







# Predictive Models of Psychological Distress, Quality of Life, and Adherence to Medication in Breast Cancer Patients: A Scoping Review

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**Purpose:** An interplay of clinical and psychosocial variables affects breast cancer patients' experiences and clinical trajectories. Several studies investigated the role of socio-demographic, clinical, and psychosocial factors in predicting relevant outcomes in breast cancer care, thus developing predictive models. Our aim is to summarize predictive models for specific psychological and behavioral outcomes: psychological distress, quality of life, and medication adherence. Specifically, we aim to map the determinants of the outcomes of interest, offering a thorough overview of these models.

**Methods:** Databases (PubMed, Scopus, Embase) have been searched to identify studies meeting the inclusion criteria: a breast cancer patients' sample, development/validation of a predictive model for selected psychological/behavioral outcomes (ie, psychological distress, quality of life, and medication adherence), and availability of English full-text.

**Results:** Twenty-one papers describing predictive models for psychological distress, quality of life, and adherence to medication in breast cancer were included. The models were developed using different statistical approaches. It has been shown that treatment-related factors (eg, side-effects, type of surgery or treatment received), socio-demographic (eg, younger age, lower income, and inactive occupational status), clinical (eg, advanced stage of disease, comorbidities, physical symptoms such as fatigue, insomnia, and pain) and psychological variables (eg, anxiety, depression, body image dissatisfaction) might predict poorer outcomes.

**Conclusion:** Predictive models of distress, quality of life, and adherence, although heterogeneous, showed good predictive values, as indicated by the reported performance measures and metrics. Many of the predictors are easily available in patients' health records, whereas others (eg, coping strategies, perceived social support, illness perceptions) might be introduced in routine assessment practices. The possibility to assess such factors is a relevant resource for clinicians and researchers involved in developing and implementing psychological interventions for breast cancer patients.

**Keywords:** breast cancer, predictive model, psychological distress, quality of life, adherence, predictors

## Introduction

With more than two million new cases in 2020 worldwide, Breast Cancer (BC) is the most frequent form of cancer for incidence and prevalence and the first in mortality among women.<sup>1</sup> Moreover, BC's impact extends beyond its clinical implications, affecting various psychological, relational, and social dimensions and impairing globally patients' Quality of Life (QoL).<sup>2-5</sup>

Psychological distress, a state of emotional suffering characterized by various combinations of anxious and depressive symptoms, is widespread among BC patients in every stage of the disease, from diagnosis to survivorship.<sup>6-8</sup> Coherently, rates of psychological disorders are higher among BC patients when compared with the general population: recent systematic reviews reported that 32.2% of BC patients suffer from depression and 41.9% from anxiety.<sup>9,10</sup> Furthermore, psychological



distress is associated with poorer clinical outcomes, such as a higher risk of cancer recurrence, poorer survival, greater all-cause and cancer-related mortality and morbidity,<sup>11–14</sup> poorer QoL, and lower adherence to medication.<sup>13</sup>

QoL refers to how patients perceive their own health, considering its physical, mental, and social dimensions.<sup>15,16</sup> QoL is commonly considered one of the key outcomes for BC patients, and its improvement is often one of the main aims of psychological interventions designed for them.<sup>16,17</sup> However, although during the last decade an increase in BC patients' QoL has been reported,<sup>16</sup> there are still several disease-related factors that may undermine BC patients' QoL, such as symptoms (eg, pain and lymphedema), adverse psychological effects (eg, worries, anxiety, depressive symptoms), sexual dysfunctions, and adverse side effects.<sup>16,17</sup>

One of the issues in which psychological distress and QoL intertwine with clinical aspects is adherence to therapy.<sup>18</sup> Among BC patients with a prescription for endocrine therapy, medication adherence rates are commonly suboptimal: a recent review<sup>19</sup> reported 5-years adherence rates ranging from 33.3% to 88.6%, with an average decrease of 25.5% for each year of treatment. Non-adhering behaviors originate from a multidimensional array of factors (eg, age, comorbidities, adverse effects). Nonetheless, it is worth noting that depression and poor QoL have been associated with lower medication adherence.<sup>19–21</sup> Since optimal adherence rates are associated with better clinical outcomes and better QoL,<sup>22–24</sup> supporting BC patients in maintaining optimal adherence is a relevant and actual cancer care goal.

In summary, a complex interplay of clinical and psychosocial variables plays a relevant role in BC patients' clinical trajectories, shaping their experiences with the disease and affecting their QoL.<sup>12,23–26</sup> Several studies investigated socio-demographic, clinical, and psychosocial factors that might influence the subjective variability observed in BC patients on psychological distress, QoL, and adherence. Several predictive models have been developed through different statistical methods (eg, linear regression, logistic regression, structural equation modeling),<sup>27–31</sup> some of these models have been further validated in additional samples, testing the model in other groups,<sup>28,31</sup> and they have been eventually applied in clinical practice, particularly in patients' assessment. Indeed, the clinical utility of such predictive models lies in the fact that identifying beforehand patients at a greater risk of severe psychological distress, poor QoL, or medication non-adherence could aid the assessment of those in greater need of psychological interventions.<sup>32–35</sup>

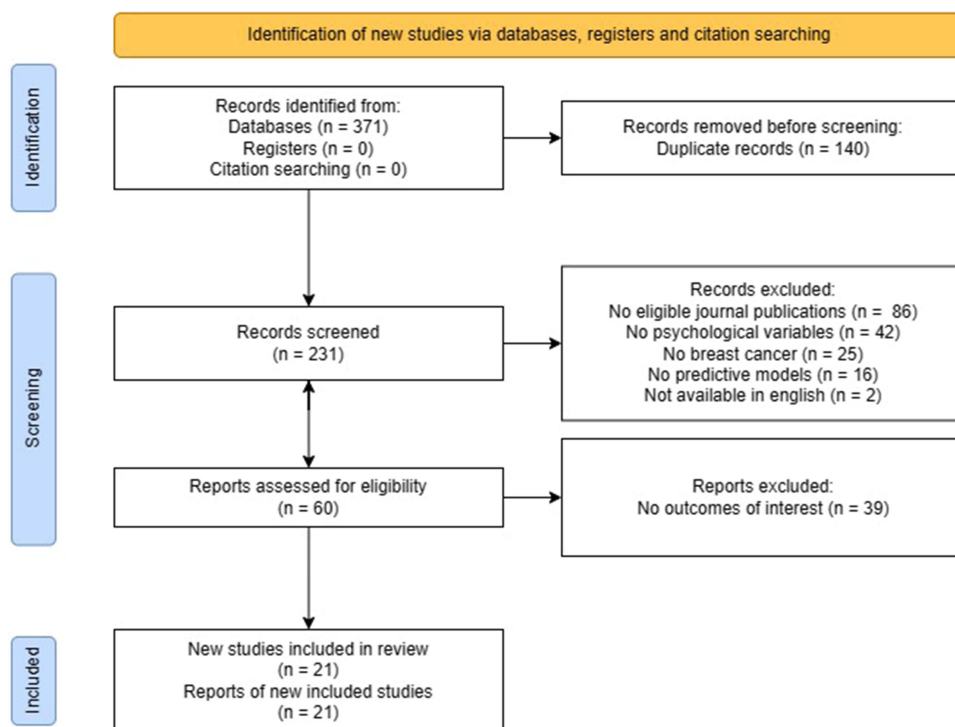
In the present paper, we reviewed studies in which models have been developed or implemented in order to predict one of the following outcomes in BC patients: (1) psychological distress and adjustment; (2) QoL; and (3) medication adherence. To our knowledge, this is the first review that takes into account models predicting these three relevant outcomes. Thus, the data here collected and commented on will be an important asset for healthcare professionals and researchers working in the field of BC care.

Coherently, the primary aim was to summarize the predictive models currently available in the health field, to report their characteristics, and to map the determinants of the three outcomes of interest. By offering an overview of the scientific literature on these themes, we aim to highlight relevant knowledge that could aid BC patients' care path, fostering optimal psychological assessment, supporting emotional wellbeing, optimal medication adherence, and good QoL. Due to the wide range of our research questions and the exploratory nature of this work, we chose to adopt the scoping review format.<sup>36</sup>

## Materials and Methods

An online search was conducted in January 2023 in order to identify relevant studies developing or using models to predict specific psychological outcomes (ie, QoL, psychological distress, adjustment, or medication adherence) in BC patients. Three online sources were screened (PubMed, Embase, and Scopus) with the following keywords: (breast cancer) AND (predictive model OR prediction model OR prognostic model OR prediction tool OR predictive tool OR prognostic tool) AND (quality of life OR depression OR anxiety OR distress OR adherence OR compliance OR psychological OR psychosocial). The search criteria did not include any restrictions on publication dates.

Following the extension for scoping reviews of the Preferred Reporting of Items for Systematic Reviews and Meta-Analyses Statement (PRISMA-ScR),<sup>37</sup> the initial selection process resulted in the identification of 371 studies. After duplicates removal, 231 articles were screened for title and abstract. Abstracts, commentaries, editorials, letters, meta-analyses, proposals, and reviews were excluded. At the end of this process, 171 studies were excluded, and 60 full-text articles were analyzed. Only research articles that satisfied the following inclusion criteria were considered: 1) study



**Figure 1** PRISMA Flow Diagram for the scoping review process.

populations consisting of BC patients; 2) development/use of predictive model; 3) psychological outcomes are predicted; 4) papers published in English.

In the screening phase, papers that did not report outcomes of our interest were excluded, as well as studies focused only on medical variables. The screening phase was independently conducted by two authors (M.P., E.F.). Interrater reliability for the assessors was calculated on a dichotomous scale using percentage agreement and Cohen's  $k$  (% of agreement: 72.64% Cohen's  $k$ : 0.377). A third author (G.E.S.) resolved discordances between raters. At the end of the process, 21 papers were selected (see [Figure 1](#) for more details). Most authors (M.P., G.E.S., E.F., I.C.) read selected articles to accept their inclusion in the study.

## Results

### Selection of Sources of Evidence

A first search in the literature identified 236 potential articles. After the screening procedure, 21 of the selected studies met the inclusion criteria for the scoping review. Specifically, nine original studies were focused on the prediction of psychological distress and adjustment, six on the prediction of QoL, and six on the prediction of adherence and treatment discontinuation.

All the included studies reported these outcomes of interest as their primary outcomes.

### Characteristics of Selected Studies

Relevant data for each included paper are reported in [Table 1](#) (psychological distress and adjustment), [Table 2](#) (QoL), and [Table 3](#) (adherence).

Concerning the prediction of psychological distress and adjustment, samples from the nine selected studies included either BC patients only ( $n = 3$ )<sup>13,38,41</sup> or patients affected by several cancer types, also including BC patients ( $n = 6$ ).<sup>30–33,39,40</sup> Studies were focused on the following outcomes, alone or in combination: self-perceived health, psychiatric disorders, psychological distress and mental health disorders (body image disturbance, self-esteem, depression, and anxiety), psychosocial adjustment (sexual, extended family, social, psychological), new onset of psychological distress or

**Table 1** Original Research Studies on the Prediction of Psychological Distress: Characteristics and Results

Author (Year), Country	Cancer Type & Sample	Study Design	Predictive Model	Outcomes	Predictors	Results
Aquil (2021), Morocco <sup>32</sup>	Mixed female cancer patients (BC N 100 Age 48.26 SD= 11.40; Gynecological cancer N 100 Age 50.94 SD= 11.33)	Cross-sectional study	Multiple regression	Mental health disorders (anxiety, depression, body image dissatisfaction)	Socio-demographic and medical characteristics	Being younger ( $p<0.001$ ), lower income ( $p<0.01$ ), and advanced stage of the disease predicted mental disorders ( $p<0.01$ ); (higher anxiety $R^2$ 0.145 $F=12.26$ ; depression $R^2$ 0.14 $F=11.89$ ; and greater body image dissatisfaction $R^2$ 0.33 $F=25.84$ ).
Ganz (2003), USA <sup>38</sup>	N 635 Breast cancer female patients (Age>65)	Prospective cohort study	Logistic regression	Self-perceived health and psychosocial adjustment	Demographic, medical characteristics, QoL, and psychosocial variables (physical functioning, mental health, social support, medical interaction)	Predictors of better psychosocial adjustment ( $R^2$ 0.29; $p=0.0001$ ) were better mental health ( $p<0.001$ ), emotional social support ( $p<0.001$ ), and better self-rated interaction with healthcare providers ( $p<0.001$ ).
Gómez-Campelo (2014), Spain <sup>33</sup>	Mixed female cancer patients (BC N 50 Age 48.36 SD= 13.27; Gynecological cancer N 50 Age 48.82 SD= 14.43)	Cross-sectional study	Multiple regression	Psychological distress (body image disturbance, self-esteem, depression, and anxiety)	Socio-demographic characteristics, medical history, and social support	Being younger ( $p<0.001$ ), inactive occupational status ( $p<0.05$ ), and post-adjuvant therapy side effects ( $p<0.05$ ) predicted body image disturbance ( $R^2$ 51.5% $F=18.34$ ) and depression ( $R^2$ 45.0% $F=14.35$ ). Anxiety ( $R^2$ 19.4% $F=4.93$ ) was predicted by post-adjuvant therapy side effects ( $p<0.01$ ).
Haun (2021), Germany <sup>39</sup>	N 496 Mixed cancer patients ( $F=269$ ; Age 64.9 SD= 10.95)	Prospective, cross-sectional study	Machine learning approach	Anxiety	Socio-demographic and medical characteristics	Physical symptoms (fatigue/weakness) ( $\beta=0.181$ ), Insomnia ( $\beta=0.122$ ), and pain ( $\beta=0.041$ ) predicted anxiety (LASSO regression: RMSE=0.370 $R^2$ 0.415).
Hong (2020), Korea <sup>40</sup>	N 203 Mixed cancer patients ( $F=136$ ; Age 57.3 SD=11.04)	Cross-sectional study	Structural equation modeling	Psychological adjustment	Symptom distress, contextual factors, Fear of Cancer Recurrence (FCR), and illness representations	Greater symptom distress, lower perceived social support and optimism, greater FCR, and negative perceptions of disease outcomes ( $\beta=0.18$ , $p<0.006$ ; $\beta=0.35$ , $p<0.001$ ; $\beta=0.25$ , $p<0.001$ respectively) predicted poorer psychological adjustment ( $\chi^2=41.2$ , GFI=0.95, $p<0.001$ ).
Morasso (2001), Italy <sup>41</sup>	N 184 Breast cancer female patients (Age<70)	Randomized controlled study	Logistic regression, multivariate analysis	Psychiatric disorders	Clinical, demographic, and psychological variables (psychological distress, anxiety, depression)	From the logistic regression analysis, increasing age ( $p=0.001$ ) and psychiatric history ( $p<0.001$ ) were associated with psychiatric disorders at follow-up: The multivariate models showed that psychological distress predicted psychiatric disorders, while the predictive value of age and psychiatric history decreased from baseline to follow-up (AUC=77.0–91.8).
Schnoll (2002), USA <sup>30</sup>	N 109 Mixed cancer patients ( $F=83$ ; Age 60.3 SD= 11)	Cross-sectional study	Structural equation modeling	Adjustment (sexual, extended family, social, psychological)	Demographic, clinical, and psychosocial variables (meaning of life, optimism, coping strategies, social support)	Higher levels of social support and meaning in life ( $\beta=0.38$ , $p<0.05$ ), and lower levels of avoidant-type coping behaviors ( $\beta=0.77$ , $p<0.05$ ) predicted higher adjustment ( $\chi^2[81]=136.42$ , $p<0.001$ ; CFI=0.94; all factor loadings $p$ 's<0.01).

Seow (2021), Canada <sup>31</sup>	N 255.494 Mixed cancer patients (F=145.632; Mean Age 64 SD= n.a.)	Retrospective, population-based, predictive study	Logistic regression	Poor performance status and severe symptoms (severe pain, dyspnea, wellbeing, and depression)	Demographic characteristics, clinical data, patient-reported outcomes, healthcare use	Lung disease, dementia, diabetes, radiation treatment, hospital admission, pain, depression, transitional performance status, issues with appetite, and receipt of home-care, increased by 10% the risk of low performance status and severe symptoms (including depression) (AUC=0.709–0.807).
Syrowatka (2018) Canada <sup>13</sup>	N 16.495 Breast cancer female patients (Age 65.7 SD= 11.8)	Population-based cohort study	Time-varying Cox proportional hazards models	New-onset psychological distress	Socio-demographic, breast cancer characteristics, and treatment received	Two predictive models were developed: (1) for the period of hospital-based treatment, and (2) for survivorship. Predictors of psychological distress in both periods were: younger age HR (95% CI) 0.91 (0.90–0.93) (1) 0.95 (0.94–0.97) (2), receipt of axillary lymph node dissection Impact at 6 months HR 0.98 (0.81–1.18) (1) 1.16 (1.05–1.28) (2), rheumatologic disease (at baseline HR 1.17 (1.07–1.28) (1) 1.23 (1.13–1.35) (2) or follow-up HR 1.34 (1.07–1.69) (1) 1.35 (1.12–1.63) (2), baseline menopausal symptoms impact at 6 months HR Proportional (1) 1.17 (1.05–1.32) (2), new opioid dispensations impact at 6 months HR 1.56 (1.29–1.87) (1) Proportional (2), emergency department visits HR 1.33 (1.21–1.47) (1) 1.47 (1.31–1.65) (2), and hospital contacts during follow-up HR 1.14 (1.03–1.25) (1) 2.32 (1.77–3.03) (2). In period (1) other predictors were: more advanced BC and chemotherapy Impact at 6 months HR 0.98 (0.81–1.18). In period (2) other predictors were: diagnosis of localized breast disease HR 1.15 (1.01–1.31), shorter duration of hospital-based treatment HR 0.94 (0.93–0.96), receipt of additional hospital-based treatment in survivorship HR 1.85 (1.33–2.59), and newly diagnosed comorbidities or symptoms (n.a.)*

**Notes:** \*The only relevant metrics reported in the paper are HRs; since this is a measure of statistical association rather than a measure of predictive validity, the reported results should be considered with caution (see Limitations section).

**Abbreviations:** QoL, Quality of Life; SD, standard deviation; F, female; n.a., not available; CFI, comparative fit index; HR, hazard ratio; RMSE, root mean squared error; GFI, goodness of fit index.

**Table 2** Original Research Studies on the Prediction of Quality of Life: Characteristics and Results

Author (Year), Country	Cancer Type & Sample	Study Design	Predictive Model	Outcomes	Predictors	Results
Liang (2022), China <sup>42</sup>	N 506 Breast cancer female patients ( Age >18)	Prospective cohort study	Meta-based univariate regressions	QoL and survivorship	Resilience, age, income, tumor characteristics, and baseline QoL	Younger age, tumor characteristics, higher resilience, and baseline QoL predicted higher QoL outcomes after one year (P<0.0001 for all; C-indexes of 0.862 (95% CI, 0.815–0.909), 0.828 (95% CI, 0.745–0.910), 0.880 (95% CI, 0.816–0.944), and 0.869 (95% CI, 0.796–0.941) respectively).
Achimaş-Cadariu (2015), Romania <sup>27</sup>	N 51 Breast cancer female patients ( Age 38.18 SD= 4.07)	Prospective randomized controlled study	Multiple linear regression	QoL	Demographic and psychological factors (emotional distress, perception of threat, anxiety, self-blame, positive reappraisal, and catastrophizing)	Emotional distress ( $\beta=-0.42$ , $p<0.001$ ) and catastrophizing as a coping strategy ( $\beta=-0.27$ , $p=0.002$ ) predicted poorer QoL. The model showed reasonable goodness of fit (F-test, $p<0.001$ ).
Ashing-Giwa (2007), USA <sup>43</sup>	N 703 Breast cancer female patients ( Age 55 SD= n.a.)	Cross-sectional study	Multivariate regression analysis	QoL	Cancer-related medical factors, general health status, psychological (emotional wellbeing), demographic, healthcare system (quality of doctor-patient relationship), socio-ecological (social support) and cultural variables	Years since diagnosis, number of comorbidities, role limitations, emotional wellbeing, quality of doctor-patient relationship, social support, and life stress predicted QoL explaining 70% of the variability ( $R^2$ 0.08 F (6630) =29.0; $p<0.001$ ).
Carmona-Bayonas (2021), Spain <sup>44</sup>	N 339 Breast cancer female patients (F= 333; Age 52 SD= n.a.)	Prospective cohort study	Constrained partial proportional odds Bayesian predictive model	QoL	Age, medical variables, perceived risk of recurrence, and baseline QoL	Six covariates (chemotherapy regimen, TNM stage, axillary lymph node dissection, perceived risk of recurrence, age, type of surgery, and baseline EORTC scores) predicted QoL (C-index=0.65 (95% HPDI, 0.63–0.67); Brier score=0.21 (95% HPDI, 0.19–0.28)).
Di Meglio (2022), France <sup>28</sup>	N 5000 Breast cancer female patients ( Age 56.3 SD= 11.2)	Prospective longitudinal cohort multicenter study	Multivariate logistic regression model	Global fatigue; Secondary outcome: physical, emotional, and cognitive fatigue	Demographic, clinical and treated-related factors, and symptoms (anxiety, depression, insomnia, pain, hot flushes)	Younger age, higher BMI, smoking behavior, physical and psychological symptoms (fatigue, anxiety, insomnia, and pain) predicted severe fatigue two years after diagnosis (AUC=0.73 (95% CI, 0.72 to 0.75)).
Giedzinska (2004), USA <sup>29</sup>	N 621 Breast cancer female patients ( Age 55.23 SD= 11.56)	Cross-sectional study	Linear regression analysis	QoL	Medical and demographic characteristics, cancer-related and psychosocial measures (depression, mental health, support, body image, sexual interest, vulnerability, emotional wellbeing)	Age, income, having had mastectomy, having had chemotherapy, and geographic location of participants predicted different aspects of QoL for different ethnic groups.*

**Notes:** \*The paper report several different predictive values for each variable and for each ethnic group considered (ie, African Americans, Whites, Latinas, Asian Americans).

**Abbreviations:** QoL, Quality of Life; SD, standard deviation; F, female; n.a., not available; AUC, area under the receiver operating characteristic curve; HPDI, highest posterior density interval.

**Table 3** Original Research Studies on the Prediction of Adherence and Treatment Discontinuation: Characteristics and Results

Author (Year), Country	Cancer Type & Sample	Study Design	Predictive Model	Outcomes	Predictors	Results
Cahir (2017), Ireland <sup>45</sup>	N 3415 Breast cancer female patients ( Age 61.4 SD= 12.6)	Population- based cohort study	Multivariate relative risks model	Non-persistence	Demographic, clinical, and treatment-related risk factors	Women aged<50 years and prescribed antidepressants resulted at greater risk, while married women and those with previous use of medications had a lower risk. However, the model has limited predictive ability (AUC=0.61).
Henry (2012), USA <sup>46</sup>	N 503 Breast cancer female patients ( Age 59 SD= n.a.)	Prospective randomized controlled study	Univariate and multivariate analysis of predictors	Treatment discontinuation	Demographics, clinical, and treatment-related characteristics	Younger age (HR, 1.4; 95% CI, 1.0 to 1.9; p=0.04), taxane-based chemotherapy (HR, 1.9; 95% CI, 0.99 to 3.6; p=0.048), and pre-existing pain (HR, 1.1; 95% CI, 1.0 to 1.2; p=0.04) predicted aromatase inhibitors discontinuation.*
Kuo (2022), Taiwan <sup>47</sup>	N 385 Breast cancer female patients ( Age 55.1 SD= n.a.)	Longitudinal observational retrospective cohort study	Multiple logistic regression	Medication-taking behavior	Demographic, clinical, and treatment-related characteristics	The top five predictors as resulting from a Borda count based on three different models (MLR, AUC=1.00; DT, AUC=0.93; ANN, AUC=0.90) were: duration of AET discontinuation, duration of AET use, age at diagnosis (younger and older patients had lower adherence), BMI (lower BMI predicted poorer adherence), and radiotherapy; vitality status, regional lymph nodes positive, comorbidities, cause of death, and type of first recurrence were other predictors.
Meneveau (2020), USA <sup>48</sup>	N 11037 Breast cancer female patients ( Age >70)	Retrospective cohort study	Stepwise selection and logistic regression	Adherence and medication initiation	Comorbidities, socio-economic measures, prescription medications, and demographics	Models were poorly predictive (AUC=0.65–0.60), demonstrating that the reasons for initiation and adherence to AET are complex and individual to the patient, and difficult to predict.
Shinn (2022), USA <sup>49</sup>	N 82 Breast cancer female patients ( Age 53–54 SD= n.a.)	Prospective study	Discrete decisional logic applied to a behavioral feedback network	Treatment discontinuation	Patient-related factors, patient-provider relationship, treatment, and comorbid factors	Low risk perception, below-median QoL, low AET-related side effects, low level of cancer recurrence worry, and median levels of general anxiety characterized the profiles leading to AET discontinuation in the simulations conducted with the models.**
Yanez (2021), USA <sup>50</sup>	N 954 Breast cancer female patients ( Age 56.6 SD= 8.9)	Randomized clinical study (post hoc analysis)	Cox proportional hazards regression	Treatment discontinuation	Medical comorbidities and QoL variables	Depression (HR, 1.82; 95% CI, 1.19–2.77; p=0.005) and poor social (HR, 1.94; 95% CI, 1.20–3.13; p=0.006) and physical wellbeing (HR, 2.12; 95% CI, 1.30–3.45; p=0.002) are significant risk factors for early discontinuation of AET.*

**Notes:** \*The only relevant metrics reported in the paper are HRs; since this is a measure of statistical association rather than a measure of predictive validity, the reported results should be considered with caution (see Limitations section). \*\*Results based on repeated logic network simulations conducted with 96 candidate decisional models over a broad range of initial demographic and behavioral profiles. No predictive values are available.

**Abbreviations:** QoL, Quality of Life; SD, standard deviation; n.a., not available; AET, adjuvant endocrine therapy; AUC, area under the receiver operating characteristic curve; HR, hazard ratio; CI, confidence interval; MLR, multiple logistic regression; DT, decision tree; ANN, artificial neural network.



other disorders. Predictive models of such studies adopted different methodologies, and the applied techniques consisted of multivariate regression analysis (logistic or linear), hazards or structural equation modeling, and machine learning approaches.

Concerning the prediction of cancer patients' QoL (Table 2), all the samples from the six selected studies included BC patients only.<sup>27–29,42–44</sup> Such studies investigated the following outcomes: QoL, survivorship, global fatigue, physical, emotional, and cognitive fatigue. Considered predictive models used several methodologies, precisely: univariate or multivariate, logistic or linear regression, and proportional odds Bayesian model.

Concerning the prediction of pharmacological adherence (Table 3), all the samples from the six selected studies included BC patients only.<sup>45–50</sup> All the studies focused on adherence to oral endocrine therapy, analyzing the following outcomes: medication adherence, medication initiation, non-persistence, medication-taking behavior, and treatment discontinuation. The predictive models used several methodologies: univariate and multivariate analysis, relative risks models, logistic regression analysis, hazard modeling, and discrete decisional logic applied to a behavioral feedback network were considered in the present review.

Consistently with the heterogeneity of the predictive models, several different metrics of models' performance are reported: these are R-squared (coefficient of determination), beta coefficient, Area Under the Curve (AUC), Concordance index (C-index), Comparative Fit Index (CFI), goodness of fit index (GFI), and root mean squared error (RMSE) (models' metrics are reported in Tables 1–3).

## Synthesis of Results

### Psychological Distress and Adjustment

As reported in Table 1, two studies used logistic regression,<sup>31,38</sup> two a multivariate regression,<sup>32,33</sup> and one a combination of both.<sup>41</sup> Two papers used structural equation modeling,<sup>30,40</sup> and one<sup>13</sup> reported a time varying cox hazard predictive model. Finally, one study<sup>39</sup> implemented a machine learning approach.

Such studies highlighted the role of socio-demographic, psychosocial, and medical characteristics as potential predictors of mental health disorders and wellbeing. For example, results showed that younger age,<sup>13,32,33</sup> lower income,<sup>32</sup> and inactive occupational status<sup>33</sup> predicted higher psychological distress. In contrast, Morasso et al<sup>41</sup> found that younger age had a protective effect on psychological symptoms.

As concerning medical factors, advanced stage of disease,<sup>13,32</sup> therapy side-effects,<sup>33</sup> radiation treatment,<sup>31</sup> receipt of axillary lymph node dissection, baseline menopausal symptoms,<sup>13</sup> and several physical symptoms such as fatigue, insomnia, and pain,<sup>31,39</sup> predicted a higher risk to develop symptoms of psychological distress.

Furthermore, mental health issues before disease onset, such as higher anxiety and depression and higher body image dissatisfaction<sup>31,32,41</sup> were predictive factors for psychological symptoms development.

As regards psychological adjustment, studies found that better mental health at baseline and high perceived emotional and social support<sup>30,38</sup> predicted better psychosocial adjustment. In contrast, lower optimism, greater fear of cancer recurrence, negative perceptions of disease outcomes, worst illness representations, and lack of perceived social support predicted poorer psychological adjustment.<sup>40</sup>

### Quality of Life

As concerning patients' QoL, as reported in Table 2, five out of six of the included studies<sup>27–29,42,43</sup> applied a predictive model obtained through univariate or multivariate logistic or linear regressions. One study developed a constrained partial proportional odds Bayesian model.<sup>44</sup>

Results show that predictors for a good QoL were as follows: high baseline QoL, high resilience, and emotional wellbeing,<sup>42–44</sup> low emotional distress or life stress, low limitations due to physical or emotional problems, and low cognitive tendency to catastrophize,<sup>27,43</sup> low perceived risk of recurrence,<sup>44</sup> not smoking,<sup>28</sup> higher income,<sup>29</sup> a good quality of doctor–patient relationship, and a high perceived social support.<sup>43</sup>

Interestingly, while two studies reported that younger age predicted higher QoL,<sup>29,42</sup> another one found that “extreme” ages (younger and older patients) were at higher risk of poor QoL,<sup>44</sup> and another one reported that younger age predicted a more significant risk of severe fatigue at two years after BC diagnosis.<sup>28</sup>



Furthermore, some physical conditions, such as Body Mass Index (BMI),<sup>28</sup> the presence of comorbidities,<sup>43</sup> or symptoms such as fatigue, anxiety, insomnia, and pain,<sup>28</sup> and several medical variables such as years since diagnosis,<sup>43</sup> tumor characteristics,<sup>42,44</sup> type of surgery or treatment received (ie, mastectomy, axillary lymph node dissection, chemotherapy),<sup>29,44</sup> accounted for a large part of the variance of QoL.

## Adherence

As reported in Table 3, the methodologies used in studies selected for adherence are heterogeneous: risk models,<sup>45</sup> logistic regressions,<sup>47,48</sup> univariate and multivariate analysis of predictors,<sup>46</sup> decisional logic applied to a behavioral feedback network,<sup>49</sup> and cox proportional hazard regression.<sup>50</sup>

These studies analyzed the predictive values of various demographic, clinical, and treatment-related risk factors. Precisely, a higher risk of non-adherence was predicted by younger age<sup>45,46</sup> or “extreme” age (younger and older),<sup>47</sup> lower BMI,<sup>47</sup> taxane-based chemotherapy, pain,<sup>46</sup> low risk perception and low level of cancer recurrence worry,<sup>49</sup> depression, general anxiety, and poor QoL.<sup>49,50</sup> Notably, two of the examined models were reported to show only poor predictive ability, as indicated by the suboptimal area under the receiver-operating characteristics curve values.<sup>45,48</sup>

## Discussion

Results show that socio-demographic and medical characteristics<sup>13,31–33,39,41</sup> were the most commonly reported predictors for psychological distress. In particular, younger age has been shown to predict the onset of psychological distress in three of the selected articles,<sup>13,32,33</sup> but one paper reported that advanced age, together with psychiatric history and baseline psychological distress, is a predictor of the occurrence of psychiatric disorders.<sup>41</sup> A possible explanation for such inconsistency might be the different definitions and measures of psychological distress used. Indeed, the outcome of interest in Morasso et al study<sup>41</sup> was the presence of a psychiatric disorder identified by a psychiatrist during an interview with the help of the Structured Clinical Interview for DSM-III-R.<sup>51</sup> In contrast, other studies assessed the presence of psychological distress through the Hospital Anxiety and Depression Scale,<sup>52</sup> the Body Image Scale,<sup>53</sup> the Beck Depression Inventory,<sup>54</sup> and the Beck Anxiety Inventory,<sup>32,33,55</sup> or through medical health records data.<sup>13</sup> Other possible explanations for this discrepancy may be found in cultural and geographical differences between the participants. Indeed, Morasso et al study<sup>41</sup> was conducted in Italy, while the others were conducted respectively in Morocco, Spain, and Canada.<sup>13,32,33</sup> Other socio-demographic factors that predict psychological distress are lower income<sup>32</sup> and inactive occupational status.<sup>33</sup> This may be explained by the fact that these socio-demographic characteristics are possible causes of psychological distress, given the uncertainty, worries, and economic difficulties they may generate. Therefore, it is reasonable to expect that, when combined with an illness such as BC, they result in greater levels of psychological distress.

Similarly, several clinical characteristics showed predictive value in psychological distress models. These were advanced stages of the tumor,<sup>32</sup> the presence of symptoms such as pain, insomnia, fatigue/weakness,<sup>33,39,40</sup> psychiatric history and baseline psychological distress,<sup>31,41</sup> comorbidities,<sup>13,31</sup> and treatment-related factors, such as adverse side-effects, hospital admissions, emergency department visits, radiation therapy, chemotherapy, opioid dispensation, and receipt of home-care.<sup>13,31,33</sup> These characteristics are all indexes of worst general clinical conditions, both on physical and psychological levels. Only three studies developed predictive models of psychological adjustment.<sup>30,38,40</sup> Interestingly, all of them highlighted the role of specific psychological determinants such as social support, coping strategies, interactions with healthcare providers, optimism, fear of cancer recurrence, and illness perceptions.<sup>30,38,40</sup> It is worth noting that four out of nine studies developing predictive models for psychological distress took into account only clinical and sociodemographic variables. Since the role of psychological variables has been suggested by the other models reviewed,<sup>30,38,40</sup> the consideration of baseline psychological variables as predictors may further improve such models. Introducing psychological assessment for BC patients in the clinical routine could increase the availability of these data, thus helping to close this gap.

Concerning QoL, predictive models have recognized a possible predictive role of psychological variables on QoL, except for Giedzinska et al.<sup>29</sup> More in detail, results showed that resilience, anxiety, emotional wellbeing/distress, quality of patient–doctor relationship, social support, perceived risk of recurrence, life stress, coping strategies, and baseline

QoL, are all psychological predictors of QoL.<sup>27,28,42–44</sup> Other commonly reported predictors were demographic and medical variables such as age, income, BMI, smoking behavior, concomitant symptoms, tumor characteristics, comorbidities, treatment regimen, and having received surgical intervention.<sup>27,29,42–44</sup> The multidimensional nature of the predictors identified is consistent with the multidimensional nature of the concept of QoL, which refers to physical, mental, and social dimensions.<sup>15,16</sup>

Finally, all the studies focusing on non-adherence considered adherence to endocrine therapy. These medicines are often taken orally, generally for five to ten years, thus charging the burden of their correct and regular assumption on the patients themselves.<sup>56</sup> Demographics and clinical variables, and treatment-related factors<sup>45–50</sup> were relevant predictors of non-adherence. Notably, depression was found to predict medication non-adherence,<sup>45,50</sup> thus confirming what has already been reported by previous studies in this field.<sup>19</sup>

It is worth noting that two of the studies focusing on adherence reported poor predictive value.<sup>45,48</sup> This further confirms the complex nature of medication-taking behaviors: the interaction of several factors and the role of patients' subjectivity make adherence to medication difficult to predict.<sup>19,20</sup>

Many of the predictors included in the considered models are easily available in patients' health records (eg, clinical history, socio-demographic variables, cancer-related or treatment-related data) and can therefore be readily used by clinicians and researchers in order to assess patients' risks. On the contrary, those predictors that are not commonly found in patients' health records (eg, coping strategies, perceived social support, illness perceptions) may be introduced in routine assessment practices in hospitals and cancer clinics.

To conclude, considering the outcomes retrieved in the current scoping review, we have shown that predictive models of distress, QoL, and adherence outcomes, although various and heterogeneous in the considered predictors and in statistical methods, generally presented good scores in the reported performance measures and metrics. Implementing such models in clinical practice might support healthcare professionals in early identifying patients at risk of psychological comorbidities, non-adherence, and a lower QoL providing tailored interventions.

## Implication and Suggestions for Research and Practice

Psychological interventions support emotional well-being and improve QoL.<sup>57,58</sup> Furthermore, they can also reduce symptoms such as pain and fatigue,<sup>59–61</sup> foster patients' adherence to medications,<sup>62,63</sup> and even improve overall survival.<sup>64,65</sup> Unfortunately, offering psychological interventions to an increasing number of BC patients may not be feasible or cost-effective.<sup>66</sup> By applying the predictive models reviewed here, it is possible to target psychological interventions to those patients who benefit the most from them, reducing healthcare-related costs and optimizing the BC care path. Specifically, the predictive models may identify patients at high risk of psychological distress, medication non-adherence, or poorer QoL. This may lead to prompt interventions reducing healthcare-related costs, and ultimately improving BC patients' outcomes.

Given the presented results of this review, it seems that younger patients who show greater levels of distress or depressive symptoms, poorer coping ability or well-being might benefit from interventions aimed at preventing psychological comorbidities and adherence. Further, interventions addressing patients' QoL are effective for patients reporting insomnia, pain, anxiety, or distress. The introduction of psychological and behavioral assessments would allow to map patients' characteristics and identify patients potentially in need of a preventive intervention, thus allowing to improve therapeutic support. Within this framework, the synthesis outlined in this work might be a relevant resource for clinicians and researchers involved in developing and implementing psychological interventions for BC patients.

## Limitations

This work has some worth-to-note limitations. First, the included studies display great heterogeneity concerning their characteristics and the applied methodologies, which may reduce the results' interpretability. The predictive models reviewed have been developed using several different statistical methods (eg, multiple logistic regression, linear regression, machine learning approaches) and different metrics have been considered to measure the models' performance (eg, ROC AUC, goodness of fit index, root mean squared error). Notably, three included studies did not report any measure of predictive validity, but only measures of statistical association (ie, hazard ratios), thus their results should be

considered with caution<sup>13,46,50</sup> (see Table 1 and Table 3); this is in line with what suggested by Varga et al<sup>67</sup> in a recent systematic review: the authors documented the frequent misuse of the term “prediction” in studies involving only statistical association analyses.

Further, the predictive models generated predictions for different specific time points along the cancer care path (eg, 6-month, 1-year, 2-year). We argued that this might partially explain the differences encountered among the results. Furthermore, the use of different questionnaires and scales to measure the outcomes of interest and the great variability in sample dimensions (ranging from 51 to 255.494 patients), may further decrease the comparability of these studies.

The decision to focus on three different outcomes has contributed to the great heterogeneity of the included studies. Yet, this may be justified by the exploratory nature of this work and by our interest in mapping the predictors of a large range of issues relevant to BC care (ie, psychological distress, QoL, and medication adherence).

Finally, among the studies on psychological distress, only three considered samples entirely composed of BC patients.<sup>13,38,41</sup> The other six explored mixed samples with different cancer types, although always including at least a sub-group of BC patients.

## Conclusion

Predictive models taken into account could aid the early-identification of those BC patients that could benefit from tailored psychological interventions. Therefore, clinicians and researchers should consider these findings when implementing routine assessments in order to intervene early whenever a high risk of poorer outcomes is highlighted.

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