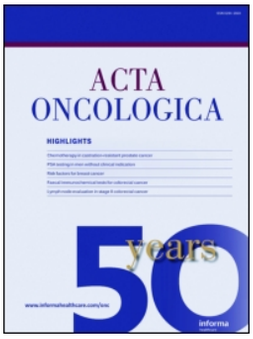

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Psychosocial determinants of adherence with oral anticancer treatment: 'we don't need no education'

Adrian A. Kaptein[a], Jan W. Schoones[b], Pim B. van der Meer[c], Ayako Matsuda[d], Michael Murray[e], Lotte Heimans[f] and Judith R. Kroep[g]

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ABSTRACT

Introduction: Given the potentially fatal consequences of inadequate adherence with oral anticancer treatment in persons with cancer, understanding the determinants of adherence is vital. This paper aims at identifying psychosocial determinants of adherence to oral anticancer treatment.

Methods: We reviewed the literature on psychosocial determinants of adherence with oral anticancer treatment, based on published literature in English, from 2015 to present. Literature searches were performed in PubMed, Embase, Web of Science, Cochrane library, Emcare, and PsychINFO, with 'cancer', 'medication adherence', 'psychology', and 'oral anticancer treatment' as search terms. The obtained 608 papers were screened by two independent reviewers.

Results: In the 25 studies identified, illness perceptions, medication beliefs, health beliefs, and depression were found to be the major psychosocial determinants of adherence to oral anticancer treatment; sociodemographic and clinical characteristics were found to be of no major importance. The quality of the identified studies as assessed by two independent reviewers was found to be acceptable overall. The majority of papers were from North America and focused on patients with breast cancer; sample size varied from 13 to 1371; adherence was assessed with questionnaires derived from various theoretical models, pill counts and electronic pharmacy records; illness perceptions reflecting adaptive coping, and medication beliefs reflecting high necessity and low concerns were found to be associated with adherence.

Conclusion: Psychosocial concepts are major determinants of adherence with oral anticancer treatment. 'Beliefs about medicines' and 'illness perceptions' in particular determine adherence with this treatment. Studies aiming at impacting adherence would benefit from interventions with a solid basis in behavioral theory in order to help health care providers explore and address illness perceptions and medication beliefs. Pre-consultation screening of adherence behavior may be a helpful supportive approach to improve adherence. Blaming the victim ('patients should be educated about the importance of adherence') is better replaced by encouraging health professionals to identify and address maladaptive psychosocial determinants of adherence.

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Oral anticancer treatment; cancer; adherence; illness perceptions; medication beliefs; psychosocial determinants

Introduction

There is discernable optimism in the introductions to many scientific papers on oral anticancer treatment. Authors state that taking the medication at home represents an important improvement over chemotherapy delivered in a hospital setting [1,2]. A disadvantage mentioned by these authors is the absence of control by health care providers over the medication-taking by patients in their homes [3,4]. All authors emphasize how 'compliance' with oral anticancer treatment is crucial, impacting directly on mortality [5]. The surprise or the disappointment in health care providers over a lack of patient adherence is often tangible. For behavioral scientists who study the subject of 'compliance', it is not really a surprise to read in virtually all papers in the area of oral anticancer treatment how sociodemographic and clinical characteristics turn out to be not related to 'compliance' while psychosocial factors are; the surprise seems to reflect the lack of or modest inclusion of psychosocial concepts in the papers' study designs. Despite this, in the Discussion sections of those papers, the mantra of '… patients, therefore, should be educated about the importance of being compliant with oral anticancer treatment' often follows [6,7].

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Supplemental data for this article can be accessed here.

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The lyric 'We don't need no education …' from the Pink Floyd song 'Another brick in the wall' articulates the direction research and clinical care, we believe, should go when it comes to oral anticancer treatment. As stated in the WHO report on Adherence to long-term therapies, 'patients need to be supported, not blamed' in their attempts to adhere to medication 'regimes' [8]. 'Compliance' refers to '… the extent to which a patient's behavior in terms of taking medication, following diets, or implementing lifestyle changes coincides with medical or health advice' [9], whereas 'adherence' is defined as 'the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider' [8] . Some researchers go one step further and prefer the word 'concordance', defined as '… a process of the consultation in which prescribing is based on partnership'. Steiner and Earnest elegantly outline some problematic issues in the concept of 'compliance': '… noncompliance exaggerates the physician's control over the process of taking medications … 'compliance' implies that the patient must take the medication as prescribed to obtain benefit … 'noncompliance 'as a term creates a clinically unjustifiable distinction between persons who take all of their pills as prescribed and those who deviate from the prescription in any way … and does not accurately represent patients' motivations for choosing to take their medications a certain way' (p. 926) [10].

Discussing the concepts of compliance, adherence, and concordance aims to outline the context of research on the degree to which patients with various types of cancer take their oral anticancer treatment as intended – as intended by prescribing health care professionals. A number of recent literature reviews have summarized the subject [11–16]. A qualitative study on oral chemotherapy adherence identified 10 papers; 'driving' and 'disabling' factors were found to be the two major determinants of adherence [11]. A meta-analysis encompassing seven studies on interventions to promote adherence to endocrine therapy in patients with breast cancer found 'bi-directional communication' between patient and health care provider to impact positively on adherence [12]. Greer and colleagues performed a systematic review of adherence with oral antineoplastic therapies and identified the problems patients report in adhering to the prescribed medication – based on empirical studies to 2015, however [13]. The systematic review by Murphy and colleagues included a fairly large number of studies (29), however, the study did not focus explicitly on psychosocial determinants to adherence [14]. The recent scoping review by Rosenberg et al. focused on interventions to enhance adherence to oral antineoplastic agents – without an explicit focus on psychosocial determinants, however [15]. Important as these papers are, they do not explicitly focus on examining psychosocial determinants of adherence with oral anticancer treatment. The two most recent review papers on adherence with oral anticancer drugs concentrate on 'factors influencing non-adherence to oral anti-neoplastic drugs' [16], and on 'interventions to enhance adherence to oral anti-neoplastic agents' [17] – without a focus on psychosocial determinants of adherence. Our paper aims to contribute to this literature, by (a) updating the literature review [2015–2020], and (b) by focusing explicitly on *psychosocial* determinants of oral anticancer treatment in persons with cancer. Given the state-of-the-art concerning 'adherence' research and clinical intervention, we focus on perceptions by patients of their illness and the associated medication, and the relation of these perceptions with adherence behavior.

Theoretical models help in conceptualizing determinants of adherence behavior. The WHO report on 'Adherence to long-term therapies' distinguishes five domains that potentially impact on adherence: social/economic, therapy-related, patient-related, condition-related, and health system/health care team factors, suggesting domains for interventions [8]. In the Common Sense Model, cognitive and emotional representations (illness perceptions) of a health threat elicit coping procedures that, after being appraised for their effectiveness in adapting to the health threat, are adjusted to or are perceived as being adequate in reducing or removing the threat. Schematically, the Common Sense Model can be summarized as: illness perceptions determine coping behavior which in its turn determines outcome. A model from the behavioral sciences with an explicit focus on targetable determinants of adherence behavior is the so-called Extended Common Sense Model [18].

In the Extended Common Sense Model, in addition to illness perceptions, medication beliefs are added to predict adherence to medication such as oral anticancer medication. The WHO model on adherence is extremely valuable in its emphasis on encompassing a wider set of determinants than only the individual patient. The Common Sense Model and its specification for adherence, the Extended Common Sense Model, offer specific psychosocial concepts (i.e. operationalized in validated questionnaires that assess illness perceptions and medication beliefs) that allow studying psychosocial determinants of adherence in one of the domains of the WHO model, i.e. the patient. The Extended Common Sense model guided our review of the literature on adherence with oral anticancer treatment. We aimed at examining characteristics in the domains of illness perceptions and medication beliefs ('specific and general representations of treatment') in relation to adherence with oral anticancer treatment in persons with cancer. Given the existing literature on this topic, our review selected papers from 2015 to present. The review focuses on recent empirical papers on adherence with oral anticancer drugs, prescribed to adult patients; the review also focuses on identifying concepts from theoretical models on adherence. The review aims at identifying determinants of adherence in patients on oral anticancer medication in order to allow intervening in these determinants with a view to achieve optimal adherence with this category of medication.

Methods

In cooperation with a trained librarian (JWS), a detailed, two-stranded search strategy was composed. The following databases were searched: PubMed, Embase, Web of Science,

COCHRANE Library, Emcare, and PsycINFO. The two search strategies used a combination of the following concepts: cancer, medication adherence, psychology, oral anticancer treatment. For the different concepts, all relevant keyword variations were used, not only keyword variations in the controlled vocabularies of the various databases, but the free text word variations of these concepts as well. The search strategy was optimized for all consulted databases, taking into account the differences of the various controlled vocabularies as well as the differences of database-specific technical variations (e.g. the use of quotation marks). The final search was performed on February 2nd, 2020. Case reports and meeting abstract references were excluded. The results were limited to articles written in English. The date limit was set to articles published from the year 2015. The bibliographic databases yielded 608 references. Full details of the search strategy can be found in Supplementary Appendix.

The CONSORT/PRISMA diagram is depicted in Figure 1.

Two reviewers reviewed the 608 abstracts of the selected papers (PBvdM, BA in psychology, and MA in Medicine; AAK, PhD in psychology), uncertainties were resolved through discussion. Twenty five papers fitted the selection criteria.

The quality of the 25 selected studies was assessed following an adaptation of the method used in a study on adherence with another category of medication [19]; the two reviewers who reviewed the abstracts allotted one point each for (1) sample size over 100, (2) use of validated assessment of adherence, (3) use of validated determinants of adherence. 'Low' quality equaled 0 points, 'medium' quality 1 or 2 points, 'high' quality 3 points.

Results

Twenty-five studies were identified (Table 1) [4,20–43].

The studies selected were performed in the USA mainly (12), with the UK (3), Germany (GER) (2) and Italy (ITA) (2) as runners-up; New Zealand (NZ), Spain (ESP), Canada (CAN), The Netherlands (NETH), Belgium (BEL), Japan (JAP) are the countries of origin of one study each. Sample sizes varied from 13 to 1,371 patients. Breast cancer was the diagnostic category studied most often in this selection of studies (18), followed by chronic myeloid leukemia CML (2) and (colo)rectal cancer (2). Adherence was assessed in a number of ways: questionnaires with solid psychometric characteristics (i.e.

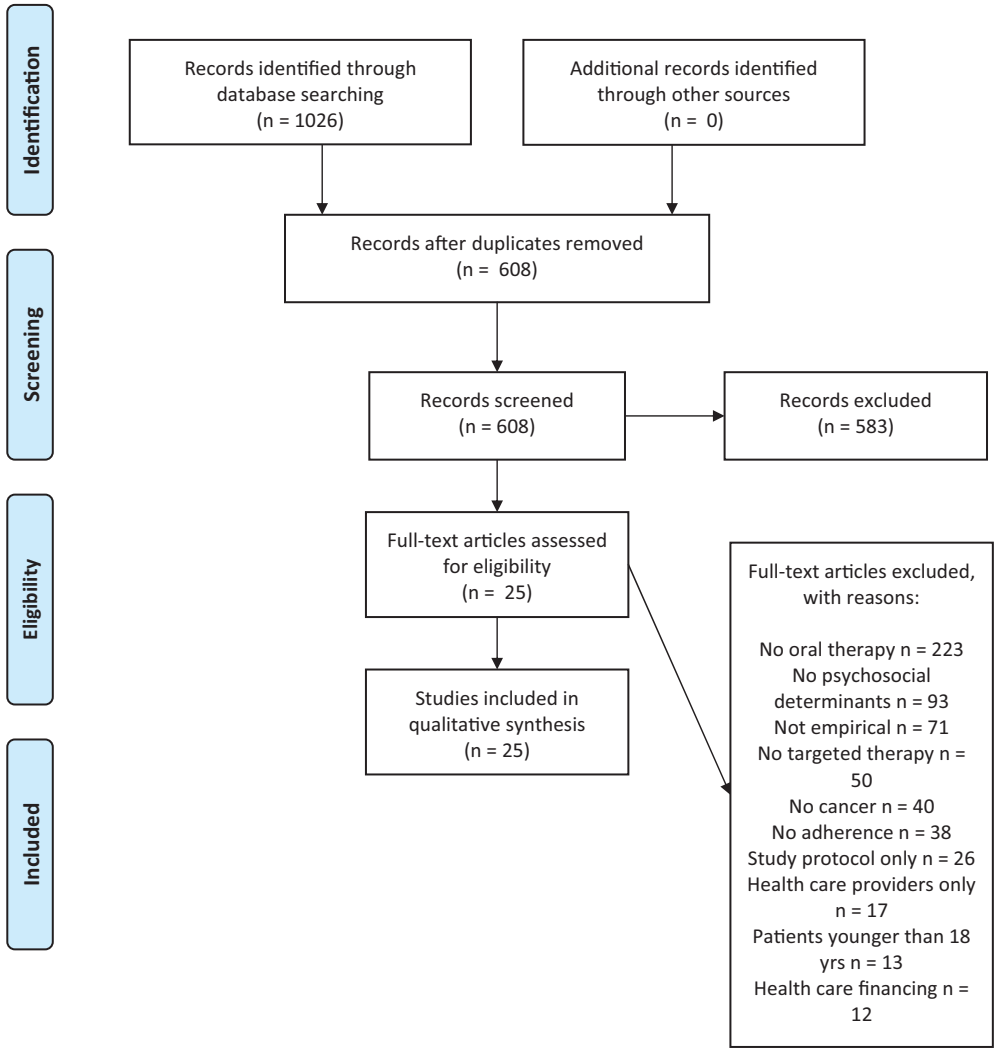

Figure 1. PRISMA diagram of literature search.

Table 1. Studies on adherence with oral anticancer treatment (2015–2020) and its psychosocial determinants.

First author; country; year	Diagnosis; number (*n*) of patients	Oral targeted therapy	Adherence assessment	Definition of non-adherence	Determinants: Concept (questionnaire used)	Results	Study quality[a]
Brier [20]; USA; 2017	Breast cancer, postmenopausal, TNM stages I-III; $n = 437$	Endocrine therapy (third generation aromatase inhibitors [AIs])	Chart review for treatment interruptions and premature discontinuation	Any time off AI therapy during prescribed treatment period or withdrawal from AI therapy before prescribed end-date	Health beliefs (perceived susceptibility; perceived benefits; perceived barriers)	Reporting greater perceived barriers to endocrine therapy: adherence ↓	medium
Bright [21]; USA; 2016	Breast cancer; $n = 1371$	Endocrine therapy (aromatase inhibitors, tamoxifen)	Online questionnaire (MMAS-8)	MMAS-8 scored continuously	Five dichotomous questions and five follow-up open ended questions on barriers and facilitators of endocrine therapy	Reporting any perceived barriers to endocrine therapy: adherence ↓; Reporting use of cognitive facilitators (self-talk): adherence ↑	medium
Bright [22] ; USA; 2018	Breast cancer, TNM stages 0-IV; $n = 130$	Endocrine therapy (anastrazole, exemestane, letrozole, tamoxifen)	A cap that fits on standard medicine bottles and records time and date each time bottle is opened and closed (MEMS)	Total doses not taken on schedule (i.e. one dose every 24-hr period) divided by the number of days between two study assessment times	Coping (modified COPE and the EAC scales); social support (ISEL-12); depression (CES-D)	Greater social support was associated with lower depressive symptoms: adherence↑	high
Buzaglo [23]; USA; 2017	Chronic myeloid leukemia (CML); $n = 318$	Oral CML medication	Self-report questionnaire (3 ordinal questions)	Skipping doses, postponing filling prescriptions, or missing a dose	Financial burden (IES); Depression	Presence of financial burden: adherence ↓; Presence of financial burden X high risk of depression: ↓	medium
Corter [24]; NZ; 2018	Breast cancer; TNM stages I-III; $n = 120$	Endocrine therapy (anastrazole, letrozole, tamoxifen)	Self-report of endocrine therapy adherence in the last 30 days	Missing any dose in the last 30 days with their endocrine therapy	Symptoms (modified BCPT); Illness perceptions (BIPQ); Medication beliefs (BMQ); Fear of recurrence (FoR); Perceived sensitivity to medications (PSM); Thoughts of stopping therapy (TST)	Lower coherence beliefs (understanding about the diagnosis of breast cancer): adherence ↓	medium
Font [4]; ESP; 2017	Rectal cancer; Clinical stages II- III; $n = 119$	Capecitabin	Simplified Medication Adherence Questionnaire (SMAQ); Pill count; MD report	$<80\%$ or $> 110\%$ calculated from the number of pills prescribed, pills returned, and days of treatment	Anxiety and depression (HADS); Quality of life (EORTC QLQ-C30)	Higher anxiety: adherence ↓	high
Hefner [25]; GER; 2018	Colorectal cancer (mainly); $n = 64$	Capecitabin	Medication Adherence Rating Scale (MARS)	MARS < 25	Patient- MD relation (PDRQ-9); Satisfaction with Information about Medicines Scale (SIMS); Medication beliefs (BMQ)	BMQ and SIMS determinants of adherence	medium
Herschman [26]; USA; 2016	Breast cancer TNM stages I – III $n = 523$	Endocrine therapy (aromatase inhibitors, tamoxifen)	Electronic pharmacy records; telephone interview	>90 days gap following endocrine therapy prescription	Quality of life (FACT-G); Treatment satisfaction (TSQM); Social support (MOS); patients breast cancer-specific distress (IES); Symptoms (modified MSQ); Patients preferred treatment decision-making roles (short form IPC); Decision-making difficulty, preferences, and considerations (ordinal questions)	Higher QOL: adherence ↑ Positive attitudes: adherence ↑	high
Hurtado [27]; USA; 2019	Breast cancer; Stages 0-III; $n = 280$	Endocrine therapy	One dichotomous question considering endocrine therapy adherence in the past two weeks	# days in the past two weeks on which endocrine therapy was not taken	Theory of Planned Behavior (TPB) dimensions: perceived control; subjective norms; attitudes; emotions	Positive attitude, perceived control, and subjective norm associated with adherence intention	medium
Iacorossi [28]; ITA; 2018	Breast cancer; $n = 27$	Endocrine therapy (anastrazole, letrozole, tamoxifen)	Face-to-face semi-structured interview	Score on interview	Fear of the drug; 'Attention to the person'; Knowledge seeking; Forgetfulness	All related to adherence	low
Iacorossi [29]; ITA; 2019	Prostate cancer; $n = 13$	Endocrine therapy (abiraterone acetate; enzalutamide)	Face-to-face semi-structured interview	Phenomenological exploration of adherence concept	Perception of obligation to take medication;	High reported adherence	low

(*continued*)

Table 1. Continued.

First author; country; year	Diagnosis; number (*n*) of patients	Oral targeted therapy	Adherence assessment	Definition of non-adherence	Determinants: Concept (questionnaire used)	Results	Study quality[a]
					Prefer oral medication over chemotherapy		
Jacobs [30]; USA; 2017	Metastatic breast cancer, chronic myeloid leukemia, non-small-cell lung cancer, renal cell carcinoma; $n = 90$	Endocrine therapy, tyrosine kinase inhibitor, capecitabine	A cap that fits on standard medicine bottles and records time and date each time bottle is opened and closed (MEMS); Self-report questionnaire (CTSQ)	The percentage of prescribed pills taken (number of cap openings compared with the number of expected cap openings during study)	Cancer-specific psychological distress (CWI); Anxiety and depression (HADS); Quality of Life (FACT-G); Satisfaction with clinician communication and treatment (FACIT-TS-PS)	Scores on CWI, HADS, FACT-G, FACIT-TS-PS all associated with adherence	medium
Karmakar [31]; USA; 2017	Breast cancer, post-menopausal; Stages 0-IV; $n = 138$	Endocrine therapy (aromatase inhibitor)	Self-report questionnaire (MMAS-8)	Score < mean MMAS-8	Self-constructed questionnaire: Perceived vulnerability; Perceived severity; Response efficacy; Response cost; Self-efficacy	Questionnaire scores related to adherence, self-efficacy in particular	medium
Kimmick [32]; USA; 2015	Breast cancer, postmenopausal, TNM stages I-III; $n = 112$	Endocrine therapy (aromatase inhibitor, tamoxifen)	Self-report questionnaire (MMAS-8)	MMAS-8 scored continuously	Symptoms (BPI-SF, BFI, MENQOL-VS, FACT-T); Self-efficacy for taking medication (modified SEAMS); Self-efficacy for communication with clinicians (PEPPI); Beliefs about Medicines (BMQ)	Higher self-efficacy for taking medication: adherence↑	high
Lambert [33]; CAN; 2018	Breast cancer, postmenopausal, stages I-III; $n = 22$	Endocrine therapy (aromatase inhibitor, tamoxifen)	Qualitative interview of patient's views on adherence	Discontinued endocrine therapy before the recommended 5 year treatment	Risk perception; Medication and necessity beliefs; Social support; Patient-provider interaction	Patients balance quality of life and quantity of life	medium
Markovitz [34]; USA; 2016	Breast cancer, stages 0-IV; $n = 133$	Endocrine therapy (e.g. aromatase, novladex, tamoxifen)	Self-report questionnaire (MMAS-4)	MMAS-4 scored continuously in correlation analyses	Depression (CES-D); Mood disturbance (POMS); Physical and cognitive symptoms (self-constructed); Social support; Internal locus of control (MHLC)	Greater depression: adherence ↓; Greater mood disturbance: adherence ↓; Greater physical and cognitive symptoms: adherence ↓; Higher levels of social support: adherence ↑	high
Mols [35]; NETH; 2020	Thyroid cancer, stages I-IV; $n = 306$	Endocrine therapy (e.g. levothyroxine)	Self-report questionnaire (MARS-5)	A score < 5 (max. score 5) for unintentional and < 20 (max score 20) for intentional non-adherence	Illness perceptions (BIPQ); Medication beliefs (BMQ); Type D behavior (DS-14)	Higher medication necessity: adherence ↑	high
Moon [36]; UK; 2017	Breast cancer, stages I-III; $n = 777$	Endocrine therapy (tamoxifen)	Self-report questionnaire (MARS-5)	A score < 5 (max. score 5) for unintentional and < 20 (max score 20) for intentional non-adherence	Social support (MSPSS); Anxiety and depression (HADS); Quality of life (FACT-ES); Information about treatment (self-constructed); Illness perceptions (IPQ-BCS); Medication beliefs (BMQ); Theory of Planned Behavior (TPB) dimensions: perceived control; subjective norms; attitudes; emotions	Attitudes and illness perceptions associated with adherence	high
Moon [37]; UK; 2017	Breast cancer, pre- and (post)menopausal; $n = 32$	Endocrine therapy (tamoxifen)	Self-report in qualitative interview	Regularly skipped or halved the medication, or took treatment breaks	Medication beliefs	Weighing up costs and benefits of treatment	medium
Moon [38]; UK; 2019	Breast cancer, pre- and (post)menopausal, stages I-III; $n = 345$	Endocrine therapy (tamoxifen)	Self-report questionnaire (MARS-5)	A score < 5 (max. score 5) for unintentional and < 20 (max score 20)	Social support (MSPSS); Anxiety and depression (HADS); Quality of life (FACT-ES); Information about treatment (self-constructed)	Low perceived behavioral control: adherence ↓; Lower perceived social support: adherence ↓;	high

(*continued*)

Table 1. Continued.

First author; country; year	Diagnosis; number (*n*) of patients	Oral targeted therapy	Adherence assessment	Definition of non-adherence	Determinants: Concept (questionnaire used)	Results	Study quality[a]
				for intentional non-adherence	Illness perceptions (IPQ-BCS); Medication beliefs (BMQ); Theory of Planned Behavior (TPB) dimensions: perceived control; subjective norms; attitudes; emotions	More negative medication beliefs : adherence ↓	
Pan [39]; GER; 2018	Breast cancer, TNM stages 0-IV; $n = 116$	Endocrine therapy (aromatase inhibitor, tamoxifen)	One question concerning adherence in the past week	<80% adherence	Side effects (GASE); Physical symptoms (GASE); Anxiety and depression (HADS); Quality of life (EORTC-QLQ-C30); Medication beliefs (BMQ)	Greater severity of side effects: adherence ↓; Lower necessity-concern beliefs: adherence ↓	medium
Verbrugghe [40]; BEL; 2017	Breast cancer; $n = 31$	Endocrine therapy (aromatase inhibitor, tamoxifen)	Semi structured interview	Not specified	Medication beliefs; Social support	Related to adherence	low
Wagner [41]; USA; 2018	Breast cancer, postmenopausal, TNM stages I-III; $n = 106$	Endocrine therapy (anastrazole, exemestane)	Time of treatment discontinuation	Early discontinuation of treatment due to reasons other than completing 5-year treatment protocol or study termination	Treatment-related symptoms (FACT-ES)	More side effects: adherence ↓	low
Walker [42]; USA; 2016	Breast cancer, stages 0-IV; $n = 106$	Endocrine therapy (aromatase inhibitor, tamoxifen)	Self-report questionnaire (adapted MMAS)	Adapted MMAS scored continuously	Emotions and perceptions (self-constructed); Endocrine therapy necessity and risk; Fear of Recurrence; Symptom attributions (BCPT); Perceptions of endocrine therapy necessity and risk (self-constructed); Emotions toward endocrine therapy (self-constructed); Fear of recurrence (self-constructed)	Positive emotions toward endocrine therapy: adherence ↑	medium
Yagasaki [43]; JAP; 2015	Gastric cancer, stages II-IV; $n = 14$	Oral anticancer agents	Semi-structured interview	–	Emotional resistance to and rational belief about taking medication	Emotions dominant regarding adherence	low

[a]Study quality was assessed based on three criteria: sample size >100 (1 point); validated assessment of adherence (1 point); validated determinants of adherence (1 point). Low quality = 0; medium quality =1-2; high quality = 3.

AIs: aromatase inhibitors; BCPT: Breast Cancer Prevention Trial Symptom Checklist; BFI: Brief Fatigue Inventory; BIPQ: Brief Illness Perception Questionnaire; BMQ: Beliefs about Medicines Questionnaire; BPI-SF: Brief Pain Inventory – Short Form; CES-D: Center for Epidemiologic Studies Depression Scale; COPE: Coping Orientation to Problems Experienced; CTSQ: Cancer Therapy Satisfaction Questionnaire; CWI: Cancer Worries Inventory; DS-14 = 14-item Type D Personality Scale; EAC: Emotional Approach Coping; EORTC-QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 30 items; ET: Endocrine Therapy; FACT-ES: Functional Assessment of Cancer Therapy – Endocrine Symptoms; FACIT-TS-PS: Functional Assessment of Chronic Illness Therapy – Treatment Satisfaction – Patient Satisfaction; FACT-G: Functional Assessment of Cancer Therapy: FACT-T: Functional Assessment of Cancer Therapy – Taxane questionnaire; GASE: Generic Assessment of Side Effects; FoR: Fear of Recurrence; HADS: Hospital Anxiety and Depression Scale; HBMABC: Health Beliefs and Medication Adherence in Breast Cancer; HLC: Health Locus of Control; IES: Impact of Events Scale; IPC: Interpersonal Processes of Care measures; IPQ-BCS: Revised Illness Perception Questionnaire; ISEL-12 = 12-item Interpersonal Support Evaluation List; MARS: Medication Adherence Rating Scale; MEMS: Medication Event Monitoring System; MENQOL-VS: Menopause Specific Quality of Life Questionnaire; MHLC: Multidimensional Health Locus of Control; MMAS: Morisky Medication Adherence Scale (- n items); MOS: Medical Outcome Study; MSPSS: Multidimensional Scale of Perceived Social Support; MSQ: Memorial Symptoms Questionnaire; PDRQ-9 = Patient Doctor Relationship Questionnaire; PEPPI: Perceived Efficacy in Patient-Physician Interactions; POMS: Profile of Mood States; PSM: Perceived Sensitivity to Medicines Scale; QOL: Quality of Life; SEAMS: Self-efficacy for Appropriate Medication Use Scale; SIMS: Satisfaction with Information about Medicines Scale; SMAQ: Simplified Medication Adherence Questionnaire; TPB: Theory of Planned Behavior; TSQM: Treatment Satisfaction Questionnaire for Medication; TST: Thoughts of Stopping Therapy.

MARS [44]: Medication Adherence Report Score; MMAS [45]: Morisky Medication Adherence Report), a medication electronic measuring system: MEMS; pill count, self-report, and health care provider report. The psychosocial determinants used in the selected studies are summarized in the fourth column of Table 1: illness perceptions, health beliefs, facilitators/barriers, coping, quality of life, and depression, appear to be the most frequently used concepts, consistent with the concepts in the Extended Common Sense Model, in particular those assessed with the Brief Illness Perception Questionnaire (BIPQ) and the Beliefs about Medicines Questionnaire (BMQ). The WHO model shows its validity by the concepts listed in the Results column of Table 1: (financial) barriers to therapy, social support, psychological issues (e.g. anxiety), depression, and self-efficacy are given in the WHO model, and mentioned as additional determinants of adherence in the Results section of our literature review.

Furthermore, depression and quality of life turn up as additional concepts associated with adherence. Adherence appears to be negatively associated with the perception by patients of psychological and financial barriers, low illness coherence, high levels of distress (anxiety, depression), low perceived behavioral control, negative medication beliefs, and fear of side effects. Adequate social support, illness perceptions that adequately represent the nature of the illness and its required medical management, high perceived necessity of the medication, and self-efficacy for taking medication appear to be associated with a higher level of adherence. These findings overall are quite in line with the established body of research on adherence [8–10]. A not quite surprising but nevertheless important finding from the literature search is how nine papers in Table 1 have been published in psychology journals; in the other selected papers, one or more psychologists usually were a part of the research team. This not only supports the validity of the search strategy, it also illustrates how many papers without authors with behavioral expertise tend to apply biomedical designs, with rather predictable results as a consequence.

The quality of the 25 papers amounted to 'low' (score 0): $n = 5$, 'medium' (score 1 or 2): $n = 12$, 'high' (score 3): $n = 8$.

Discussion

Reviewing the empirical literature on adherence with oral anticancer treatment in persons with cancer is a timely endeavor, given the rapidly increasing role of this innovative way of delivering medication (i.e. rather than intravenous chemotherapy). Given the state-of-the-art regarding adherence, in the review we focused on psychosocial determinants of adherence. Given earlier reviews, our review includes papers published from 2015 to 2020. Four percent of papers that were identified in the literature searches fitted the criterion of psychosocial determinants of adherence with oral anticancer treatment: 25 papers were the basis for our review.

Consistent with earlier work, adherence appears to be not determined by sociodemographic or clinical characteristics (except a few exceptions, e.g. [5]): more importantly appear to be determinants that are part of the Extended Common Sense Model, i.e. illness perceptions, medication beliefs, coping and more or less stable personality characteristics such as anxiety and depression [24,25,29,31,32,35,38,39]. Earlier, more or less comparable reviews published similar results (e.g. [11,46–48]): they reflect the upshot of the WHO report on adherence in identifying five categories of adherence: the patient, the condition, the treatment, the health care organization, and sociocultural/economic conditions [8]. The reviewed studies in Table 1 use a wide variety of theoretical backgrounds; not all, therefore, would fit seamlessly into the Extended Common Sense Model. Nevertheless virtually all concepts used in the studies do attempt to assess the patient's views regarding medication and the medical condition, i.e. psychosocial determinants.

The issue of interventions in adherence of persons on oral anticancer treatment is discussed in quite a few important papers. Greer et al. review 12 intervention studies and conclude that treatment monitoring especially in a pharmacy context may impact positively on adherence, although these authors caution against too much optimism [13]. A number of substantial methodological issues make for cautious interpretation. Rosenberg et al.'s study is more or less a sequel to the Greer et al. review [15]. Rosenberg et al. identify a somewhat larger number of studies and they share the critical remarks by Greer et al., regarding methodological issues in the selected empirical studies. Rosenberg et al. conclude 'some pharmacy-directed programs, particularly those that integrate monitoring or routine follow-up with a provider did demonstrate efficiency' [15].

Suggesting that 'patients should be educated' about the necessity of adhering to prescribed medication seems not to be very productive [40,49]. One might even make the case, consistent with the analyses in the WHO report on Adherence, that it is not the patient but rather the health care provider who should be educated about adherence as a complex aspect of human behavior. 'Adherence is determined to a considerable extent by cognitions (ideas, views) and emotions (anxiety, fear, denial) about the medication and the illness', would be the main message about adherence (cf. Jacobs et al., who emphasize the importance of exploring illness perceptions and medication beliefs in efforts to motivate patients to continue taking their oral anticancer treatment 30]. Recently, ASCO/NCODA Standards appear to integrate these suggestions to a certain extent, which must be judged as encouraging [50].

We acknowledge a few limitations of our work. Although the literature search was performed according to state-of-the-art requirements (i.e. CONSORT, PRISM), the selection of papers from the literature search may have been biased. Furthermore, given the great variation in virtually all major aspects of the included studies, it was not feasible to rate the included studies on a set of predefined criteria.

In line with the previous reviews, our review points at some suggestions for intervention: 'explore illness perceptions and medication beliefs, discuss them and attempt to have patients agree with more adaptive and constructive perceptions' seems to be the 'take home message'. Cognitive behavioral therapy offers theoretical and empirical expertise

in this area. Theoretical models on adherence behavior (e.g. the Extended Common Sense Model 18] could be used as a guiding principle in intervention research [51]. Recently, Weinman and colleagues published such a study: based on a theoretically based model about behavior change, the authors developed a brief screening tool to help patients disclose any hesitations they may have in using prescribed medications without confronting them with all too explicit and therefore possibly threatening items about non-adherence [52]. The screening tool was found to correlate strongly with the core questionnaire in the Extended Common Sense Model (i.e. the Beliefs about Medicines Questionnaire, BMQ). The authors suggest using the screening tool in order to assess adherence in a valid manner, without social desirability effects. Another promising approach in attempts to help patients adhere with their oral targeted therapy was published recently [53]. The authors discuss a Therapeutic Patient Education (TPE) programme, consisting of two specific components: 'self-care skills, referring to both an understanding of the disease and the appropriation of specific care techniques crucial for self-management, and psychosocial skills, which are related to patient empowerment, whereby patients play a more active role in their care' (p. 537). The TPE is based on psychological theory on behavior change that is similar to the Common Sense Model of Self-Regulation. The authors are cautiously optimistic about the effects of TPE on adherence with oral anticancer treatment . Future research should help in refining intervention methods that may help patients who are prescribed oral anticancer treatment to incorporate their medication behavior into self-management behavior of their illness and its treatment.

We conclude that the material reviewed in this paper supports the view that in order to address and maximize adherence with oral anticancer treatment in persons with cancer, psychosocial determinants deserve attention first and foremost. Identifying illness perceptions and medication beliefs and encouraging their adaptive functions seems to be a worthwhile undertaking in this category of patients. Behavioral scientists would be important in assisting health care providers in these efforts.

Disclosure statement

The authors report no conflict of interest.

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