

Section 1

Introduction and methods

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Triple negative breast cancers are defined by the lack of progesterone and oestrogen receptors, and HER2 proteins. Triple negative breast cancers are an aggressive form of breast cancer that typically affects younger women, has a poor prognosis, and lack of targeted therapies.

In 2019, there were 19,371 new cases of breast cancer reported in Australia⁵. Approximately 12 to 17% of all breast cancers are triple negative, that is an estimated 3000 new cases of triple negative breast cancer in Australia 2019.

A PubMed search was conducted in 2021 to identify studies reporting patient experience, patient reported outcomes, and quality of life studies in the triple negative breast cancer community. Studies conducted more than 10 years ago were excluded, and studies that included multiple types of breast cancers that did not report triple negative breast cancers separately (as a subgroup) were excluded. There were 12 studies identified of between six and 902 participants. There was only one study identified that interviewed participants or used qualitative methods, this study was focused on African Americans diagnosed with triple negative breast cancer.

This PEEK study appears to be among the largest cohorts of women diagnosed with triple negative breast cancer that includes a structured interview and it also covers the most domains.

Introduction

Triple negative breast cancers are defined by the lack of progesterone and oestrogen receptors, and HER2 proteins^{1,2}. Triple negative breast cancers are an aggressive form of breast cancer that typically affects younger women, has a poor prognosis, and lack of targeted therapies^{3,4}.

In 2019, there were 19,371 new cases of breast cancer reported in Australia⁵. Approximately 12 to 17% of all breast cancers are triple negative³, that is an estimated 3000 new cases of triple negative breast cancer in Australia 2019.

Personal Experience, Expectations and Knowledge (PEEK)

Patient Experience, Expectations and Knowledge (PEEK) is a research program developed by the Centre for Community-Driven Research (CCDR). The aim of PEEK is to conduct patient experience studies across several disease areas using a protocol that will allow for comparisons over time (both quantitative and qualitative components). PEEK studies give us a clear picture and historical record of what it is like to be a patient at a given point in time, and by asking patients about their expectations, PEEK studies give us a way forward to support patients and their families with treatments, information and care.

The research protocol used in PEEK studies is independently driven by CCDR. PEEK studies include a quantitative and qualitative component. The quantitative component is based on a series of validated tools. The qualitative component is the result of two years of protocol testing by CCDR to develop a structured interview that solicits patient experience data and provides patients with the opportunity to provide advice on what they would like to see in relation to future treatment, information and care. The structured interview has also been designed so that the outcomes of PEEK studies can inform policy, research, care, information, supportive care services and advocacy efforts.

Participants

To be eligible for the study, participants needed to have been diagnosed with triple negative breast cancer, have experienced the healthcare system in Australia, be 18 years of age or older, be able to speak English, and be able to give consent to participate in the study.

Ethics

Ethics approval for this study was granted (as a low or negligible risk research study) by the Centre for Community-Driven Research Ethics Committee (Reference CS_Q4_03).

Data collection

Data for the online questionnaire was collected using Zoho Survey (Zoho Corporation Pvt. Ltd. Pleasanton, California, USA, www.zoho.com/survey). Participants completed the survey in 2021.

There were five researchers who conducted telephone interviews and used standardised prompts throughout the interview. The interviews were recorded and transcribed verbatim. Identifying names and locations were not included in the transcript. All transcripts were checked against the original recording for quality assurance. Interview data was collected in 2021.

Online questionnaire (quantitative)

The online questionnaire consisted of the 36-Item Short Form Health Survey (SF36) (RAND Health)⁶, a modified Cancer Care Coordination Questionnaire for Patients (CCCQ)⁷, the Short Fear of Progression Questionnaire (FOP12)⁸, and the Partners in Health version 2 (PIH)⁹. In addition, investigator derived questions about demographics, diagnosis, treatment received and future treatment decisions making were included.

Structured Interview (qualitative)

Interviews were conducted via telephone by registered nurses who were trained in qualitative research. The first set of interview questions guided the patient through their whole experience from when symptoms were noticed up to the present day.

Questionnaire analysis

Statistical analysis was conducted using R included in the packages “car”, “dplyr” and “ggplot2” (R 3.3.3 GUI 1.69 Mavericks build (7328)). The aim of the statistical analysis of the SF36, CCCQ, FOP12, and PIH responses was to identify variations by disease stage, physical function, year of diagnosis, age, location of residence, education status and socio-economic status. Scales and subscales were calculated according to reported instructions⁶⁻⁹.

The location of participants was evaluated by postcode using the Australian Statistical Geography Maps (ASGS) Remoteness areas accessed from the Australian Bureau of Statistics¹⁰.

The level of socio-economic status of participants was evaluated by postcode using the Socio-economic Indexes for Areas (SEIFA) accessed from the Australian Bureau of Statistics¹¹.

For comparisons by age, a one-way analysis of variance (ANOVA) analysis was conducted. A Tukey HSD test was used post-hoc to identify the source of any differences identified in the one-way ANOVA test. Where the assumptions for the one-way ANOVA were not met, a Kruskal-Wallis rank sum test on care was conducted with post-hoc pairwise comparisons using Wilcoxon rank sum test. When the assumption of equal variances were not met, a Welch one-way test was used with post-hoc pairwise t-tests with no assumption of equal variances.

For all other comparisons between groups, a two-sample t-test was used when assumptions for normality and variance were met, or when assumptions were not met, a Wilcoxon rank sum test with continuity correction was used. Questions where participants were asked to rank preferences were analysed using weighted averages. Weights were applied in reverse, the most preferred option was given the largest weight equal to the number of options, the least preferred option was given the lowest weight of 1.

Structured interviews analysis

A content analysis was conducted using conventional analysis to identify major themes from structured interviews. Text from the interviews were read line-by-line by the lead researcher and then imported into NVivo 8 (QSR International)/MaxQDA. Each question within the interview was individually analysed. Initial categories and definitions were identified and registered in NVivo 8 (QSR International)/MaxQDA. The minimum coded unit was a sentence with paragraphs and phrases coded as a unit.

A second researcher verified the codes and definitions, and the text was coded until full agreement was

reached using the process of consensual validation. Where a theme occurred less than 5 times it was not included in the study results, unless this result demonstrated a significant gap or unexpected result.

Position of this study

A PubMed search was conducted in 2021 to identify studies reporting patient experience, patient reported outcomes, and quality of life studies in the triple negative breast cancer community. Studies conducted more than 10 years ago were excluded, and studies that included multiple types of breast cancers that did not report triple negative breast cancers separately (as a subgroup) were excluded.

There were 12 studies identified of between six and 902 participants. There was only one study identified that interviewed participants or used qualitative methods, this study was focused on African Americans diagnosed with triple negative breast cancer¹².

There were 11 studies that collected patient experience/patient reported data by questionnaire. The two largest studies of 902 and 190 participants with triple negative breast cancer respectively, were multi-national drug clinical trials^{13,14}. There were three other clinical trials identified that collected patient reported outcomes, two were conducted in USA, and had between 37 and 38 triple negative breast cancer participants^{15,16}, one trial conducted in Spain with 73 participants¹⁷.

There was one study conducted in China focused on patient activation with 121 participants¹⁸, and one study conducted in the USA focused on health-related quality of life of 83 participants¹⁹. There were two studies conducted in North America that focused on clinical trial participation that included between 15 and 74 participants^{20,21}. One study was focused on lifestyle changes, conducted in the USA with 23 participants²², and one USA study of 13 participants focused on coping²³.

PEEK is a comprehensive study covering all aspects of disease experience from symptoms, diagnosis, treatment, healthcare communication, information provision, care and support, quality of life, and future treatment and care expectations.

Table 1.1: PEEK position

Author, Year	Location	Number of participants	Data collection	Focus	PEEK SECTION								
					2: Health status, co-morbidities	3: Diagnosis experience	4: Decision making	5: Treatment, healthcare system use	6: Information, communication and self-management	7: Care, support and navigating healthcare system	8: Quality of life, mental health, relationships	9: Expectations, preferences and messages	
Adams et al, 2020 ¹³	International	902	Questionnaire	Clinical trial	x								
Rugo et al, 2019 ¹⁴	International	190	Questionnaire	Clinical trial	x								
Shen et al, 2020 ¹⁸	China	121	Questionnaire	Patient activation	x				x	x			
Vadaparampil et al, 2017 ¹⁹	USA	83	Questionnaire	HRQOL	x							x	
Jacobs et al, 2017 ²⁰	Canada	74	Questionnaire	Clinical trial participation				x					
Manso et al, 2015 ¹⁷	Spain	73	Questionnaire	Clinical trial	x								
Filho et al, 2021 ¹⁶	USA	38	Questionnaire	Clinical trial	x								
Anders et al, 2014	USA	37	Questionnaire	Clinical trial	x								
Swisher et al, 2015 ²²	USA	23	Questionnaire	Lifestyle changes	x								
Kuderer et al, 2017 ²¹	USA	15	Questionnaire	Clinical trial participation		x	x					x	
Watkins et al, 2017 ²³	USA	13	Questionnaire	Coping								x	
Bollinger et al, 2018 ¹²	USA	6	Interview	Biopsychosocial challenges				x	x	x		x	

Abbreviations and terminology

ASGS	The Australian Statistical Geography Standard from the Australian Bureau of Statistics, defines remoteness and urban/rural definitions in Australia
CCDR	Centre for Community-Driven Research
dF	Degrees of Freedom. The number of values in the final calculation of a statistic that are free to vary.
f	The F ratio is the ratio of two mean square values, used in an ANOVA comparison. A large F ratio means that the variation among group means is more than you'd expect to see by chance.
HER2	Human epidermal growth factor receptor 2
FOP	Fear of Progression. Tool to measure anxiety related to progression
IQR	Interquartile range. A measure of statistical dispersion, being equal to the difference between 75th and 25th percentiles, or between upper and lower quartiles.
p	Probability value. A small <i>p</i> -value (typically ≤ 0.05) indicates strong. A large <i>p</i> -value (> 0.05) indicates weak evidence.
PEEK	Patient Experience, Expectations and Knowledge
PIH	Partners in Health
SD	Standard deviation. A quantity expressing by how much the members of a group differ from the mean value for the group/
SEIFA	Socio-Economic Indexes for Areas (SEIFA) ranks areas in Australia according to relative socio-economic advantage and disadvantage. This is developed by the Australian Bureau of Statistics.
SF36	Short Form Health Survey 36
t	t-Statistic. Size of the difference relative to the variation in your sample data.
Tukey HSD	Tukey's honestly significant difference test. It is used in this study to find significantly different means following an ANOVA test.
W	The W statistic is the test value from the Wilcoxon Rank sum test. The theoretical range of W is between 0 and (number in group one) x (number in group 2). When W=0, the two groups are exactly the same.
χ^2	Chi-squared. Kruskal-Wallis test statistic approximates a chi-square distribution. The Chi-square test is intended to test how likely it is that an observed distribution is due to chance.

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