we are grateful for the valuable input received from representatives on this committee. A representative from Primary Health Network has reviewed all correspondence developed for PCPs.

ETHICS AND DISSEMINATION

Ethics approval for this study has been granted by the PMCC Human Research Ethics Committee (EC00235): HREC/101142/PMCC.

Retrospective and prospective data collected on clients attending catchment clinics are obtained under a waiver of consent, as approved by the PMCC Human Research Ethics Committee. This is because it is impractical to

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consent these women, and there is sufficient protection of their privacy and confidentiality as names will not be used, and reporting of the study results will not allow individuals to be identified. Clients attending the catchment clinics who then attend the PCMed Service have the option to 'opt out' of having their data collected and analysed. All clients attending the PCMed Service, regardless of the referring clinic, are invited to participate in the study (including a survey, follow-up telephone calls and an optional interview) via a patient information and consent form (online supplemental file 1). Clinician consent to use data collected about them is implied if the clinicians return the survey and/or participate in the interview.

Manuscripts detailing research findings will be submitted to peer-reviewed journals for publication. Data will be presented at national and international conferences and scientific meetings. In addition, results will be disseminated to stakeholders through relevant specialty networks (by way of newsletters, webinars and educational meetings). For example, breast surgeons will be notified through the Breast Surgeons of Australia and New Zealand Society[50] by way of an electronic newsletter. Family Cancer Clinicians will be notified through the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer website.[51] Australian PCPs will be notified through the Royal Australian College of General Practitioners[52] by way of educational webinars.

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Contributors KLW, the primary author, led the writing of this manuscript by producing drafts, responding to edits and suggestions by the coauthors and editing the paper for final submission. All authors contributed to the conception and design of the intervention (PCMed Service) and concurrent evaluation. KAP obtained funding for the study and is responsible for the overall content as guarantor. All authors reviewed the work and approved the final version of the manuscript. All authors are accountable for all aspects of the work and KAP is responsible for the overall content as guarantor.

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Competing interests KAP has received funding for an unrelated clinical trial, paid to the Peter MacCallum Cancer Centre, from AstraZeneca. SMi has received payment from Volpara Health Australia for work on education material and payment in kind for consumer representative activities at the Peter MacCallum Cancer Centre.

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2.9 Summary

This chapter, supported by Appendix 1, outlines the methodological approach used to evaluate the PCMed Service within the scope of this thesis. The following chapters present the results of this evaluation. Chapter 3 specifically describes the baseline use of RRMeds in a historical cohort of women attending Catchment Clinics prior to implementation of the PCMed Service.

PART II: RESULTS

Chapter 3: Pre-Implementation Uptake of RRMeds

3.0 Introduction

This chapter presents the findings from the retrospective chart review undertaken to address Aim 1 of this thesis: to determine RRMed use among eligible women who attended Catchment Clinics prior to the implementation of the PCMed Service. These findings contextualise local practice before service implementation and establish a pre-implementation baseline against which RRMed uptake among women attending Catchment Clinics post-implementation of the PCMed Service can be evaluated in the future, once data are mature.

3.1 Results

3.1.1 Study population (historical control sample) and patient characteristics

Between November 14, 2022, and April 5, 2023, 100 consecutive eligible participants in the historical control sample attended a Catchment Clinic and were included in the analysis. Participant characteristics are presented in Table 3.1.

Participants were aged between 21 and 70 years, with a mean age of 45.8 years (SD 12.1years) and a median age of 47 years (IQR 37, 55). Most participants were born in Australia (n=83, 83%), and none required an interpreter. Among participants with available data, almost all were recorded as non-Indigenous, with 1 participant recorded as Aboriginal.

Marital status was incompletely recorded; however, among participants with available data, 64.1% were married or in a de facto relationship. Socioeconomic status was derived from residential postcode data using the Australian Bureau of Statistics Socio-Economic Indexes for Areas (SEIFA), specifically the Index of Relative Socio-economic Disadvantage (IRSD).[105] Most participants (n=77, 77%) resided in the two least disadvantaged quintiles (Q4 and Q5).

Individual risk factors are also summarised in Table 3.1. Risk factors were not mutually exclusive; participants could therefore have more than one risk factor. The most common recorded risk factor was any family history of breast cancer, documented in 73 participants (73%). This category included all participants with a recorded family history of breast cancer, including those who also had other risk factors such as LCIS or ADH; it should therefore not be interpreted as family history alone. Other recorded risk factors included thoracic irradiation in 19 participants (19%), LCIS in 5 participants (5%), and ADH in 2 participants (2%). Among the 5

participants with LCIS, 2 also had a recorded family history of breast cancer, 2 did not, and family history was not recorded for 1 participant. Among the 2 participants with ADH, 1 also had a recorded family history of breast cancer.

Mean 10-year breast cancer risk was 7.7% (SD 5.6), calculated on 81 participants; 62 who met the 10-year risk eligibility criterion (≥5%) and 19 who had previous thoracic irradiation. For participants who had previous thoracic irradiation, 10-year risk estimates were derived from Swerdlow et al.,[38] which did not provide residual lifetime risk estimates. Mean residual lifetime risk was 22.4% (SD 8.2) calculated on the remaining 19 participants, none of whom had prior thoracic irradiation. Of these, 15 did not meet the 10-year risk eligibility criterion of at least 5% and 4 participants had no 10-year risk estimate documented.

As this was a retrospective chart review, data completeness was dependent on documentation within the electronic medical record. Some variables, including education level, were not routinely captured. Missing data were present for several variables, including Indigenous status (n=19, 19%), marital status (n=22, 22%), parity (n=18, 18%), and family history (n=2, 2%), as shown in Table 3.1. These limitations should be considered when interpreting the participant characteristics of the sample.

Table 3.1. Participant characteristics on historical control sample (n=100)

Characteristic	**Category**	**n (%) or mean +/-(SD)**
Age	Mean (SD)	45.8 (12.1)
	Median (IQR)	47 (37, 55)
	Range	21,70
Country of Birth	Australia	83 (83)
	Not Australia	16 (14)
	Not recorded	1 (1)
Need for Interpreter	Yes	0 (0)
	No	100 (100)
Indigenous status	Non-Indigenous	80 (80)
	Aboriginal	1 (1)
	Torres Strait Islander	0 (0)
	Aboriginal and Torres Strait Islander	0 (0)
	Not recorded	19 (19)
Marital Status	Single	25 (25)
	Married or de facto	50 (50)
	Divorced / separated	3 (3)
	Widowed	0 (0)
	Not recorded	22 (22)
Socioeconomic Status (SEIFA IRSD)	Q1 (most disadvantaged)	2 (2)
	Q2	9 (9)
	Q3	12 (12)
	Q4	23 (23)

	Q5 (least disadvantaged)		54 (54)
Parity	0		27 (27)
	1		18 (18)
	2		24 (24)
	3		10 (10)
	4		3 (3)
	Not recorded		18 (18)
Individual risk factors	Any family history of breast cancer	Yes	73 (73)
		No	25 (25)
		Not recorded	2 (2)
	History of LCIS		5 (5)
	History of ADH		2 (2)
	History of ALH		0 (0)
	History of thoracic irradiation		19 (19)
Multiple risk factors (overlapping categories)*	Family history and LCIS	Yes	2 (2)
		No	2 (2)
		Not recorded	1 (1)
	Family history and ADH		1(1)
	Family history and ALH		0 (0)
	Family history and thoracic irradiation	Yes	0 (0)
		No	18 (18)
		Not recorded	1 (1)
10-year breast cancer risk	n=81*		7.7 (5.6)
Residual lifetime risk	n=19**		22.4 (8.2)

Footnote:
Unless otherwise stated, percentages are based on the total sample denominator (n=100). Risk factor categories are not mutually exclusive; therefore, participants may appear in more than one row under individual risk factors. “Any family history of breast cancer” includes all participants with a recorded family history, including those with LCIS, ALH, ADH, or thoracic irradiation. Family history may include first- or second-degree relatives.
SEIFA = Socio-Economic Indexes for Areas; IRSD = Index of Relative Socio-economic Disadvantage; LCIS = lobular carcinoma in situ; ADH = atypical ductal hyperplasia; ALH = atypical lobular hyperplasia; IQR = interquartile range; SD = standard deviation. *10-year breast cancer risk was calculated for participants who either had prior thoracic irradiation, which precludes calculation of residual lifetime risk, or met the 10-year risk eligibility criterion of ≥5%.
**Residual lifetime risk was calculated for participants who did not meet the 10-year risk eligibility criterion, or where 10-year risk data were unavailable, and who had no prior thoracic irradiation.

3.1.2 Catchment Clinic attendance and clinician discipline

Of the 100 participants in the historical control sample, 40 (40%) attended PMCC Breast Surgical Oncology Clinic, 25 (25%) attended the RMH Familial Cancer Centre, 20 (20%) attended

the PMCC Familial Cancer Centre, and 15 (15%) attended the PMCC Late Effects Clinic. Table 3.2. summarises Catchment Clinic attendance and clinician discipline.

Clinician discipline varied by clinic, with the PMCC Breast Surgical Oncology Clinic exclusively surgeon-led, the Familial Cancer Centres involving a mix of medical oncologists, geneticists, and genetic counsellors, and the PMCC Late Effects Clinic involving radiation oncologists and haematologists.

Table 3.2: Catchment Clinic attended and clinician discipline by participant

Catchment Clinic	**Clinician Discipline**	**Participants n (%)**
PMCC Breast Surgical Oncology Clinic	Breast Surgeon	40 (100)
RMH Familial Cancer Centre	Geneticist Medical Oncologist Genetic Counsellor Breast Surgeon	3 (12) 14 (56) 8 (32) 0 (0)
PMCC Familial Cancer Centre	Geneticist Medical Oncologist Genetic Counsellor	5 (24) 7 (33) 8 (38)
Late Effects Clinic	Radiation Oncologist Haematologist	9 (64) 6 (36)
Footnote: Percentages are calculated within clinic unless otherwise stated. PMCC = Peter MacCallum Cancer Centre; RMH = Royal Melbourne Hospital.		

3.1.3 Documented discussion and use of risk-reducing medications

In this historical cohort, a discussion regarding RRMeds was documented in the medical records of 4 participants (4%). Documented discussion by clinic, together with RRMed prescribing within 12 months of the Catchment Clinic consultation, is summarised in Table 3.3. All documented discussions about RRMeds occurred in the Familial Cancer Centres, including 3 participants at the PMCC Familial Cancer Centre and 1 participant at the RMH Familial Cancer Centre. No documented discussions regarding RRMeds were identified among participants attending the PMCC Breast Surgical Oncology Clinic or the PMCC Late Effects Clinic. All consultations in which an RRMed discussion was documented were conducted by medical oncologists.

Within 12 months of the Catchment Clinic consultation, 1 participant (1.0%) in the historical control sample was prescribed an RRMed.

Table 3.3: Documented risk-reducing medication discussion and use by Catchment Clinic within 12 months in the historical control sample (n=100)

Clinic	Participants attendees, n	Documented RRMed discussion, n (%)	RRMed use within 12 months, n (%)
PMCC Breast Surgical Oncology Clinic	40	0 (0)	0 (0)
RMH Familial Cancer Centre	25	1 (4)	0 (0)
PMCC Familial Cancer Centre	20	3 (15)	1 (1)
PMCC Late Effects Clinic	15	0 (0.0)	0 (0)
Total sample	100	4 (4)	1 (1)

Footnote:
Documented RRMed discussion are calculated using the number of participants attending each clinic as the denominator. The percentage for RRMed prescribed within 12 months in the total row is calculated using the total sample denominator (n=100).
RRMed = risk-reducing medication; PMCC = Peter MacCallum Cancer Centre; RMH = Royal Melbourne Hospital.

3.2 Summary of Key Findings

In this retrospective chart review of 100 consecutive eligible participants in the historical control sample, documentation of RRMed discussions prior to implementation of the PCMed Service was uncommon. Only 4 participants (4.0%) had a RRMed discussion documented in the medical record. All documented discussions occurred within the Familial Cancer Centres at RMH or PMCC and were conducted by medical oncologists. Within 12 months of the Catchment Clinic consultation, 1 participant (1.0%) was prescribed an RRMed.

These findings indicate a very low, baseline documentation of RRMed discussion and prescribing prior to implementation of the PCMed Service. The following chapter (Chapter 4) presents data on RRMed uptake following implementation of the PCMed Service.

Chapter 4: Risk-Reducing Medication Uptake Among PCMed Service Attendees

4.0 Introduction

This chapter presents the findings of the interim analysis undertaken to address Aim 2 of this thesis: to determine the RRMed uptake among eligible participants attending the PCMed Service to 31 December 2024 who had no contraindications to use. Uptake was assessed 6 months after the decision consultation, defined as the consultation at which a decision regarding RRMed use was made. Owing to the small sample size available for this interim analysis, participant characteristics associated with uptake are presented descriptively, as no formal inferential analyses of factors associated with uptake were conducted.

4.1 Results

4.1.1 Participant flow, contraindications and participant characteristics

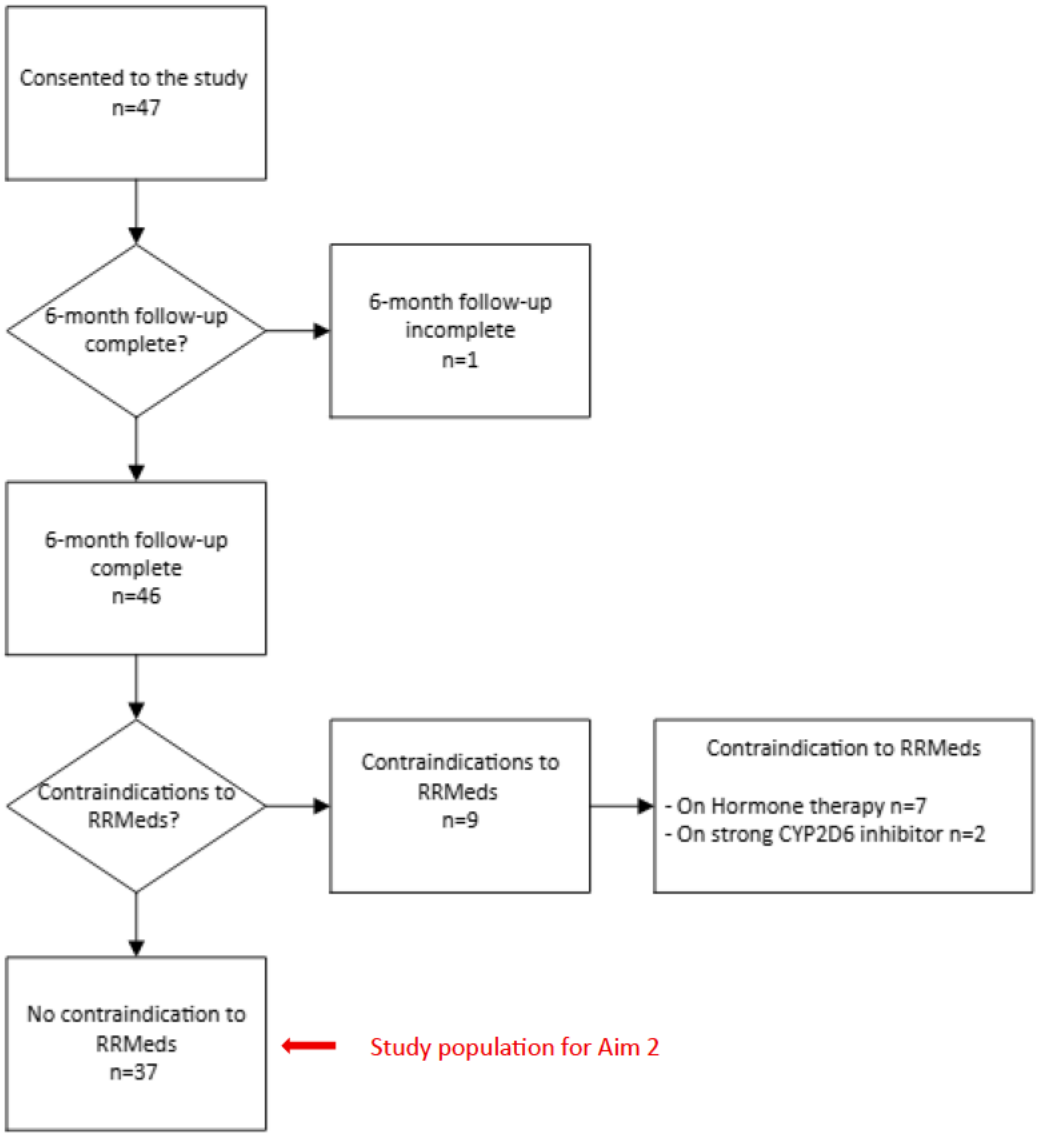
Between December 2023 and December 2024, 57 eligible women attended the PCMed Service, of whom 47 (82%) consented to participate in the study. This time period was selected to ensure that all participants included in the interim analysis had the opportunity to complete 6 months of follow-up before the interim analysis data lock at 30 June 2025. One participant was excluded because 6-month follow-up had not been completed at the time of data extraction, leaving 46 participants with outcome data.

Of these, 37 participants had no contraindications to RRMed use at the time of the decision consultation and formed the primary analytical sample for this interim analysis. Contraindications at the time of the decision consultation are presented in Table 4.1, and participant flow is shown in Figure 4.1.

Table 4.1: Contraindications to risk-reducing medication use at the decision consultation (n=9)

Contraindication to RRMed	Participants n=9 n (%)
Hormone Use	7 (77.8)
Concurrent use of a strong CYP2D6 inhibitor	2 (22.2)
Footnote: Contraindications were defined on page 2 of the published study protocol, reproduced in Chapter 2, page 41).	

Figure 4.1 Participant Flowchart for Aim 2



The analysis for this chapter focuses on the 37 participants with no contraindication to RRMed use. A summary of participant characteristics for this group is provided in Table 4.2. Additional descriptive characteristics for all participants with 6-month outcome data (n=46) are presented in Appendix 3 (Table A3.1).

Participants included in the interim analysis were aged 33 to 67 years, with a mean age of 52.0 years (SD 9.1). Most participants were born in Australia (32/37, 86%) and most did not require an interpreter (36/37, 97%). Most participants were married or in a de facto relationship (28/37, 76%), and almost half had completed a university degree (18/37, 49%). Most participants resided in relatively advantaged areas, with (27/37, 73%) living in the 2 least disadvantaged regions (Q4 and Q5).

Individual risk factors are also summarised in Table 4.2. Risk factors were not mutually exclusive; therefore, participants could have more than one risk factor recorded. The most common recorded risk factor was any family history of breast cancer (25/37, 68%), followed by thoracic irradiation (10/37, 27%), LCIS (7/37, 19%), ALH (3/37, 8%), and ADH (2/37, 5%). Approximately one-third of participants were nulliparous (12/37, 33%).

Among participants with available risk estimates, mean 10-year breast cancer risk was 11.6% (SD 8.2). Residual lifetime risk was able to be assessed for 27 participants, with a mean of 35.2% (SD 15.7). The remaining 10 participants had a history of prior thoracic irradiation, which precluded calculation of residual lifetime risk.

Table 4.2: Baseline characteristics of participants with no contraindications to risk-reducing medications (n=37)

Characteristic	**Category**	**Prospective sample n = 37**
Age	Mean (SD)	52.0 (9.1)
	Median (IQR)	52 (14)
	Range	33,67
Country of birth, n (%)	Australia	32 (86.5)
	Not Australia	5 (13.5)
Indigenous status, n (%)	Non-Indigenous	37 (100)
	Aboriginal	0 (0)
	Torres Strait Islander	0 (0)
	Aboriginal & Torres Strait Islander	0 (0)
Need for interpreter, n (%)	Yes	1 (2.7)
	No	36 (97.3)
Marital status, n (%)	Single	5 (13.5)
	Married/de-facto	28 (75.7)
	Divorced/separated	3 (8.1)
	Widowed	1 (2.7)
Education level, n (%)	Never attended school	0 (0)
	Year 11 or below	1 (2.7)
	Year 12 or equivalent	7 (19)
	TAFE, vocational	10 (27)
	University degree	18 (48.6)
	Prefer not to say	1 (2.7)
Socioeconomic Status (SEIFA), n (%)	Q1 (most disadvantaged)	2 (5.4)
	Q2	2 (5.4)
	Q3	6 (16.2)
	Q4	13 (35.1)
	Q5 (least disadvantaged)	14 (37.8)
Parity, n (%)	0	12 (32.4)
	1	6 (16.2)
	2	10 (27)
	3	9 (24)
Individual risk factors*, n (%)	Any family history of breast cancer	25 (67.6)

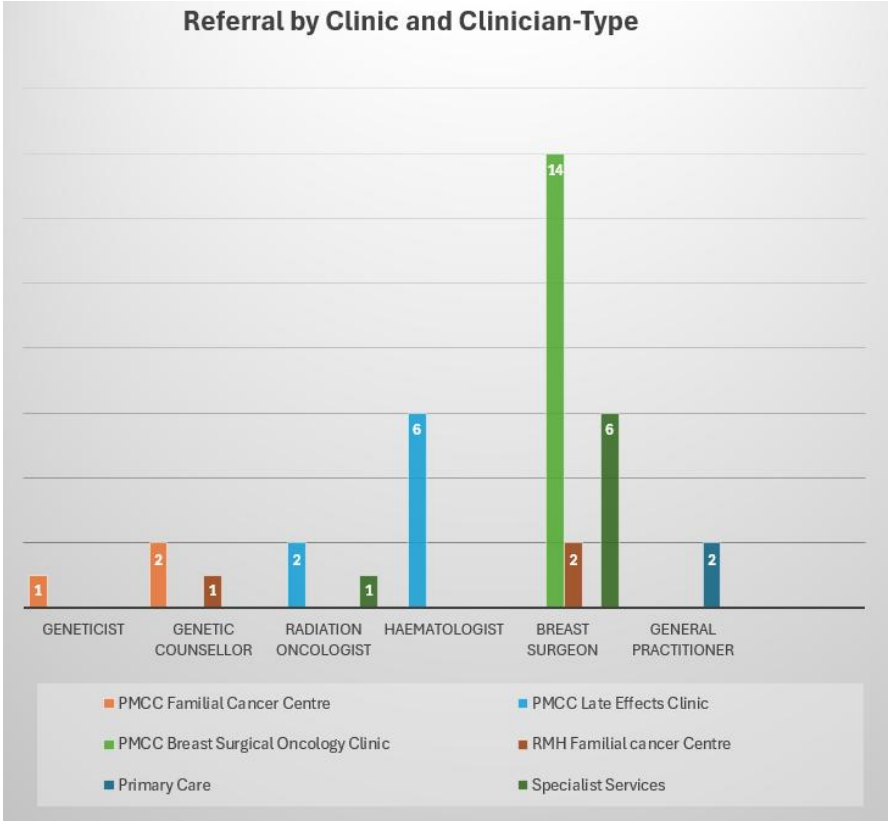
	History of LCIS	7 (18.9)
	History of ADH	2 (5.4)
	History of ALH	3 (8.1)
	History of thoracic irradiation	10 (27)
Multiple risk factors*, n (%)	Family history and LCIS	5 (13.5)
	Family history and ADH	1(2.7)
	Family history and ALH	1(2.7)
	Family history and thoracic irradiation	3 (8.1)
Number of first-degree relatives with breast cancer, n (%)	0	7 (18.9)
	1	12 (32.4)
	2	3 (8.1)
	3	3 (8.1)
10-year breast cancer risk, mean (SD)		11.6 (8.2)
Residual lifetime risk, mean (SD)	In participants assessed n=27	35.2 (15.7)
	Unable to be assessed** n=10	

Footnote:
*Risk factor categories are not mutually exclusive; participants may appear in more than one row under individual or multiple risk factors. Unless otherwise stated, percentages are based on the total sample denominator (n=37). 'Any family history' may include first- or second-degree relative. The number of first-degree relatives with breast cancer is presented for the full sample; a value of 0 indicates no affected first-degree relatives and may include participants with no family history or family history limited to second-degree relatives**.**
**Participants not able to be assessed for residual lifetime risk had prior thoracic irradiation, which precluded calculation of this estimate.

4.1.2 Referral Characteristics

Referral source and referring clinician type are shown in Figure 4.2. Most participants were referred from the PMCC Breast Surgical Oncology Clinic (14/37, 38%), and the most common referring clinician type was a breast surgeon (22/37, 59%). Referrals from the PMCC Familial Cancer Centre and the RMH Familial Cancer Centre were less common (3/37, 8% each), and referrals from primary care were least common (2/37, 5%), noting that the PCMed Service had not been promoted to primary care at commencement of this study.

Figure 4.2: Referral source and referring clinician-type



4.1.3 Risk-reducing Medication (RRMeds) Uptake

Among the 37 participants with no contraindications to RRMed use at the time of the decision consultation, 20 (54.1%) commenced a RRMed within 6 months.

For this analysis, participants were classified as being at average, moderate, or high risk of breast cancer using their 10-year risk estimate and the Royal Australian College of General Practitioners (RACGP) guideline.[45] The RACPG guideline defines moderate risk as a 1.5- to 3-fold increase in risk, and high risk as a greater than 3-fold increase in risk, relative to the age-specific population risk.[45] This approach was employed because it enabled descriptive comparison of RRMed uptake between moderate-risk and high-risk participants. This distinction was important for the current analysis and supports comparison with published literature using similar risk categories. In contrast the American Society of Clinical Oncology (ASCO)[43] and National Comprehensive Cancer Network (NCCN) guidelines,[44] identify women at increased risk for the purpose of considering RRMeds but do not provide an equivalent distinction between moderate-risk and high-risk groups. The National Institute for Health and Care Excellence (NICE) criteria[103] were also not directly applicable because this study sample included participants with a history of previous thoracic irradiation for whom the risk

assessment was estimated using published risk data[38] rather than the risk assessment tools specified in the NICE guideline.[103]

Using the RACGP classification,[45] 1 participant (2.7%) was categorised as being at average risk, 15 participants (40.5%) as moderate risk, and 21 participants (56.8%) as high risk. The participant classified as average risk met study eligibility due to a history of prior thoracic irradiation before age 35 years, with the irradiation delivered at least 5 years prior. However, a RRMed was not recommended or offered, as this would have been inconsistent with current clinical practice guidelines.[16, 43]

RRMeds uptake was highest among participants classified as high risk, with 17/21 (81.0%) initiating therapy within 6 months, compared to 3/15 (20%) participants classified as moderate risk. The distribution of individual risk factors among participants classified as moderate risk and high risk is shown in Figures 4.3 and 4.4, respectively.

Figure 4.3: Distribution of individual risk factors among participants classified as moderate risk

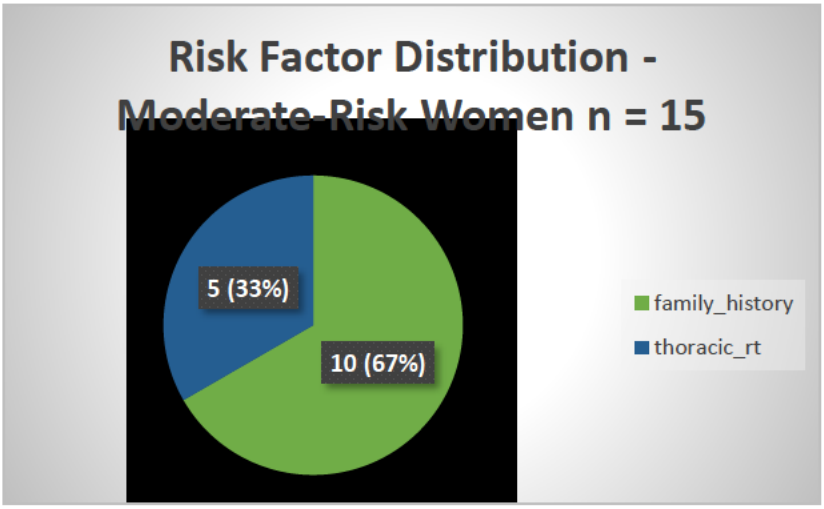
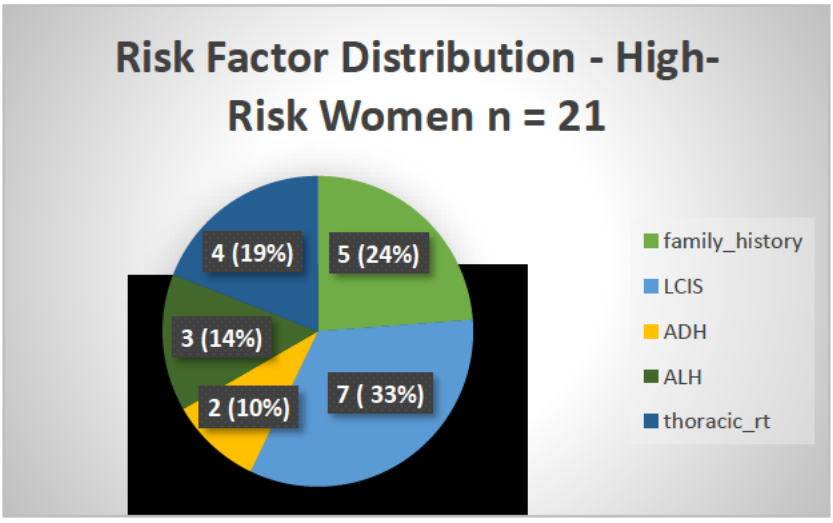


Figure 4.4: Distribution of individual risk factors among participants classified as high risk



Beyond risk category, descriptive differences in uptake were also observed across selected clinical subgroups. All participants with AH (5/5, 100%) initiated an RRMed within 6 months, and uptake was also high among participants with a personal history of LCIS (6/7, 85.7%). By contrast, uptake appeared broadly similar across most sociodemographic characteristics, including age, country of birth, marital status, education level, parity, and number of first-degree relatives with breast cancer. No clear descriptive differences were observed according to family history of breast cancer or history of thoracic irradiation. A full descriptive summary of participant characteristics stratified by RRMed uptake is provided in Table A3.2 in Appendix 3. Given the small sample size, these findings should be interpreted cautiously, as no formal inferential analyses of factors associated with uptake were undertaken.

4.2 Summary of key findings

In this interim analysis, RRMed uptake among PCMed Service attendees without contraindications to use was high, with 20 of 37 participants (54.1%) commencing a RRMed within 6 months of the decision consultation. Uptake was highest among participants classified as high risk and among those with benign proliferative breast diseases, including AH and LCIS. These patterns are consistent with published literature and are considered further in Chapter 6.

These findings are descriptive and should be interpreted cautiously due to the small sample size. No formal inferential analyses of factors associated with uptake were undertaken. Direct comparison with the historical control sample is also not made in this chapter because the analytic samples were defined differently.

Chapter 5: Delivery of the PCMed Service: Findings on Feasibility, Fidelity and Adaptations

5.0 Introduction

This chapter presents findings from an interim process evaluation of data relevant to Aim 3 of this thesis: to determine the feasibility and fidelity of the PCMed Service intervention, and to identify adaptations that occurred during implementation within a real-world clinical setting. The analysis includes service delivery data collected prospectively through to 30 June 2025.

Feasibility was defined as the extent to which the PCMed Service could be accommodated within routine clinical practice and delivered with available resources in a sustainable manner.[89, 106] Fidelity was defined as the extent to which the PCMed Service was delivered[88] according to the core components of the planned intervention described in Appendix 2. Findings are presented descriptively in this chapter, with broader interpretation of their implications for service sustainability, and future scale-up provided in Chapter 6.

To systematically capture adaptations and the barriers and facilitators to implementation relevant to Aim 3, a prospective research journal was maintained throughout implementation, from December 2023 to 30 June 2025. This research journal was completed monthly by the NP, who was both the clinician delivering the PCMed Service and the author of this thesis. This dual clinician-researcher role enabled direct observation and real-time documentation of how the PCMed Service was implemented and adapted in routine clinical practice.[90] However, it also necessitated reflexive acknowledgment that the author's involvement in service delivery may have influenced how implementation experiences were observed, recorded, and interpreted.[93]

The research journal structure was informed by two complementary implementation science frameworks. The Framework for Reporting Adaptations and Modifications–Expanded (FRAME)[107] guided systematic documentation of what was modified, when the modifications occurred, whether they were planned or reactive, and their alignment with the intended service model. The Capability, Opportunity, Motivation–Behaviour (COM-B) model within the Behaviour Change Wheel[108] was used to interpret barriers and enablers to implementation across capability, opportunity, and motivation domains. Research journal data were subsequently reviewed to identify implementation barriers, adaptations, and contextual factors that informed interpretation of the quantitative service-delivery findings reported in this chapter, consistent with mixed-methods intervention frameworks where qualitative process

data are deliberately integrated to explain quantitative outcomes.[90, 92] The full PCMed research journal is provided in Appendix 4.

5.1 Measures of Feasibility and Fidelity

Feasibility and fidelity were assessed using prospectively collected service-level data aligned with the published protocol and the planned intervention model described in Appendix 2. As outlined in Chapter 1, references to telehealth in this thesis refers to video-based consultations.

No a priori percentage thresholds were specified for assessing feasibility or fidelity. These domains were assessed using the indicators outlined below, with findings interpreted against the planned service model rather than pre-defined criteria for acceptable performance. Appendix 2 describes the intended intervention, not quantitative thresholds for feasibility or fidelity.

Feasibility was assessed through indicators reflecting whether the PCMed Service could be accommodated within existing clinical workflows and delivered with available resources. Given that the PCMed Service was designed as a predominantly telehealth-delivered model, demonstration of feasibility of telehealth delivery was considered fundamental to the viability of the intervention in routine practice. Feasibility indicators included:

- the extent to which the PCMed Service could be delivered by telehealth as the primary modality, including assessment of the proportion of consultations successfully conducted via telehealth and identification of circumstances requiring alternative delivery modes;
- consultation duration, interpreted in relation to standard institutional scheduling practices at PMCC, where new patient appointments are generally allocated 60 minutes and review appointments 30 minutes;
- number of consultations required before prescription or discharge;
- participant attendance at planned follow-up;
- frequency, duration, and clinical reasons for additional Post-Prescription Ad hoc Consultations; and
- volume, duration, and reasons for hotline telephone service use.

Fidelity was assessed through indicators reflecting adherence to core intervention components specified in the planned PCMed Service model, Appendix 2. These indicators included:

- consultation modality: predominant use of telehealth, with face-to-face delivery reserved for participants unable to access telehealth, and telephone consultations avoided where possible for planned consultations (Initial, Repeat, and Post-Prescription Consultations);
- provider type: delivery of most consultations by the NP, consistent with the planned clinician allocation described in Section 5.2;
- consultation pathway: delivery of the intended sequence including Initial Consultation, Repeat Consultation where required, and planned Post-Prescription Consultation following RRMed commencement;
- timing of planned Post-Prescription Consultation within 8–10 weeks of RRMed commencement, as specified in the intervention model; and
- attendance at the planned Post-Prescription Consultation which is interpreted as both a fidelity indicator (reflecting a specified component of the intervention) and a feasibility indicator (reflecting participant engagement and practical ability to complete follow-up).

Consultation modality, specifically telehealth delivery, was assessed as both a feasibility and fidelity indicator. As a feasibility indicator, it reflected whether the PCMed Service could function as a telehealth model in routine practice. As a fidelity indicator, it reflected adherence to the planned telehealth-first delivery mode specified in the intervention design. To emphasise the fundamental importance of demonstrating feasibility of telehealth delivery for the viability of this service model, consultation modality findings are presented first within the feasibility section (Section 5.3.4.1), with cross-reference to fidelity implications.

Hotline availability was not independently audited and therefore, hotline data were interpreted as evidence of use of the planned support pathway rather than as a standalone measure of fidelity.

Data were collected prospectively, with consultation type, modality, duration, and clinician involvement recorded in real time.

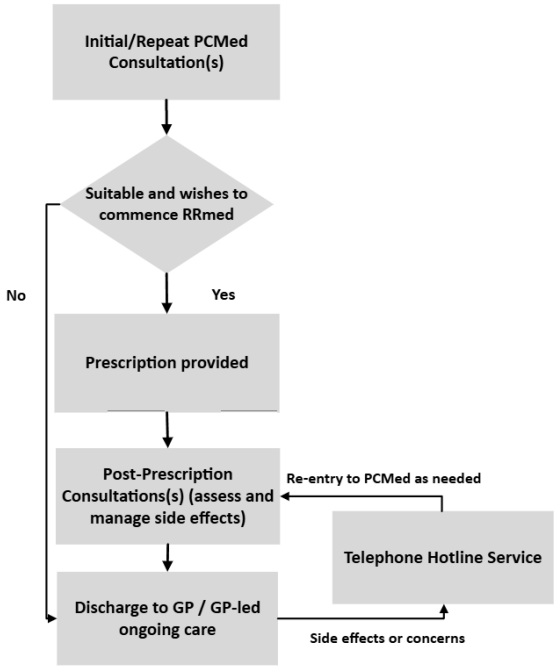
5.2 Planned PCMed Service Intervention

The planned PCMed Service intervention is described in Appendix 2 and summarised in Figure 5.1. The PCMed Service was designed as a collaborative NP-medical oncologist model, delivered predominantly by video-based telehealth, to facilitate informed decision-making and safe initiation of RRMeds for women at increased risk of breast cancer.

Most consultations were intended to be conducted by the NP, with a minority conducted by the medical oncologist. The NP was to review the referral and Pre-Service Questionnaire to determine the appropriate clinician for the Initial Consultation. Women with substantive medical problems or issues that might not be resolved by the NP were to be allocated to the medical oncologist.

The intended clinical pathway comprised an Initial PCMed Consultation, Repeat Consultation where required for women who remained undecided or required additional clinical review, RRMed prescribing for women who were suitable and wished to commence treatment, a planned Post-Prescription Consultation occurring 8–10 weeks following medication commencement, transfer to general practitioner (GP)-led ongoing care, and access to hotline telephone support with re-entry to the Service if clinically indicated.

Figure 5.1: PCMed Service Pathway



The intervention specified that the PCMed Service would be delivered primarily by video-based telehealth, and face-to-face consultations were to be arranged for women unable to attend by telehealth due to technological barriers, accessibility issues, or preference. Telephone consultations were to be avoided where possible for planned consultations, as they do not allow visual assessment and limit the quality of therapeutic communication, though telephone was recognised as appropriate for brief, problem-focused ad hoc reviews.

The PCMed Service saw its first women in clinic on 14 December 2023. Initially, the PCMed Service was not broadly advertised, with referrals received primarily received from the participating Catchment Clinics. As the PCMed Service became established, referrals were also received from clinicians external to the Catchment Clinics.

The following sections present findings on the feasibility and fidelity of this planned intervention. Results are organised to first provide an overview of service delivery (Section 5.3.1), then to describe the population and referral pathways (Sections 5.3.2–5.3.3), present findings on feasibility and fidelity (Sections 5.3.4–5.3.5), before concluding with implementation challenges and adaptations identified during service delivery (Section 5.3.6).

5.3 Results

5.3.1 Overview of Service Delivery

A prospective sample of all consenting, eligible participants (n=73) who attended the PCMed Service between 14 December 2023 and the data lock at 30 June 2025 was included in this interim process evaluation. Unlike the uptake analysis presented in Chapter 4, this evaluation did not require 6-month follow-up for inclusion and therefore utilised all available service-delivery data up to the interim data lock.

Over the study period, 153 consultations were delivered. These comprised Initial Consultations, Repeat Consultations for participants who remained undecided after the Initial Consultation, planned Post-Prescription Consultations scheduled after commencement of a RRMed, and unplanned Post-Prescription Ad hoc Consultations requested to address additional concerns or emerging clinical issues.

The characteristics of participants attending the PCMed Service and the referral pathways through which they accessed the PCMed Service are described in Sections 5.3.2 and 5.3.3, respectively, before presenting feasibility and fidelity findings.

5.3.2 Participant characteristics

A prospective sample of all consenting, eligible participants (n=73) who attended the PCMed Service between 14 December 2023 and the data lock at 30 June 2025. Unlike the uptake analysis presented in Chapter 4, this evaluation did not require 6-month follow-up for inclusion and therefore used all available service-delivery data up to the interim data lock.

Participant characteristics are presented to contextualise the population in which the PCMed Service was implemented. They are not primary feasibility or fidelity outcomes, but provide information relevant to interpreting service delivery, and consultation complexity.

Participant characteristics are summarised in Table 5.1. The process evaluation sample included 73 participants, with a mean age of 51.1 years (SD 9.2). Most participants were born in Australia, did not require an interpreter, were married or in a de facto relationship, and lived in areas of greater socioeconomic advantage. Individual risk factors were not mutually exclusive. The most common recorded risk factor was any family history of breast cancer, followed by thoracic irradiation and LCIS. These characteristics provide context for interpreting PCMed Service delivery but were not primary indicators of feasibility or fidelity.

Table 5.1 Baseline characteristics of all participants who attended PCMed Service between 14 December 2023 and the data lock at 30 June 2025 (n=73)

Characteristic	**Category/metric**	**Prospective sample n=73**
Age at PCMed Attendance	Mean (SD)	51.1 (9.2)
	Median (IQR)	52 (58,44)
	Range	29, 67
Sex	Female	73 (100.0)
Country of birth, n (%)	Australia	64 (87.7)
	Not Australia	9 (12.3)
Need for interpreter, n (%)	Yes	1 (1.4)
	No	72 (98.6)
Indigenous status, n (%)	Non-Indigenous	73 (100.0)
	Aboriginal	0 (0.0)
	Torres Strait Islander	0 (0.0)
	Aboriginal & Torres Strait Islander	0 (0.0)
Marital status, n (%)	Single	8 (10.9)
	Married/de-facto	60 (82.2)
	Divorced/separated	4 (5.5)
	Widowed	1 (1.4)
	Not recorded	0 (0.0)
Education level, n (%)	Never attended school	0 (0.0)
	Year 11 or below	3 (4.1)
	Year 12 or below	8 (11.0)
	TAFE, vocational	21 (28.8)
	University degree	40 (54.8)
	Prefer not to say	1 (1.4)
Socioeconomic Status (SEIFA), n (%)	Q1 (most disadvantaged)	3 (4.1)
	Q2	5 (6.8)
	Q3	13 (17.8)

	Q4	23 (31.5)
	Q5 (least disadvantaged)	29 (39.7)
Individual risk factors*, n (%)	Any family history of breast cancer	51 (69.8)
	History of LCIS	15 (20.5)
	History of ADH	2 (2.7)
	History of ALH	5 (6.8)
	History of thoracic irradiation	15 (20.5)
Multiple risk factors*, n (%)	Family history and LCIS	10 (13.7)
	Family history and ADH	1 (1.4)
	Family history and ALH	2 (2.7)
	Family history and thoracic irradiation	4 (5.5)
Number of first-degree relatives with breast cancer, n (%)	0	37 (50.7)
	1	26 (35.6)
	2	6 (8.2)
	3	4 (5.5)
Parity, n (%)	0	20 (27.4)
	1	12 (16.4)
	2	21 (28.8)
	3	19 (26.0)
	4	1 (1.4)
10-year breast cancer risk, mean (SD)	Able to be assessed n=72	12.4 (9.21)
	Not able to be assessed** n=1	
Residual lifetime risk, mean (SD)	Able to be assessed n = 58	36.32 (17.33)
	Not able to be assessed** n=15	

Footnote:
*Risk factor categories are not mutually exclusive; Participants may have multiple risk factors and therefore appear in more than one category.
"Any family history" may include first- or second-degree relative. The row "number of first-degree relatives with breast cancer" is reported for all participants; a value of 0 indicates no affected first-degree relatives (participants may have no family history or family history limited to second-degree relatives**.**
**10-year or residual lifetime risk could not be calculated for participants with prior thoracic irradiation.

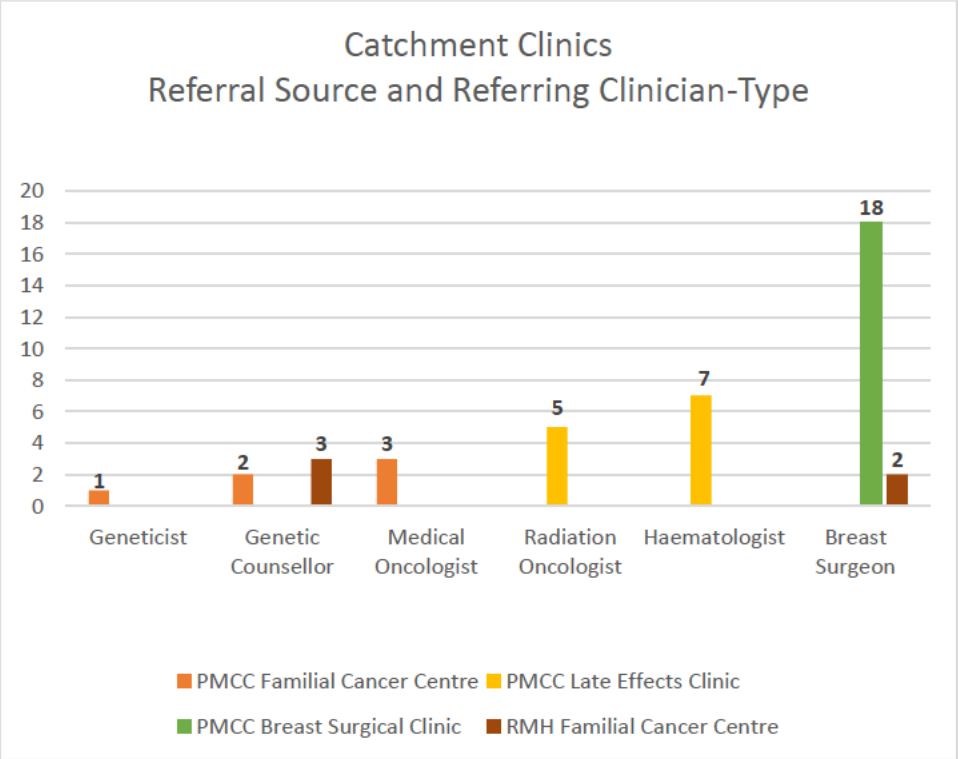
5.3.3 Referral characteristics

Referral source and referring clinician type for participants referred from Catchment Clinics and from sources external to Catchment Clinics are shown in Figures 5.2 and 5.3, respectively. Classification was based on the origin of referral rather than service title alone, and therefore similar service types could appear within both Catchment Clinic and external referral pathways.

Among referrals originating from Catchment Clinics, the largest number were from the Peter MacCallum Cancer Centre (PMCC) Breast Surgical Oncology Clinic, followed by the PMCC Late

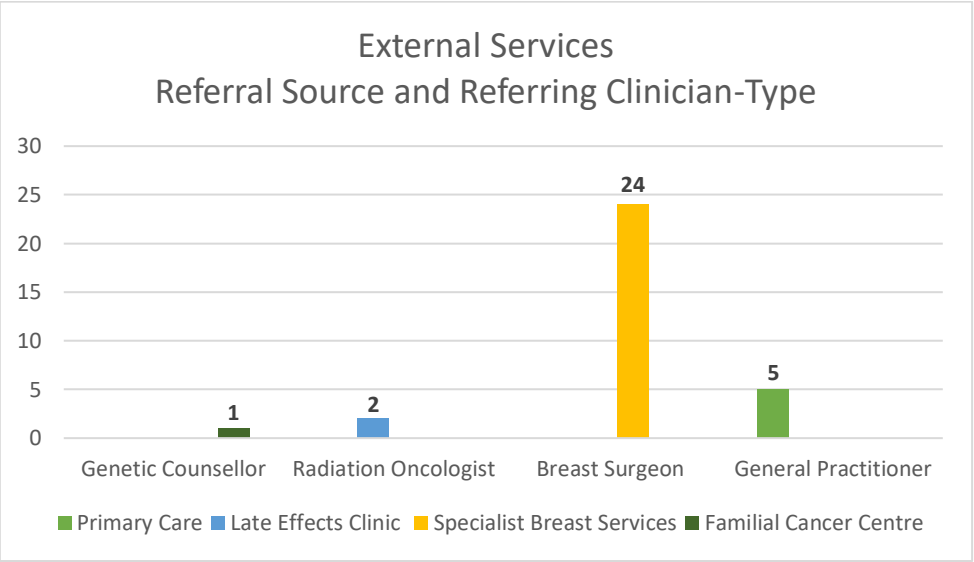
Effects Clinic, PMCC Familial Cancer Centre, and the RMH Familial Cancer Centre. Referring clinician type varied across these sources, reflecting the multidisciplinary settings from which the PCMed Service received referrals. Referrals from sources external to Catchment Clinics arose from Primary Care and other external specialist services, including breast, familial cancer/genetics, and late effects services. Together, these findings indicate that the PCMed Service was accessed through both internal referral pathways and broader external referral networks.

Figure 5.2: Referral source and referring clinician type for participants referred from Catchment Clinics



Note: Catchment Clinic referrals were classified according to the origin of referral. PMCC = Peter MacCallum Cancer Centre; RMH = Royal Melbourne Hospital; BU = Breast Unit; FCC = Familial Cancer Centre; LEC = Late Effects Clinic.

Figure 5.3: Referral source and referring clinician type for participants referred from sources external to Catchment Clinics



Note: Referral groups were classified according to the origin of referral. Accordingly, similar service types may appear in both Figures 5.1 and 5.2. For example, the Familial Cancer Centre reflected a similar service type but was classified as an external site, as it was not a Catchment Clinic. Similarly, Late Effects Clinics shared the same service title but were external to the participating Catchment Clinics.

Having described the participant population and referral pathways, the following sections present findings on feasibility and fidelity of service delivery.

5.3.4 Feasibility of Service Delivery

Feasibility was assessed through indicators reflecting whether the PCMed Service could be accommodated within existing clinical workflows and delivered with available resources in a sustainable manner. These indicators included consultation duration, number of consultations required before prescription or discharge, participant engagement with planned follow-up, additional ad hoc reviews, and hotline use.

5.3.4.1 Feasibility of Telehealth Delivery

Consultation modality by type is shown in Table 5.2. Overall, video-based telehealth was successfully utilised as the dominant modality, with 142 of 153 consultations (92.8%) conducted via telehealth. However, feasibility of telehealth is most meaningful assessed in relation to the intended planned telehealth consultations, namely the Initial, Repeat, and the Post-Prescription Consultations. Among these 144 planned consultations, 140 (97.2%) were conducted by video-based telehealth, 3 (2.1%) were conducted face-to-face, and 1 (0.7%) was conducted by telephone. This indicates feasibility of telehealth delivery in routine practice and high fidelity to the intended telehealth-first model.

Table 5.2: Consultation modality by type

Consultation type	Telehealth n (%)	Face-to-Face n (%)	Phone n (%)	Primary Reason for non-telehealth delivery
Initial (n=73)	72 (98.6)	1 (1.4)	0 (0)	Lacked the technology for telehealth.
Repeat (n=42)	40 (95.2)	1 (2.4)	1 (2.4)	Lacked the technology for telehealth; Complementary medication review (Phone)
Post-Prescription (n=29)	28 (96.6)	1 (3.4)	0 (0)	Lacked the technology for telehealth.
Post-Prescription Ad hoc (n=9)	2 (22.2)	0 (0)	7 (77.8)	Responsive assessment and management of new concerns.
Total (n=153)	142 (92.8)	3 (2.0)	8 (5.2)	

Footnote:
Initial = first consultation in the PCMed Service. Repeat = subsequent consultation for participants who required more time to decide whether to commence an RRMed, or who needed additional review of issues relevant to commencing treatment. Post-Prescription = planned consultation after initiation of a risk-reducing medication.
Post-Prescription Ad hoc = unplanned consultations initiated after prescription to address new concerns. Planned consultations include Initial, Repeat, and Post-Prescription Consultations.

The 3 face-to-face consultations all related to a single participant who lacked the technology required for telehealth, representing a specific access barrier affecting 1 individual participant across their consultation pathway. The single planned telephone consultation was an additional Repeat Consultation undertaken to review complementary medication use.

Post-Prescription Ad hoc Consultations were responsive, unplanned reviews and were not expected to follow the same telehealth structure as planned consultations. Most of these consultations were conducted by telephone (7/9, 77.8%), reflecting their flexible and time-sensitive purpose.

5.3.4.2 Consultation Duration

Consultation duration, stratified by type is presented in Table 5.3. Consultation length was interpreted primarily as a feasibility indicator, as the PCMed Service intervention (Appendix 2) did not prescribe fixed consultation durations. Rather, consultation scheduling reflected usual institutional practice at PMCC, where Initial Consultations are generally allocated 60 minutes and subsequent review consultations are allocated 30 minutes.

Most Initial Consultations (41/73, 56.2%) lasted 30–44 minutes, with a proportion (17/73, 23.3%) lasting 45–59 minutes, and a smaller proportion (15/73, 20.5%) lasting 15-29 minutes. No Initial Consultations exceeded 60 minutes. Repeat Consultations were generally shorter, with most (40/42, 95.2%) completed within 29 minutes. Planned Post-Prescription Consultations were typically brief, with most (21/29, 72.4%) completed in less than 15 minutes.

Similarly Post-Prescription Ad hoc Consultations were completed in less than 15 minutes. These findings support the feasibility of delivering the PCMed Service within routine clinical workflows.

Table 5.3: Duration of Consultations, stratified by type (n=153)

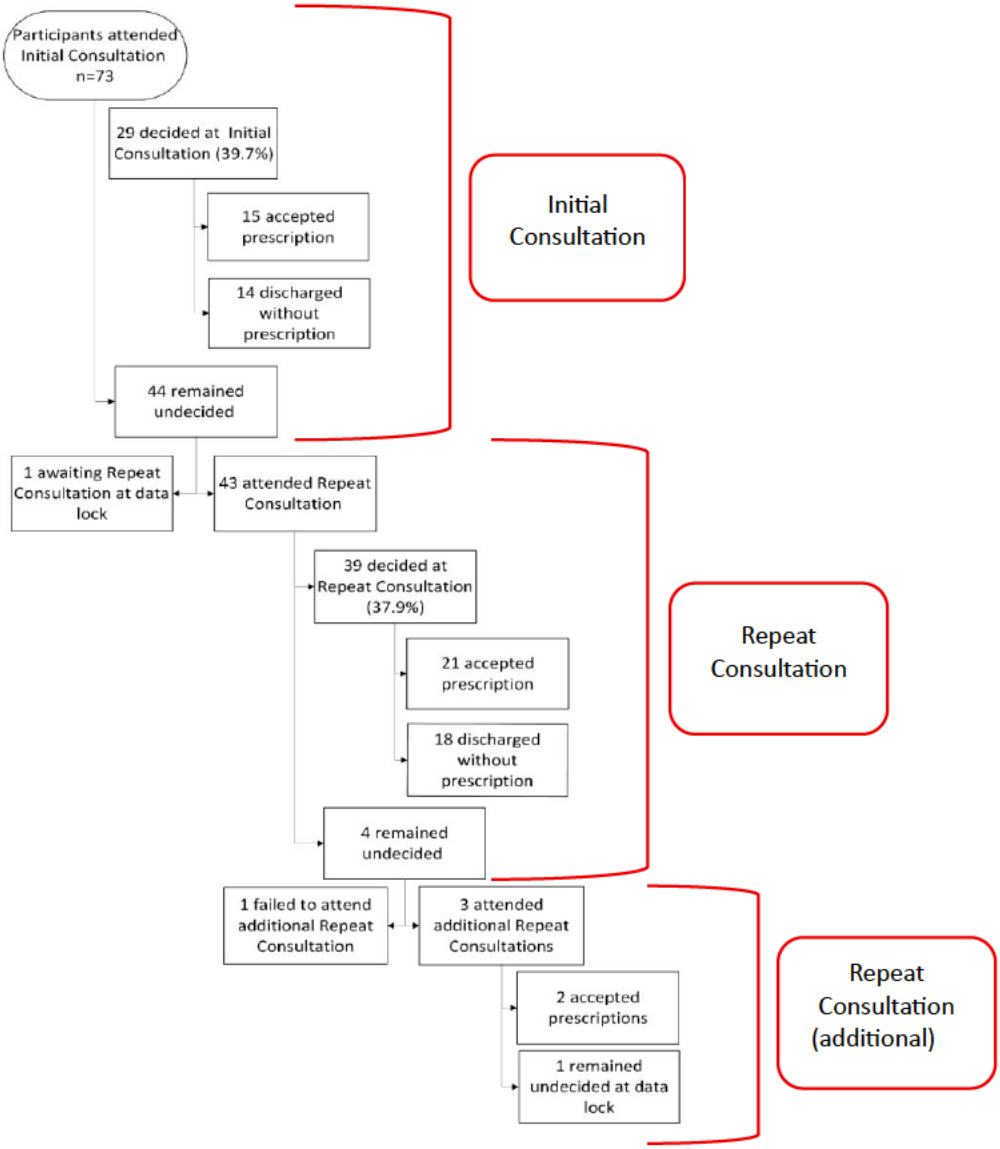
Consultation Type	**< 15 minutes n (%)**	**15-29 minutes n (%)**	**30-44 minutes n (%)**	**45-59 minutes n (%)**	**> 60 minutes n (%)**	**Total n**
Initial (n=73)	0 (0.0)	15 (20.5)	41 (56.2)	17 (23.3)	0 (0)	73
Repeat (n=42)	18 (42.9)	21 (50.0)	3(7.1)	0 (0)	0 (0)	42
Post Prescription (n=29)	21 (72.4)	8 (27.6)	0 (0)	0 (0)	0 (0)	29
Post-Prescription Ad-hoc (n=9)	8 (88.9)	1 (11.1)	0 (0)	0 (0)	0 (0)	9
TOTAL	**47 (30.7)**	**45 (29)**	**44 (29)**	**17 (11)**	**0 (0)**	**153**
Footnote: Initial Consultations were allocated 60 minutes, and review Consultations 30 minutes, consistent with usual institutional practice. Time required for pre-consultation preparation, documentation, prescribing, and communication with referrers or GPs was not systematically recorded.						

5.3.4.3 Number of Consultations required before prescription or discharge

Most participants reached a decision regarding RRMed use within 2 consultations or fewer, supporting both the feasibility of the consultation pathway and fidelity to the planned intervention. The pathway to decision is shown in Figure 5.4.

Of the 73 participants, 29 (39.7%) reached a decision at the Initial Consultation. Among those who remained undecided, a further 39/73 (53.4%) reached a decision after the Repeat Consultation. Only a small number of participants required more than 2 consultations to reach a decision.

Figure 5.4: Consultation pathway to decision regarding RRMed use among participants attending the PCMed Service (n=73)



5.3.4.4 Attendance at the planned Post-Prescription Consultation

All participants who accepted a prescription were scheduled for a Post-Prescription Consultation. At the time of this interim analysis, 29 of these scheduled consultations fell within the study period and were therefore included in the planned interim analysis. Of these, 27 participants (93.1%) attended the planned Post-Prescription Consultation, indicating high fidelity to the intended follow-up pathway and high participant engagement with the PCMed Service. The 2 participants who did not attend the planned Post-Prescription Consultation, had not commenced the medication, and therefore did not require clinical review of treatment tolerability. One participant considered her risk insufficient to warrant treatment and the other wanted additional time to consider whether to commence a RRMed.

5.3.4.5 Post-Prescription Ad hoc Consultations

Beyond the planned follow-up pathway, 7 of 29 participants (24.1%) who initiated a RRMed required at least 1 Post-Prescription Ad hoc Consultation, with 9 consultations conducted in total. Reasons for ad hoc reviews are shown in Table 5.4. Post-Prescription Ad hoc Consultations arose through several pathways, including a message received from a referring clinician via the hospital's electronic medical record (EMR) system, issues identified during the study 6-month study follow-up telephone call, concerns arising at a planned Post-Prescription Consultation, email communication, and administrative contact. Of the 9 Post-Prescription Ad hoc Consultations, 2 arose following participant contact with the hotline telephone service (described separately in Section 5.3.2.6).

Clinical reasons for ad hoc review included clarification or assessment of possible side effects, management of ongoing symptoms, medication-related decision-making, prescription issues related to medication supply, and competing health concerns requiring medication deferral.

Post-Prescription Ad hoc Consultations are interpreted primarily as a feasibility indicator, reflecting the additional support burden required beyond the planned pathway. However, they were also consistent with the intended PCMed Service intervention, as the intervention explicitly allowed additional Post-Prescription Ad hoc Consultations where needed.

Table 5.4: Reason and number of Post-Prescription Ad hoc Consultations per participant

Participant	Trigger / source of contact	Number of consultations	Primary reason for adhoc review
ID 5	Hotline contact	1	Ceased medication due to concern about possible side effects.
ID 50	Message from referring clinician via hospital EMR system	1	Experiencing urinary frequency, hair thinning and flattened mood on tamoxifen 20mg daily.
ID 68	Issue identified during 6-month study follow-up phone call	1	Experiencing fluid retention on tamoxifen 20mg daily.
ID 84	Hotline contact	2	Experiencing dry cough on tamoxifen 20mg daily. Additional Post-Prescription (Ad-hoc) generated.
ID 158	Receipt of abnormal bone density scan results	1	Prescribed anastrozole 1mg daily.
ID 161	Email contact	1	Prescription request – On low dose tamoxifen and prescribed 10mg tamoxifen tablets. National shortage of

			10mg tablets and required a prescription using 20mg tablets.
ID 253	Contact made to Administration Officer	2	Request to reschedule Post-Prescription review as had not started RRMed due to unrelated health concerns; Additional Post-Prescription (Ad-hoc) generated as part of follow-up.

5.3.4.6 Hotline Telephone Service Use

Use of the dedicated hotline was low over the approximately 19-month study period. A total of 6 calls were received, all from women participants. The reason for these calls, their duration, and whether they generated additional consultations are presented in Table 5.5. Notably, although telephone support was explicitly offered to GPs in handover documentation following transfer of care, no calls were received from GPs during the study period. This finding is discussed further in Chapter 6, Section 6.6.2, in the context of primary care integration and sustainability.

Reasons for calling included onset of dry cough, fatigue, concern about potential side effects, clarification regarding the timing of medication administration, and postmenopausal bleeding. Of the 6 hotline calls, 2 resulted in a Post-Prescription Ad hoc Consultation (as reported in Section 5.3.2.5), while the remainder were managed through advice alone. Most calls were brief, with 4 of 6 lasting less than 5 minutes and the 2 lasting 5 to 10 minutes.

Table 5.5: Reason for hotline calls and duration

Caller	Caller-type	Reason for call	Duration (minutes)	Generated ad hoc review
ID 84	Participant	Experiencing dry cough after commencing of tamoxifen 20 mg daily.	5 - 10	Yes
ID 129	Participant	Whether to cease medication for air travel.	< 5	No
ID 135	Participant	Experiencing Grade 1- Fatigue 10 days after commencing anastrozole 1mg daily.	5 to 10	No
ID 5	Participant	Ceased medication due to concern for future side effects.	< 5	Yes
ID 264	Participant	Clarifying time of day to take medication	< 5	No
ID 302	Participant	Experiencing postmenopausal vaginal bleeding 10 days after commencing tamoxifen 20mg daily.	< 5	No
Footnote: Participant refers to an individual (women) who had attended the PCMed Service.				

5.3.5 Fidelity to the Planned Intervention

Fidelity was assessed through indicators reflecting adherence to core intervention components specified in the planned PCMed Service model (Appendix 2). As noted in Section 5.3.4.1, consultation modality has been addressed within the feasibility section given its fundamental importance to demonstrating viability of the telehealth service model. This section presents findings on three remaining fidelity indicators: provider type and clinician allocation (Section 5.3.5.1), delivery of the intended consultation pathway (Section 5.3.5.2), and timing of Post-Prescription Consultations (Section 5.3.5.3).

5.3.5.1 Provider Type and Clinician Allocation

Of the 153 consultations, most (131/153, 85.6%) were conducted by the NP alone, 5 (3.3%) solely by the medical oncologist, and 17 (11.1%) involved both clinicians.

Joint consultations were conducted for training or clinical supervision purposes (n=15) and less commonly, for more complex cases requiring collaborative assessment (n=2). Consultations conducted solely by the medical oncologist occurred due to NP leave (n=2), referrer request for medical oncologist review (n=2), or case complexity (n=1).

The predominance of NP-delivered consultations was consistent with fidelity to the provider allocation component of the planned model, which specified that most consultations would be conducted by the NP, with a minority conducted by the medical oncologist (Appendix 2). The pattern also suggests feasibility of delivering the PCMed Service primarily through the NP role, with medical oncologist support.

5.3.5.2 Delivery of the Intended Consultation Pathway

Fidelity to the intended consultation pathway was high. All participants who accepted a prescription for a RRMed were scheduled for a planned Post-Prescription Consultation, consistent with the intervention protocol. At the time of the interim analysis, 29 planned Post-Prescription Consultations fell within the study period and were eligible for inclusion in this analysis.

Among the 27 participants (93.1%) attended the planned Post-Prescription Consultation. As reported in Section 5.3.2.4, the two participants who did not attend had not commenced the prescribed medication. Among participants who did not commence a RRMed, discharge processes aligned with the intervention model, with participants and their referring clinicians advised that the participant could re-enter the PCMed Service if circumstances or preferences

changed. This demonstrates fidelity to the intended support model, which included flexibility for women to revisit their decision and re-access the PCMed Service at a later time.

5.3.5.3 Timing of Planned Post-Prescription Consultation

Among the 27 participants who commenced a RRMed and attended the scheduled Post-Prescription Consultation, the median time from medication commencement to review was 7.9 weeks (IQR 6.1–8.5 weeks). Timing of review in relation to the planned 8–10-week timeframe is presented in Table 5.6.

Fifteen participants (55.6%) were reviewed within the planned 8–10-week timeframe as specified in the planned PCMed Service intervention (Appendix 2). A further 7 participants (25.9%) were reviewed between 6 and less than 8 weeks after medication commencement, and 5 participants (18.5%) were reviewed before 6 weeks after medication commencement. These reviews occurred earlier than intended relative to medication commencement, most commonly because the Post-Prescription Consultation was scheduled after prescription, but participants delayed commencing the medication. No participants were reviewed more than 10 weeks after medication commencement.

Beyond the quantitative indicators of feasibility and fidelity presented above, the prospectively maintained research journal identified implementation challenges and service adaptations that contextualise these findings.

Table 5.6: Timing of attended planned Post-Prescription Consultations after RRMed commencement (n=27)

Timing of Post-Prescription Consultation	**n/N (%)**
Occurred within 8–10 weeks of RRMed commencement	15/27 (56%)
Occurred after 10 weeks	0/27 (0%)
Occurred between 6 and 8 weeks	7/27 (26%)
Occurred before 6 weeks	5/27 (18%)

5.3.6 Implementation Challenges and Service Adaptations

Although the PCMed Service was delivered largely in accordance with the planned intervention, the prospectively maintained research journal identified several implementation challenges and required adaptations during the study period.

The most persistent challenge was lower than anticipated referral volume from the Catchment Clinics. Additional referral related barriers included clinician uncertainty regarding eligibility criteria and variability in the completeness of referral information. In some referrals, the pre-referral risk assessment appeared to focus primarily on familial or genetic factors, while co-

existing benign high-risk breast lesions, such as LCIS or AH, were not clearly documented or incorporated into the overall risk assessment.

The research journal highlighted the resource intensity of clinician-led pre-service preparation. Manual review of referral information, confirmation of eligibility, and completion or interpretation of risk assessments, and follow-up communication to clarify incomplete referral information were time-consuming. Participant understanding of their breast cancer risk also varied at the time of initial contact, ranging from detailed awareness of personal risk estimates to limited understanding of why they had been referred.

Although telehealth was successful overall, isolated technical difficulties were encountered, including connectivity issues. One participant required face-to-face delivery across all consultations due to lack of access to technology and requirement for an interpreter. These instances demonstrated that some flexibility in consultation modality remained necessary despite the predominantly telehealth-based model.

Most challenges documented in the research journal were managed through use of flexibility already built into the intervention design, such as offering face-to-face consultations where telehealth was not feasible, rather than requiring modification to the core service model. Two substantive adaptations were identified during implementation.

First, the process for risk assessment was adapted to increase use of participant self-completed risk assessment via iPrevent.[50, 51] This adaptation was introduced to streamline pre-service preparation, reduce clinician workload, and improve efficiency without altering the consultation content or clinical decision-making process.

Second, discharge and follow-up processes were adapted to provide greater flexibility for women participants who commenced a risk-reducing medication. Rather than formally discharging participants immediately after stabilisation on treatment, ongoing care was transferred back to the referring clinician or GP while participants remained notionally linked with the PCMed Service. This approach allowed participants to re-access specialist review if clinical concerns arose, without requiring a new referral. This adaptation was consistent with the intervention's intended support model, which included re-entry pathways for participants requiring additional specialist input.

Neither adaptation altered the core intervention structure, which remained a predominantly telehealth-delivered, NP-medical oncologist model with the planned consultation pathway and post-prescription support mechanisms. The implications of these implementation challenges and adaptations for service sustainability and future scale-up are interpreted in Chapter 6.

5.4 Summary of Key Findings

This chapter presents findings from the planned interim process evaluation of the feasibility and fidelity of the PCMed Service. Overall, the PCMed Service was delivered largely in accordance with the planned intervention model.

Fidelity to the planned telehealth-first model was high, particularly among planned consultations. The NP autonomously delivered most consultations, with medical oncologist input used selectively for supervision, training, clinician availability, referrer request, or clinical complexity. Most participants reached a decision regarding RRMed use within 1 or 2 consultations, and attendance at the planned Post-Prescription Consultation was high among those who commenced a RRMed.

The need for additional Post-Prescription Ad hoc Consultations was limited, and hotline use was low over the study period. However, these additional reviews were triggered through multiple routes, indicating that the hotline was one component of a broader post-prescription support pathway rather than the only mechanism for re-contacting the PCMed Service.

Fidelity to the exact 8–10-week Post-Prescription Consultation timing criterion was partial, with 55.6% of attended reviews occurring within the planned window. Reviews outside the window occurred earlier, not later than planned, and were usually explained by delayed medication commencement after prescription. As a result, appointments scheduled after prescription sometimes occurred sooner than intended relative to actual treatment initiation.

Implementation challenges related primarily to referral processes, referral completeness, pre-service risk assessment, and the workload associated with preparation and coordination around consultations. Only minor pragmatic adaptations were identified, and these did not substantially alter the core intervention model. The PCMed Service demonstrated strong feasibility as a predominantly telehealth, NP-medical oncologist model, with high fidelity to most core intervention components, supporting its viability for future implementation and scale-up.

Chapter 6: Discussion and Conclusion

6.0 Introduction

This chapter synthesises the findings of the Graduate Student Committee-endorsed interim analysis of a defined subset of outcomes from the larger PCMed mixed-methods evaluation, "*Evaluation of a telehealth service to support breast cancer prevention medication uptake: a protocol of a mixed methods study"*. Specifically, this thesis focused on pre-implementation use of RRMeds among participants attending the PCMed Service, early findings on feasibility and fidelity to the planned intervention, and adaptations required during implementation. Accordingly, this chapter interprets the findings within the scope of the thesis while situating them within the wider evidence-implementation gap of breast cancer prevention.

This chapter first summarises the key findings before considering their implications for understanding the evidence-implementation gap in primary breast cancer prevention, the potential role of a dedicated telehealth service in addressing this gap, and the feasibility of implementing such a model within routine clinical practice. The findings are then discussed in relation to implementation theory, specifically the Knowledge to Action Framework (KTA),[99] before discussing implications for routine clinical practice, primary care integration, policy, equity, and sustainability. The chapter concludes by outlining the strengths and limitations of the present thesis and identifying how the work reported here, if confirmed in the final analysis of the larger PCMed mixed-methods evaluation, may support future refinement of the PCMed Service, inform service development and potential scale-up, and provide a foundation to advancing implementation of breast cancer prevention in routine clinical practice.

6.1 Summary of Key Findings

This thesis confirmed a substantial evidence-implementation gap in the use of RRMeds for breast cancer prevention. In the historical control sample of women attending Catchment Clinics prior to the implementation of the PCMed Service, documented discussion of RRMeds was uncommon and prescribing was rare. By contrast, among PCMed attendees who had no contraindication to their use, more than half commenced a RRMed within 6 months of the decision consultation. Uptake was high among participants classified as being at high risk of breast cancer which included participants with AH or LCIS. The PCMed Service was delivered largely as intended, with high use of telehealth, care delivered predominantly by the NP, high attendance at planned follow-up, and limited use of unplanned support. Only minor adaptations were required during implementation.

6.2 Interpreting the Evidence-Implementation Gap

The findings from the retrospective chart review of women who attended Catchment Clinics prior to PCMed Service implementation, suggest that, in routine care, breast cancer risk identification was not consistently translated into discussion of medication- based prevention. In this historical cohort, only 4% of eligible participants had a documented discussion about RRMeds in their medical record, and only 1% were recorded as having commenced a RRMed within 12 months of their Catchment Clinic consultation. These findings suggest that, in this setting, low uptake of RRMeds was likely influenced by limited discussion of RRMeds as an available prevention strategy. Women cannot make an informed decision about preventative medication if the option is not raised or explained. The low rate of clinician discussions about RRMeds is therefore likely to have contributed to the very low rate of RRMed use observed in the historical sample.

The clinical implications of absent or inconsistent discussion are substantial. Without structured counselling, many women at increased risk may remain unaware that medication-based prevention is an option, thereby limiting opportunities for informed and value-concordant decision-making.[81, 109] In this context, access to prevention may depend more heavily on a woman's ability to seek information independently, ask specifically about preventive options, or navigate specialist pathways.[76, 109] This places greater responsibility on women to identify and pursue preventative care themselves, creating the potential for inequitable access, particularly for women with lower health literacy, fewer resources, or more limited access to specialist care.[109] Conversely, when women receive structured, evidence-based counselling, uptake and decisional satisfaction may improve.[110-112] Interventions incorporating shared decision-making processes and decision support tools also have shown to improve knowledge, support informed choice, and reduce decisional conflict.[112]

Without clear, evidence-based guidance, misconceptions regarding harms may further deter RRMed uptake. Persistent concerns about adverse effects are well described in the literature, including risk of endometrial cancer risk and venous thromboembolism with tamoxifen, as well as the stigma associated with taking what is perceived to be a "cancer drug".[17, 77, 113] Importantly these risks may be overestimated or applied inaccurately when they are not contextualised according to medication type, menopausal status, and individual risk profile. For example, endometrial cancer risk is not increased with aromatase inhibitors or raloxifene, and the increased risk associated with tamoxifen is primarily relevant to postmenopausal women.[1] Some women may also confuse chemoprevention with chemotherapy or anticipate toxicities

that are not typical of preventative endocrine therapy.[71, 77, 113] These concerns reinforce the importance of accurate, personalised counselling that directly addresses misconceptions and distinguishes preventive therapy from treatment for active cancer.

This interpretation is consistent with both Australian and international literature on breast cancer prevention, which identifies clinician-initiated discussions as a critical first step in the pathway to RRMed uptake.[17, 71, 79, 81, 109, 114-117] Australian research has identified several barriers that may contribute to missed discussions, including limited clinician knowledge of RRMeds, low confidence in quantitative risk assessment, time constraints within routine consultations, and uncertainty regarding whose role it is to discuss and prescribe preventative therapy.[17, 76, 82] Similar barriers have also been reported internationally, particularly in primary care and specialist settings where preventive medication may be deprioritised in favour of acute concerns, screening, or surveillance, and where clinicians may feel insufficiently prepared to counsel women about chemoprevention.[66, 71, 78, 83]

That this pattern was observed within a tertiary metropolitan cancer service is notable, as one might expect discussion and use of preventive medication to be higher in such a setting. However, access to structured risk-management pathways may vary according to the source and level of breast cancer risk, as well as the clinic through which a woman is managed. At PMCC, women with high familial or genetic risk may be seen through familial cancer services and then referred to a dedicated high-risk management clinic for ongoing risk management once genetic assessment is complete.[121, 122] In that setting, discussion of RRMeds would be expected to occur as part of a dedicated risk-management consultation. However, this pathway is not necessarily available to all women at increased risk. Women at moderately increased familial risk may not be seen face-to-face in familial cancer services because of high service demand and may instead receive written management advice. Consequently, they may not have an opportunity to be referred onward to the high-risk management clinic for a structured discussion of medication-based prevention. Similarly, women whose increased risk is defined by benign high-risk breast lesions, such as AH or LCIS, may continue to be managed in breast surgical services rather than in familial cancer or high-risk management clinics. Women with prior thoracic irradiation may also be referred to breast surgical services for surveillance, which may create an implicit assumption that discussion of RRMeds will occur elsewhere.

Across these pathways, consultations may appropriately focus on surveillance, surgical management, treatment-related late effects, genetic assessment, or lifestyle advice. However, in the absence of an explicitly designated clinician or service responsible for medication-based prevention across all risk groups, discussion of RRMeds may be deferred, assumed to be

addressed elsewhere, or diluted within broader risk-management consultations. Although this cannot be confirmed from the present data, such fragmentation may be compounded by limited clinician confidence, variable familiarity with RRMeds, and uncertainty regarding role responsibility for preventive counselling.

At the same time, some women with AH or LCIS may have been attending breast clinics for several years, and the retrospective chart review may not have captured an earlier consultation at which preventive medication was discussed. Taken together, these findings suggest that specialist setting alone does not guarantee access to preventive discussion. Rather, an explicit pathway linking risk identification to counselling and prescribing might be required, with clear responsibility allocated to clinicians who have the expertise, time, and service structure to provide a focused discussion of medication-based prevention.

The findings therefore support the interpretation that the evidence–implementation gap for RRMeds is driven, at least in part, by failure to consistently translate risk identification into a structured discussion of medication-based prevention. This distinction is important. Decisions about RRMeds are widely recognised as "preference-sensitive", meaning that there are no single correct choice and decisions must be both evidence-informed and aligned with each woman's values and preferences.[79, 81, 112, 118-119] However, shared decision-making cannot occur unless the option is first raised. In this sense, discussion is a necessary precondition for informed uptake. The findings of this thesis suggest that in routine care prior to implementation of the PCMed Service, many eligible women may not have reached the point at which they were supported to consider RRMeds as an available prevention option.

At the same time, these findings must be interpreted in light of the limitations of retrospective chart review. Absence of documentation does not definitively establish that discussion did not occur. In a busy clinical environment, clinicians may briefly mention preventive medications without recording the conversation. Some women may also have received counselling elsewhere, such as in primary care, private specialist settings, or other services not captured in the audited records. In addition, chart review cannot assess the quality, depth, or decisional adequacy of any discussion that was documented. The present study therefore cannot determine why discussions were infrequently recorded, nor whether this reflected true non-discussion, incomplete documentation, or care delivered outside the audited records. Nevertheless, even with these limitations the practical implication remains important which is that very few women in the historical control sample had documented evidence of having progressed from risk identification to medication-based prevention.

These findings strengthen the rationale for a dedicated intervention, such as the PCMed Service, which was designed to directly address the point at which routine clinical practice appears to falter. By establishing a defined and accessible pathway for prevention discussion, prescribing and follow-up, the PCMed Service aimed to bridge the gap between identifying increased breast cancer risk and supporting informed decisions about medication-based prevention. The next section examines RRMed uptake among women who attended the PCMed Service, while recognising that the most appropriate assessment of service impact will require comparison of RRMed uptake among eligible women seen in Catchment Clinics before and after implementation of the PCMed Service, to determine whether this structured pathway was associated with improved uptake of RRMeds.

6.3 Interpreting RRMed Uptake Among PCMed Service Attendees.

Among participants who attended the PCMed Service, RRMed uptake was high. Of the 37 participants with no contraindications to RRMed use at the time of their decision consultation, 20 (54.1%) commenced a RRMed within 6 months. These findings cannot be directly compared with the historical Catchment Clinic findings because the two groups are not equivalent. Women who attended the PCMed Service had already been referred to, accepted, and attended a dedicated medication-prevention consultation, and therefore may have differed from the broader population of eligible women seen in Catchment Clinics prior to PCMed Service implementation. This creates the potential for referral and self-selection bias. Accordingly, these findings should be interpreted as describing medication initiation among women who engaged with the PCMed Service, rather than as evidence that the PCMed Service increased uptake compared with routine clinical practice. Nevertheless, the findings suggest that, among attendees, a structured pathway for counselling, prescribing, and follow-up can support informed initiation of RRMeds.

It is also important to recognise that the PCMed Service population comprised women without a diagnosis of breast cancer who were considering medication for primary prevention. In this context, participants were required to weigh a future reduction in cancer risk against the possibility of current side effects and the burden of long-term medication while otherwise feeling well.[81, 85, 119] This ‘trading morbidity dilemma’, where healthy women are asked to accept the potential of adverse effects for an abstract future benefit, may help explain why uptake of preventive medication is often low in routine clinical practice.[79, 119] The choice to initiate chemoprevention is a highly preference-sensitive decision, which reinforces the

importance of structured, personalised counselling to elicit women's values and support informed decision-making.[110, 112, 119]

The finding is notable in the context of previous Australian and international literature, in which uptake of preventive endocrine therapy has generally been low outside clinical trial settings.[16, 71, 72] It also adds to evidence from studies of decision support interventions, including the web-based RealRisks decision aid and the provider-facing Breast Cancer Risk Navigation Tool.[112, 120] These studies have shown that decision aids can improve decision-making, breast cancer risk perception, chemoprevention knowledge, informed choice, and short-term decisional outcomes.[112, 120] However, improvements in knowledge and decision quality have not consistently translated into medication initiation.[112, 120-121] In the RealRisks pilot study, 9 of 37 (24%) high-risk women expressed interest in chemoprevention after using the decision aid, yet none had commenced medication at 6 months.[120] Similarly, in the larger randomised trial evaluation RealRisks together with the provider-facing Breast Cancer Risk Navigation Tool, uptake remained very low at 6 months, with no meaningful difference between intervention and control groups 2.1% vs. 3.5% and overall uptake remained below 5% in both groups.[112] These findings suggest that decision aids are valuable for supporting preference-sensitive decisions, but on their own, may not be sufficient to change preventive medication initiation.

The contrast between those studies and the present findings is informative, rather than a criticism of RealRisk or decision aids more broadly. Decision support tools primarily address cognitive and decisional determinants of uptake, such as understanding of risk, knowledge of medication benefits and harms, and clarity about personal preferences.[118, 120] These are necessary components of shared decision-making, particularly given the value-sensitive trade-offs involved in taking a daily preventive medication for breast cancer risk reduction.[118, 121] However, women who are informed and interested may still face practical and service-level barriers, including concerns about potential side effects, uncertainty about clinical responsibility for discussing and prescribing RRMeds, limited clinician confidence in counselling women about RRMeds, and limited integration between decision support and prescribing.[112, 113, 122] By comparison, the PCMed Service combined personalised risk communication with specialist counselling, prescribing capacity, follow-up, and access to ongoing support. In this sense, the PCMed Service extended beyond decision support alone: it provided an implementation pathway through which RRMeds could be discussed, initiated, and monitored. Critically, it also addressed practical barriers such as prescribing confidence, role clarity, and follow-up responsibility, which decision aids alone cannot resolve. This may help explain why

uptake was high in the present study, whereas improvements in knowledge and informed choice in prior decision-aid studies did not necessarily translate into medication initiation.[112, 120]

Uptake also differed by breast cancer risk category, with numerically high initiation among participants classified as high-risk (17/21, 81%) than moderate-risk (3/15, 20%).[45] Although the sample size was small, the high uptake observed among participants in this interim analysis, is broadly consistent with the finding from the BC-Predict study,[111] in which uptake of preventive medication was also higher among women at high risk than among those at moderate risk following a risk consultation.[111] However, this comparison should be interpreted cautiously, as BC-Predict used NICE risk categories,[103] whereas the present study used the RACGP guideline,[45] and these classifications are not directly equivalent. Even so, the findings are consistent with the possibility that women who perceive a greater absolute benefit from treatment may be more willing to initiate a RRMed.

Descriptive differences in uptake were also observed across selected clinical subgroups. All participants with AH (5/5, 100%) initiated a RRMed within 6 months, and uptake was also high among participants with a personal history of LCIS (6/7, 85.7%). These high initiation rates are consistent with guideline recommendations[43, 44] and the evidence base supporting preventive endocrine therapy in these pathology-defined higher-risk groups.[9] They are also broadly consistent with targeted interventions reported in the literature. For example, Brewster et al. reported high prescribing rates among women with newly diagnosed AH or LCIS,[115] and Cornell et al. found that women with high-risk intraepithelial lesions were more likely to initiate and persist with preventive medication than women whose eligibility was based on calculated risk alone.[110] Taken together, these findings suggest that a dedicated decision consultation service may be particularly valuable for women whose risk profile is defined by a high risk lesion, where the potential benefit of preventative medication is both clinically well supported and more tangible in practice.

The findings also align with literature suggesting clinician recommendation and access to specialist counselling are among the strongest influences on RRMed uptake.[17, 109, 114, 116] Previous studies have shown that women are more likely to consider chemoprevention when they receive clear, personalised information from a clinician who is able to explain the balance between benefit and harm in the context of their own risk.[79, 81, 110] The present study extends this literature by suggesting that a dedicated service model may be particularly effective because it addresses both sides of the implementation problem: it provides women with the opportunity for informed decision-making and simultaneously reduces the practical barriers

that clinicians face in initiating these discussions and prescribing medication in routine clinical practice.[76, 81, 83, 123]

At the same time, the present findings should not be taken to mean that structured counselling alone is sufficient to ensure uptake in all eligible women. Even within the PCMed Service, not all participants initiated a RRMed, and the broader literature makes clear that concerns about adverse effects, uncertainty about long-term medication use, and personal attitudes towards taking preventive medications remain important barriers.[71, 77, 79, 81, 109] The findings of this interim analysis therefore support a more nuanced interpretation: structured discussion is a necessary first step, but the decisions about RRMeds are preference-sensitive and require consultation time for shared decision making, discussion of individual values and priorities, exploration of benefits and concerns about potential side effects, and long term medication use.[112, 118, 119] Uptake is therefore most likely to improve when that discussion occurs within a service model that also addresses prescribing, follow-up, and continuity of support. The larger PCMed Service mixed-methods evaluation described in the published protocol (Chapter 2) will further examine reasons for non-initiation of RRMeds and may help clarify the relative contribution of patient preferences, medication concerns, clinician recommendation, prescribing pathways, and other service-level factors.

These findings strengthen the rationale for the PCMed Service as more than an informational intervention. Rather, it appears to function as an implementation strategy that converts identification of elevated breast cancer risk into a realistic opportunity for informed uptake of preventive medication. Nevertheless, a critical implementation challenge remains in regard to reach and engagement. In this context, reach refers to the extent to which eligible women are offered and attend the PCMed Service, while engagement refers to their willingness and ability to take up the opportunity for specialist prevention counselling.[124] Evidence suggests that fewer than half of women informed they are at increased risk accept invitations to attend prevention clinics.[111] Accordingly, while the PCMed Service appears effective for those who attend, its population impact will depend on adoption and referral success. The findings of the larger PCMed Service mixed-methods evaluation described in the published protocol (Chapter 2) will quantify adoption, that is the proportion of eligible women who attend the PCMed Service following a Catchment Clinic appointment in which the PCMed Service is discussed. Understanding the motivators and barriers to attendance, is vital to develop and to evaluate engagement strategies that enable the benefits of the PCMed Service model to be realised at scale.

6.4 Feasibility, Fidelity and Adaptations

The interim process evaluation indicates that the PCMed Service was both feasible to deliver within routine clinical practice and implemented with a high degree of fidelity to the planned intervention (Appendix 2). Crucially, this model effectively facilitated remote shared decision-making, a collaborative process that is essential for preference-sensitive choices like initiating RRMeds.[112, 118] Telemedicine technologies have been shown to foster virtual interactions that successfully support this remote shared-decision making.[125, 126] The present findings confirm that telehealth can effectively facilitate these collaborative processes in the context of preventive medication counselling. Planned consultations were conducted almost exclusively by telehealth, with 140 of 144 planned consultations (97.2%) delivered in this mode, and telehealth accounting for 142 of 153 consultations (92.8%) overall. The NP delivered the large majority of consultations autonomously (85.6%), demonstrating that NPs can effectively guide patients through complex shared decision-making processes. Furthermore, most participants who decided did so within 2 consultations, attendance at the planned Post-Prescription Consultation was high (27/29, 93.1%), and demand for additional support was relatively low, with only 9 Post-Prescription Ad hoc Consultations and 6 hotline calls over approximately 19 months. Taken together, these findings suggest that the PCMed Service model successfully integrated share decision-making into a real-world clinical setting, was delivered as intended, and was feasible within the practical constraints of a real-world clinical setting.

The high use of telehealth is particularly relevant in the Australian context, where geographic distribution affects access to specialist services; approximately one-quarter of the population (around 27%) live outside major cities, in areas classified as Inner Regional, Outer Regional, Remote, or Very Remote under the Australian Statistical Geography Standard (ASGS).[127] In this context, a telehealth prevention service is inherently attractive because it reduces travel burden, time away from work and family responsibilities, and practical barriers associated with attending specialists services in person, without compromising outcomes.[128] Importantly, telehealth may also improve equity for culturally and linguistically diverse populations when supported by video-compatible interpreter services,[129] with Australian evidence indicating high acceptability and use among those requiring interpreters.[130] The present findings therefore support telehealth not only as a mode of delivery with high fidelity, but also as a model with potential relevance for improving access to preventive care across geographically dispersed populations.

At the same time, the small number of face-to-face consultations highlights that telehealth cannot be assumed to be universally accessible. Importantly, the 3 face-to-face consultations documented in this study all related to a single participant who lacked the technology required for telehealth and required interpreter support.

However, this case should not be interpreted as evidence that telehealth is inherently unsuitable for people requiring interpreter services. Rather it highlights that telehealth can be successfully delivered to culturally and linguistically diverse (CALD) populations when appropriate, patient-centric support systems are implemented.[129] An Australian survey found that people from CALD backgrounds who require interpreters find video consultations just as acceptable as those who do not require interpreters.[130] Importantly, among those who require an interpreter for their appointments, the vast majority (84.71%) have experienced video consultations, compared to only 14.29% who have only used phone consultations.[130] This high level utilisation of video telehealth use among interpreter-requiring patients challenges assumptions that this group faces insurmountable technological barriers. Indeed, research warns of an implicit medical bias whereby some clinicians may preferentially offer telephone consultations rather than video because they incorrectly assume CALD patients lack the digital literacy, internet connectivity, or devices needed for video calls.[130] This assumption can actually hinder access, as video platforms are often necessary for proper interpreter integration.[130]

In the present study, the barrier was not language or cultural background per se, but the convergence of limited technology access and interpreter requirements in a specific individual case. This distinction is important: the evidence suggests that most people requiring interpreters can and do successfully use video telehealth when given the opportunity. The single participant in this study who required face-to-face delivery represents a specific circumstance where technology access was genuinely unavailable, rather than a generalisable finding about CALD populations or interpreter-requiring patients.

These findings reinforce that equitable implementation of telehealth requires several key enablers: (1) avoiding assumptions about digital capability based on language or cultural background, and defaulting to video rather than telephone for planned consultations requiring interpreter support;[130] (2) proactive assessment of actual technology access and digital capability during referral and triage, rather than making assumptions;[129] (3) reliable access to professional interpreter services that are compatible with video telehealth platforms;[129-130] (4) technical and administrative support to assist patients with platform access where needed;[129] and (5) retained flexibility for face-to-face delivery in the specific circumstances where genuine technology barriers cannot be overcome.[129] When these conditions are met, telehealth can

serve as an effective and acceptable mode of delivery for diverse populations, including those requiring interpreter services. When they are not, face-to-face alternatives must remain accessible to prevent inequitable exclusion from preventive care.[129]

The NP-medical oncologist model was also strongly supported by the findings. Most consultations were delivered by the NP, with medical oncologist involvement reserved for supervision, training, leave coverage, referrer preference, or clinical complexity. This suggests that a prevention-focused NP model may be a practical way to address workforce constraints in a field where time,[131] role ambiguity, and limited prescribing confidence have previously been identified as barriers to risk-reducing medication use.[66, 86] However, if such a model is to become a realistic and scalable component of care, several enabling conditions would need to be in place. These include formal governance and escalation pathways, structured access to medical oncologist support for complex cases, and targeted training in breast cancer risk assessment, risk communication, contraindication assessment, prescribing, and management of adverse effects. Standardised referral criteria and documentation templates would also be important to ensure consistent triage and efficient pre-service work-up. In addition, the model would require sustainable funding, administrative support, and the continued integration with primary care, so that ongoing prescribing and monitoring can be shared safely once treatment has been initiated and stabilised. In this sense, the findings suggest not only that the NP role was feasible in this service, but also that broader implementation would require intentional workforce planning rather than simple replication. It is also important to acknowledge that the service was delivered by a single NP, which limits the generalisability of these findings; evaluation across practitioners and sites would be necessary to determine whether similar feasibility and outcomes can be achieved at scale (see Section 6.7).

The consultation pathway itself also appeared feasible. Most participants reached a decision regarding medication within 2 consultations, supporting the practicality of a model in which an Initial Consultation is followed, where needed, by one or more Repeat Consultations before a final decision is made. This is important because decisions about RRMeds are inherently preference-sensitive and often require time for reflection.[112, 118-119] The findings suggest that providing this time did not generate excessive service burden. Consultation duration was interpreted primarily as a feasibility indicator rather than a measure of fidelity, because the intervention did not prescribe fixed consultation lengths. Instead, durations reflected routine institutional practice, with Initial Consultations generally allocated 60 minutes and review consultations 30 minutes. Most consultations were completed within or below those timeframes, indicating that the model could be delivered within existing workflow structures.

Follow-up demands were also modest. Attendance at the planned Post-Prescription Consultation was high, suggesting that participants who accepted a prescription were willing and able to engage with the scheduled consultation. The small number of Post-Prescription Ad hoc Consultations and hotline telephone calls indicates that the service did not generate substantial unplanned demand. Importantly, however, the ad hoc consultations also show that some degree of flexible support remained necessary. These consultations were generated through multiple pathways, including hotline telephone contact, clinical messages from referrers, issues arising at planned consultations, and concerns identified during broader study follow-up. This is consistent with the intended intervention, which explicitly allowed responsive post-prescription review when required. From an implementation perspective, these findings suggest that scalability of the service would depend not on eliminating this responsive support, but on ensuring that systems are in place to absorb it efficiently.

Only minor pragmatic adaptations were required during implementation. The most important adaptation related to the substantial resource intensity of pre-service preparation. The research journal documented that manual review of referral information, confirmation of eligibility criteria, completion or interpretation of the risk assessments, and follow-up communication to clarify incomplete referral information were time-consuming tasks that created workload burden and reduced consultation efficiency. To address this, greater use of participant self-completed risk assessment via iPrevent[50] was introduced to streamline preparation and reduce clinician workload.

However, this adaptation only partially addressed the underlying challenge. The research journal also identified variability in the completeness of referral information and clinician uncertainty regarding eligibility criteria as persistent barriers. In some referrals, pre-referral risk assessment appeared to focus primarily on familial or genetic factors, while co-existing benign high-risk breast lesions, such as LCIS or AH, were not clearly documented or incorporated into the overall risk assessment. This variability required additional clinician time to reconcile information across multiple systems and clinical records.

These findings highlight an important consideration for future scalability: if preventive services rely heavily on specialist-led manual pre-assessment, they may become resource-intensive and difficult to expand. Future implementation may benefit from continued use of self-assessment or automated eligibility screening tools, standardised referral templates with mandatory fields for risk factors and eligibility criteria, and integration of risk assessment data across electronic medical record systems. For example, automated software that flags eligible women based on documented risk factors (e.g., family history, breast density, pathology alerts for high-risk

lesions) could reduce manual workload and improve consistency. Similarly, clinical decision support tools embedded within referral pathways could prompt referring clinicians to complete structured risk assessments before referral, reducing downstream burden on the prevention service. A scalable model will therefore likely require not only streamlined risk-assessment workflows and clear referral standards, but also technological infrastructure that supports automated eligibility screening and data integration across services.

A second adaptation related to discharge and follow-up processes, which were modified to provide greater flexibility for women who commenced a RRMed. Rather than formally discharging participants immediately after stabilisation on treatment, ongoing care was transferred back to the referring clinician or GP while participants remained notionally linked with the PCMed Service. This approach allowed women to re-access specialist review if clinical concerns arose, without requiring a new referral. This adaptation was consistent with the intervention's intended support model, which included re-entry pathways for women requiring additional specialist input.

Overall, these findings suggest that the PCMED Service was delivered with high fidelity to its core design and was feasible within routine clinical practice. More broadly, they indicate that a telehealth, NP-led prevention service could form part of a realistic service response to the evidence–implementation gap in breast cancer prevention, provided that future scale-up is accompanied by robust governance, workforce development, administrative support, technological infrastructure to support automated eligibility screening and risk assessment, and explicit integration with primary care and specialist referral pathways.

6.5 Theoretical Integration: The Knowledge to Action Framework

The findings of this thesis can be interpreted usefully through the Knowledge to Action (KTA) Framework,[99] outlined in Chapter 2, Section 2.3. This framework was selected to guide the broader evaluation of the PCMed Service Within this framework, the knowledge creation component for RRMeds was already well established before implementation of the service. Therefore, the central problem was not lack of evidence, but failure to translate this knowledge into routine clinical practice.

The findings from the retrospective chart review help define the known evidence–implementation gap. In the historical control sample, very few participants had a documented discussion about RRMeds, and use of these medications was rare. Interpreted through the KTA Framework, this reflects a breakdown early in the action cycle: although women at increased risk were being identified within specialist services, the knowledge that preventive medication

was an evidence-based option was not consistently being translated into a structured clinical discussion, prescribing pathway, or follow-up process. In this sense, the findings illuminate a gap between risk identification and knowledge use.

The PCMed Service can be understood as an implementation strategy to bridge that gap by adapting existing knowledge to the local context and embedding it within a practical service model. Rather than generating new clinical evidence about the efficacy of risk-reducing medications, the service sought to operationalise what was already known by creating a dedicated pathway for counselling, prescribing, and follow-up. This included a telehealth-first model, a NP-led consultation pathway, access to specialist prescribing support, and structured post-prescription review. These features represent an attempt to move beyond awareness of evidence towards its routine application in clinical care.

The uptake findings suggest that, among women who attended the PCMed Service, the structured pathway effectively supported knowledge use and medication initiation. However, it is important to acknowledge that the historical sample and the PCMed Service attendees represent different cohorts that cannot be directly compared. Women who attended the PCMed Service had already been referred to, accepted, and attended a dedicated prevention consultation, suggesting they may have been more interested in or receptive to preventive medication than the broader population of eligible women. This creates potential for self-selection bias, whereby the observed uptake among PCMed attendees may reflect both the effectiveness of the PCMed Service model and the characteristics of women who chose to engage with it. Accordingly, while the contrast between low documented discussion in the historical sample (4%) and high RRMed initiation among PCMed attendees without contraindications (54.1%) is striking, this should not be interpreted as definitive evidence that the service caused an increase in population-level uptake. Rather, within the KTA Framework, these findings indicate that the PCMed Service successfully operationalised existing knowledge into a practical clinical pathway that facilitated informed decision-making and RRMed initiation among those who engaged with it. Whether the PCMed Service increases RRMed uptake at a population level will require evaluation of adoption and reach, comparing RRMed uptake among all eligible women seen in Catchment Clinics before and after service implementation, an analysis that will be addressed in the larger PCMed mixed-methods evaluation once data are mature.

The process findings reported in Chapter 5 are also important within this framework. High use of telehealth, predominant delivery by the NP, efficient progression through the consultation pathway, and high attendance at planned follow-up suggest that the service was not only

implemented but implemented in a way that was workable within routine clinical practice. These findings speak to later phases of the action cycle, including monitoring knowledge use, evaluating outcomes, and considering the conditions required for sustained knowledge use. The minor adaptations observed during implementation, such as greater use of participant self-completed risk assessment, are also consistent with the iterative nature of the framework, which recognises that implementation requires refinement in response to local context.

At the same time, the findings also highlight that the KTA process remains incomplete. This thesis focused on a subset of outcomes from the larger PCMed Service mixed-methods evaluation as outlined in Chapter 1, Section 1.1.1. As such, provides only an interim view of implementation. Important questions remain regarding adoption, acceptability, persistence, cost, and equitable reach, all of which are necessary to determine whether the service can be sustained and scaled. Thus, within the KTA Framework, this thesis contributes most clearly to the stages of identifying the evidence–implementation gap, implementing a context-specific intervention, and providing early evaluation of its use and deliverability. The complete evaluation, will assess population-level impact, service acceptability, cost-effectiveness, and sustainability, as outlined in the published protocol (see Chapter 2, Section 2.8.1).

6.6 Clinical, Primary Care, Policy, Equity, and Sustainability Implications

The findings from this interim analysis have important implications for clinical practice, primary care integration, health system policy, equity, and service sustainability. This section addresses each of these domains in turn.

6.6.1 Clinical Practice Implications

From a clinical perspective, the findings suggest a dedication prevention pathway may address several barriers that currently limit RRMed discussions and uptake in routine specialist care. A centralised PCMed Service may reduce the time burden on referring clinicians, particularly breast surgeons and familial cancer clinicians, allowing greater focus on surveillance, surgical care, and management of complex familial or genetic presentations, while ensuring eligible women receive structured, evidence-based counselling regarding RRMeds. By providing a referral pathway for medication-based prevention, such a service may also reduce role ambiguity and uncertainty about whose responsibility it is to initiate these discussions.

This model is also relevant to survivorship (“Late Effects”) services that manage women treated with chest radiation for childhood, adolescent, or young adult cancers and who have treatment-related elevations in breast cancer risk. In these settings, routine clinical practice has

traditionally prioritised coordination of intensified breast surveillance, and the retrospective chart audit suggested that RRMed discussions were not documented. Providing a dedicated, specialist prevention pathway offers “Late Effects” clinicians a practical mechanism to translate risk identification into an accessible, individualised prevention discussion and prescribing pathway, without displacing the core survivorship focus on long-term follow-up and surveillance.

The PCMed Service intervention supports informed, values-based decisions and may counter common misconceptions and stigma by providing consistent, evidence-based counselling. For safe and timely initiation, clinicians require clear guidance on eligibility assessment. Decision aids and training in shared decision-making may further strengthen consultation quality and patient experience, though as discussed in Section 6.3, decision support alone may be insufficient without an accompanying implementation pathway that addresses prescribing, follow-up, and role clarity.

6.6.2 Primary Care Integration

Integration with primary care is central to the sustainability and scalability of a specialist-initiated prevention model. The PCMed Service was designed to transfer ongoing prescribing and monitoring to GPs once a RRMed had been initiated and stabilised. To support this transition, GPs received detailed handover documentation, including a summary of the prevention consultation, risk assessment, contraindication screening, shared decision-making process, medication type, dose and intended duration, monitoring recommendations, advice regarding treatment cessation, the Clinical Oncology Society of Australia clinician guide for RRMeds,[1] and contact details for telephone support from the PCMed Service.

Despite this structured handover process, no telephone calls were received from GPs during the study period. This may indicate that the written guidance was sufficient to support ongoing management. However, alternative explanations are also possible. GPs may have been uncertain about when or how to access telephone advice, reluctant to contact a specialist service informally, or more likely to manage issues independently or re-refer formally. It is also possible that the study period was too short to capture queries arising during longer-term RRMed use, or that some women discontinued treatment before GP management issues emerged.

This finding suggests that effective primary care integration requires more than written handover and the availability of specialist advice. Future implementation should examine whether GP handover documentation is received, understood and used in practice, and

whether additional strategies are needed to support confidence in ongoing RRMed management. These may include GP education, clearer thresholds for telephone advice versus formal re-referral, decision-support tools, and monitoring of prescribing, adverse-effect management and treatment persistence after transfer of care.

The study, described in the published protocol in Chapter 2, Section 2.8.1, will explore GP acceptability and may help identify barriers to ongoing primary care management, including reasons telephone support was not used. Future implementation should prioritise co-design with primary care to ensure that specialist initiation of RRMeds is matched by feasible and actively supported continuation pathways. Without this, transfer of care may remain incomplete, potentially contributing to treatment discontinuation, uncertainty about ongoing management, or transfer of responsibility back to specialist services, thereby limiting sustainability and scalability.

6.6.3 Policy Implications

From a policy perspective, clearer delineation of roles and responsibilities across primary care, familial cancer services, breast screening programs, and oncology is needed to reduce ambiguity that can inhibit initiation of preventative medication discussion. Funding models should explicitly support preventive pathways, including dedicated nurse-led prevention consultations with appropriate governance, training, and specialist backup. Investment in workforce development is likely required, including education for GPs and practice nurses in primary care-based monitoring and side-effect management, and well as expansion of the NP workforce with prevention capabilities.

Investment in technological infrastructure is also critical. This includes automated eligibility screening systems that identify and flag women at increased risk based on documented pathology (e.g., AH, LCIS), family history algorithms, breast density data, and prior treatment history (e.g., thoracic irradiation). Strengthening information technology (IT) should also encompass electronic prompts, standardise referral templates with mandatory risk factor fields, referral decision support, and embedded decision aids to support consistency and reduce missed opportunities. Such technological enablers may be essential to reduce manual workload, improve scalability, and ensure consistent identification of eligible women across diverse clinical settings.

Emerging changes in population risk identification may further increase the need for scalable prevention pathways. BreastScreen is now routinely reporting mammographic density to clients and their GPs,[132] reinforcing the importance of breast density as a risk factor.[33] This

creates an opportunity to embed validated risk assessment and stratification processes that identify women at increased risk. Integrating breast density alongside other known risk factors into risk assessment tools, can improve risk discrimination and support informed decision-making about screening and prevention,[133] and these risk-stratified approaches have been shown to be feasible in practice.[111] However, increasing risk awareness without an accessible prevention pathway, has the potential to widen the existing evidence-implementation gap. A dedicated service such as the PCMed Service could provide the necessary bridge from risk identification to evidence-based preventive action, particularly given evidence that women receiving density notification may have increased intentions to seek GP advice.[134]

6.6.4 Equity Considerations

Equity and sustainability considerations are central to any scale-up. A centralised telehealth model may improve access for rural and remote populations.[135] Evidence also demonstrates that video telehealth is acceptable and feasible for culturally and linguistically diverse (CALD) populations requiring interpreter services, with Australian data showing that 84.71% of interpreter-requiring patients successfully use video consultations.[130] However, equity cannot be assumed, and clinicians must avoid implicit bias that may lead to preferential use of telephone over video for CALD patients, as this can inadvertently reduce access to appropriate interpreter-supported care (as discussed in Section 6.4).

Uptake and outcomes must be examined across groups that are culturally, linguistically, and geographically diverse, those with low health literacy, and those from lower socioeconomic backgrounds. Technological barriers must also be considered: while telehealth improves geographic access, it may disadvantage women with limited digital literacy, unreliable internet access, or language barriers requiring interpreter support, as demonstrated by the single participant in this study who required face-to-face delivery across all consultations due to combined technology and interpreter needs (Section 6.4). Culturally and linguistically appropriate decision support, reliable access to video-compatible interpreter services, and targeted engagement strategies will be essential to avoid widening disparities.[129]

For these reasons, future service design should incorporate co-design with patients, interpreters, primary care clinicians, specialist services, and implementation stakeholders to ensure that telehealth pathways are acceptable, accessible, and feasible in routine practice. This should include attention to modality choice, interpreter integration, digital support, referral processes, follow-up responsibilities, and escalation pathways. Sustainability will require integration into routine workflows, ongoing workforce training, stable funding, and

governance structures that specify accountability, quality assurance, and cross-site consistency in referral, counselling, initiation, and monitoring.

6.6.5 Economic and Sustainability Implications

Finally, economic implications are important for policy translation. Although dedicated prevention services incur upfront costs, including staff time and training, downstream savings may occur if increased RRMed uptake reduces breast cancer incidence among appropriately selected high-risk women. Although the cost evaluation is outside the scope of this thesis, the larger PCMed mixed-methods evaluation will assess the cost of delivering the PCMed Service from a healthcare provider perspective, as described in the published protocol, Chapter 2, Section 2.8.1. Further economic modelling, including consideration of long-term clinical outcomes and health system costs, may be required to inform policy decisions regarding broader implementation and national scale-up.

6.7 Strengths and Limitations

This thesis has several important strengths. First, it evaluates a novel, real-world clinical service designed to address clearly identified evidence–implementation gap in breast cancer prevention. Rather than examining chemoprevention uptake in a trial-only setting, the study assessed how a dedicated telehealth service functioned within routine clinical care, increasing the practical relevance of the findings for future service planning and implementation. Second, the inclusion of a historical control sample provided important context, demonstrating the magnitude of the pre-existing evidence-implementation gap. Third, the evaluation was guided by an established implementation science framework, the KTA Framework, which provided an evidence-based structure for assessing not only whether the intervention worked among attendees, but also how and why it functioned in practice. This theory-driven approach enabled systematic examination of the translation of evidence into routine care, identification of implementation barriers and facilitators, and explicit consideration of feasibility, fidelity, and adaptations required for real-world delivery. By grounding the evaluation in implementation science principles, this thesis provides findings that guide future scale-up, service refinement, and broader implementation strategies**.** Fourth, the prospective evaluation of service delivery using predefined indicators of uptake, feasibility, and fidelity strengthened the internal coherence of this thesis and enabled assessment of whether the intervention was delivered as intended. Finally, the thesis examined the service from multiple implementation perspectives, including baseline care, uptake among attendees, and early process outcomes, thereby providing a more comprehensive understanding of how the service functioned in practice.

Several limitations should also be considered. First, this thesis presents an interim analysis of the larger PCMed Service mixed-methods evaluation and findings are therefore based on relatively small sample sizes, particularly in the prospective uptake analysis. The sample size precluded robust inferential modelling and means that subgroup findings should be interpreted cautiously. Second, the study was conducted within a single tertiary cancer centre and its referral network, which may limit generalisability to other settings with different referral pathways, workforce structures, and patient populations. Third, the use of a historical retrospective chart review means that the study relied on the completeness and quality of clinical documentation. A lack of documented discussion does not definitively establish that discussion did not occur, and some women may have received counselling outside the audited records. In addition, chart review could not assess the quality, depth, or decisional adequacy of any discussion that was recorded. Fourth, the historical control sample and PCMed Service attendees represent different cohorts that cannot be directly compared. Women who attended the PCMed Service had already accepted a prevention consultation, creating potential self-selection bias. The high uptake among PCMed Service attendees may therefore reflect both the service pathway and participant characteristics, not service impact alone. The observational design, combined with confounding differences between time periods, precludes causal inference regarding service effectiveness. Population-level impact assessment will require before-and-after comparison at the Catchment Clinic level, as planned in the larger PCMed mixed-methods evaluation. Fifth, the PCMed Service was delivered by a single NP limiting the generalisability of feasibility and fidelity findings. Although the model effectively supported RRMed initiation and follow-up, outcomes may reflect the NP's specific expertise, communication style, and clinical experience, particularly as they also served as lead investigator. This may have enhanced protocol fidelity and service quality. Broader implementation should therefore be evaluated across multiple practitioners and settings to determine whether the model remains feasible, effective, and consistent at scale, and whether additional training, standardisation, or clinical support is required. Finally, some variables were derived from routinely collected data and area-level proxies such as Socio-Economic Indexes for Areas, which may not fully reflect individual-level circumstances and may therefore introduce some misclassification.

Taken together, these strengths and limitations suggest that the thesis makes a useful contribution to understanding implementation of a novel prevention service, while also underscoring the need for continued evaluation with larger samples, longer follow-up, and broader assessment of adoption, acceptability, persistence, equity, and cost.

6.8 Recommendations for Future Research

Further research is required to build on the findings of this interim analysis and support translation of the PCMed Service into broader clinical practice. The recommendations below are organised according to priority domains for future investigation.

6.8.1 Completion of the Planned Mixed-Methods Evaluation

A priority for future work is completion of the planned mixed-methods evaluation, which will examine outcomes beyond the scope of this thesis. These include the impact of the PCMed Service at the Catchment Clinic level using a before-and-after implementation design, as well as adoption, participant and clinician acceptability, reasons for non-uptake, treatment persistence, and cost, as outlined in Chapter 2, Section 2.8.1. These outcomes are needed to determine whether the promising uptake observed among women who attended the PCMed Service can be achieved at sufficient scale and reach to influence broader patterns of preventive care.

6.8.2 Reach, Adoption, and Engagement

Future research should also distinguish clearly between reach, adoption, and engagement when evaluating the broader impact of the service. In this context, reach refers to the extent to which the PCMed Service extends to the eligible population,[136] adoption refers to the extent to which referral pathways and clinicians use the PCMed Service in routine practice,[89] and engagement refers to the extent to which referred participants actively attend and participate in consultations and follow-up.[137] This distinction is important because a service may be feasible and effective for those who attend yet still have limited broader impact if eligible women are not reached, referral pathways are inconsistently used, or participation declines after initial contact.

A related priority is to better understand reach and engagement. Although uptake among attendees of the PCMed Service was encouraging, the overall effect of the model will depend on whether eligible women are identified, informed about the service, and willing to attend. Further work is therefore needed to evaluate referral pathways, invitation timing, patient navigation strategies, and other mechanisms to improve service use among women who are eligible but may not otherwise engage. Attention should be given to women managed across fragmented pathways, including familial cancer, breast surgical services, late effects (survivorship), and primary care settings.

6.8.3 Equity and Diversity

Further research is also needed to evaluate equity. Future research should assess whether uptake, PCMed Service use, and outcomes differ according to language, health literacy, socioeconomic position, geographic location, and access to specialist care. This is particularly important in the Australian context, where geography and uneven access to specialist services may affect preventive care. Equity-focused research should also examine the effectiveness of strategies such as culturally and linguistically appropriate decision support, interpreter-supported care, and targeted outreach for underserved populations. Future research should also evaluate implementation strategies to address implicit bias in telehealth modality selection. The present study identified that people requiring interpreter services can successfully engage with video telehealth,[130] yet clinician assumptions about digital capability may lead to inappropriate use of telephone consultations, which can hinder interpreter integration.[130] Research is needed to determine whether clinician training, decision support tools, or standardised triage protocols can reduce such bias and ensure that video telehealth is offered equitably across diverse populations.

6.8.4 Scalability, Sustainability, and Primary Care Integration

An additional priority is the assessment of scalability and sustainability. The present findings suggest that a telehealth, NP-led model is feasible, but wider implementation would require careful evaluation of workforce capability, governance arrangements, referral processes, funding mechanisms, and integration with primary care. In particular, future research should examine primary care integration through co-design with GPs to determine whether current handover and support systems are meeting their needs. Although no calls from GPs were received during the study period despite telephone support being offered (Section 6.6.2), absence of identified problems does not confirm absence of problems. GPs may be managing uncertainties or challenges without seeking specialist consultation, or the study timeframe may have been too brief to capture the full trajectory of ongoing care. Co-design research should therefore actively seek GP perspectives on handover documentation quality, confidence in ongoing prescribing, experiences of managing RRMed-related issues, and barriers to accessing support. Understanding how specialist initiation of RRMeds can be linked effectively with GP-led ongoing care will be essential for a sustainable model of care.

6.8.5 Nurse Practitioner Model

Evaluation of the NP-led model across multiple practitioners and settings is also a research priority. The present study involved a single NP, and it cannot be assumed that similar

feasibility, fidelity, or uptake outcomes would be achieved with different practitioners or in diverse clinical contexts. Future research should assess whether the model can be effectively delivered by NP with varying levels of experience in breast cancer risk assessment and prevention counselling, and should identify the training, competencies, clinical support structures, and governance arrangements required to ensure consistent service quality and patient outcomes. Multi-site evaluation would also allow assessment of how local context, referral pathways, and integration with primary care influence service delivery and sustainability.

6.8.6 Risk Assessment Pathways and Technological Solutions

Another important area for further investigation relates to risk assessment pathways. The implementation observations in this thesis suggest that some referral pathways may not consistently integrate hereditary and pathology related risk factors. Larger studies are warranted to determine whether this contributes to under recognition of women who may be eligible for preventive intervention and to evaluate how risk assessment tools and referral processes can be better integrated across services. Future research should also evaluate the effectiveness and feasibility of automated eligibility screening systems, including algorithms that flag women based on documented pathology, family history data, breast density, and treatment history. Such technological solutions may be critical to improving scalability, reducing clinician workload, and ensuring consistent identification of eligible women across diverse clinical settings.

6.8.7 Persistence, Adherence, and Long-Term Outcomes

Finally, longer term research is needed to evaluate the downstream clinical and economic consequences of this model. This includes persistence with and adherence to RRMeds, adverse effects, quality of life, and the potential impact of improved uptake on breast cancer incidence and health-system costs. Understanding why women discontinue RRMeds, and identifying strategies to support long-term adherence, will be critical for maximising the preventive benefit of this intervention. Such work will be important for informing policy, service planning, and future national scale-up.

6.9 Conclusion

This thesis evaluated a novel telehealth service designed to support the initiation of RRMeds for women at increased risk of breast cancer. Using an implementation science framework (KTA

Framework), this thesis examined pre-implementation baseline care, uptake among service attendees, and early process outcomes including feasibility, fidelity, and required adaptations.

The findings confirmed substantial evidence–implementation gap prior to PCMed Service introduction, with very low documented discussion and use of preventive medication in routine care at participating specialist sites. In contrast, among participants who attended the PCMed Service and had no contraindications to treatment, uptake of RRMed was high (54.1% at 6 months). The PCMed Service was also feasible to deliver and was implemented with a high degree of fidelity to the planned intervention, with telehealth and a NP-medical oncologist model functioning effectively within routine clinical practice.

Taken together, these findings suggest that the central problem in routine care may not simply have been low willingness to use preventive medication, but failure to consistently provide women with an accessible pathway for informed discussion, prescribing, and follow-up. The PCMed Service appears to offer a practical response to this gap by translating established evidence into a structured clinical model. By creating an explicit pathway that addresses both the decisional and practical barriers to RRMed uptake, the service demonstrates that it is possible to operationalise guideline-recommended primary breast cancer prevention in real-world clinical practice.

However, important limitations must be acknowledged. This thesis presents interim findings based on a small sample, and women who attended the PCMed Service may have differed from the broader eligible population because of self-selection bias. Direct comparison between the historical control sample and PCMed attendees is not methodologically appropriate for assessing population-level service impact. Furthermore, the PCMed Service was delivered by a single NP within a single tertiary cancer centre, limiting generalisability. Findings from the completed mixed-methods evaluation will be necessary to determine whether this model achieves sufficient adoption, acceptability, supports persistence and adherence to RRMeds, is justified from a cost perspective, and increases RRMed uptake at a population level among all eligible women seen in Catchment Clinics.

Nonetheless, this thesis contributes important early evidence that a dedicated, prevention-focused telehealth service can support use of RRMeds among engaged participants and can be delivered with fidelity within routine clinical workflows. If findings from the completed evaluation confirm population level impact and demonstrate acceptability to participants and clinicians, this model could inform the development of scalable prevention pathways that address a long-standing evidence-implementation gap in breast cancer prevention. Given the

proven efficacy of RRMeds and the persistent under-use of these interventions in routine care, such implementation strategies are urgently needed to translate prevention evidence into meaningful reductions in breast cancer incidence among women at increased risk.

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Appendices

Appendix 1: Full Study Protocol

Note on appendix numbering

Appendix 1 contains the full study protocol and associated protocol appendices. To avoid confusion with the thesis appendices, appendices that formed part of the original study protocol are labelled as protocol appendices within Appendix 1. Where a protocol appendix duplicates material already presented elsewhere in the thesis, this is indicated and the material is not reproduced.

Appendix 1.1 Study Protocol

SUPPORTING UPTAKE OF BREAST CANCER PREVENTION MEDICATIONS AND MINIMISING TREATMENT DISCONTINUATION: A PROCESS EVALUATION

Version 5, 6 March 2025

Investigators

Prof Kelly-Anne Phillips – Medical Oncology Lead for the Preventing Cancer with Medication (PCMed) Service, PMCC

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VERSION HISTORY

Version 5, 06 March 2025

The primary reason for this protocol amendment is the addition of Aim 8; i.e. to evaluate persistence with RRMeds for women who choose to commence a preventive medication.

This involves data collection at two additional time points (2 years and 4.5 years).

In addition, editorial changes have been made following a comprehensive review of the protocol to amend minor in-text errors and promote greater clarity. This includes clarifying the time point for inviting eligible clinicians to complete a questionnaire and (optional) semi-structured interview.

Applicable section number(s)/title	**Nature of revision**
BACKGROUND **1.3 Use of Breast Cancer Risk-Reducing Medications in Australia**	The definition of "persistence" has been added to this section to promote clarity.
AIMS **2.2 Specific Aims**	"Aim 8" has been added to the protocol to evaluate women's persistence with RRMeds at 2 years and (for those women planned for a 5 year course) 4.5years after commencement of the RRMed.

	Persistence with RRMeds is vital information given these medications are given for 3-5 years and low persistence has been identified as an in issue in previous research. Prior versions of the protocol have recognised persistence as an important issue; however, the addition of this aim was only felt to be of value if uptake of RRMeds was relatively high. Preliminary data is now suggestive that collection of persistence data would be valuable given the high rates of uptake of RRMeds for women who attend the PCMed Intervention.
METHODS 3.2 Participants <u>iii) Active follow up</u>	Additional information is provided in this section to promote clarity around the participants who will receive phone calls during active follow-up and the timing of these phone calls. This includes the addition of follow-up phone calls to women who commence RRMeds at 2yrs and 4.5 yrs (the later being relevant only to women planned for a 5 year course) which is relevant to data collection for Aim 8.

3.2.2 Eligibility of Clinicians	Minor editorial change to clarify the recruitment process for Eligible Clinicians.
3.3 Identification of Eligible Women and Clinicians 3.3.3.2 Recruitment of Women to Participate in Aim 8. 3.3.4 Recruitment of Clinicians (Aim 5)	Given that Aim 8 was added to the protocol in March 2025, this section has been added to provide clarity regarding the reconsent process for women who were recruited to the study prior to the addition of Aim 8. Minor editorial change. For "eligible clinicians", participant recruitment and completion of the intervention (questionnaires and semi-structured interviews) has been defined in previous versions of the protocol as being "at the end of the study period". For clarity, "at the end of the study period" in this context, refers to when sufficient clinicians have made referrals to the Service that it is feasible for the sample size to be met. The wording of the protocol in this section (3.3.4) and other relevant

	sections (3.2, 3.5.3, 3.6.2, 4.0) has been changed to reflect this.
3.5 Study Consent Process 3.5.2 Dual Opt-out and Opt-In Consent for Women who attend the PCMed Service	Minor editorial change to reflect that women will be asked to consent to follow-up phone calls at 2 years and 4.5years (for women planned for a 5 year course) if they choose to commence a RRMed.
3.6 Data Collection 3.6.2 Prospective Data Collection	"Data Collection at 2 years" and "Data Collection at 4.5 years" are new sections that have been added to reflect data collection at these time points for Aim 8.
4.0 ENDPOINTS 8) Persistence	The addition of Endpoint 8 has been made to reflect data collection specific to Aim 8.
5.0 STATISTICAL ANALYSIS AND SAMPLE SIZE CONSIDERATIONS 5.2.3 Aim specific analyses	The plans for statistical analysis of data collected for Aim 8 have been described.
REFERENCES	Updated for clarity.
APPENDICES	

Appendix A – The PCMed Service Intervention Appendix F – Email invitation for semi-structured interview for Clinicians Appendix G – Telephone scripts for data collection at 6 and 12 months, 2years and 4.5years.	References updated for clarity. Minor editorial changes have been made to the wording in Appendix F "Email to Clinicians" to improve clarity. Updated to include a telephone script to reconsent women for ongoing participation in the study (where relevant) if they had already provided consent prior to this Protocol Amendment (March 2025). Appendix G has also been updated with a telephone script for the planned phone calls at 2years and 4.5years.
PATIENT INFORMATION AND CONSENT FORM	Updated to reflect the addition of Aim 8 to the protocol.

Version 4, 8 August 2024 The primary reason for this protocol amendment is to elaborate on the methods for the semi-interviews evaluating the acceptability of the PCMed Service. In addition, editorial changes have been made following a comprehensive review of the protocol to amend minor in-text errors and promote greater clarity.	
Applicable section number(s)/title	**Nature of revision**

STUDY GLOSSARY	Addition of the term "Catchment Clinics". This term refers to the specialty clinics relevant for aims 1 and 2 of the study. The term has replaced the need to name the individual specialty clinics throughout the study protocol. These minor editorial changes are not referred to again in this document.
BACKGROUND **1.1 Breast Cancer Overview** **1.2 Barriers to Clinicians Discussion and Prescribing Risk-Reducing Medications** **1.8 The PCMed Service Responds to the Evidence-Implementation Gap** **1.9 Embedding Health Services Research into the PCMed Service**	Update of in-text citations to reflect changes in References. In-text citations amended due to error in previous protocol. Abbreviations of services inserted. Addition of in-text citation previously omitted.
AIMS 2.2 Specific Aims	Rewording of Aims to promote clarity.
METHODS **3.2 Participants** iii) Active follow-up 3.2.1 Eligibility of Women	Additional information provided to promote clarity around the participants who will receive phone calls during active follow-up and the timing of these phone calls.

	Separation of eligibility criteria for women in the prospective and retrospective components to provide further clarity. Change of female to "assigned female at birth".
3.3.3.1 Recruitment of women for the PCMed Service Acceptability Interview	New section expanding on the methods for interviews, in particular the recruitment and sampling strategy.
3.3.4 Recruitment of Clinicians (Aim 5)	Addition of information provided on the recruitment and sampling strategy.
3.5 Study Consent Process 3.5.3 Clinicians	Option for clinicians to indicate on the TFA questionnaire if they wish to be approached for the interview has been removed. All eligible clinicians will be invited to participate in an interview by email.
3.6 Data Collection 3.6.1 Historical Cohort (retrospective component) for Aim 1	Addition of parity due to accidental omission.
3.6.2 Prospective Data Collection *Data Collection at 12 months*	Rewording of section to promote clarity.
Interviews with Women	Additional information provided on the development of the interview guide for

	women and software to be used in the thematic analysis.
Interviews with Clinicians	Additional information provided on the development of the interview guide for clinicians and software to be used in the thematical analysis.
4.0 ENDPOINTS 5) Acceptability	Addition of Endpoints for semi-structured interviews.
6) Evaluation of service delivery	Minor editorial changes to improve clarity. Change in timeline with <u>all</u> variables to be assessed at the end of the study period.
5.0 STATISTICAL ANALYSIS AND SAMPLE SIZE CONSIDERATIONS <u>5.2.3 Aim Specific analyses</u> *Aim 5*	Additional information inserted on data analysis for interviews.
REFERENCES	Reference 1 and 2 updated to reflect.
APPENDICES **APPENDIX A: THE PCMED INTERVENTION** **Eligibility for PCMed Service**	The insertion of new documents Removal of criteria that women (in the prospective component) needs to be an existing patient of the PMCC Family Cancer Centre (FCC), Breast Unit (BU) or Late Effects Clinic (LEC) or external GP or RMH FCC or BU or RWH BU to reflect

APPENDIX E: TFA Questionnaire for Clinicians **APPENDICES** **LIST OF APPENDICES**	current practice (that is, the PCMed Service accepts referrals if all other eligibility criteria met). Some minor editorial changes. Question 9 asking clinicians if they consent to being approached for a phone interview has been removed. All clinicians will be contacted via email and invited to participate. Consent is implied if they choose to participate in the interview. Development of new documents pertaining to the semi-structured Interviews. 1. Telephone call to request and consent participants participation in semi-structured interviews" (APPENDIX C). 2. Email inviting clinicians to participate in semi-structured interview (APPENDIX F). 3. Interview Guide for semi-structured interview with women (APPENDIX I). 4. Interview Guide for semi-structured interview with clinicians (Appendix K). Renaming of Appendices due to the insertion of the new documents above.
VERSION CONTROL Initial PCMed Service Protocol Version 3, 20 September 2023.	

PCMed Service Protocol Version 4, 27 November 2023. PCMed Service Protocol Version 5, 14 March 2024.	Renamed PCMed Service Protocol Version 1, 20 September 2023 due to error. Renamed PCMed Service Protocol Version 2, 27 November 2023. Renamed PCMed Service Protocol Version 3, 14 March 2024.

Version 3, 14 March 2024 Changes to the protocol are summarised below.
Primary reason for the protocol amendment was the addition of Royal Melbourne Hospital Familial Cancer Centre (RMH FCC) as a study site to improve recruitment for Aims 1 and 2 (see sections 2.2; 3.3.1 and 3.3.2). Addition of reason for declining referral to the PCMed Service if readily available (section 3.3.2, paragraph 2).

Version 2, 27 November 2023 Changes to the protocol are summarised below
Minor editorial changes have been made to two documents, The "Explanatory Pamphlet" and Appendix C Initial Consultation appointment letter with PICF with the later document renamed to "Research Invitation with PICF". The minor changes were a result of consumer feedback received when consumer testing of our processes for intake into the Preventing Cancer with Medications (PCMed) Service were undertaken and to accommodate the capability of the REDCap database which was built after initial ethics submission.

Version 1, 20 September 2023
Initial Creation

STUDY GLOSSARY

Term	Definition
Active follow-up	This is the phase where women who attend the PCMed Service and consent to the study are followed up with a questionnaire, phone calls and an optional telephone interview
AH	Atypical hyperplasia
AIs	Aromatase inhibitors
BU	Breast unit
Catchment Clinics	Catchment Clinics refers to the Royal Melbourne Hospital Familial Cancer Clinic (RMH FCC), the Peter MacCallum Cancer Centre Familial Cancer Centre (PMCC FCC), the PMCC Breast Unit (PMCC BU) and Peter MacCallum Late Effects Clinic (PMCC LEC).
DCIS	Ductal carcinoma in situ
EMR	Electronic medical record
EPIC	The database management system for electronic medical records
FCC	Familial cancer centre
GPs	General practitioners
Initial Consultation	The first consultation in the PCMed Service in which the woman will receive personalised information on her breast cancer risk and the pros and cons of risk-reducing medications
LCIS	Lobular carcinoma in situ
LEC	Late-effects clinic
NWAU	National Weighted Activity Unit - a measure of health service activity, expressed as a common unit, against which the National Efficient Price (NEP) is paid
Parkville Precinct	Hospital network consisting of the Peter MacCallum Cancer Centre, Royal Melbourne Hospital and Royal Women's Hospital
PCMed Service	Preventing Cancer with Medications Service
PICF	Participant information and consent form
PMCC	Peter MacCallum Cancer Centre
Post-Prescription Consultation	A planned consultation after a prescription for risk-reducing medication is provided to a woman. This will be booked 8-10 weeks after commencing this medication
Post-Prescription Consultations (ad hoc)	Unplanned consultations requested by the of the woman or her referring clinician or GP to address concerns during the treatment period

Pre-Service Questionnaire	A form to be completed by women prior to attending the Initial Consultation. This form will request information to confirm eligibility for the PCMed Service and help to streamline the Initial Consultation
PURN	Patient Unit Record Number
REDCap	A secure web platform to capture data for research purposes
Repeat Consultation	A subsequent consultation for women who did not take a prescription at the Initial Consultation. This will generally occur within 3 months from the Initial Consultation
Risk Assessment Tool	Online tools that enable healthcare professionals to calculate an individual's future risk of breast cancer risk, e.g., CanRisk, iPrevent, IBIS Breast Cancer Risk Evaluation Tool
Risk Management Consultation	Consultation with the referring clinic where information is provided on a woman's personal risk of breast cancer and options to manage this risk
RMH	Royal Melbourne Hospital
RRMeds	Risk-reducing medications
RWH	Royal Women's Hospital
SERMs	Selective estrogen receptor modulators
SEIFA	Socio-Economic Indexes for Areas ranks areas according to socio-economic advantage or disadvantage using Census data
TFA	Theoretical Framework of Acceptability

1.0 BACKGROUND

1.1 Breast Cancer Overview

Breast cancer is a major public health problem in Australia. It is the most common cancer in women and is the leading cancer cause of disease burden[1]. In 2018, the average lifetime risk (before age 80 years) for a breast cancer diagnosis in Australian women was 11.6%[1]. However, approximately 20% of women are at considerably higher risk due to either genetic or non-genetic factors[2]. Importantly, many breast cancers can be prevented[3].

1.2 Breast Cancer Risk-Reducing Medications Overview

One strategy found to be efficacious to prevent breast cancer is the use of cancer preventing medications. These risk-reducing medications (RRMeds), a single tablet daily, can reduce the relative risk of breast cancer by 30%-60% if taken for 3-5 years[4-13]. RRMeds include the selective estrogen receptor modulators (SERMs), tamoxifen and raloxifene, and the aromatase inhibitors (AIs), anastrozole and exemestane. Tamoxifen is the only RRMed that is appropriate for pre- or peri-menopausal women. Post-menopausal women can choose between the SERMS or the AIs. These medications are often well-tolerated. The most common side-effects are vasomotor symptoms, but there are a range of other possible side-effects depending on which drug is chosen[4-13]. They can also have rare serious side-effects; tamoxifen increases the risk for endometrial cancer in post-menopausal women and both SERMs increase thrombosis risk, while the AIs increase risk of osteoporosis[4-13]. Guidelines recommend consideration of RRMeds for Australian women who have a breast cancer risk that is at least 1.5 times the population risk [14-16].

1.3 Use of Breast Cancer Risk-Reducing Medications in Australia

Despite evidence and guidelines supporting the use of RRMeds, currently only 2% of Australian women, who know they are at increased risk for breast cancer, have used prevention medications[17]. International data also reports low uptake of RRMeds in women with uptake around 8.7% in non-trial settings[18]. For women who use preventative medications, long term persistence is an important factor to ensure women experience the full preventative effect of the medication. Persistence is defined as the act of continuing the medication for the defined duration. A meta-analysis examining data on persistence found low long-term persistence, with persistence declining over time [18]. Trials with 5-year follow up data, found long-term persistence with tamoxifen ranged from 61% to 81%, with several studies reporting lower persistence with tamoxifen compared to the placebo and raloxifene arms,[18] suggesting side effects may be a contributing factor. Some studies suggested persistence with RRMeds was higher in woman with lower depressive symptoms with no sociodemographic factors associated with persistence [18]. Data suggests providing the opportunity for a personalised discussion including the risks and benefits of RRMeds and the provision of ongoing specialist support for women using RRMeds may be of benefit.

1.4 Barriers to Use of Risk-Reducing Medications by Women at Increased Risk

Most women at increased risk of breast cancer have never heard of RRMeds [19]. Lack of awareness of their existence is obviously a strong barrier to using these medications. In our research, among women who knew of their existence, lack of information and concern about side-effects (which is potentially exacerbated by lack of information) are both strong barriers to using these medications[19]. These barriers for women may, at least in part, be consequences of lack of clinician knowledge (see Section 1.5) with resultant inability of clinicians to impart tailored and appropriate information to each woman.

1.5 Barriers to Clinicians Discussing and Prescribing Risk-Reducing Medications

In Australia there is a major gap in terms of a medical workforce that is willing to manage women at moderate risk of breast cancer (i.e., 1.5-3 times population risk). These women are key candidates for cancer preventing medications, as surgical prevention is usually not appropriate for this risk level, and RRMeds are efficacious in this subgroup. Our research has shown that breast surgeons and Family Cancer Clinicians consider that they do not have capacity to manage moderate-risk women (as they are already at full capacity managing women with breast cancer and high-risk women respectively)[20], and that general practitioners (GPs) generally lack the knowledge to manage them[21]. Thus, most of these women do not get a risk-reducing intervention, despite the fact that almost 50% of breast cancers occur in this group. This is a major unmet need in breast cancer control.

At least one third of GPs who manage women at increased risk of breast cancer are unaware that RRMeds exist. GPs who <u>are</u> aware of these medications generally do not feel they have the required knowledge about the medications to initiate them for their patients[19]. In fact, only 3% of GPs feel "very confident" in providing information to women about these medications, and only 31% of GPs felt it was their role to write an initial prescription. Not enough knowledge or training was the strongest barrier to prescribing for 60% of GPs.

For breast surgeons who manage women at increased risk of cancer, only 3% had never heard of RRMeds and 56% felt "very confident" in providing information to women about these medications. Most (81%) were willing to write an initial prescription, although only a minority (43%) thought it was their role to write ongoing scripts. The major barrier to prescribing for breast surgeons was concern about the side-effects of the medications; this was the strongest barrier for 40%. The next most common strongest barrier was lack of knowledge or training (15%). An important minority (14%) identified lack of time in a consultation as the strongest barrier[19].

We have also previously shown that most Family Cancer Clinicians have never prescribed RRMeds and that, again, lack of knowledge is a major barrier to these clinicians even discussing the subject with women[20].

1.6 Specialist Support a Key Facilitator for Clinicians to Discuss and Prescribe Risk-Reducing Medications

The ability to access specialist support and clear guidance was identified by 59% of GPs and 27% of breast surgeons as the strongest potential facilitator for prescribing RRMeds[19].

1.7 The Evidence-Implementation Gap

Thus, currently there is a large evidence-implementation gap, with few women being offered RRMeds despite their clear efficacy and guidelines that suggest they are a standard of care option. Our research suggests that lack of a medical workforce capable of, and willing to, discuss and initiate prescription of these medications is a major driver of this evidence-implementation gap.

Given the sparse uptake of RRMeds across the Australian community currently, it is unlikely that socioeconomic, cultural, and linguistic factors currently play a major role. A UK study revealed no socio-demographic determinants of cancer preventing medication uptake, but all participants had to have been to a clinic to discuss their breast cancer risk[23]. Interest in having a personal breast cancer risk assessment is greater in women on higher incomes[24], so any strategy to increase uptake of RRMeds should evaluate whether uptake is influenced by these factors.

1.8 The PCMed Service Responds to The Evidence-Implementation Gap

As a response to our research showing that lack of workforce capability is at least in part driving the identified evidence-implementation gap, and following stakeholder consultation, the Peter MacCallum Cancer Centre (PMCC) will launch the novel Preventing Cancer with Medications (PCMed) Service (see Appendix A). This Service will be a consultative telehealth Service with the primary aim of initiating evidence based RRMeds for women at increased risk of breast cancer and supporting women and their referring clinicians and GPs throughout the prolonged treatment period.

In the initial phase covered by this research protocol, the Service will accept women referred by specialists from the Familial Cancer Centre (FCC), Breast Unit (BU), and Late Effects Clinic (LEC), within the Parkville Precinct (PMCC, Royal Melbourne Hospital (RMH) and Royal Women's Hospital (RWH)), as well as from doctors external to these sites. These will be women at increased risk of breast cancer due to a family history of the disease, a personal history of lobular carcinoma in situ (LCIS) or atypical hyperplasia (AH), or history of chest irradiation. It is expected that women attending the aforementioned clinics will have a discussion regarding their breast cancer risk and possible risk management options (subsequently referred to in this protocol as the "Risk Management Consultation"). If eligible for referral to the PCMed Service, they will receive information on the PCMed Service (verbal and a pamphlet), and a referral will be generated as appropriate.

1.9 Embedding Health Services Research into the PCMed Service

This protocol describes research that will be conducted to evaluate the implementation of the new PCMed Service, which is a complex intervention. Figure 1 describes a Knowledge to Action Framework, which is a conceptual framework that can be used to describe the concept of moving knowledge into action[25]. It integrates the roles of knowledge creation (depicted in the centre of the below diagram) and

knowledge application (labelled the 'Action Cycle'). Figure 2 illustrates the adaption of the Knowledge to Action Framework to RRMeds for breast cancer and highlights how and where the study described in this protocol fits. As detailed in the overview above, the knowledge creation component for breast cancer RRMeds is complete (although of course knowledge is always being honed). This protocol specifically relates to the components of the action cycle highlighted in the red boxes in Figure 2.

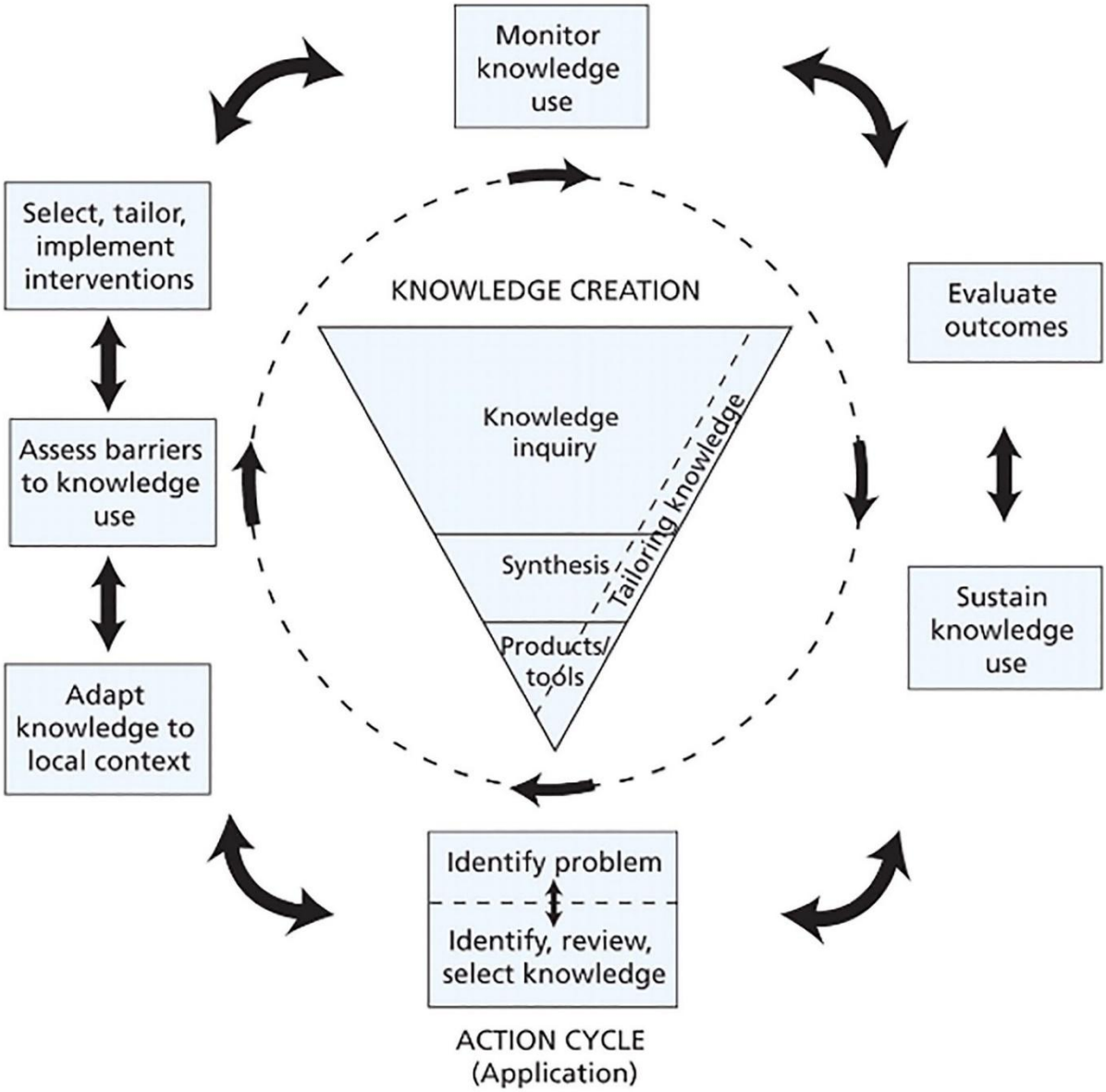

Figure 1: The Knowledge to Action Process[25]

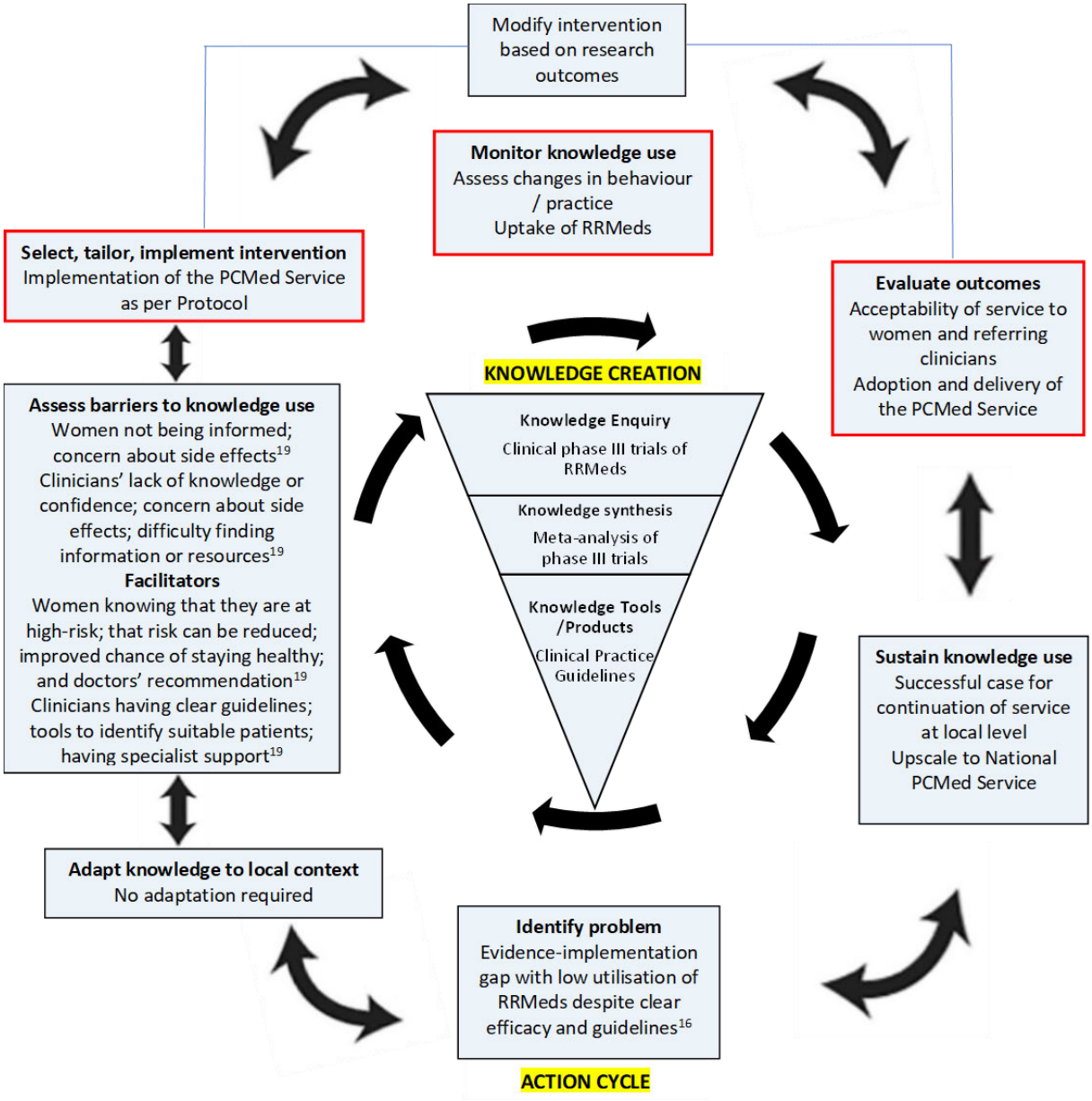

Figure 2: The Knowledge to Action Cycle adapted for Breast Cancer Risk Reducing Medications

The key research questions are whether the PCMed Service is associated with increased use of RRMeds, is well-adopted and is deliverable as planned, and is acceptable to clients and clinicians. The cost of the new Service will also be assessed.

The results of this research will be used internally within PMCC to provide an evidence-base for funding an ongoing clinical Service. However, it will also be used more broadly by key stakeholders to inform the planning of a potential scale-up phase of the PCMed Service. The ultimate vision is for scale-up to a national PCMed telehealth Service, potentially in partnership with other institutions and cancer peak bodies.

2.0 AIMS

2.1 Overarching Aim

The overarching aim is to explore the process and impact/effectiveness of implementing a new clinical service aimed at supporting the uptake of, and persistence with, breast cancer prevention medications.

2.2 Specific Aims

1) To determine whether the PCMed Service is associated with an increased use of RRMeds by women at increased risk of a 1st breast cancer who attended the RMH FCC, or the PMC clinics (FCC/BU/LEC) (hereafter referred to as the "Catchment Clinics", compared with the use of RRMeds in a historical cohort of similar women who attend the Catchment Clinics prior to the PCMed Service implementation. This will be assessed at approximately 12 months after the last Risk Management Consultation in the Catchment Clinic.

2) To describe the adoption of the PCMed intervention by women who attended the Catchment Clinics. Specifically, the proportion of eligible women that attend at least one PCMed consultation within 6 months of a Catchment Clinic Risk Management Consultation where the PCMed Service is discussed.

To explore the characteristics associated with adoption of the PCMed intervention (age, socioeconomic status (SEIFA), marital status, indigenous status, country of birth (Australia/not Australia), need for interpreter, referral source (clinic i.e. FCC, LEC or BU and referring clinician type i.e. geneticist, medical oncologist, radiation oncologist, breast surgeon, other), estimated 10-year and 20-year breast cancer risk, estimated residual life-time breast cancer risk, history of breast biopsy, history of LCIS/AH, history of chest irradiation, parity, marital status, education level, number of 1st degree relatives with breast cancer).

Note aims 1 and 2 will only use data on women who attended the Catchment Clinics. It will not include data on women referred from other sources such as the RWH BU, the RMH BU or other doctors within or external to the Parkville Precinct. This is because the historical cohort data (needed for aim 1) will not be readily available nor will the number of potentially eligible women seen at those sites (needed for aim 2).

3) To determine the uptake of RRMeds 6 months after attendance at the PCMed Service in women who have no contraindications for prescription of

RRMeds at the Initial or (if required) the Repeat Consultation.

To explore the characteristics associated with uptake (age, socioeconomic status (SEIFA), indigenous status, country of birth (Australia/not Australia), need for interpreter, referral source (FCC/BU/LEC/external service etc), referring clinician type, estimated 10-year breast cancer risk, estimated residual life-time breast cancer risk, history of breast biopsy, history of LCIS/AH, history of chest irradiation, parity, marital status, education level, and number of 1st degree relatives with breast cancer).

4) To explore the reasons for not taking up RRMeds in the 6 months after attending the PCMed Service in women (who had no contraindications for prescription of RRMeds at the Initial or Repeat Consultation(s). Their self-reported intention to take RRMeds in the future will also be explored.

5) To evaluate the acceptability of the Service:

a. For woman who use the Service, and
b. For clinicians working within the Catchment Clinics (regardless of whether or not they refer to the PCMed service) and for other referring clinicians (e.g. from RMH, RWH, GPs and other external sites).

6) To evaluate the delivery of the PCMed Service intervention (as described in Appendix A), and any adaptations required. Specifically:
    a. To determine the proportion of consultations that are conducted by telehealth rather than face to face or phone, and the reasons for requiring face to face consultations or phone if required.
    b. To describe the proportion of consultations conducted by the nurse practitioner (NP) versus a medical oncologist (MO) or the combination.
    c. To describe the approximate duration of the consultations (<15 minutes, 15-29 minutes, 30-44 minutes, 45-59 minutes, >1 hour).
    d. To describe the number of consultations required before a prescription is written, or the woman is discharged from the Service.

e. To determine the number of women who do not attend the Post-Prescription Consultation and the reason why (e.g., no side-effects of concern; ceased the medication; did not take the medication).
f. To determine the number and approximate duration (as per 6c. above) of additional Post-Prescription Consultations required and the reasons for them.
g. To describe the number, approximate duration (<5 mins, 5-10 mins, 11-20 mins, >20 mins) and nature of patient, referrer, or GP calls to the hotline.
h. To explore what factors, influence each of a-g (age, socioeconomic status (SEIFA), indigenous status, country of birth (Australia/not Australia), need for interpreter, referral source (FCC/BU/LEC/external service) and referring clinician type, marital status, education level, name of medication commenced (if any).
i. To document any unintended consequences of the PCMed Service implementation.

7) To evaluate the cost to PMCC of delivering the PCMed Service by reporting:
   a. the amount of funding received per woman through activity-based funding,
   b. the cost of service-delivery per woman through micro-costing, and

the difference between funding (a) and cost (b).

8) To evaluate women's persistence with RRMeds at 2 years and 4.5 years (the latter only relevant for women having a 5 year planned course) after commencement. Reasons for ceasing RRMeds and characteristics associated with persistence with RRMeds will be explored.

Aims 3-8 will include data from all women who consent to this research and who attend the PCMed Service during the study timeframe (regardless of whether the referrals originated from Catchment Clinics or from doctors external to these sites).

3.0 METHODS

3.1 Study Design / Setting

The study is an implementation pilot of a new complex intervention (the PCMed Service) based in a specialist cancer centre.

3.2 Participants

This study will include 2 types of participants:

1) women at increased risk of breast cancer and
2) clinicians.

And 2 components

1) a retrospective component (historical controls - women only, no clinicians)
2) a prospective component – this component has four parts:
    - i) data collection via EPIC and clinic database audit (under a waiver of consent) on all women from Catchment Clinics who are eligible to attend the PCMed Service but who do not attend the PCMed Service (this is required for Aims 1 and 2).
    - ii) data collection via EPIC and clinic database audit (under an opt out consent process) on all women from Catchment Clinics who attend the PCMed Service (this is required for Aims 1 and 2).
    - iii) Active follow-up of women who attend the PCMed Service and consent to this study (regardless of which referring clinic they came from). Women will be actively followed up after Service attendance with a questionnaire, telephone calls and an optional telephone interview. In regard to the telephone calls, the first call will occur at 6 months after the Initial or Repeat Consultation with the PCMed Service where a decision was made regarding RRMeds. All women regardless of whether they have commenced a RRMed will receive this phone call. For women who attended a Catchment Clinic a phone call will occur at 12 months after the Risk Management Consultation in the Catchment Clinic (regardless of whether they have commenced a RRMed or not). All women who commence a RRMed will also be followed up with a telephone call at 2 years and (in the case of those having a planned 5 year course) at 4.5 years after RRMed commencement to assess persistence.
    - iv) clinicians at the referring clinics will receive a questionnaire and optional telephone interview.

3.2.1 Eligibility of Women

Note, eligibility criteria to attend the PCMed Service are outlined in Appendix A. The following criteria relate to inclusion in the research outlined in this study protocol.

For historical controls (retrospective component):

a. Assigned female at birth.
b. Attendee of a Catchment Clinic
c. Aged between 20 and 70 years at the time they have their most recent Risk Management Consultation.
d. Residual lifetime breast cancer risk at least 20%[26] or 10-year risk of at least 5%[27], or history of LCIS or atypical hyperplasia[28], or prior thoracic irradiation before the age of 35 and the radiation was given at least 5 years prior[29].
e. Does not require germline genetic testing to further clarify risk.
f. Not eligible for the PMCC or RMH Breast and Ovarian Cancer Risk Management Clinic (i.e., those with a pathogenic variant in a major breast cancer predisposition gene and those who are untested 1st degree relatives of carriers).
g. No history of invasive breast cancer or ductal carcinoma in situ (DCIS).
h. No history of bilateral mastectomy.
i. No prior or current use of RRMeds at the time of the Risk Management Consultation.

For prospective component:

a. Assigned female at birth.
b. Age between 20 and 70 years.
c. Residual lifetime breast cancer risk at least 20%[26] or 10-year risk of at least 5%[27], or history of LCIS or atypical hyperplasia[28], or prior thoracic irradiation before the age of 35 and the radiation was given at least 5 years prior[29].
d. Does not require germline genetic testing to further clarify risk.
e. Not eligible for the PMCC or RMH Breast and Ovarian Cancer Risk Management Clinic (i.e., those with a pathogenic variant in a major breast cancer predisposition gene and those who are untested 1st degree relatives of carriers).
f. No history of invasive breast cancer or ductal carcinoma in situ (DCIS).
g. No history of bilateral mastectomy.
h. No prior or current use of RRMeds.
i. Written informed consent (for attendees of the PCMed Service).

3.2.2 Eligibility of Clinicians

- All clinicians who saw eligible women in the Catchment Clinics during the prospective study period (whether or not they referred any women to the PCMed Service).
- All clinicians external to Catchment Clinics (e.g., RMH, RWH, GPs) who referred women to the PCMed Service during the prospective study period.

3.3 Identification of Eligible Women and Clinicians

3.3.1 Historical Controls (retrospective component) for Aim 1

Historical controls will be consecutive eligible women who attended any of the Catchment Clinics. They will have attended those clinics in the same months of the year

(but in the year prior) as the women who are included in the prospective component to ensure study results are not biased by any seasonal variation in uptake of RRMeds. They will be identified using the FCC database and EPIC. Data will be abstracted from EPIC and the FCC database (waiver of consent).

3.3.2 Prospective Data Collection for Aim 1 and 2 for Women Who do not Attend the PCMed Service

Only women attending Catchment Clinics will be relevant to these aims. Data will be collected on consecutive women attending the Catchment Clinics from the study commencement date (14/11/2023). The Catchment Clinics will be actively encouraged to refer women to the PCMed Service. Clinics will be pre-screened for eligible women and clinicians reminded about the new PCMed Service, and a pamphlet provided (see Appendix B) so they can introduce the Service to potentially eligible women. Reasons for declining a referral to the PCMed Service will be recorded if this information is readily available.

"Recruitment" of these consecutive women will cease when the sample size of consenting women who do attend the PCMed Service has been reached (see 5.1 Sample Size). These women will be identified using the EPIC database and data will be abstracted from EPIC and the FCC database where relevant (waiver of consent).

3.3.3 Recruitment for Women who Attend the PCMed Service

All women who attend the PCMed Service will be invited to participate in this research. They will have the option of opting out of having their data abstracted (for Aims 1 and 2) from EPIC and the FCC database. They will be specifically invited to provide written informed consent for active follow-up, i.e., a questionnaire, follow-up phone calls and an optional telephone interview as outlined below in section 3.6.2. Only women who provide consent for this active follow-up will be included in aims 3-8. They will be identified as they are referred to the PCMed Service. They will be invited to participate by email/post at least 2 weeks prior to their attendance at the PCMed Service.

3.3.3.1 Recruitment of women for the PCMed Service Acceptability Interview

A subset of consenting women will be invited to participate in interviews regarding their experience of the Service (Aim 5). Women will be contacted by phone following their last planned PCMed consultation and invited to participate in an interview regarding their experience of the Service (see Appendix C). A purposive sampling framework, using quota sampling,[30] has been devised, to ensure a representative cross section of the sample population is recruited for the interview. Quota sampling will allow for a minimum number of cases to be recruited to each of the pre-specified demographic categories:

- Age: (20-39 years); (40-55years); (>55years).
- Residence (Metro/Regional/Rural)
    - Residence will be defined using the Accessibility/Remoteness Index of Australia Plus (ARIA+) Remoteness Area Categories 0-4,[31] whereby:
        - Metropolitan areas are Remoteness Area Category 0;
        - Regional areas are Remoteness Area Category 1; and
        - Rural areas are Remoteness area category 2-4.

Referring Clinic: Familial Cancer Clinic, Breast Unit, Late-Effects Clinic, General Practice, Other.

Women will be recruited until saturation is reached. Based on the expertise of the research group, the sample size estimated to achieve "theoretical saturation" is approximately 15-20 women.[32,33] As such, the minimum quota to be recruited to each category will be attempted as outlined below, noting that each single woman will contribute to the quotas of all of the pre-specified demographic categories. It is prospectively acknowledged that it may not be possible for all quotas to be met.

- Age:
    - At least 3 woman who are 20-39 years;
    - At least 3 woman who are 40-55 years;
    - At least 3 woman who are >55 years.
- Residence:
    - At least 3 woman who are from a metropolitan area (ARIA 0);
    - At least 3 woman who are from a regional area (ARIA 1);
    - At least 3 woman who are from a rural area (ARIA 2-4[31]).
- Referring clinic:
    - At least 2 women are referred by the LEC;
    - At least 2 women are referred by the FCC;
    - At least 2 women are referred by Breast Unit;
    - At least 2 women are referred by GPs;
    - At least 2 women are referred from "other" sources.

As the women are being invited to interview, these quotas will be monitored to establish whether they are being met. By using these minimum quotas, this strategy will ensure that key groups are represented in the sample, whilst still providing flexibility in the final sample composition. To start with, 2 women from each referring clinic (FCC, LEC, Breast Unit, GP and other) will be recruited. After these 10 women are recruited, the quotas for age and residence categories will also be monitored for subsequent participants. Subsequent sampling will aim to ensure that as many of the pre-specified quotas across all categories are met.

3.3.3.2 Recruitment of Women to participate in Aim 8.

Given that Aim 8 was added to the protocol in 2025 (i.e. after study commencement), additional advice regarding recruitment of women to allow for the evaluation of persistence with RRMeds is provided here.

Women who were recruited to this study prior to the addition of "Aim 8", and who have commenced RRMeds, will be invited to reconsent using the amended PICF to allow them to receive follow-up phone calls at 2 years and (for those having a planned 5 year course) at 4.5 years after medication commencement. This invitation will be made using the telephone script (Appendix G) at the time the 6 or 12 month follow-up phone call (whichever is first). Women who provide verbal consent for the additional call(s) will be sent (emailed or mailed) the revised Patient Information and Consent

Form (PICF v2) to sign. Any woman who has additional questions regarding this consent process will be offered an additional telehealth appointment to discuss.

Women who were recruited to this study prior to the addition of "Aim 8", and who have already received their final planned follow-up phone call (at 6 or 12 months), will not be contacted and will not be invited to participate in the collection of data for "Aim 8".

3.3.4 Recruitment of Clinicians (Aim 5)

Eligible clinicians will be identified from i) RMH or PMCC FCC, PMCC BU (surgeons only) and PMCC LEC and ii) from referrals received from RMH BU, RWH and external doctors. A subset of these will be invited to participate in interviews regarding their experience of the Service (Aim 5). Recruitment will be stratified using a purposive sampling framework that has been devised, using quota sampling[30], to ensure a representative cross section of clinicians including clinic type (Familial Cancer Clinic, Breast Unit, Late Effects Clinic, General Practice, other), speciality (medical oncology, radiation oncology, breast surgery, haematology, geneticist, genetic counsellor or general practice, and sex (male/female) are included.

Recruitment will commence once sufficient clinicians have made referrals to the PCMed Service, such that it is feasible for the sample size to be met. Clinicians will then be recruited until saturation is reached. Based on the expertise of the research group, the sample size estimated to achieve "theoretical saturation" is approximately 15-20 clinicians.[32,33] As such, the minimum quota to be recruited to each category will be attempted as outlined below, noting that each clinician will contribute to the quotas of all of the pre-specified demographic categories. It is prospectively acknowledged that it may not be possible for all quotas to be met.

- Sex:
    - At least 5 women;
    - At least 5 men.
- Clinic Type:
    - At least 3 clinicians from Breast Unit;
    - At least 3 clinicians from the Late Effects Clinic;
    - At least 3 clinicians from the FCC;
    - There is no prespecified quota from General Practice and "other", given these clinicians were not specifically targeted for referrals.
- Specialty:
    - At least 1 Medical Oncologist;
    - At least 1 Radiation Oncologist;
    - At least 1 Breast Surgeon;
    - At least 1 Haematologist;
    - At least 1 Geneticist/genetic counsellor;
    - There is no prespecified quota of GPs or External Specialists, given that these clinicians were not clinician groups targeted for referrals.

As clinicians are selected for interview, these quotas will be monitored to establish whether they are being met. To start with, 1 clinician from each specialty will be recruited. After 5 clinicians are recruited, the quotas for sex and clinic type categories

will also be monitored when recruiting subsequent clinicians. Subsequent sampling will aim to ensure that as many as possible of the pre-specified quotas across all categories are met.

3.4 The Intervention

The PCMed Service will be a consultative, telehealth Service co-led by a nurse practitioner and a medical oncologist. It is described in detail in Appendix A.

Eligible women attending the PCMed Service will be offered an Initial Consultation with either a nurse practitioner or a medical oncologist (see Appendix D). In the Initial Consultation women will be offered a discussion about their personal breast cancer risk and personalised information regarding the risks and benefits of RRMeds.

Women who do not want to take RRMeds or for whom RRMeds are not appropriate, will be referred back to their referring clinician or GP.

For women who want to commence RRMeds a prescription will be provided at the Initial Consultation or at a Repeat Consultation (as needed). All women supplied with a prescription for RRMeds will be booked for an 8-to10-week Post-Prescription Consultation to assess toxicities.

A hotline telephone Service will be provided for emergent concerns for referring clinicians, GPs and the women attending the Service. Further ad hoc Post-Prescription Consultations will be allowed if requested by the woman or her referring doctor or GP.

The PCMed Service intervention is illustrated in a flow chart below (Figure 3).

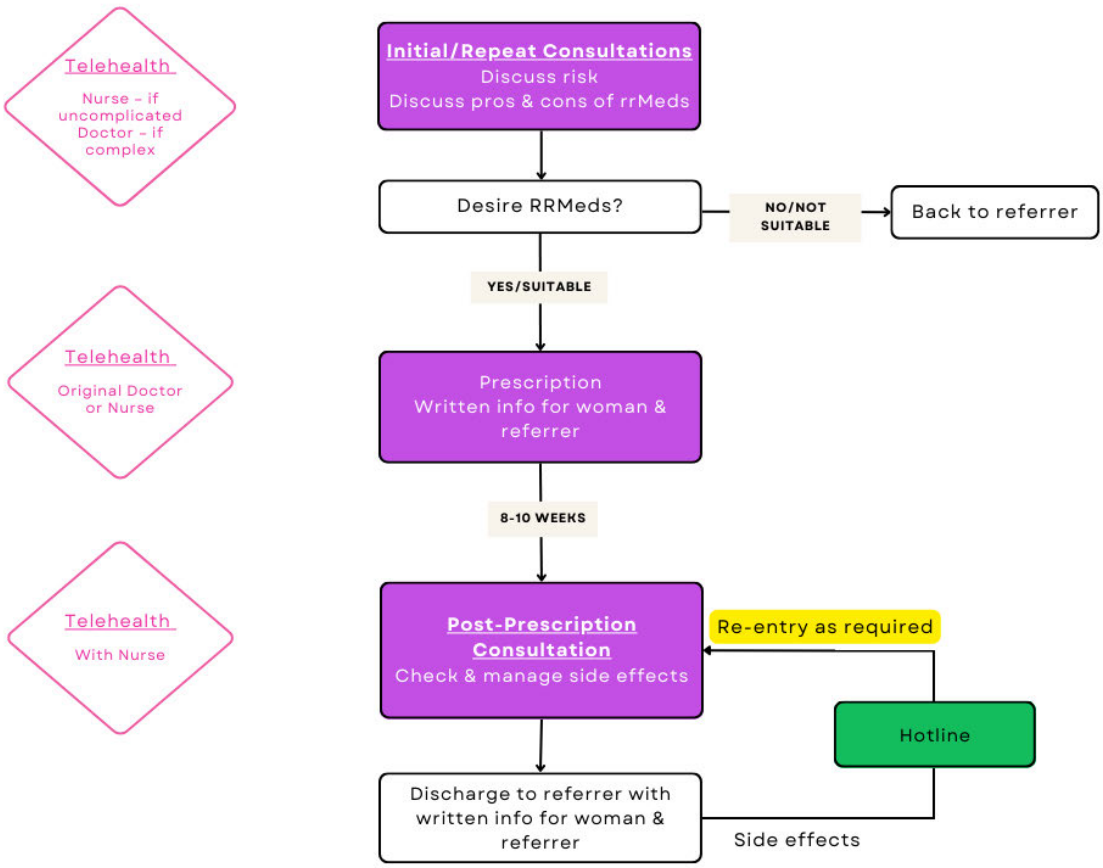

Figure 3: PCMed Service Intervention

3.5 Study Consent Process

3.5.1 Waiver of Consent for Historical Controls and Prospective Women who do not Attend the PCMed Service

A waiver of consent is requested to collect and analyse both prospective and historical control chart data on women attending the Catchment Clinics who meet eligibility for the PCMed Service. It is essential for aim 2 of this study that the denominator of eligible women coming through the Catchment Clinics is known so that we can determine the adoption of the new Intervention. It is impractical to consent these women, there is little risk of harm and there is no reason to believe that they would not consent if asked. There is sufficient protection of their privacy and confidentiality as names will not be used and reporting of the study results will not allow individuals to be identified, the benefits of the research in terms of optimising development of a new breast cancer prevention service (which if successful will reduce breast cancer incidence in the population) outweighs any harm associated with not seeking consent.

3.5.2 Dual Opt-out and Opt-In Consent for Women who attend the PCMed Service

Women who do not attend the PCMed Service will have their data collected and analysed for aims 1 and 2 under a consent waiver. This approach is not appropriate for women who do attend the PCMed Service, as it is not viable to argue that it is impractical to consent these women. Thus, women who do attend the PCMed Service will have the option of opting out (see Appendix D) of having their data abstracted from EPIC and the FCC database. If they do not opt out the data will be collected and analysed as per this protocol.

Conversely, an opt-in consent process will be used for the prospective active follow-up data collection for the women in this study who attend PCMed Service (Aims 3-8). That is, they will be invited to consent via a Participant Information and Consent Form (PICF) to a questionnaire, follow-up phone calls at 6 and 12 months, as well as at 2 years and (for those having a planned 5 year course) at 4.5 years if they choose to commence an RRMed. They will also be invited to consent to an optional telephone interview. If they consent, they can still change their mind and decline the interview when contacted about it.

Women who do not require an interpreter and who have a valid personal email address will be emailed a PICF in the form of an e-Consent. Women who do not have a personal email address will have the PICF posted to them.

Women who require an interpreter will have the PICF explained to them in their own language by a certified interpreter at the time of their Initial Consultation at the PCMed Service. The circumstances around the use of an interpreter, if required, will be documented in the electronic medical record (EMR).

Those who do not return the PICF will receive an email reminder, and/or a telephone call unless they have opted out of having their data abstracted from EPIC and the FCC database (for Aims 1 and 2).

3.5.3 Clinicians

The Theoretical Framework of Acceptability[34] (TFA) questionnaire, along with an explanatory email (see Appendix E), will be emailed to all eligible clinicians. Completion of the TFA questionnaire will be considered implied consent to use the TFA data. Clinicians will have the option to email the researchers to say they are not interested in participating. For those who do not opt out or respond, a reminder will be emailed at 1 week and again 3 weeks after the first invitation was sent.

All eligible clinicians will be invited to participate in a semi-structured telephone interview (Appendix F). Clinicians will be asked to provide a contact telephone number and suggest an interview time if they are willing to participate. Consent to use the data will be implied if they participate in the interview. Clinicians can indicate if they do not wish to participate via reply email. If no response is received, a reminder email will be sent.

3.6 Data Collection

3.6.1 Historical Cohort (retrospective component) for Aim 1

Historical data will be sourced from EPIC and the RMH and PMCC FCC database. Data collected will include: patient unit record number (PURN), initials, date of birth, Indigenous status, country of birth, postcode, marital status, parity, education level, whether interpreter required, clinic where last Risk Management Consultation took place, type of clinician seen (e.g. geneticist, medical oncologist etc.), date of last Risk Management Consultation, whether RRMeds were discussed and whether at 12 months after the last Risk Management Consultation there was documentation that the woman had commenced RRMeds. If there was no discussion of RRMeds and there is no documentation of use, it will be assumed the woman did not use RRMeds. If RRMeds were discussed but there is no documentation regarding whether they were used by the woman at 12 months after the last Risk Management Consultation, staff from the clinic in which they were seen for Risk Management will contact the woman to ask this. This follow-up of the actions taken after consultation, although admittedly rarely done due to resource limitations, can be considered a standard of care rather than specifically for research purposes. The relevant Units have agreed to this approach.

3.6.2 Prospective Data Collection

From EPIC and during Consultations:

Data on all eligible women who attend a Catchment Clinic and receive a Risk Management Consultation will be sourced from EPIC, and the RMH or PMCC FCC database (where relevant). Data collected at the time of the last Risk Management Consultation will include: patient unit record number (PURN), initials, date of birth, Indigenous status, country of birth, postcode, marital status, parity, education level, whether interpreter required, clinic where last Risk Management Consultation took place, type of clinician seen (e.g. geneticist, medical oncologist etc.), date of last Risk Management Consultation, whether RRMeds were discussed and whether the PCMed Service was discussed (or a pamphlet about the Service given).

For women in this group who subsequently attend the PCMed Service, further information will be collected during the consultations and from EPIC, including name and email address for the purposes of emailing electronic questionnaires (or name and postal address for the purposes of mailing hard-copy questionnaires), referring clinician name and type, date of referral, clinic from which they were referred, appointment type (e.g., Initial Consultation, Repeat Consultation, date of appointment, mode of consultation (i.e., telehealth, telephone, face-to-face) education level, menopausal status, hormone level results (if done), family history, history of LCIS or AH, history of chest irradiation (if so age at irradiation, dose, whether alkylating chemotherapy has been received, whether pelvic radiation has been received), 10 year, 20 year and residual lifetime risk of breast cancer, risk assessment tool used, use of hormonal contraception at time of clinic visit, use of menopausal hormone therapy at time of clinic visit, use of anti-coagulants (current and ever), current use of CYP2D6 inhibitors, other concomitant medications, history of osteoporosis, bone density scan results (if done), history of thrombosis (including deep venous thrombosis, pulmonary embolism,

stroke), history of other cancers (type and presumed prognosis), smoking status, currently trying to conceive, pregnant or lactating or planning pregnancy within the next 3 years, any difficulty swallowing or taking tablets, lactose intolerance, whether eligible for RRMeds (which ones and if not why not), whether woman indicated interest in taking RRMeds, whether prescription for RRMeds was accepted, RRMed type recommended, type prescribed, and duration of consultations (which will be manually recorded by the attending clinician).

If telephone calls were received via the 'Hotline', additional data will include who the caller was (e.g., woman, carer, referring clinician, GP), reason for the call (e.g., concerns related to treatment, general information needed), and outcome of the call (e.g., interruption of RRMeds, cessation of RRMeds, change in RRMeds).

Data Collection at 6 months
At 6 months after the Initial or Repeat Consultation, women will receive a telephone call (see Appendix G). Data collected will include whether RRMeds were commenced (Y/N), the date of commencement (if not previously recorded), whether RRMeds were ceased (Y/N), reason for ceasing RRMeds (if applicable), intent to use RRMeds in the future (Y/N), if no intention to use RRMeds then the reason for not intending to use RRMeds, and factors that would facilitate use of RRMeds.

Data Collection at 12 months
Data will be collected at 12 months after the Risk Management Consultation in the Catchment Clinic at which the woman was deemed suitable for referral to the PCMed Service (regardless of whether she was referred or not).

For women who aren't consented to active follow-up, and who do not attend PCMed Service, this data will be collected under a waiver of consent from EPIC as per section 3.6.1. Data collected will include uptake of RRMeds (Y/N).

For women who do consent to active follow-up, this data will be collected via a telephone call (Appendix G). Data collected at this telephone call will include uptake of RRMeds (Y/N), the date of commencement (if not previously recorded), were RRMeds ceased (Y/N), reason for ceasing RRMeds (if applicable), intent to use RRMeds in the future (Y/N), if no intention to use RRMeds then the reason for not intending to use RRMeds (as applicable).

Data Collection at 2 years
Data collection at this time point is only relevant to women who have commenced a RRMed. Data will be collected 2 years after the woman has commenced a RRMed and will include whether the RRMeds were permanently ceased (Y/N), if so, when they were ceased, reason(s) for ceasing the RRMed (if applicable), whether they sought medical advice regarding the reason for ceasing, and if so with whom (GP/PCMed Service/breast specialist/other), whether they would consider re-starting the same or a different RRMed in the future and if so what factors would facilitate that.

Data Collection at 4.5 years

Data collection at this time point is only relevant to women who have commenced a RRMed with a planned 5 year course. Data will be collected approximately 4.5 years after the woman has commenced a RRMed and will include whether RRMeds were permanently ceased (Y/N), if so, when they were ceased, reason(s) for ceasing RRMeds (if applicable) whether they sought medical advice regarding the reason for ceasing, and if so with whom (GP/PCMed Service/breast specialist/other), whether they would consider re-starting the same or a different RRMed in the future and if so what factors would facilitate that.

Theoretical Framework for Acceptability (TFA) Questionnaire
Consenting women participating in the research will receive a Cover Letter and TFA questionnaire (see Appendix H) via email or post after their PCMed Initial or Repeat Consultations. This questionnaire will take less than 5 minutes to complete. If no response received, 2 reminders will be sent out at 1 to 2 weeks and then 3 to 4 weeks after the initial invitation sent.

Eligible Clinicians will also receive a Cover Letter and TFA Questionnaire (see Appendix E) by email. This questionnaire will take less than 5 minutes to complete.

The number of clinicians who do not participate, their sex, clinic type and specialty will be collected and reported as part of the study.

Interviews with Women
An interview guide, consisting of a list of semi-structured questions has been developed by study investigators including medical oncologists, a nurse practitioner, and an implementation scientist (Appendix I). The interview guide aims to explore the acceptability of the PC Med Service for women, including their perception of the clinic before, during and after attendance. The interview guide was formulated with the Theoretical Framework of Acceptability (TFA) in mind.[34] The TFA comprises seven constructs that guide the assessment of acceptability of an intervention from the perspective of participants (and those delivering the intervention).[34] In formulating the guide, only the constructs felt to be relevant to the participant's experience of the PCMed Service were used to formulate questions – these included affective attitude, self-efficacy, burden, intervention coherence and perceived effectiveness. The ethicality and opportunity cost constructs were not perceived as being relevant to the intervention being assessed.

The interview guide will be pilot tested with the first two women. Refinement of research questions will be made based on the pilot test. Interviews will be conducted by telephone. The interviewer will highlight the purpose of the interview, address the terms of confidentiality, and provide contact details for the participant to contact, if they wish, on completion of the interview. Interviews will be audio recorded, transcribed professionally and de-identified, and analysed thematically using NVIVO[35] software. We will recruit participants until saturation of themes is reached.

Data analysis will occur simultaneously with data collection. Data analysis is described in Section 5.2.3 "Specific Aim Analyses – Aim 5".

Interviews with Clinicians
A separate interview guide with semi-structured questions for clinicians has also been developed by study investigators including medical oncologists, a nurse practitioner and an implementation scientist (Appendix J). The interview guide aims to explore the acceptability of the PC Med Service for referring clinicians, including the referral process and any interactions they had with the Service (regardless of whether they actually referred any women to the service or not). The interview guide will be pilot tested with the first clinician. Refinement of research questions will be made based on the pilot test. Interviews will be conducted via telephone, and will be audio recorded, transcribed, and analysed thematically using NVIVO[35] software. Interviews will be de-identified after transcription. Recruitment of clinicians will stop once saturation of themes is reached.

Data analysis will occur simultaneously with data collection. Data analysis is described in Section 5.2.3. "Specific Aim Analyses – Aim 5"

Data Collection to evaluate Cost of PCMed Delivery (Aim 7)
Micro-costing entails making an inventory of all resources needed for service delivery. The data to calculate the cost of service-delivery over the study duration will not require additional data collection to that described above. Data used will include the number and duration of all consultations, type of consultation, who provided the service (nurse practitioner or medical oncologist), involvement of interpreter during consultation as well as the duration of calls received via the 'Hotline'.

Data on the time spent by the administration officer to support the activities of the PCMed Service (making appointments, taking hotline telephone calls to direct to nurse practitioner, mailing notifications) will not be collected because the time spent per woman is expected to be negligible. A reasonable estimate will be used instead. The hourly cost of the administration officer, nurse practitioner, medical oncologist/s and interpreter(s) will be determined by the recorded activity and salaries as per Awards and Enterprise Agreements.

The data to calculate the level of funding received per women will be extracted from EPIC records. As the PCMed Service will use Activity Based Funding[36], all consultations (including type and mode) and the person undertaking the consultation (nurse practitioner or medical oncologist) will be recorded in EPIC. All consultations that meet the funding requirements are considered 'Service Events' with each 'Service Event' allocated a National Weighted Activity Unit (NWAU). Data on those 'Service Events' for all individuals participating in the study will be extracted by the PMCC Reporting System (DASH). By assigning a monetary figure assigned to each NWAU the amount of funding can be calculated.

Research Journal
A formal research journal (see Appendix G) will be kept by the nurse practitioner informed by the FRAME fidelity framework and the COM-B behaviour change framework. Influences on the Service and the nurse practitioner role will be recorded

alongside changes to the PCMed Service Process and rationale for the change. Any unintended consequences of the implementation of the PCMed Service will be documented.

3.7 Data Storage and Security

Data will be kept strictly confidential according to the National Statement on Ethical Conduct in Human Research 2007 and the Australian Code for Responsible Conduct of Research 2007.

Patient research data will be stored electronically where possible, on a specialised, secure web-based database (REDCap) or in secure folders in the Peter MacCallum Cancer Centre network drives.

Audio recordings from the interviews will be transcribed and de-identified. The de-identified transcriptions and audio files will be kept on a password-protected computer and stored in secure folders in the Peter MacCallum Cancer Centre network drive.

Any laptop or desktop computer used for this study will be password-protected with no data stored on an external hard drive, CD or USB. Any paper records will be kept in a locked cabinet in a room with controlled access at the Peter MacCallum Cancer Centre.

Research data will only be visible to and accessed by members of the Research Team who are directly involved with the administration, collection, or analysis of the data.

Patient data, including transcriptions will only be analysed in a coded form. Individual patients will not be identifiable from the presented or published material.

Per the Australian Code for Responsible Conduct of Research 2018, research data, including audio files and transcriptions, will be stored for a minimum period of 5 years from the date of the last publication. Once this date is reached, these files will be destroyed by erasure unless further approval for retention is obtained.

4.0 ENDPOINTS

1) Primary Endpoint: Use of RRMeds at 12 months after a Risk Management Consultation in a Catchment Clinic.
2) Attendance by women at PCMed Service at 6 months following documented discussion on PCMed Service at Risk Management Consultation.
3) Use of RRMeds at 6 months after the Initial Consultation at PCMed Service or Repeat Consultation if required.
4) Reason for non-use of RRMeds at 6 months after first consultation at PCMed Service (or after Repeat Consultation if required).
5) Acceptability:
    a. Acceptability of the PCMed Service (as per the Theoretical Framework of Acceptability (TFA) questionnaire) for woman 2 to 3 weeks after the Initial of Repeat Consultation/s if a Repeat Consultation required.
    b. Acceptability of the PCMed Service for clinicians as assessed by the TFA questionnaire.

c. Acceptability of the PCMed Service for women who use the service, assessed via a semi-structured qualitative interview following their last planned PCMed consultation.
d. Acceptability of the PCMed Service to clinicians, assessed via semi-structured interview.

6) Evaluation of service delivery will be assessed using the following variables at the end of the study period:
    a. Number of consultations conducted by telehealth, face-to-face, or Reason for consultation not being conducted by telehealth.
    b. Number of consultations undertaken by nurse practitioner and/or medical oncologist.
    c. Duration of every consultation.
    d. Number of consultations required before a prescription is written for RRMeds.
    e.
        i. Number of failures to attend (FTA) the post-prescription consultation.
        ii. Reason for failure to attend the post-prescription consultation.
    f. Number of ad hoc Post-Prescription Consultations required after the 1st post-prescription consultation.
    g.
        i. Number of calls to Hotline over a period of 6 months.
        ii. Duration of call.
        iii. Reason for call.
    h. Factors that influence delivery of service as per protocol.
    i. Unintended consequences of PCMed Service.
7) Evaluation of the cost-of-service delivery:
    a. Funding received by the PCMed Service per woman who uses RRMeds.
    b. Funding received by the PCMed Service per woman attending the Service.
    c. Cost of the PCMed Service per woman who uses RRMeds.
    d. Cost of the PCMed Service per woman attending the Service.
    e. Difference between (a) and (c).
    f. Difference between (b) and (d).
8) Persistence with RRMeds
    a. At 2 years after commencement of the RRMed
    b. At 4.5 years after commencement of the RRMed (only relevant for women having a 5 year planned course).

5.0 STATISTICAL ANALYSIS AND SAMPLE SIZE CONSIDERATIONS

5.1 Sample Size

Aim 1

Based on national data[17] we expect that 2% of women who attended the Catchment Clinics prior to the commencement of the PCMed intervention (i.e., the historical controls) will have used RRMeds. We consider an increase in use from 2% to 20% to be clinically significant, given the PCMed Service is a complex intervention. A prospective sample size of 57 women attending the PCMed Service will provide 80% power to detect a minimum change from 2% to 20% at a 5% significance level. The sample size of consecutive consented women attending the PCMed Service will be 63 for this study, to account for a 10% drop out/loss to follow-up.

Table 1: Sample size scenarios* - sample size per arm

	Post-implementation uptake				
Pre-implementation uptake	**10%**	**15%**	**20%**	**25%**	**30%**
1.0%	121	72	50	38	30
2.0%	162	86	57	42	33
2.5%	189	95	61	45	34
5.0%	474	160	88	59	43
7.5%	2084	304	134	80	55
10.0%	N/A	726	219	113	72

*Minimum sample size required in each of the prospective and historical cohorts presuming 80% power at the 5% significance level.

If the use of RRMeds in the historical controls is > 2%, a larger sample size may be needed as per table 1 above. For example, if the historical use is 5%, a sample size of 59 + 10%, i.e., 65 will be required to show an increase from 5% to 25%. A protocol amendment will be submitted if a change in sample size is required once the historical control data are available.

We will identify 100 consecutive historical controls. If 0% of these use RRMeds, we will extend the sample to a total of 150.

Aim 2

For aim 2 (adoption of the PCMed Service) we will prospectively collect data on eligible women attending the Catchment Clinics until we have 63 consented women that actually attended the PCMed Service. Thus, the sample size is not fixed. We will have collected some data on other women after that time, but we will not use that in the analysis.

Aim 5 interviews

To investigate findings from the TFA questionnaire, follow-up interviews will be conducted. (n≈15-20 for each of women and clinicians). This number should allow for reaching concept density. The clinician sample is expected to include geneticists, genetic counsellors, oncologists, breast surgeons, haematologists, and radiation oncologists.

5.1.1 Analysis sets

The primary analysis set will consist of all eligible women who attend the PCMed Service and the historical controls. The secondary analysis set will consist of all eligible

women attending Catchment Clinics (regardless of whether they subsequently attend the PCMed Service), and the historical controls.

5.1.2 Interim analysis

An interim analysis may be conducted to ensure both the prospective and historical cohorts are sufficiently powered to permit comparison of the primary endpoint. Additional sample may be recruited as required.

5.2 Statistical Analyses

All statistical analyses will be undertaken in Stata version 17 (StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC.) and R version 4.0.5 (The R Foundation for Statistical Computing, Vienna, Austria).

5.2.1 General – descriptive statistics

Categorical variables will be summarised using frequency and percentage. Continuous variables will be summarised using mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Incidence rates will be expressed as the count of events divided by the number of subjects and/or per unit time as appropriate and expressed as point estimates with associated 95% confidence intervals and presuming an underlying Poisson or negative binomial distribution.

5.2.2 General – inferential statistics

Comparisons of event proportions between the prospective cohort and historical controls will be conducted using a chi-square test or Fisher's exact test as appropriate. Associations between participant characteristics and study outcomes will be explored using univariable and multivariable logistic, Poisson and/or negative binomial regression as indicated. Multivariable models will be assessed for collinearity and interactions between explanatory covariates. Adjustment for clinic effects will be conducted by including the clinic ID as a random effect in the aforementioned models. The final selection of test or model type will be confirmed upon initial review of the collected data with consideration given to the number of available events for each outcome. For all analyses, $p<0.05$ will be considered significant.

5.2.3 Aim specific analyses

Aim 1

The proportion of women who start RRMeds within 12 months of a cancer Risk Management Consultation in the Catchment Clinic will be summarised pre- and post-implementation of the PCMed Service using descriptive statistics as detailed in section 5.2.1. Proportions will be compared using a chi-square or Fisher's exact test. Differences in the distribution of confounders between the historical and prospective cohorts will be managed using adjusted regression as described in section 5.2.2. This analysis will use the primary analysis set as described in 5.1.1.

Aim 2

The proportion of women who attended each Catchment Clinic for a Risk Management Consultation and received a discussion and / or information about the PCMed Service and who subsequently attended the PCMed Service within 6 months of a Risk Management Consultation will be summarised using descriptive statistics as per section 5.2.1. Associations between participant characteristics and the likelihood of adoption will be analysed using logistic regression as described in section 5.2.2. This analysis will use the secondary analysis set as described in section 5.1.1. Descriptive statistics will be used to summarise reason/s for declining a referral to the PCMed Service as an exploratory endpoint.

Aim 3

The proportion of women (without contraindications) who had used RRMeds within 6 months of their Repeat Consultation will be summarised using descriptive statistics as per section 5.2.1.

Aim 4

Reason for non-use of RRMeds at 6 months after the Initial Consultation at PCMed Service (or after Repeat Consultation if required) will be summarised using descriptive statistics as per section 5.2.1.

Aim 5

Acceptability – Theoretical Framework for Acceptability (TFA) Questionnaire metrics will be summarised using descriptive statistics as per section 5.2.1.

Semi-structured interview data will be analysed both inductively and deductively. The Theoretical Framework for Acceptability will act as the coding framework for deductive analysis.

Interviews will be transcribed in full and de-identified. All transcripts will be read in conjunction with the original audio recording to check for accuracy. Two authors (SL and WC) will independently code several interviews and determine the level of agreement on coding the data. After 6 interviews with women, and 5 interviews with clinicians (one with each referring specialty), a summary of the themes with supporting quotes will be generated. Themes will be reviewed by co-investigators for feedback regarding the themes and any refinements required for the interviews. After 15 interviews (with women and clinicians respectively), the coding framework capturing the full range of comments will be developed and reviewed by co-authors. After interview 15 (with women and clinicians respectively), new interviews will be reviewed in light of the coding framework to determine whether saturation of the main themes has been achieved. The final coding framework will be reviewed by all authors. Regular research meetings will continue where analysis will be discussed with the research team, particularly any areas of complex coding.

Aim 6

Evaluation of service delivery will be summarised using descriptive statistics as per section 5.2.1.

Aim 7
Associated costs and funding received through Activity Based Funding will be summarised using descriptive statistics as per section 5.2.1.

Aim 8
The proportion of women who commence a RRMed and persist with taking it at 2 years and 4.5 years will be summarised using descriptive statistics as per section 5.2.1. Reasons for non-persistence will also be summarised using descriptive statistics.

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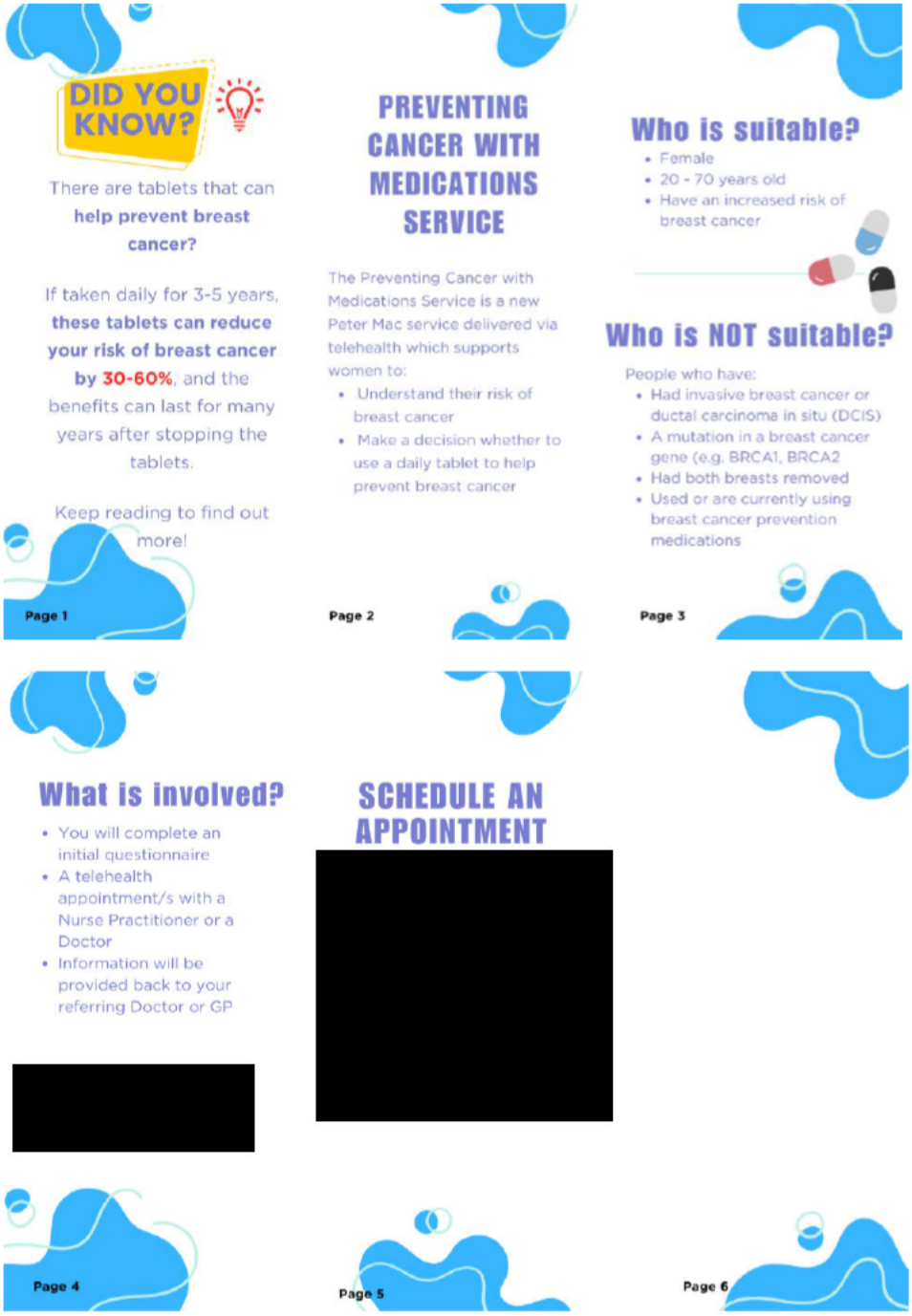
Appendix 1.2 Protocol Appendix A – The PCMed Service Intervention

Not reproduced as include in Appendix 2 of this thesis.

Appendix 1.3 Protocol Appendix B – PCMed Service Pamphlet



DID YOU KNOW?

There are tablets that can **help prevent breast cancer?**

If taken daily for 3-5 years, **these tablets can reduce your risk of breast cancer by 30-60%**, and the benefits can last for many years after stopping the tablets.

Keep reading to find out more!

Page 1

PREVENTING CANCER WITH MEDICATIONS SERVICE

The Preventing Cancer with Medications Service is a new Peter Mac service delivered via telehealth which supports women to:

- Understand their risk of breast cancer
- Make a decision whether to use a daily tablet to help prevent breast cancer

Page 2

Who is suitable?

- Female
- 20 - 70 years old
- Have an increased risk of breast cancer

Who is NOT suitable?

People who have:

- Had invasive breast cancer or ductal carcinoma in situ (DCIS)
- A mutation in a breast cancer gene (e.g. BRCA1, BRCA2
- Had both breasts removed
- Used or are currently using breast cancer prevention medications

Page 3

What is involved?

- You will complete an initial questionnaire
- A telehealth appointment/s with a Nurse Practitioner or a Doctor
- Information will be provided back to your referring Doctor or GP

[redacted]

Page 4

SCHEDULE AN APPOINTMENT

[redacted]

Page 5

Page 6

Appendix 1.4 Protocol Appendix C – Telephone call to request and consent participants in semi-structured interviews

Version 1, 31/07/2024



APPENDIX C

Telephone call to request and consent participants for semi-structured interviews (by research assistant)

Introduction
Hi (insert name), I'm (name and role) from the PC Med Service at the Peter MacCallum Cancer Centre. This was the Service you attended in (insert month attended) where you had a discussion regarding your breast cancer risk and the pros and cons of taking medication to lower your risk.

Reason for call
I'm calling because you signed a consent for the research component of the PC Med Service. I'd like to ask if you would be interested in participating in a telephone interview to help us research the acceptability of the Service by gaining an understanding of your experience with the service.

Time expectation
The interview will be with my colleague Dr Sarah Latham and should take approximately 20-30 minutes. We'll schedule it at a time that's convenient for you. Anything you say in the interview will remain confidential and can't be linked back to you.
If you don't want to participate in the interview, please know that this won't interfere with your care at Peter Mac.

Consent to Continue
Would you be happy to participate in this interview?
Shall we schedule a time whilst we're on the phone now?

End call
Thank you for your time.

Appendix 1.5 Protocol Appendix D – Research Invitation with PICF

Version 3, 10/09/2024

APPENDIX D: Research Invitation with PICF

Dear [insert name],

Welcome to the Preventing Cancer with Medications (PCMed) Service. This is a new Service to help you to decide whether a tablet medication to reduce your chance of getting breast cancer is right for you. Your first appointment (*If telehealth appointment insert:* will be a telehealth video call and) is expected to take approximately 45 minutes.

Research

(Remove highlighted sections for women referred external to the PMCC FCC, BU and LEC as Opt-out not relevant. These women will not be included in Aims 1 and 2)

To assess this new Service, we are conducting research. It involves two parts:

Part 1: Pre-Service Information Collection

1. We want to understand if attendance at the PCMed Service influences the uptake of tablet medication to reduce breast cancer risk. To achieve this, we will collect and analyse information from your medical record that is collected as part of your routine care at the clinic from which you were referred to the PCMed Service. This will include information about you and your health. If you would like to find out more about this, or if you do not wish to have this information included in the research, contact the Research Team by replying to this email or via telephone (03) 8559 8632.

Part 2: Service Experience

We want to understand how useful the Service is and whether changes are needed to improve the Service. To understand this, we would like to collect information about your interaction and experience with the PCMed Service. This information will be collected when you attend your PCMed Service appointments, from follow-up telephone calls, a brief questionnaire, and an optional telephone interview. This part is only relevant to you if you do not opt out of Part 1, as above

Please (*insert as applicable:* ***read the*** *(if for mail out)* ***OR*** **click on the link below for the** *(if REDCap) OR* **read the attached** *(if sending as pdf))* **Patient Information and Consent Form (PICF)** to find out more about this important research and to let us know if you would like to be involved. (*insert:* Please return the PICF in the pre-paid envelope enclosed *(if for mail out)).*

(*Insert as applicable:* **REDCap link to e-Consent Form (PICF)**
If the link above does not work, try copying the link into your web browser:
https://redcap.petermac.org.au/surveys/

[redacted]

PCMed Study_ Information and Consent (PICF) V1_06-09-2023.pdf
Yours sincerely,

[redacted]

Appendix 1.6 Protocol Appendix E – Invitation-Explanatory email to Clinicians

Version 1, 6/09/2023

APPENDIX E: Invitation – Explanatory email to clinicians

Dear [insert name],

Re: Study [insert PMC number]- Supporting uptake of breast cancer prevention medications and minimising treatment discontinuation: a process evaluation

Please consider completing the 2–3minute multiple choice, online questionnaire regarding the new Preventing Cancer with Medications Service (PCMed Service) at the Peter MacCallum Cancer Centre. We are asking you to complete this questionnaire even if you have never referred a patient to the Service.

The PCMed Service is a world-first approach, trying to increase evidence-based uptake of medications that reduce the risk of breast cancer for women who have never had cancer, but who are at increased risk for the disease. The new service responds to our previous published research findings showing that lack of clinician knowledge and confidence was a barrier to discussing and prescribing these medications[1]. It is hoped that this specialist telehealth service to discuss and initiate risk-reducing medications will enhance uptake and persistence with these medications.

Health Services Research has been built into The PCMed Service to formally evaluate it. Clinicians who referred women to the PCMed Service or who saw eligible women in their clinics, are being invited to participate in this research.

The questionnaire, found using the link below, asks you to assess your experience with the PCMed Service. We understand that the questionnaire may arrive at an inconvenient time but are hoping that you will be able to spare a few minutes to contribute to our research. A reminder email will be sent in one week if we do not hear back from you and then again three weeks after that.

Redcap questionnaire link here

The answers you provide will be confidential to the researchers and the results of the research will be published in a form that will not allow individuals to be identified.

[redacted]

Thank you for taking the time to assist us with this important research.

Yours sincerely,

[redacted]

[1] Macdonald C, Saunders CM, Keogh LA, Hunter M, Mazza D, McLachlan SA, Jones SC, Nesci S, Friedlander M, Hopper JL, Emery JD, Hickey M, Milne RL, Phillips KA. Breast Cancer Chemoprevention: Use and Views of Australian Women and their Clinicians. *Cancer Prev Res (Phila).* 2021 Jan;14(1):131-144. doi: 10.1158/1940-6207.CAPR-20-0369.

Appendix 1.6 Protocol Appendix E – TFA Questionnaire for Clinicians

Version 2, 31/07/2024

APPENDIX E:

TFA Questionnaire for Clinicians

This questionnaire contains eight questions / statements that require an answer. This should only take five minutes to complete. Please choose the option that best fits with your experience of the PCMed Service.

1. Do you like or dislike the PCMed Service?

Strongly dislike	Dislike	No opinion	Like	Strongly like

2. How much effort did it take for you to discuss, and refer eligible patients to, the PCMed Service?

No effort at all	A little effort	No opinion	A lot of effort	Huge effort

3. How well does the PCMed Service fit with your values?

Not at all well	Not well	No opinion	Well	Very well

4. The PCMed Service increases the likelihood that women will use medication to reduce their breast cancer risk.

Strongly disagree	Disagree	No opinion	Agree	Strongly agree

5. It is clear to me how the PCMed Service helps women to reduce their breast cancer risk:

Strongly disagree	Disagree	No opinion	Agree	Strongly agree

6. How confident do you feel about referring eligible patients to the PCMed Service?

Not at all confident	Not confident	No opinion	Confident	Very confident

7. Discussing and referring eligible patients to the PCMed Service interfered with my other priorities:

Strongly disagree	Disagree	No opinion	Agree	Strongly agree

8. How acceptable is the PCMed Service to you?

Completely unacceptable	Unacceptable		No opinion	Acceptable	Completely acceptable

Appendix 1.7 Protocol Appendix F – Email invitation semi-structured interviews-Clinicians

Version 2, 06/03/2025

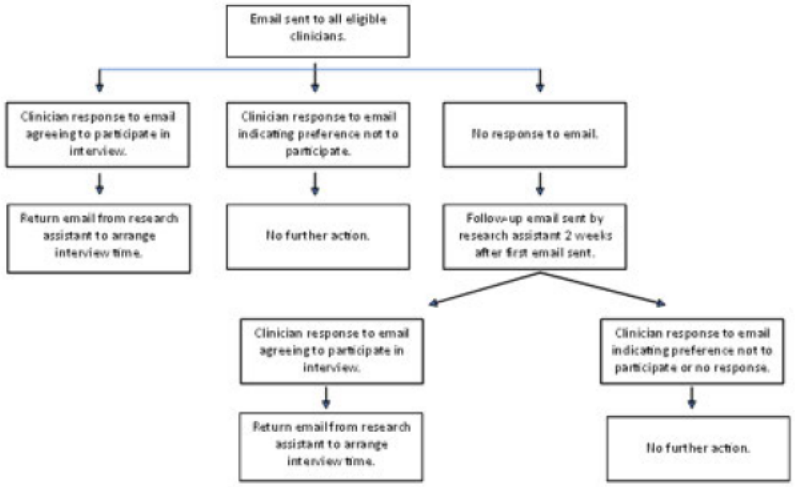
APPENDIX F:

Email Invitation

[redacted]

- Eligible clinicians include:
  - *Clinicians who have reviewed eligible women in the PMCC FCC, BU or LEC during the prospective study period (whether or not they've referred any women to the PCMed Service) and all Clinicians external to PMCC (i.e. RWH, RMH, GPs) who referred women to the PC Med Service during the prospective study period.*

Email Invitation Schema



Version 2, 06/03/2025

Email Template
To: "Eligible Clinician"
Subject/Header: PCMED SERVICE Research Study – Clinician Feedback Opportunity

Dear "Eligible Clinician" (insert name of doctor),

RE: Participation in a research study: ~20 minute interview

You are invited to participate in a research interview regarding the PCMed Service which is being piloted at Peter Mac. Your feedback regarding the Service will help us to determine whether the Service will continue, and whether any adjustments need to be made.
We are interested in your feedback, regardless of whether or not you have referred a patient.
The interview will be conducted by a medical oncologist and researcher, Dr Sarah Latham, who is not directly involved in the Service and will be audio recorded. All feedback will be confidential.

What Is the PCMED SERVICE?
The PC Med Service (Preventing Cancer with MEDications Service) aims to provide women at increased risk of breast cancer with personalised information to help them decide if they want to take medications to reduce their breast cancer risk.

What should I do if I am happy to be interviewed about PCMed?

- Please reply to this email and include:
  - Your phone number
  - Some suggested days and times over the next month that may suit you to participate in the phone interview.
  - Once confirmed, we will follow up with a calendar invite.

What should I do if I no longer want to participate in a research interview?

- Please reply to this email with the words "No thanks". This will ensure you do not receive follow-up emails.

Kind regards,

[redacted]

Version 2, 06/03/2025

Email Invitation Reminder

To: Referring Clinician
Subject/Header: REMINDER: PCMED SERVICE Research Study – Opportunity for Feedback

Dear "Eligible Clinician" (insert name of doctor),

RE: Participation in a research study: ~20 minute interview

You are invited to participate in a research interview regarding the PCMed Service which is being piloted at Peter Mac. Your feedback regarding the Service will help us to determine whether the Service will continue, and whether any adjustments need to be made.
We are interested in your feedback, regardless of whether or not you have referred a patient.
The interview will be conducted by a medical oncologist and researcher, Dr Sarah Latham, who is not directly involved in the Service and will be audio recorded. All feedback will be confidential.

What Is the PCMED SERVICE?
The PC Med Service (Preventing Cancer with MEDications Service) aims to provide women at increased risk of breast cancer with personalised information to help them decide if they want to take medications to reduce their breast cancer risk.

What Should I Do If I Am Happy to be Interviewed About PCMed?

- Please reply to this email and include:
  - Your phone number
  - Some suggested days and times over the next month that may suit you to participate in the phone interview.
  - Once confirmed, we will follow up with a calendar invite.

What Should I Do If I No Longer Want To Participate in a Research Interview?

- Please reply to this email with the words "No thanks". This will ensure you do not receive follow-up emails.

Kind regards,



Appendix 1.8 Protocol Appendix G – Telephone Scripts for data collection at 6 and 12 months

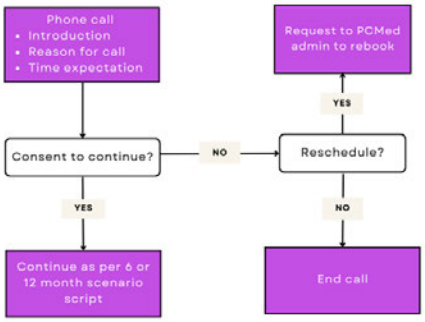
Version 1, 6/09/2023

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

APPENDIX G:

Telephone calls for data collection at 6 and 12 months (by research assistant)

Introduction
Hi (insert name) this is (name and role) from the PCMed Service at the Peter MacCallum Cancer Centre. This was the Service you attended in (insert month attended) where you had a discussion regarding your breast cancer risk and the pros and cons of taking breast cancer preventions.
Reason for call
You are receiving this phone call because you consented to participate in the research component of our Service.
Time expectation
This should only take about 5 minutes.
Consent to continue
Are you happy to answer some questions now?
Can we reschedule for another time?
End call
Thank you for your time.
We will call you again in (insert the month that the 12-month phone call is due). *You will receive an appointment 2 weeks prior to this time.*



Version 1, 6/09/2023

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

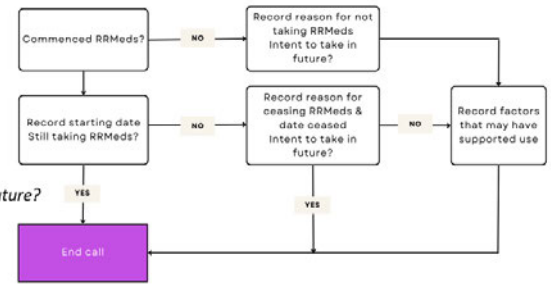
Telephone calls for data collection at 6 months

Scenario 1: Women who received a prescription for RRMeds at the Initial or Repeat Consultation

Uptake of RRMeds
Did you commence the tablets that were prescribed to reduce your risk of breast cancer?
Commenced RRMeds
When did you commence these tablets?
Are you still taking the tablets?
Did not commence RRMeds
Can I ask the reason you did not commence these tablets?
Do you intend to take in the future?
Commenced RRMeds then stopped
Can I ask you the reason for stopping these tablets?
When did you stop taking these tablets?
Would you consider taking tablets to reduce your breast cancer risk in the future?
No intention to use RRMeds in the future
Are there any factors that may have supported (select: you to take OR your ongoing use of) these tablets?
Intention to take in future
When do you think, you may want to commence (OR restart as appropriate) these tablets?

- Immediate future: *I can arrange an appointment with the PCMed Service to discuss this with you?*
- Not immediate future: *Your doctor (insert Referring Clinic) or GP can refer you back to the service when you feel you are read to consider taking these tablets to reduce you breast cancer risk.*

End call
Thank you for your time. We will call you again in (insert the month that the 12-month phone call is due). You will receive an appointment 2 weeks prior to this time.



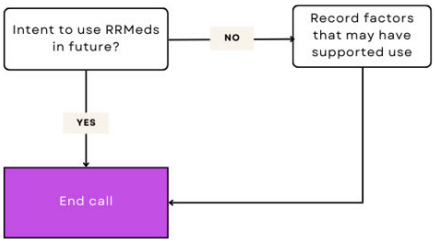
Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Scenario 2: Women who DID NOT receive a prescription for RRMeds at the Initial or Repeat Consultation

Intent to use RRMeds in future
Would you consider taking tablets to reduce your breast cancer risk in the future?
No intention to take RRMeds in future
Are there any factors that may have supported you to take tablets to reduce your breast cancer risk?
Intention to take in future
When do you think, you may want to consider taking tablets to reduce your breast cancer risk?

- *Immediate future: I can arrange an appointment with the PCMed Service to discuss this with you.*
- *Not immediate future: Your doctor (insert Referring Clinic) or GP can refer you back to the service when you feel you are read to consider.*

End call
Thank you for your time. We will call you again in (insert the month that the 12-month phone call is due). You will receive an appointment 2 weeks prior to this time.



Version 1, 6/09/2023

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

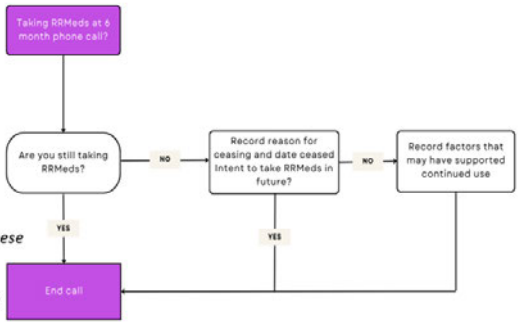
Telephone call for data collection at 12 months

Scenario 1: Women who commenced RRMeds and were still taking these at the 6-month (data collection) telephone call

Commenced RRMeds
It has been recorded that you commenced tablets to reduce your risk of breast cancer.
Can you tell me when you started (only if not recorded)?
Are you still taking these tablets?
Commenced RRMeds and stopped
Can I ask you the reason for stopping these tablets?
When did you stop taking these tablets?
Would you consider using these tablets again in the future?
No intention to use RRMeds in the future
Are there any factors that may have supported the ongoing use of these tablets?
Intention to take in future
When do you think you may want to restart these tablets?

- *Immediate future: I can arrange an appointment with the PCMed Service to discuss this with you.*
- *Not immediate future: Your doctor (insert Referring Clinic) or GP can refer you back to the service when you feel you are ready to consider taking these tablets to reduce you breast cancer risk.*

No intention to use RRMeds in the future
Are there any factors that may have supported your ongoing use of these tablets?
End call
Thank you for your time.



Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Scenario 2: Women who commenced RRMeds and it was recorded they ceased at the 6-month (data collection) telephone call

Commenced and ceased RRMeds at the 6-month telephone call

I see from the last phone call last (insert month of the 6-month phone call) *that you had stopped the tablets prescribed to reduce your breast cancer risk.*
Is this still the case?

No intention to use RRMeds in the future

Are there any factors that may have supported your ongoing use of these tablets?

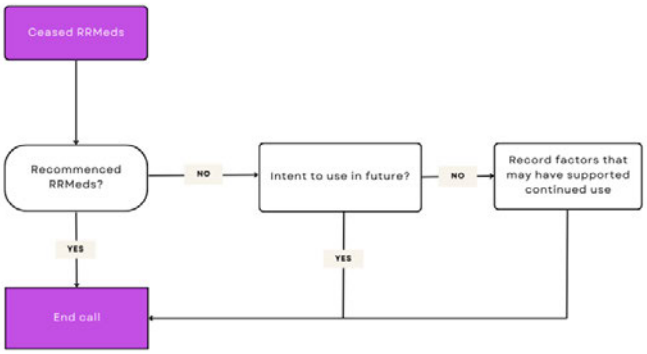
Intention to take in future

When do you think, you may want to commence (OR restart as appropriate) these tablets?

- *Immediate future: I can arrange an appointment with the PCMed Service to discuss this with you.*
- *Not immediate future: Your doctor (insert Referring Clinic) or GP can refer you back to the service when you feel you are ready to consider taking these tablets to reduce you breast cancer risk.*

End call

Thank you for your time.



Version 1, 6/09/2023

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Scenario 3: Women who had never received a prescription for RRMeds at the 6-month (data collection) telephone call

Never commenced RRMeds

I see you did not receive a prescription to take tablets to reduce your breast cancer risk.
Do you intend to take these tablets in the future?

No intention to use RRMeds in the future

Are there any factors that may have supported you to take these tablets?

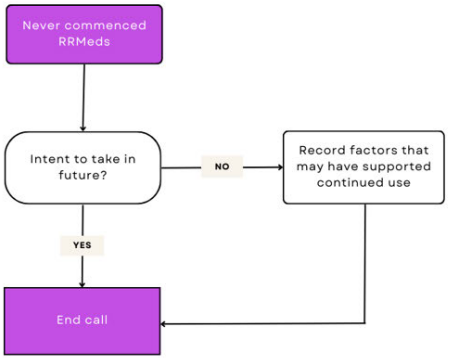
Intention to take in future

When do you think, you may want to commence these tablets?

- *Immediate future: I can arrange an appointment with the PCMed Service to discuss this with you.*
- *Not immediate future: Your doctor (insert Referring Clinic) or GP can refer you back to the service if OR when you feel you are ready to consider taking these tablets to reduce you breast cancer risk.*

End call

Thank you for your time.



Appendix 1.9 Protocol Appendix H - Invitation - Cover Letter Email to Women

Version 1, 6/09/2023

APPENDIX H: Invitation - Cover Letter Email to Women

Dear [insert name],

Re: Supporting uptake of breast cancer prevention medications and minimising treatment discontinuation: a process evaluation

You recently had an appointment with the PCMed Service through the Peter MacCallum Cancer Centre. You agreed to being involved in research that is evaluating the usefulness and acceptability of this new Service.
Below is a link to a short questionnaire about your experience of the Service. This questionnaire should only take you a few minutes to complete. We understand that the questionnaire may arrive at an inconvenient time but are hoping that you will be able to spare the few minutes it takes to complete to contribute to our important research.
The answers you provide will be confidential to the researchers and the results of the research will be published in a form that will not allow individuals to be identified.

Redcap questionnaire link here

[redacted]

Thank you for taking the time to assist us with this important research.

Yours sincerely,

[redacted]

Appendix 1.9 Protocol Appendix H - Invitation - Cover Letter Email to Women

Version 1, 6/09/2023

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia
Victoria Australia

APPENDIX H: TFA Questionnaire for Women

TFA Questionnaire for Women

This questionnaire contains eight questions / statements that require an answer. This should only take five minutes to complete. Please choose the option that best fits with your experience of the PCMed Service.
Your feedback will help us improve the PCMed Service!

1. How comfortable were you with your overall experience with the PCMed service?

Very uncomfortable	Uncomfortable	No opinion	Comfortable	Very comfortable

2. How easy was it for you to contact, and have your appointment/s with the PCMed service?

Very difficult	Difficult	No opinion	Easy	Very easy

3. How well does the PCMed service fit with your values?

Not at all well	Not well	No opinion	Well	Very well

4. The PCMed service has increased the likelihood that I will use medication to reduce my breast cancer risk.

Strongly disagree	Disagree	No opinion	Agree	Strongly agree

5. It is clear to me how attending the PCMed Service will help me to start on medications to reduce my breast cancer risk if I choose to.

Strongly disagree	Disagree	No opinion	Agree	Strongly agree

6. How confident did you feel about engaging with the PCMed service?

Very unconfident	Unconfident	No opinion	Confident	Very confident

7. My involvement with the PCMed service interfered with my other priorities.

Strongly disagree	Disagree	No opinion	Agree	Strongly agree

8. How acceptable was the PCMed service?

Completely unacceptable	Unacceptable	No opinion	Acceptable	Completely acceptable

Thank you for completing this questionnaire!

Appendix 1.10 Protocol Appendix I – Interview Guide Women

Version 1, 31/7/2024

APPENDIX I: Participant Questionnaire

Participant Questionnaire

Opening Introduction

- Thank you for participating in this interview about the Preventing Cancer with MEDications Service, also known as PCMed.
- Introduction of self:
    - My name is Sarah Latham.
    - I am a doctor and researcher working at Peter Mac.
    - I don't work in the Preventing Cancer with Medication Service, but my research aims to understand how people experience the Service so it can be improved in the future if needed.

- During this interview I will be asking you questions about your experience with the Service and I'm interested in any feedback you have to offer about the Service.

- The interview will last for approximately 20-30 minutes.
- You can stop at any time. If there are any questions you want to skip at any time, please let me know.
- With your permission I will record this interview, which will be stored and then transcribed professionally. All your identifying details will be removed from the transcript to ensure it remains confidential.
- All files will be saved until 5 years have passed since we last published the results of this study, for instance in a journal article. Files will then be destroyed.
- I may quote your words in a journal article but will make sure it is done in such a way that you cannot be identified from the quote.
- Are you happy to proceed with this interview?
- Ok, I will start the audio-recording now.

Appendix 1.11 Protocol Appendix J – Interview Guide Clinician

Version 1, 31/7/2024

APPENDIX J: Clinician Questionnaire

Eligible Clinician Questionnaire

Opening Introduction

- Thank you for participating in this interview about the Preventing Cancer with MEDications Service, also known as PCMed.
- Introduction of self:
    - My name is Sarah Latham.
    - I am a medical oncologist and research fellow working at Peter Mac.

- During this interview I'd be interested to hear about your experience with the PCMed Service.

- The interview will last for about approximately 20minutes.
- You can stop the interview at any time and if there are any questions you want to skip at any time, please let me know.
- With your permission I will record this interview, which will be stored and then transcribed professionally. All your identifying details will be removed from the transcript to ensure it remains confidential.
- All files will be saved for an additional 5 years from the date of last publication and then they will be destroyed.
- I will analyse the information that you share with me today, along with what I collect from other interviews, to identify what the service is doing well and ways they can improve.
- I may use phrases you share with me when we disseminate out findings but will make sure you cannot be identified in any way.
- Are you happy to proceed with this interview?
- Ok, I will start the audio-recording now.

Appendix 1.12 Protocol Appendix K – PCMed research journal

Version 1, 6/09/2023

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

APPENDIX K: PCMed research journal

Aim: to capture longitudinal data on barriers and enablers to implementation of the new PCMed Service, adaptations made and the role of the PCMed Service nurse practitioner

When: monthly

Population: PCMed Service nurse practitioner

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response:
Over the last month, what has helped the take up of the PCMed service? *
Response:
What adaptations have been made to the service over the last month? **
Response:
Have there been any unintended consequences from this service? If so, what?
Response:
Is there anything that would facilitate your role?
Response:
Do you have any other thoughts/comments
Response:

* This may relate to capability such as skills and knowledge; opportunity such as resources or the social influences of others, and motivation such as beliefs about consequences of the service, professional identity[1].

** What the change was, when it happened, who decided on the change, why - including planned or unplanned changes - and what was the impact of the change[2].

1. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci.* 2011 Apr 23;6:42. doi: 10.1186/1748-5908-6-42.
2. Wiltsey Stirman, S, Baumann, AA, Miller CJ. The FRAME: an expanded framework for reporting adaptations and modifications to evidence-based interventions. *Implementation Sci.* 2019 Jun 6;14(1):58. doi: 10.1186/s13012-019-0898-y.

Appendix 2: The PCMed Service Intervention

Eligibility for PCMed Service

i. Female.
ii. Aged between 20 and 70 years.
iii. Residual lifetime breast cancer risk at least 20%[21] or 10-year risk of at least 5%[22], or history of LCIS or atypical hyperplasia, or prior thoracic irradiation before the age of 35 and the radiation was given at least 5 years prior.
iv. Does not require germline genetic testing to further clarify risk (those who do should be referred to the FCC and can then be re-referred to the PCMed Service as needed).
v. Not eligible for the PMCC Breast and Ovarian Cancer Risk Management Clinic (i.e., no pathogenic variant in a breast cancer predisposition gene and not an untested 1st degree relatives of a carrier).
vi. No history of invasive breast cancer or DCIS.
vii. No history of bilateral mastectomy.
viii. No prior or current use of medication to reduce breast cancer risk. (If current or prior use of RRMeds women should see the original clinician).

Referral Pathways

Referral pathway from PMCC and RMH Family Cancer Centres (FCCs)
Currently, women without a personal history of invasive breast cancer who are identified with a potentially increased risk of breast cancer due to family history are referred to the Family Cancer Centre by their GP or other clinicians for consideration of genetic testing. A CanRisk assessment is undertaken to formally assess their risk. Currently this assessment only uses family history, but it is likely that it will soon also consider lifestyle factors that contribute to risk.

The majority of women at moderate or high risk are offered an FCC appointment. Some women are offered genetic testing. Those found to have a germline mutation in a breast cancer predisposition gene, and their untested 1st degree relatives are referred to the Breast and Ovarian Cancer Risk Management Clinic (and will thus not be eligible for the PCMed Service). However, most women at increased risk either do not undergo a genetic test and/or do not have a mutation. These women are sent back to the referring clinician for ongoing management. Anecdotally, it is thought that very few of these ultimately use RRMeds. *These are a target group for the PCMed Intervention.*

Referral Pathway from PMCC and RMH and RWH Breast Unit (BU)

Women with a recent or previous history of isolated lobular carcinoma in situ (LCIS) or atypical hyperplasia (AH) have a 4-10 times population risk of subsequent invasive breast cancer. RRMeds are a standard of care for these women based on national and international guidelines[26-28]. Anecdotally few of these women are offered RRMeds. *These are a target group for the PCMed Intervention.*

Referral Pathway from Late Effects Clinic (LEC)

Women who have had thoracic irradiation before the age of 35 (e.g., for Hodgkin's Disease) are at high risk for invasive breast cancer[29]. These women attend the Late Effects Clinic. *These are a target group for the PCMed Intervention.*

Referral Logistics – FCC/BU/LEC

Clinicians seeing women eligible for the PCMed Service (should) discuss RRMeds as a standard of care option and will discuss attendance at the PCMed Service in that context. Women will also receive a pamphlet (see Appendix 2) from the FCC/BU/LEC clinician about the PCMed Service. If the woman immediately indicates she is keen to attend, the clinician should put in an EPIC referral to the PCMed Service. If the woman needs time to consider whether they would like to attend PCMed, the woman can email the PCMed Service later and the Service will request a referral from the FCC/BU/LEC clinician.

Activity Based Funding (rather than Medicare billing) will be used for the PCMed Service, so an internal referral from the FCC/BU/LEC clinician to the PCMed Service through EPIC will suffice, and these do not expire provided the woman is not discharged from the FCC/BU/LEC.

Delivery of the PCMed Service

Pre-Service Attendance Work Up

The Pre-Service Attendance Work Up is illustrated in a flow chart below (Figure 4).

Referrals will be received from FCC/BU/Late Effects clinicians OR as a direct enquiry from woman (after having received the PCMed Explanatory Pamphlet). Occasional referrals are expected from external doctors and specialists at RWH and RMH during this pilot phase.

PCMed Service administration staff to email women who are referred to the PCMed Service with a link to a Pre-Service Questionnaire. The purpose of the PCMed Pre-Service Questionnaire is to confirm eligibility to the PCMed Service, determine if the Initial Consultation should be booked with the nurse practitioner or medical oncologist, ensure the

woman can attend the consultation via telehealth, and that relevant health information is available to maximise consultation time to address breast cancer risk and use of RRMeds.

The medical oncologist should see patients who have substantive medical problems or issues that may not be able to be resolved by the nurse practitioner.

Information from the Referral and the PCMed Pre-Service Questionnaire will be checked by the nurse practitioner. If the woman meets Service eligibility criteria and can attend the Initial Consultation via telehealth (video call) the nurse practitioner will liaise with the PCMed Service administration staff to make the Initial Consultation appointment. For woman who cannot attend by telehealth, a face-to-face consultation will be arranged. Telephone consultations are allowed but are to be avoided. Most consultations will be conducted by the nurse practitioner, with a minority conducted by the medical oncologist.

The administration staff will convey information on the Initial Consultation date and time (target KPI within 2 months of referral) to the woman.

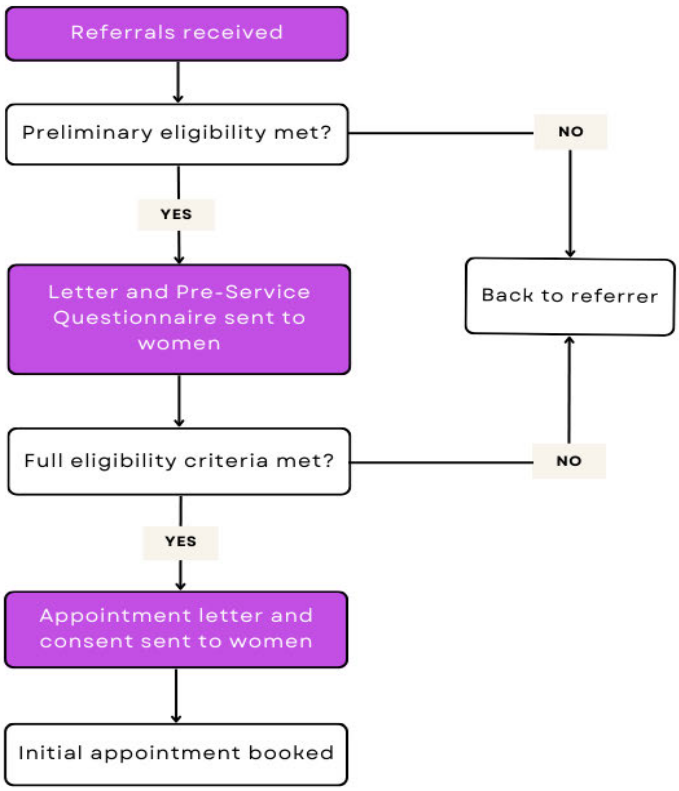


Figure 4: PCMed Service Pre-Service Attendance Work Up

Preparation for Initial Consultation

In preparation for the woman's Initial Consultation the nurse practitioner will determine client's breast cancer risk (10-year, 20 year and residual lifetime) and enter the risk assessment into EPIC. The breast cancer risk will be determined as follows:

- FCC clients – will already be available from the CanRisk assessment done in FCC. Breast Unit clients – nurse practitioner to calculate risk using online IBIS tool (risk is based only on age at diagnosis of LCIS/AH). Nurse may need to review histology report in EPIC to confirm atypical hyperplasia / LCIS (and no associated ductal carcinoma in situ (DCIS) or invasive breast cancer). Women who do not have LCIS or AH (e.g. women referred due to a family history of breast cancer) will be asked to complete iPrevent and return the output. Late Effects clients – nurse practitioner to use risk estimation table in Swerdlow paper[29] (based on Pre-Service Questionnaire and details in EPIC).
- Clients referred from services external to the Catchment Clinics – those with LCIS or atypical hyperplasia will have their risk estimated using the IBIS tool (based on lesion type and age). Others will be asked to complete iPrevent and return the output (note this will not currently give 20-year risk).

Initial consultation

- History from the Referral and Pre-Service Questionnaire will be checked, and other relevant history will be obtained. This will include social, medical (including current medications) and reproductive history (including menopausal status, whether currently lactating and desire for, and timing of future pregnancy).
- Presence/absence of contraindications to RRMeds as documented in the most recent Clinical Oncology Society of Australia (COSA) guide[16] will be specifically documented.
- Menopausal status will be determined. Consider post-menopausal only if:
    - Aged 60 years or older
    - Bilateral oophorectomy
    - Younger than 60 years old with uterus present but with amenorrhoea for >12 months in the absence ofanother explanation (e.g., continuous pill use, Mirena IUD, pregnant or breastfeeding) or
    - Aged 40-59 without a uterus and with FSH level >30IU/L.
- Clarification of the client's understanding of their breast cancer risk.

- Enquiry as to whether the client desires specific numerical information regarding their risk:
    - If “yes” then disclosure of the 10-year, 20-year and lifetime risks that have been formally estimated using CanRisk/IBIS tool/Swerdlow paper (see pre-Service work-up above), and statement that consideration of RRMeds is recommended for them based on national and international guidelines.
    - If “no” then general discussion about which Cancer Australia/eviQ risk category, they fall into and that consideration of RRMeds is recommended for them based on national and international guidelines.
- Discussion of the names and mechanisms of action of RRMeds relevant to that woman (i.e., tamoxifen if pre or peri--menopausal, OR tamoxifen, raloxifene or anastrozole if post-menopausal) Utilisation of COSA patient information document as basis for discussion[16].
- Discussion of the potential breast cancer risk reduction in absolute terms (calculation of estimates as per box below):
    - Women will be told their estimated absolute 20-year and 10-year BC risk without RRMeds, followed by the range of approximate breast cancer risk if they take a 3 to 5-year course of RRMeds. The range will reflect between a 30% and 50% relative reduction in breast cancer risk, consistent with COSA patient information[16], and reflecting differences in results of the randomised trials. The risk reduction will be described i) in percentages and ii) where CanRisk and iPrevent have been used in a pictogram consistent with best practice in risk communication.

Worked example of absolute risk reduction calculation

If estimated 20-year BC risk is 15%

Risk can be approximately reduced to between [15% x 0.5] and [15% x 0.7] with RRMeds

Thus, the woman’s baseline 15% breast cancer risk at 20 years becomes (approximately) between 8% and 11% if she uses RRMeds for 3-5 years.

- Discussion of other benefits and side-effects of the relevant RRMeds using the COSA patient information sheet[16].

- Discussion of costs of the medications.
- The client will have had the opportunity to ask questions and seek clarification throughout and also at the end following delivery of the benefits and side-effects information.
- Client will be asked what they think of the information they have heard
- If women are keen to proceed with RRMeds they will be offered a 1st prescription in this consultation. If not, they will be offered a Repeat Consultation within 3 months (women will be asked how long they think they will need before the next appt) to consider further.
- All women will be provided with evidence-based information regarding lifestyle risk factors for breast cancer (e.g., from reliable sources such as government-endorsed health websites, or peak condition-specific organisations). However, these issues will not be discussed in any length in the consultation. It is expected that the referring doctor or GP will address these non-medication related issues.

Repeat Consultation

(only for women who did not take a prescription the Initial Consultation)

- Will generally occur within 3 months of the Initial Consultation.
- Women will have the opportunity to ask any follow-up questions.
- If women are keen to proceed with RRMeds they will be offered a 1st prescription for RRMeds at this visit.
- If the woman is uncertain, she will be encouraged to take a prescription to minimise telephone calls to the Service.

Post-Prescription Consultation

(only for women who received a prescription at the Initial or Repeat Consultation)

- Will occur at 8-10 weeks after commencing RRMeds.
- Women will be assessed for side-effects with a discussion on proactive management of side-effects/issues.
- Will include review of a bone density scan (organised locally by the GP) for women who have been prescribed an aromatase inhibitor and are having no problematic symptoms at 6 weeks. Women who do have problematic symptoms at this time are unlikely to stay on the AI and thus a bone density is not required.

- Women who do not have any side-effects of concern will be able to email the Service and cancel this appointment if desired. If this occurs a formal note will be made in EPIC.

Ad Hoc Post-Prescription Consultations

- Additional consults can be arranged as required either to address questions before starting RRMeds or to address side-effects during the 3-to-5-year course of medication.

Communications and Informational Material

To Women (with copies to referring clinician and GP)

After the Initial Consultation, within 2 working days, clients will be emailed (or posted if no email) written information on their risks, the estimated absolute risk reduction with RRMeds and a summary of their current thinking and that of the PCMed clinician regarding the most appropriate RRMeds regimen. The letter will include general information regarding minimising modifiable risk factors for breast cancer (alcohol, obesity, inactivity) and general information regarding breast cancer screening relevant to their risk level. They will also receive the COSA patient information about RRMeds[16].

When a decision to try RRMeds has been made a letter will be sent to the woman.

- For these clients who accept a prescription, the letter will contain detailed information on side-effects of the specific RRMed chosen, and advice on what to do in the event of side-effects.
- For those who decline RRMeds, the letter will contain a summary of the reasons for declining. If appropriate these women will be informed that the PCMed Service will be available to them for further discussions about RRMeds after 12 months, should they desire.

To Clinicians

Once a decision has been made about RRMeds, the referring clinician and GP will receive a letter with the following information:

- Summary of the woman's 10-year, 20-year, and residual lifetime breast cancer risks and how those can be reduced with RRMeds.
- General information regarding minimising modifiable risk factors for breast cancer (alcohol, obesity, inactivity).
- Recommendation regarding breast cancer screening relevant to the woman's risk level.
- On the PCMed Service Hotline.

- COSA information for clinicians on RRMeds[16].
- Clinicians will also receive a letter after the Post-Prescription Consultation and after any ad hoc Post-Prescription Consultations with repeat hotline information.

Hotline Telephone Service

There will be a hotline service to support women and their clinicians. They will be able to call during staffed hours to obtain advice. Calls from women will attract Activity Based Funding.

Appendix 3: Characteristics for participants with 6-month outcome data

Table A3.1 Baseline characteristics of all participants with 6-month outcome data (n=46)

Characteristic	Category	Prospective sample n = 46
Age	Mean (SD)	50.6 (9.2)
	Median (IQR)	53 (12.8)
	Range	29,67
Country of Birth, n (%)	Australia	39 (84.8)
	Not Australia	7 (15.2)
Indigenous status, n (%)	Non-Indigenous	46 (100.0)
	Aboriginal	0 (0.0)
	Torres Strait Islander	0 (0.0)
	Aboriginal & Torres Strait Islander	0 (0.0)
Need for interpreter, n (%)	Yes	1 (2.2)
	No	45 (97.8)
Marital status, n (%)	Single	7 (15.2)
	Married/de-facto	35 (76.1)
	Divorced/separated	3 (6.5)
	Widowed	1 (2.2)
Education level, n (%)	Never attended school	0 (0.0)
	Year 11 or below	1 (2.2)
	Year 12 or equivalent	7 (15.2)
	TAFE, vocational	13 (28.3)
	University degree	24 (52.2)
	Prefer not to say	1 (2.2)
Socioeconomic Status (SEIFA), n (%)	Q1 (most disadvantaged)	2 (4.3)
	Q2	3 (6.5)
	Q3	8 (17.4)
	Q4	16 (34.8)
	Q5 (least disadvantaged)	17 (37.0)
Parity, n (%)	0	16 (34.8)
	1	8 (17.4)
	2	12 (26.1)
	3	10 (21.7)
Referral source, n (%)	PMCC Familial Cancer Centre	4 (8.7)
	PMCC Breast Surgical Oncology Clinic	15 (32.6)
	PMCC Late Effects Clinic	12 (26.1)
	RMH Familial Cancer Centre	4 (8.7)
	Primary Care	3 (6.5)
	External Specialist Service	8 (17.4)
Referring Clinician Type, , n (%)	Geneticist	1 (2.2)
	Genetic Counsellor	4 (8.7)
	Medical Oncologist	1 (2.2)
	Radiation Oncologist	6 (13.0)
	Haematologist	7 (15.2)
	Breast Surgeon	23 (50.0)

	Nurse	1 (2.2)
	General practitioner	3 (6.5)
Individual risk factor*, n (%)	Any family history of breast cancer	30 (65.2)
	History of LCIS	7 (15.2)
	History of ADH	2 (4.3)
	History of ALH	3 (6.5)
	History of thoracic irradiation	15 (32.6)
Multiple risk factors*, n (%)	Family history and LCIS	5 (10.9)
	Family history and ADH	1 (2.2)
	Family history and ALH	1 (2.2)
	Family history and thoracic irradiation	4 (8.7)
Number of first-degree relatives with breast cancer, n (%)	0	23 (50.0)
	1	16 (34.8)
	2	4 (8.7)
	3	3 (6.5)
10-year breast cancer risk, mean(SD)	Able to be assessed n=45	11.8 (8.2)
	Unable to be assessed** n= 1	
Residual lifetime risk mean(SD)	Able to be assessed n=31	35.2 (15.7)
	Unable to be assessed** n =15	
Footnote: *Risk factor categories are not mutually exclusive; participants may appear in more than one row under individual or multiple risk factors. Unless otherwise stated, percentages are based on the total sample denominator (n=46). "Any family history" may include first- or second-degree relative. The number of first-degree relatives with breast cancer is presented for the full sample; a value of 0 indicates no affected first-degree relatives and may include participants with no family history or family history limited to second-degree relatives. **Participants not able to be assessed for residual lifetime risk had prior thoracic irradiation, which precluded calculation of this estimate.		

Table A3.2: Participant characteristics stratified by RRMed uptake status

Characteristic	Category	RRMed Uptake n=20	No RRMed Uptake n=17
Age	Mean (SD)	51.1(9.4)	53 (8.9)
	Median (IQR)	51 (14)	56 (10)
	Range	33, 66	39,67
Country of Birth, n (%)	Australia	17 (85)	15 (88.2)
	Not Australia	3 (15)	2 (11.8)
Indigenous status, n (%)	Non-Indigenous	20 (100.0)	17 (100.0)
	Aboriginal	0 (0.0)	0 (0.0)
	Torres Strait Islander	0 (0.0)	0 (0.0)
	Aboriginal & Torres Strait Islander	0 (0.0)	0 (0.0)
Need for interpreter, n (%)	Yes	1 (5.0)	0 (0.0)
	No	19 (95.0)	17 (100.0)
Marital status, n (%)	Single	3 (15.0)	2 (11.8)
	Married/de-facto	17 (85.0)	11 (64.7)
	Divorced/separated	0 (0.0)	3 (17.6)

	Widowed	0 (0.0)	1 (5.9)
	Not recorded	0 (0.0)	0 (0.0)
Education level, n (%)	Never attended school	0 (0.0)	0 (0.0)
	Year 11 or below	1 (5.0)	0 (0.0)
	Year 12 or below	3 (15.0)	4 (23.5)
	TAFE, vocational	6 (30.0)	4 (23.5)
	University degree	9 (45.0)	9 (53.0)
	Prefer not to say	1 (5.0)	0 (0.0)
	Not recorded	0 (0.0)	0 (0.0)
Socioeconomic Status (SEIFA), n (%)	Q1 (most disadvantaged)	1 (5.0)	1 (5.9)
	Q2	2 (10.0)	0 (0.0)
	Q3	1 (5.0)	5 (29.4)
	Q4	8 (40.0)	5 (29.4)
	Q5 (least disadvantaged)	8 (40.0)	6 (35.3)
Parity, n (%)	0	8 (40.0)	4 (23.5)
	1	2 (10.0)	4 (23.5)
	2	5 (25.0)	5 (29.5)
	3	5 (25.0)	4 (23.5)
	4	0 (0.0)	0 (0.0)
Referral source, n (%)	PMCC Familial Cancer Centre	0 (0.0)	3 (17.6)
	PMCC Breast Surgical Oncology Clinic	7 (35.0)	7 (41.2)
	PMCC Late Effects Clinic	4 (20.0)	4 (23.5)
	RMH Familial Cancer Centre	1 (5.0)	2 (11.8)
	Primary Care	2 (10.0)	0 (0.0)
	External Specialist Service	6 (30.0)	1 (5.9)
Referring Clinician Type, n (%)	Geneticist	0 (0.0)	1 (5.9)
	Genetic Counsellor	0 (0.0)	3 (17.6)
	Medical Oncologist	0 (0.0)	0 (0.0)
	Radiation Oncologist	2 (10.0)	1 (5.9)
	Haematologist	2 (10.0)	4 (23.5)
	Breast Surgeon	14 (70.0)	8 (47.1)
	Nurse	0 (0.0)	0 (0.0)
	General practitioner	2 (10.0)	0 (0.0)
Individual risk factors*, n (%)	Any family history of breast cancer	12 (60)	13 (76.5)
	History of LCIS	6 (30.0)	1 (5.9)
	History of ADH	2 (10.0)	0 (0.0)
	History of ALH	3 (15.0)	0 (0.0)
	History of thoracic irradiation	4 (20.0)	6 (35.3)
Multiple risk factors*, n (%)	Family history and LCIS	4 (20.0)	1 (5.9)
	Family history and ADH	1 (5.0)	0 (0.0)

	Family history and ALH	1 (5.0)	0 (0.0)
	Family history and thoracic irradiation	1 (5.0)	2 (11.8)
Number of first-degree relatives with breast cancer, n (%)	0	8 (40.0)	4 (23.5)
	1	2 (10.0)	4 (23.5)
	2	5 (25.0)	5 (29.5)
	3	5 (25.0)	4 (23.5)
	4	0 (0.0)	0 (0)
10-year breast cancer risk	Mean (SD)	12.01 (8.47)	11.56 (8.15)
Residual lifetime risk	In participants assessed	43.59 (14.0) (n=16)	25.09 (14.0) (n=11)
	Unable to be defined**	n = 4	n = 6

Footnote:
*Risk factor categories are not mutually exclusive; participants may appear in more than one row under individual or multiple risk factors. Unless otherwise stated, percentages are based on the total sample denominator (n=46).
“Any family history” may include first- or second-degree relative. The number of first-degree relatives with breast cancer is presented for the full sample; a value of 0 indicates no affected first-degree relatives and may include participants with no family history or family history limited to second-degree relatives.
**Participants not able to be assessed for residual lifetime risk had prior thoracic irradiation, which precluded calculation of this estimate.

Appendix 4: PCMed Research Journal

PCMed research journal **entries documenting barriers, enablers, adaptations and reflections on the nurse practitioner role** during implementation of the PCMed Service (December 2023 to June 2025). All entries were completed by Katrina West, the thesis author and PCMed Service nurse practitioner.

Aim: to capture longitudinal data on barriers and enablers to implementation of the new PCMed Service, adaptations made and the role of the PCMed Service nurse practitioner

* This may relate to capability such as skills and knowledge; opportunity such as resources or the social influences of others, and motivation such as beliefs about consequences of the service, professional identity[1].

** What the change was, when it happened, who decided on the change, why - including planned or unplanned changes - and what was the impact of the change[2].

When: Monthly

Population: PCMed Service nurse practitioner

PCMed research journal

Month: December 2023

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
As the PCMed Service represented a new model of care within existing hospital systems, early implementation required navigation of organisational processes that sat outside usual clinical practice which I found challenging. This included learning how to align the new service with established EMR naming conventions, referral workflows and hospital reporting requirements. Clarifying the appropriate service name and EMR terminology was necessary before the referral template could be finalised. Similarly, establishing the NP clinic required clarification of the correct clinic coding and funding classification and required collaboration with administrative and finance teams who may not be familiar with nurse practitioner clinics. This highlighted the importance of understanding hospital funding and reporting systems when developing a new clinical service. Eligibility assessment also required refinement during early implementation. For women attending the PMCC Familial Cancer Centre, residual lifetime risk and 10-year risk were not routinely documented in the EMR, making eligibility for the PCMed Service difficult to determine from existing records. Accessing individual risk assessment information therefore became an important early process improvement to support accurate identification of eligible women.
Over the last month, what has helped the take up of the PCMed service? *
Response: Over the last month, take-up of the PCMed Service was supported by active problem-solving during early implementation and teamwork. Working with the EMR team to clarify the service name and referral terminology enabled development of the referral templates and made the service more visible and accessible to referrers. Collaboration with administrative and finance

teams to ensure correct NP clinic coding also supported appropriate service establishment within hospital reporting and funding systems. A communication plan was developed to introduce the novel PCMed Service and included: presentations about the PCMed Service and the concurrent evaluation, were delivered to Catchment Clinic teams. Clinician resources were developed (information scripts for lanyards; and Information Sheets on Service, including eligibility criteria); email reminders were sent to clinicians in Catchment Clinics when recruitment commenced; a PCMed Service page was developed on CONNECT (hospital website); and clinicians were reminded when potentially eligible women were identified through pre-screening.
What adaptations have been made to the service over the last month? **
Response: No adaptation to the Service
Have there been any unintended consequences from this service? If so, what?
Response: No unintended consequences
Is there anything that would facilitate your role?
Response: Clinical training and supervision. Weekly meetings with Service lead to discuss implementation issues and improvements.
Do you have any other thoughts/comments
Response: Significant effort required to establish both the clinical service and research processes simultaneously. "You don't know what you don't know" was very relevant during establishment.

Month: January 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: While the following are not implementation barries they were some challenges that I faced and include: Confusion for one clinician regarding eligibility criteria leading to a one eligible woman not being informed about PCMed because residual lifetime risk was <20% despite meeting the 10-year risk >5% criterion, demonstrating need for clearer communication pathways. Inability to send enclosures with letters to referrers and clients due to limitations of the hospital EMR system. Difficulty quantifying risk in a woman with prior thoracic irradiation due to inability to confirm treatment field.

One woman thought telehealth meant telephone rather than video-based consultation.
Over the last month, what has helped the take up of the PCMed service? *
Eligibility criteria were clarified by email to clinicians, with emphasis on both residual lifetime risk and 10-year risk thresholds. Supporting information that could not be sent as EMR enclosures was converted to links in correspondence, and the COSA clinician information was inserted into letters. Clinic templates were refined once they were used in practice. Self-directed learning and supervision from the lead medical oncologist supported safe early implementation. Clearer language about video-health was used to reduce misunderstanding about the consultation modality.
What adaptations have been made to the service over the last month? **
Response: No adaptations to the Service.
Have there been any unintended consequences from this service? If so, what?
Response: No unintended consequences identified.
Is there anything that would facilitate your role?
Response: Ongoing clinical training and supervision. Weekly meetings with Service lead.
Do you have any other thoughts/comments
Response: During early implementation the importance of clear communication about eligibility, study purpose and telehealth processes were highlighted.

Month: February 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: A woman was referred who was eligible for genetic testing, requiring clarification of the referral pathway. Telehealth technical issues occurred during some consultations, including occasions when telehealth staff could not be contacted. Two consultations had to be completed by telephone, which was not ideal.

Over the last month, what has helped the take up of the PCMed service? *
Clarification that women requiring genetic testing should first be referred to the Familial Cancer Centre, then to PCMed if still appropriate after testing. Flexibility in completing consultations by telephone, while not ideal, ensured that the consultation could still proceed rather than requiring cancellation.
What adaptations have been made to the service over the last month? **
Response: No adaptations to Service.
Have there been any unintended consequences from this service? If so, what?
Response: Telephone used as a back-up modality when telehealth failed.
Is there anything that would facilitate your role?
Response: Continued access to supervision and pathway clarification. More reliable telehealth support and clearer troubleshooting processes.
Do you have any other thoughts/comments
Response: Pathway clarification for genetics was important early and likely to remain relevant. Telehealth is feasible overall but requires knowledge and access to operational support to function optimally.

Month: March 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: Some women referred to PCMed appeared not to have a clear understanding of their breast cancer risk before attending, suggesting variability in pre-referral counselling and baseline risk communication.
Over the last month, what has helped the take up of the PCMed service? *
Response: Personalised explanation of individual breast cancer risk during consultations appeared important in supporting understanding and decision-making.
What adaptations have been made to the service over the last month? **

Response: No adaptations to Service.
Have there been any unintended consequences from this service? If so, what?
Response: No unintended consequences identified.
Is there anything that would facilitate your role?
Response: Ongoing supervision and case discussion.
Do you have any other thoughts/comments
Response: Understanding whether women appreciate their level of risk before attending remains an important consideration for referral and counselling processes.

Month: April 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: The following were not implementation barriers but provided a learning opportunity: Some referred cases involved risk profiles that were more complex than initially apparent. For example, one woman attending the Familial Cancer Centre primarily because of a strong family history of colorectal cancer also had a sister with breast cancer, requiring careful consideration of whether and how breast cancer prevention discussions should be incorporated. A 21-year-old woman met eligibility due to residual lifetime risk but not 10-year risk during pre-screening. This created a service implementation challenge because she was technically eligible by lifetime risk but not currently an appropriate candidate for medication discussion, requiring clear explanation about timing and future reassessment.
Over the last month, what has helped the take up of the PCMed service? *
Response: These nuanced cases helped develop clearer explanations around timing of intervention, future reassessment, and reasons for not recommending immediate medication.
What adaptations have been made to the service over the last month? **
Response: No adaptations to Service.
Have there been any unintended consequences from this service? If so, what?

Response: No specific unintended consequences identified.
Is there anything that would facilitate your role?
Response: Ongoing supervision regarding management of borderline or age-dependent prevention cases.
Do you have any other thoughts/comments
Response: Ongoing supervision regarding management of borderline or age-dependent prevention cases. These cases highlighted the importance of distinguishing eligibility for referral from current suitability for risk-reducing medication. Consideration was given to how best to discuss reassessment and possible future re-referral for women eligible on lifetime risk alone but not currently suitable for medication.

Month: May 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: A woman requiring an interpreter was unable to link into telehealth despite assistance and therefore required face-to-face review. Telehealth was not equally accessible for all women, particularly where interpreter support and digital literacy issues were combined.
Over the last month, what has helped the take up of the PCMed service? *
Response: Flexibility in offering face-to-face review when telehealth was not feasible supported engagement.
What adaptations have been made to the service over the last month? **
Response: No adaptations to Service.
Have there been any unintended consequences from this service? If so, what?
Response: Inability to use Telehealth to attend created additional administrative burden and highlighted the need to retain flexibility in consultation modality.
Is there anything that would facilitate your role?
Response: Reliable access to interpreter-supported telehealth processes and contingency pathways for failed telehealth connections.

Do you have any other thoughts/comments
Response: Although telehealth is central to the service model, it cannot be assumed to be universally accessible.

Month: June 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: Some referrals involved complexity beyond current nurse practitioner scope or confidence, requiring escalation to the medical oncologist. This included women with ATM-related risk, where further expertise was required.
Over the last month, what has helped the take up of the PCMed service? *
Response: Ongoing clinical supervision and case review were helpful, particularly for complex cases and escalation decisions.
What adaptations have been made to the service over the last month? **
Response: No adaptations occurred.
Have there been any unintended consequences from this service? If so, what?
Response: No unintended consequences identified.
Is there anything that would facilitate your role?
Response: Continued structured clinical supervision and opportunities to review complex cases.
Do you have any other thoughts/comments
Response: Clinical supervision and case discussion remained important in determining when to escalate and what key information to discuss. These more complex cases reinforced the importance of clear escalation pathways within a nurse practitioner-led prevention model.

Month: July 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: Unexpected contraindications or other medical issues (for example, endometriosis and Factor V Leiden carrier status) sometimes required literature review and additional specialist input before treatment decisions could be made. This delayed treatment planning and created uncertainty about when follow-up appointments should be booked.
Over the last month, what has helped the take up of the PCMed service? *
Response: Case discussion and supervision supported management planning where unexpected issues arose.
What adaptations have been made to the service over the last month? **
Response: No adaptations to Service.
Have there been any unintended consequences from this service? If so, what?
Response: When additional review was required, follow-up appointments sometimes needed to be delayed, rescheduled or left pending until advice was received. This increased administrative work and could prolong the time from initial consultation to a final treatment decision.
Is there anything that would facilitate your role?
Response: Clearer pathways for women requiring review of contraindications or other medical issues.
Do you have any other thoughts/comments
Response: Timing and sequencing of appointments will be important operational issues if the service is expanded. As the service grows, the introduction of structured pre-clinic case discussions, including input from medical oncology and pharmacy, is likely to improve planning and reduce avoidable delays.

Month: August 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: Referral numbers remained low from Catchment Clinics.
Over the last month, what has helped the take up of the PCMed service? *

Response: Ongoing visibility of the Service and reminders to referrers remained important. Continued efforts to maintain awareness of the Service among referrers included emailing clinicians seeing eligible women, placing notes in the EMR system to alert clinician.
What adaptations have been made to the service over the last month? **
Response: No adaptations to Service.
Have there been any unintended consequences from this service? If so, what?
Response: Low referral volume has implications for recruitment targets and for evaluating uptake of RRMeds and adoption of the service.
Is there anything that would facilitate your role?
Response: More consistent referrals and engagement with Catchment Clinics.
Do you have any other thoughts/comments
Response: Low referral rates from Catchment Clinics remain one of the most persistent implementation challenges.

Month: September 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: In one case a woman who did not appear to meet criteria based on the pre-service questionnaire but did meet criteria when iPrevent (risk assessment) was completed. This highlighted that incomplete or inaccurate information at referral can lead to under-recognition of eligibility. Manual assessment of risk remained time-consuming.
Over the last month, what has helped the take up of the PCMed service? *
Response: Completion of iPrevent helped identify women who were in fact eligible when this was not initially apparent. Having women to complete iPrevent placed less burden on the nurse practitioner and improved completeness of information before consultation.
What adaptations have been made to the service over the last month? **

Response: Greater use of iPrevent adopted to streamline risk assessment and improve completeness of information before consultation.
Have there been any unintended consequences from this service? If so, what?
Response: Reliance on incomplete referral information had the potential to miss eligible women.
Is there anything that would facilitate your role?
Response: Using iPrevent as the PCMed standardised validated risk assessment tool for all women.
Do you have any other thoughts/comments
Response: These experiences reinforced the value of pre-service risk assessment in improving efficiency and reducing inappropriate exclusion.

Month: October 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: Some Familial Cancer Centre referrals appeared to focus on familial risk without accounting for benign proliferative breast lesions such as LCIS, which independently increase breast cancer risk. This was not an isolated incident.
Over the last month, what has helped the take up of the PCMed service? *
Response: Detailed review of pathology history alongside family history improved recognition of women at higher risk who may benefit from discussion of risk-reducing medication.
What adaptations have been made to the service over the last month? **
Response: No adaptations to Service.
Have there been any unintended consequences from this service? If so, what?
Response: The experience highlighted that Familial Cancer Centre referrals may appropriately prioritise familial and genetic risk but may not consistently incorporate benign proliferative breast lesions into breast cancer risk assessment. This creates a potential risk of underestimating eligibility for preventive intervention at the point of referral. The case was discussed with the referring clinicians

and escalated to my professional lead, enabling the issue to be considered at a service-lead level and informing broader referral pathway improvement.
Is there anything that would facilitate your role?
Response: Better integration of hereditary and pathology-related risk information across referral pathways.
Do you have any other thoughts/comments
Response: These cases suggest that comprehensive risk assessment processes are essential for accurate referral and eligibility determination.

Month: November / December 2024

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: No barriers to Service implementation
Over the last month, what has helped the take up of the PCMed service? *
Response: Additional follow-up enabled review of treatment tolerance and safe continuation planning. The experience highlighted that some elements of stable follow-up could be managed by the GP in future scale-up.
What adaptations have been made to the service over the last month? **
Response: No adaptations to Service.
Have there been any unintended consequences from this service? If so, what?
Response: One woman attended her planned Post-Prescription Consultation review but had not started medication due to unrelated health issues. This raised concerns about inefficient use of clinic resources and how best to avoid such appointments when medication has not yet commenced. A phone review was arranged after Post-Prescription Consultation to reassess once the bone density scan was completed. Additional follow-up used to support treatment interruption and rechallenge.
Is there anything that would facilitate your role?
Response: Clearer shared-care arrangements with GPs for stable follow-up and monitoring.

Do you have any other thoughts/comments
Response: Follow-up appointments may become more resource-intensive if investigations such as bone density scans are not completed before review. These cases support the importance of flexibility in follow-up, while also highlighting opportunities for shared care with GPs in future scale-up and the need to educate women to reschedule if they have not commenced the prescribed RRMed.

Month: January / February 2025

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: iPrevent could not assess risk for monozygotic twins, requiring use of CanRisk instead.
Over the last month, what has helped the take up of the PCMed service? *
Response: Use of clinical guidelines supported management advice. Alternative validated tools such as CanRisk were useful where iPrevent could not be used.
What adaptations have been made to the service over the last month? **
Response: No adaptations required. A good learning experience in knowing the limitations of risk assessment tools
Have there been any unintended consequences from this service? If so, what?
Response: A GP inquiry about vaginal estrogen use leading to required guideline-based review to support safe advice and unplanned correspondence. Referral rates from Catchment Clinics remained low throughout the study period. This reflected annual review patterns in the Breast Unit and Late Effects Clinic, and more restrictive referral pathways in Familial Cancer Centres, where many women either required genetic testing or were directed to high-risk management clinics rather than the PCMed Service.
Is there anything that would facilitate your role?
Response: Understanding all limitations of the Risk Assessment tools. Easy access to guidelines (such as saving as favourites on computer). Additional administrative or research support for pre-screening and follow-up of potentially eligible women, sending reminders for clinicians, and ongoing promotion of the Service.
Do you have any other thoughts/comments

Response: Case highlighted the importance of understanding the limitation of the Risk Assessment Tools to ensure accuracy of risk estimation.

Month: March 2025

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: Nil Barriers identified.
Over the last month, what has helped the take up of the PCMed service? *
Response: Clarification of questionnaire responses, helped prevent inappropriate exclusion and improved assessment accuracy.
What adaptations have been made to the service over the last month? **
Response: No adaptations to Service.
Have there been any unintended consequences from this service? If so, what?
Response: Answer provided in the pre-service questionnaire required follow-up phone calls to clarify information that had been entered
Is there anything that would facilitate your role?
Response: Administrative support has reduced burden.
Do you have any other thoughts/comments
Response: Incomplete or inaccurate pre-service information can increase administrative workload.

Month: April 2025

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: No barriers identified.
Over the last month, what has helped the take up of the PCMed service? *

Response: Nil identified.
What adaptations have been made to the service over the last month? **
Response: No adaptations to Service
Have there been any unintended consequences from this service? If so, what?
Response: A woman was referred by an external breast surgeon for support with side effects, specifically hot flushes while taking low-dose tamoxifen (not initiated in the PCMed Service). Decision made to see the woman. Although this type of referral may support persistence, it is not entirely clear whether it sits within the intended core role of the service.
Is there anything that would facilitate your role?
Response: Clear policy regarding whether and how the service should support women already established on medication elsewhere.
Do you have any other thoughts/comments
Response: Persistence support is clinically valuable but may require clearer service boundaries.

Month: May / June 2025

Over the last month, what barriers have there been to the implementation of the PCMed Service? *
Response: No barriers identified.
Over the last month, what has helped the take up of the PCMed service? *
Response: Nil identified.
What adaptations have been made to the service over the last month? **
Response: Women stable on RRMeds are not formally discharged at this stage. Instead, care is transferred back to the GP with a written management and monitoring plan, while the woman remains linked to the PCMed Service for medication-related advice or concerns if needed. Practically, this could occur by documenting the transfer plan in the EMR, sending a letter to the GP and woman, and advising women to contact PCMed if medication-related issues arise. A report template could be developed in EMR to identify women who commenced and RRMeds and then a 6-monthly audit

could occur to ensure women are then formally discharged after completion of treatment (3 to 5 years) or permanent cessation of medication.
Have there been any unintended consequences from this service? If so, what?
Response: Women contacted Service after being discharged. If formally discharged from the service once stable on a risk-reducing medication, subsequent urgent contact does not generate VINAH funding. This has implications for funding workflows and service design.
Is there anything that would facilitate your role?
Response: Clearer processes.
Do you have any other thoughts/comments
Response: This highlighted the importance of developing standard operating procedures as implementation issues arise. Clear documentation is needed to distinguish GP-led stable monitoring from formal discharge, particularly while women remain on RRMeds.

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