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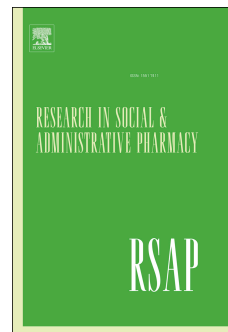
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Patients' lived experiences with antineoplastic medicines for the management of malignant solid tumours: a systematic review

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1 **Patients' lived experiences with antineoplastic medicines for the management of malignant solid**
2 **tumours: a systematic review**

3
4 **Abstract**

5
6 **Background:** Antineoplastic medicines affect the patients' physical and psychosocial well-being posing
7 challenges for patients, caregivers and healthcare professionals. However, little is known about the
8 patients' lived experience with medicines (PLEM) for antineoplastic treatment. It is the lived experience
9 that gives meaning to each individual's perception of a particular phenomenon which is influenced by
10 internal and external factors relevant to the individual.

11
12 **Objectives:** To critically appraise, synthesise and present the available evidence of patients' lived
13 experience with antineoplastic medicines prescribed for the management of malignant solid tumours.

14
15 **Method:** A systematic literature search was conducted in six electronic databases for articles published in
16 English with no date restrictions. The search terms were related to beliefs, practice and burden in relation
17 to patient, antineoplastic medicines, tumours and lived experience. Study selection, quality assessment
18 and data extraction were performed independently by 2 reviewers. Research findings were analysed using
19 narrative and meta-synthesis approaches.

20
21 **Results:** The search retrieved 31,004 articles with only 10 studies satisfying the inclusion and exclusion
22 criteria. These studies were published between 2005 and 2016 in Europe (n=6), America (n=3) and Asia
23 (n=1). Nine themes were identified to contribute to the patients' lived experience with antineoplastic
24 medicines. These were (a) influence from family members, healthcare professionals, media and culture,
25 (b) general attitude towards medicine, (c) accepting medicine, (d) modifying or altering medicine regimen
26 or dose, (e) medicine characteristics, (f) medicine routine, (g) medicine adverse events, (h) medicine and
27 social burden and (i) healthcare associated medicine burden. Patients tend to undergo a continuous
28 process of reinterpretations of their experience with medicines throughout their treatment journey.

29
30 **Conclusion:** The use of antineoplastic medicines has a profound effect on the patients' lives. Further
31 longitudinal in-depth studies are required to provide deeper insight into PLEM and support patients in
32 their treatment journey.

33
34 **Keywords:** solid tumor; antineoplastic medicines; patients' lived experience with medicine;
35 medicine-taking practice; medicine-related beliefs; medicine-related burden
36

37
38 **Abbreviations:**

39 PLEM - Patients' Lived Experience with Medicines

40 CASP - Critical Appraisal Skills Programme

41 EPHPP - Effective Public Health Practice Project

42 PRISMA-P - Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol

43 PROSPERO - International Prospective Register of Systematic Reviews
44

45 Introduction

46 Cancer is a group of related diseases featured by uncontrolled growth and dissemination of abnormal
47 cells; with more than 80% of all cancers being solid tumours.^{1,2} Cancers with the highest incidence
48 amongst both genders are solid tumours in the breast, lung, colorectum and prostate. More than 18 million
49 patients were newly diagnosed with cancer worldwide in 2018.³ It is being projected that by 2030 the
50 number of newly diagnosed cancer cases will rise to over 22 million per year predicted on the basis of an
51 aging population and adoption of behaviours linked with socio-economic development. Hence it is being
52 considered as an enormous international health burden growing at an alarming pace.^{2,4,5}

53
54 Antineoplastic medicines, which are often used as part of the treatment in combination with surgery and
55 radiation, interfere with cell growth resulting in apoptosis of cancer cells. Over the years, advances in
56 cancer care have led to prolonged cancer remission and management even when cure cannot be achieved.
57 Hence cancer is being considered as a chronic condition.^{2,6} The number of cancer survivors in America is
58 expected to increase from 15.5 million in 2015 to 20 million by 2026.⁷

59
60 Patients, themselves, are primarily responsible for the management of their health. Patient participation
61 within the healthcare systems includes the involvement of the patient in decision making, expressing
62 opinions about different treatment methods such as sharing of information, feelings and cooperating with
63 the healthcare professionals' advice. The concept of enabling active patient participation is increasingly
64 noted as a key component in the redesign of healthcare services and also as means to improve patient
65 safety.^{8,9}

66
67 The medicine experience incorporates the patient's description of his expectations, concerns, beliefs,
68 cultural, ethical and religious influences on medicine-taking behaviour. Cipolle *et al.* (2004) developed
69 the concept of medicine experience defined as "the sum of all the events a patient has in his/her lifetime
70 that involves drug therapy." This approach is emphasised in the practice of pharmaceutical care as it
71 focuses on patient-centred approach by providing direct care to patients based on their medicine-related
72 needs.¹⁰ Similarly, Shoemaker and Ramalho de Oliveira in 2008 defined "the medication experience as an
73 individual's subjective experience of taking a medication in his daily life."¹¹ The concept of lived
74 experience stresses the fact that only those who have experienced the phenomena can communicate their
75 real experience to the outside world.^{12,13} A conceptual model of patients' lived experience with medicines
76 was compiled in a metasynthesis of qualitative studies by Mohammed *et al.* (2016). As depicted in
77 Figure 1, this incorporated medicine-related burden, medicine-related beliefs and medicine-taking
78 practice. These concepts will in turn affect the patients' wellbeing and health-related quality of life
79 together with therapeutic outcomes.¹⁴

80
81 Healthcare professionals' behaviours, family members and peers influence the patient's beliefs towards
82 medicines. The intensity of medicine-related burden and the coping skills of the individual influence the
83 patient's attitude and behaviour to the use of medicines. Positive attitudes arise from trust in healthcare
84 professionals, positive medicine experience and achievement of the desired therapeutic outcomes. The
85 medicine-related beliefs with the effect of the medicine-related burden influence the medicine-taking
86 practice.^{14,15} Medicine-related burden incorporates the medicine regimen, characteristics, adverse events
87 together with the social and healthcare effects. Mohammed *et al.* (2016) showed that intolerable medicine
88 burden often resulted in non-adherence and poor treatment outcomes.¹⁴ In addition, a study on 97
89 Australian participants identified medicine-related burden as one of 4 interrelated components of
90 treatment burden (financial, time, travel and healthcare access burden) operating in a cyclical manner.¹⁶

91
92 The focus of cancer care is centred on improving patient experience by understanding the burden they
93 meet in everyday life, as well as the unmet needs of treatment such as treatment adverse effects and
94 quality of life. These insights can be achieved through direct and constructive interactions with
95 patients.^{9,17}

96
97 The increasing number of publications including systematic reviews in the field of oncology indicates that
98 the care of cancer patients persists as a clinical research priority. The majority of the systematic reviews
99 evaluated cancer drug treatment effectiveness, safety and supportive care interventions.¹⁸ Despite this,
100 systematic reviews about medicine experiences of adult cancer patients undergoing antineoplastic
101 treatment are lacking. The aim of this systematic review was to critically appraise, synthesise and present
102 the available evidence of patients' lived experiences of antineoplastic medicines prescribed for the
103 management of malignant solid tumours.

104 **Method**

105 **Protocol registration**

106 A systematic review protocol was developed in accordance with the Preferred Reporting Items for
107 Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) standards.¹⁹ The protocol was then
108 registered with International Prospective Register of Systematic Reviews (PROSPERO)
109 [PROSPERO2016:CRD42016048457] to avoid unplanned duplication of work.²⁰

110 **Eligibility criteria**

111 Studies were included in the systematic review if:

- 112 • the recruited patients were aged ≥ 18 years irrespective of their gender, ethnicity and stage of disease
113 and were receiving antineoplastic medicines for the management of malignant solid tumours in any
114 setting; and
- 115 • the views, experiences and behaviours of patients in receiving antineoplastic medicines from their
116 perspective were reported; and
- 117 • the study incorporated all the 3 aspects of the patients' lived experience with medicines concept:
118 medicine-related beliefs, medicine-related burden and medicine-taking practice as outcome measures.

119
120 Studies were excluded if they investigated the patient experience in experimental studies rather than the
121 'real world' setting, they included experiences of patients taking antineoplastic medicines solely for
122 palliative intent, studies reported in a non-English language or published as conference abstracts and grey
123 literature.

124 **Search strategy**

125 A database search strategy using specified search terms and their different combinations was created in
126 consultation with the research team. The key concepts of the patients' lived experience with medicines,
127 extracted from the model developed by Mohammed *et al.* (2016), were medicine-related burden, medicine
128 related-beliefs and medicine-taking practice. The search focused on these concepts in relation to patient,
129 antineoplastic medicines, malignant solid tumours and lived experience. Concept mapping was utilised as
130 an aid to consider all aspects of the topic and identify keywords that may be used for the search. The
131 search strategy was then adapted to meet the specifications of the different databases.

132 A systematic literature search was conducted in six databases: Cumulative Index to Nursing and Allied
133 Health Literature (CINAHL), Medline, Cochrane Database of Systematic Reviews, Embase, International
134 Pharmaceutical Abstracts and PsycArticles. The manual search of related studies in the references of
135 identified publications was carried out to identify additional potentially relevant papers.

136 **Study Review**

137 Screening was performed first on titles, then on abstracts and then followed by full papers in accordance
138 to the inclusion and exclusion criteria. A random sample of 10% of the retrieved titles and abstracts and
139 the whole list of full papers were screened independently by 2 members of the research team for

140 consistency of inclusion/exclusion and to enhance the reliability of the process. Any disagreement was
141 resolved following discussion and consensus was reached within the research team.

142 **Quality assessment**

143 Studies were appraised using quality appraisal forms adapted from the Critical appraisal skills programme
144 (CASP)²¹ and Equator Network²² for qualitative research together with the quality assessment tool of the
145 Effective public health practice project (EPHPP) for quantitative research.²³ Quality assessment was
146 performed independently by 2 reviewers. Any disagreements were discussed and resolved by consensus.

147 **Data extraction and synthesis of results**

148 Data extracted from the articles included specific details about the populations, study setting, research
149 design, method, salient findings and study limitations. The research findings of the quantitative and
150 qualitative studies were analysed using narrative and meta-synthesis approaches respectively. This
151 systematic review implemented the qualitative meta-interpretative synthesis (QIMS) methodology for
152 qualitative studies in an attempt to “create a new, deeper, and broader understanding” of the
153 phenomenon.²⁴ QIMS allows the extracted data to be analysed through a process of coding, theme
154 extraction, theme synthesis and triangulation.^{25,26} After repeatedly reading the included studies, sections
155 identified to fall within one of the 3 main categories: (1) medicine-related beliefs, (2) medicine-taking
156 practice and (3) medicine-related burden in accordance to the model of Mohammed *et al.*
157 (2016) were extracted and reported verbatim in line with the corresponding theme. The quotes, if
158 available, were pulled directly from the study. This was independently done by the first researcher and
159 another researcher within the team to ensure that all extracts within the study were identified and grouped
160 in the same category. Then the studies were translated into each other. Proposed themes and sub-themes
161 were put forward by all researchers through an iterative process. The theme synthesis process utilises
162 triangulation to enhance dependability and trustworthiness of the findings. Triangulation is based on 4
163 processes, namely methods, sources, analysts and theoretical perspectives.^{24,25}

164 **Bias**

165 The risk of bias was minimised by the application of the following measures:

- 166 • A random sample of 10% of studies identified during the database search was independently
167 assessed for relevance by two independent reviewers.
- 168 • Quality assessment using standardised critical appraisal instruments and data extraction of all
169 selected papers was conducted by two independent reviewers prior to inclusion in the review.
- 170 • Disagreements were resolved by consensus after discussion with the research team.

172 **Results**

173 **Study selection**

174 As shown in the Prisma flow diagram²⁷ (Figure 2), the combined search yielded 31,004 titles. A total of
175 10 studies met the inclusion criteria and were included in the systematic review.²⁸⁻³⁷ Two studies were
176 quantitative studies and 8 studies followed qualitative methodology.

177 **Description of the selected studies**

178 The characteristics of the included studies are summarised in Table 1. Studies were published between
179 2005 and 2016 and were conducted on 3 continents: Europe (n=6), America (n=3) and Asia (n=1).
180 Sample sizes ranged from 1 to 92 participants. Qualitative studies were conducted on 153 patients in total
181 whilst quantitative studies investigated 154 patients. Four studies included solely male participants whilst
182 only 1 study involved only female participants in the sample population. Six studies investigated patients

183 suffering from a single cancer type: advanced non-small cell lung cancer (2 studies), breast cancer (3
184 studies) and colorectal cancer (1 study). The remaining 4 studies did not focus on any particular cancer
185 type but involved patients suffering from various solid tumours. The treatment strategy varied across all
186 10 studies. Two studies focused on patients receiving capecitabine, two studies included patients
187 receiving erlotinib or completed adjuvant antineoplastic treatment (fluorouracil, epirubicin and
188 cyclophosphamide treatment protocol) respectively and the other six studies involved patients receiving
189 different antineoplastic treatment protocols.

190 The majority of studies (n=8) used a range of qualitative methods which included focus groups (1 study),
191 open interviews (2 studies), semi-structured interviews (2 studies) or multi-method approach consisting of
192 observational study with semi-structured interviews with or without the use of field diary (3 studies).
193 Two further studies used a quantitative approach where data was collected using patient-reported ques-
194 tionnaires, blood sampling and patient's medical files.

195
196 Out of the 10 studies, 3 studies did not state at which point in the patient's cancer journey the interview
197 was conducted. Six studies collected data during the patient's treatment phase whilst 1 study took a
198 retrospective look at patients who had completed chemotherapy within the previous year. Qualitative data
199 of included studies were analysed using content analysis, grounded theory and ethnography. Hence this
200 systematic review satisfied the 4 triangulation processes.

201 **Quality assessment of the included studies**

202 The quality assessment of the included studies is summarised in Appendices 1-4. The strengths of the
203 studies included a clear research aim in 80% (n=8) of the studies, an appropriate study design and the
204 attainment of ethical approval in all the studies except one where it was unclear whether ethical approval
205 was granted. The results obtained in the majority of the studies (n=8) clearly addressed the original
206 research question and the key findings were explained in detail.

207 The weaknesses of the selected studies included the lack of justification for the final sample size in the
208 manuscript (n=2) and the lack of discussion on the limitations of findings such as triangulation, bias and
209 confounders (n=8). The latter clarifies the extent to which the findings offer an accurate representation of
210 the phenomenon under study, hence affecting the validity and reliability of research findings.

211 **Data synthesis**

212 The studies included in this systematic review did not provide a standard definition of the patients' lived
213 experience with medicine. Nine themes emerged to highlight the patients' lived experience with
214 antineoplastic medicines in patients suffering from solid tumours: medicine-related beliefs (two themes),
215 medicine-taking practice (two themes) and medicine-related burden (five themes). The themes and
216 subthemes generated from this systematic review were mapped and presented in line with the structure of
217 the PLEM model (Figure 3) adapted from the conceptual model of Mohammed *et al.* (2016).
218 Modifications in the adapted model included the elimination of medicine related burden, magnitude and
219 coping skills from the main theme of medicine-related beliefs and the inclusion of the sub-themes within
220 the model to ensure a clear understanding.

221 **Medicine-related beliefs**

222 The identified themes within medicine-related beliefs included (a) influence of healthcare professionals,
223 family members, media and culture as well as (b) general attitude towards medicine.

224 *(a) Influence of family members, healthcare professionals, media and culture*

225 Chemotherapy, as a treatment, was found to be unique in being considered “*as the source of suffering*”
 226 both culturally and medically.³¹ Suffering encompassed both a meaning and a value for each cancer
 227 patient. The myths and stigma associated with cancer treatment may have silencing effects and may
 228 influence the patient’s behaviour resulting in patients seeking support at a later stage of treatment.^{28,31}

229
 230 Patients tend to follow the healthcare professionals’ treatment recommendation to base their decision on
 231 whether to initiate treatment or not. The trust of the patient in the healthcare professionals’ attitudes and
 232 their relationship act as a driving force in their treatment decision and has a strong positive influence on
 233 compliance with the medicine.^{28,33} “*I don’t know if I’m that brave yet, but if my doctors assured me this*
 234 *was a good move, this was a good move for me, I feel confident enough in [my doctor] to follow his*
 235 *advice.*”³³

236
 237 Family members have also shown to be highly influential on patients’ beliefs and this was reflected in the
 238 patients’ decisions regarding treatment. Patients disclosed their feelings of responsibility towards their
 239 family members as they felt obliged to survive even if this was associated with suffering and
 240 restrictions.^{33,35}

241 “*Yes, I just thought that if something comes back again and I say no, then I have to look my family and*
 242 *friends in the eye and say I could have prevented it, perhaps. Now, if something comes back again, I can*
 243 *say I did everything I could. Cancer is bad enough without someone saying: It’s your own fault!!*”³⁵

244
 245 Media and support groups have been found to strongly influence the cancer patient’s beliefs. Newly
 246 diagnosed cancer patients may even obtain a false picture about cancer and its treatment from these
 247 sources and this may provoke unnecessary anxiety.^{29,31} Cultural aspects also affect patients’ outlook on
 248 cancer and its treatment as different cultures have diverse views on life, death and pain in general.^{28,31}

249
 250 (b) *General attitude of the patient towards medicine*

251 Chemotherapy is considered as one of the current treatment strategies that may lead to a disease-free
 252 future and ultimately to survival.²⁸ Studies showed that prior to the initiation of treatment patients already
 253 had pre-conceived notions and expectations about their treatment. A commonly expressed idea amongst
 254 patients is that chemotherapy “*hurt the good cells and really hurting the cancer cells.*”^{30,31,35} Several
 255 feelings were expressed by patients at initiation of treatment with antineoplastic medicines. These
 256 included hope^{28,33}, anxiety, stress^{29,35}, fear and also acceptance to carry the burden of side effects.³⁵ It
 257 was noted that although chemotherapy provides grounds for “*hope*”³³, this is a highly feared form of
 258 treatment that is commonly considered to be as bad or worse than the experience of cancer itself.^{30,31}
 259 Patients expressed concerns related to aesthetic adverse effects such as hair loss, feeling of sickness and
 260 dependency on intake of medicines.³⁰ “*When I found out that I was going to have chemotherapy my whole*
 261 *world came apart. It was the worst thing I could imagine.*”³⁰ As treatment cycles progressed, patients
 262 reported to feel calmer and more peaceful (mean value of the mental component of SF-12 Health Survey
 263 improved from 47.1±7.5 at baseline to 50.4±5.4 at cycle 5).³⁷

264
 265 When looking to the future, patients pondered if their current chemotherapy would be successful or
 266 whether they would require to continue or change treatment. Patients were also concerned about the
 267 frequency of follow-up visits with the oncologist, the monitoring of symptoms in relation to the disease
 268 and the adverse effects in relation to treatment.^{28,29} Notwithstanding the fact that the negative feelings
 269 particularly in relation to the side effects symptoms were still fresh in the patients’ minds, patients were
 270 worried about their ability to continue with further chemotherapy sessions whilst coping with experience
 271 of their previous treatment.²⁹ “*...But I can’t think about if I were to find out that the cancer had spread,*
 272 *(and if I were to need more treatment)—how would I then manage to go through chemotherapy again,*
 273 *now that I know about everything, now that I have all the answers.*”²⁹ At the same time however they
 274 anticipated the time when their treatment would be completed and were looking forward to a normal life.

275 Some patients argued that they perceived their life to have changed forever and were concerned about
 276 continuing to live their life without treatment but with a lack of energy and a fear of disease recurrence.
 277 “After treatment I want to begin with a trip to the archipelago (islands that lie outside Stockholm)
 278 because that is where I get strength, and I come out of there different, if you compare it to when you are
 279 in the city or town. I have been so close to death and gone through this treatment—well, it is present all
 280 the time..I am going through counselling right now, since I don’t want to put my family through the
 281 motions all the time..”²⁹

282

283 **Medicine-taking practice**

284 The themes generated in relation to medicine-taking practice were (a) accepting medicine and (b)
 285 modifying or altering medicine regimen or dose.

286 *(a) Accepting medicine*

287 Qualitative studies revealed that upon receiving the news of suffering from the life-threatening condition
 288 of cancer, the focus shifted from diagnosis to treatment and survival.³⁵ Patients also wanted to know the
 289 intent of treatment to be able to decide whether to undergo treatment and live longer; “if this disease has
 290 no cure you can tell me, because in this case I do not wish any treatment. ...He told me that that depends
 291 on the case: if the disease is already too advanced, it is not worth to treat!”²⁸

292

293 Patients claimed to be highly adherent to antineoplastic medicines.^{32,34,35} Quantitative studies in patients
 294 receiving erlotinib showed that the mean adherence was $96.8\% \pm 4.0$.³⁴ Using the pill count method
 295 patients treated with capecitabine showed a high adherence rate with only 8% (n=7) consuming less than
 296 95% of treatment whilst one patient was taking “more than 105% of the prescribed dose.”³⁷

297 The treatment-free period between treatment cycles was medically prescribed interruption from treatment
 298 either in accordance with the treatment protocol or due to adverse effects. Patients associated these breaks
 299 as periods of relief and freedom from constraints to the medicine plan such as “holidays”³⁵ or as
 300 burdensome periods with adverse effects with “fear of recurrence.”³³ This emphasised the importance of
 301 involving the patient in treatment decision making and explanation of treatment.

302

303 Along the treatment journey, patients were building up their knowledge about the effects of
 304 chemotherapy, interpreting the physical reactions experienced and developing coping mechanisms. Hence
 305 these patients underwent a continuous process of reinterpreting their situation.²⁸ Collectively, patients
 306 described the treatment journey in cancer as a “degrading experience and anxiety-provoking” as these
 307 patients had to manage various side effects along the treatment phase. A fear of “change” was highly
 308 emphasised; this did not only include the physical appearance especially in women but also the loss of the
 309 normal routine and their identity as they may be considered as a cancer case.^{29,30} Although patients were
 310 learning to accept the illness, they still wanted to maintain control over their body.³⁰

311

312 *(b) Modifying or altering medicine regimen or dose*

313 Patients, especially those receiving parenteral chemotherapy treatment, expressed their concern regarding
 314 dose reduction and postponement of chemotherapy regimen by healthcare professionals.³¹ “When the
 315 oncologist offered to administer more chemotherapy cycles with a lowered dose, she enquired whether
 316 this would still provide the optimal benefit and the oncologist replied “They’ve lowered lots of
 317 people”...She was scared and had enquired with the oncologist whether this will cause the cancer to grow
 318 faster.”³¹ Self-reported non-adherence measured by MARS showed increasing rates of modifications in
 319 treatment over time ranging from 16% (n=12) at cycle 1 to 29% (n=16) at cycle 5.³⁷ Qualitative
 320 comments noted that cancer patients receiving oral antineoplastic medicines may self-alter their
 321 prescribed treatment regimen resulting in either under or over dosing of the treatment. The underdosing

phenomenon may occur by unintentionally missing or deliberately skipping a dose to reduce the severity of unbearable adverse effects such as gastrointestinal symptoms. On the other hand, overdosing may occur when some patients claimed to consume the remaining forgotten medicines at the end of the cycle and a patient even admitted that “he did not always respect the break in-between cycles.”^{32,34,37} Delays in chemotherapy schedule and dosage reduction have instilled fears in making the tumour “grow faster” and promote recurrence. Most people receiving cytotoxic chemotherapy seek to obtain certainty over uncertainty. The importance of taking treatment exactly as prescribed and receiving “100% dose” was emphasised by the majority of patients.^{31,32}

Medicine-related burden

Five themes emerged for medicine related burden, these were (a) medicine characteristics (b) medicine routine (c) medicine adverse events (d) medicine and social burden (e) healthcare associated medicine burden.

(a) Medication characteristics

The patients’ experience in relation to medicine characteristics was adversely influenced by the dosage form of treatment,³¹ colour of the parenteral infusion bag²⁹ and tablet size.³⁵ Patients recalled their physical revulsion to the intake of oral antineoplastic formulation due to the size and form of the tablets that may be too difficult to swallow, profound throat discomfort and the metallic after-taste.³⁵

Patients remarked that watching the nurse wearing the personal protective wear and following the procedure to initiate the parenteral infusion created an appalling experience to the patient. This made them recall that ultimately they would be experiencing adverse effects from such treatment. A patient metaphorised his feeling as being “chained” to the infusion line. “*Especially the moment when the nurse entered the room wearing protective gear and started the infusion, to be hooked up and to see the chemotherapy infuse the blood vessel, and to know that this also will give some side effects was a terrifying experience.*”²⁹

(b) Medicine routine

In the qualitative studies, medicine routine burden considered aspects that related to the identification of challenges in adapting to the incorporation of antineoplastic treatment into the patient’s lifestyle and strategies to overcome these challenges. Patients made great effort to adhere to the prescribed doses and schedules of chemotherapy due to the continuous awareness of the life-threatening nature of the illness metaphorised as “*pills dominate the mind.*”^{32,35} This attitude was the “only task that was not delegated to others” as they felt that they “invested all their energy” so as to feel “actively engaged in fighting against” cancer.³⁵

It appears that patients develop individualised treatment strategies to assist them with the adherence procedure such as counting of tablets, preparing the tablets from the day before, storing the medicinal product in a “*clearly visible prominent place*” or setting alarm on their mobile phone. More than 70% of patients stated that they relied on the reminder method to support their treatment regimen. No association was established between adherence as monitored with Medication Event Monitoring System and the practice of the reminder method for erlotinib intake.³⁴ The use of the reminder method was noted in more than 60% of patients receiving capecitabine at cycle 1 (61.5%, n=47), 3 (66.2%, n=44) and 5 (73.2%, n=41).³⁷

Despite the patients’ determination to precisely adhere to the prescribed medicine plan, patients identified barriers that could interfere with the adherence process. These include uncertainty in taking the correct number of tablets, skipping the exact time for intake, disruption in their daily routine and running out of

370 pills.³⁵ Thirteen percent of patients (n=10) did not adjust the administration of capecitabine with meal
371 times at cycle 1, a behaviour that increased by 10.9% towards cycle 5.³⁷ This is comparable with 21%
372 (n=8) of patients in the study by Timmers *et al.* (2015) who did not follow the advice of taking erlotinib
373 under fasting conditions at 1 month. Using the generalised estimated equations, the occurrence of ocular
374 symptoms ($p=0.031$) and stomatitis ($p=0.005$) were found to be significantly increased with incorrect
375 intake of erlotinib without food.³⁴

376
377

(c) *Medicine adverse events*

378 Adverse events were considered as one of the most challenging aspects of living with antineoplastic
379 medicines. Patients referred to different adverse effects which ranged from minor to severe life-
380 threatening effects with the psychological and physical impact of these adverse effects affecting the
381 patients' quality of life.^{28,30,32,35,36} A cognitive decline manifested as lack of concentration, deteriorating
382 memory and dizziness was noted during and after antineoplastic treatment.^{30,35} Few participants reported
383 of suffering from mild cognitive impairment described as "empty head" and "fog" which adversely
384 affected their concentration.³⁶ A few patients considered it strange to suffer from symptoms caused by the
385 treatment and not from the actual illness.³⁰

386

387 The extent and severity of adverse effects due to antineoplastic treatment played a huge role in many
388 patients' attitudes.^{29,33} A female patient expected to feel better with every chemotherapy cycle however
389 she was frustrated when she started feeling side effects again.²⁸ All patient-reported symptoms were
390 reported to worsen from baseline to 1 month of treatment with erlotinib (with the exception of headache).
391 Rash, fatigue and cough were the three most common patient-reported symptoms after 2 months.³⁴ Thirty
392 three percent of patients blamed side effects for the discontinuation of treatment with capecitabine prior to
393 completion of the 5th cycle. The commonest patient-reported symptoms with capecitabine at cycle 5 were
394 hand and foot syndrome, fatigue and flatulence. In view that these patients had already reported the
395 symptoms at baseline, were pre-treated and/or receiving capecitabine concomitantly with
396 oxaliplatin/irinotecan, it is difficult to attribute these adverse effects solely to capecitabine.³⁷

397 The majority of patients were still experiencing side effects after stopping treatment, with effects being
398 cumulative and worsening over time. However, several patients were surprised to experience relatively
399 few side effects during their course of chemotherapy, both for orally and parenterally administered
400 antineoplastic treatment.³¹

401

402 The aspect of "suffering" is so ingrained with the experience of chemotherapy that it is not even
403 recognised as an adverse effect of treatment.³¹ Hence patients failed to recognise adverse effects from
404 these medicines and refrained to inform the healthcare professionals about the occurrence and severity of
405 adverse effects they experienced.^{28,32,35} The patient's ability to tolerate the adverse effects is associated
406 with the concept of making an effort to achieve cure or disease control and may be considered as the
407 "price to pay" for treatment efficacy.³² Patients face adverse effects differently, they either accept to
408 support their adverse effects and have a fatalist attitude or they resort to complementary medicine such as
409 phototherapy, homeopathy and hypnosis. The focus groups discussions revealed that patients wait
410 between 3 and 8 days prior to consulting medical advice. Some cancer patients even tried to hide or
411 minimise their adverse effects by either not considering them as severe or by preferring not to talk about
412 them.^{32,35} The latter may be the result of feeling afraid that the oncologist would change their treatment
413 and hence reduce the possibility of a positive response. Few patients felt uncomfortable to speak about
414 adverse effects during every appointment or to discuss specific intimate adverse effects such as vaginal
415 dryness.^{30, 32, 35}

416

417 (d) *Medicine and social burden*

418 Despite having treatment, patients put all their efforts to be as positive as possible and lead a normal life.
 419 They realised the significance of every day and felt determined to appreciate their lives.^{30,36} *“But because
 420 of the experience of illness, I realize how precious each day and normal life is.”*³⁰
 421

422 Antineoplastic medicines affect the patient’s social life which is directly related to their quality of life.
 423 Patients experienced social isolation often due to altered relationships with family members and
 424 friends.^{29,30,35,36} This may be the result of adverse effects, complex treatment regimen or social stigma. As
 425 treatment became the focal point of the cancer patients’ lives, this also dominated both their social and
 426 family life. *“I stopped playing with the orchestra in November of last year. That also has something to do
 427 with (name of medication); I got shaky and it had a few other side effects than with (intravenous)
 428 chemo.”*³⁵ Patients described this period as hard to get through and they focused all their efforts on their
 429 feelings. *“And then there was the constant worry that the lab tests wouldn’t be good so that everything
 430 would have to be postponed, and my whole life was about this..”*³⁰
 431

432 In contrast, cancer patients recognised the support provided by family members for proper medicines use
 433 and the benefits of support groups.^{29, 30, 33, 35, 36} The illness was described as a dramatic, traumatic and
 434 insane experience for the family. Family members offer paramount support to cancer patients, with the
 435 role of the spouse often considered as a *“lifeline”*.³⁰ The partners were specifically identified as providing
 436 aid in the patients’ daily life such as doing the household chores as this allows the patients to rest when
 437 they felt tired.³⁵ However there were other patients who felt as if their family did not take any extra
 438 consideration. The necessities of time and support to the patient from their relatives was usually
 439 overlooked, demonstrating the importance that relatives are aware of the patient’s requirements.³⁰
 440

441 Patients also spoke about the impact of treatment on the patients’ work and financial income bringing
 442 about instability in life. *“Chemotherapy brings a lot of anxiety, because I don’t know if I can accept an
 443 order for or not. You know, there is no lack of work, but if you don’t deliver as promised the costumers
 444 forget about you. It’s bad time for work now.... But it’ll become better.”*²⁸ Patients, predominantly
 445 females, voiced a sense of gratitude for being granted sick leave during their treatment period. This
 446 provided time to completely devote their life to themselves. Patients disclosed their difficulties in
 447 returning back to their workplace. They described feeling pressured from society and healthcare
 448 professionals to return to their workplace as early as possible. The patients’ inner worry was that their
 449 employer expected to receive the same work output like before their diagnosis. Some women explained
 450 that specific work environments, such as working with children, may result in a higher risk of contracting
 451 infections. This may have contributed to their decision not to return to work during treatment. Some
 452 women narrated that when they spoke about cancer at the work place; this proved to be taken negatively
 453 both by employers and work colleagues.³⁰ *“But then I noticed, and when I came back and started to work
 454 full-time my boss came to me and said that this position I had applied for had gone to someone else
 455 because I had to think of my illness.”*³⁰ Those cancer patients who persisted with the working life had
 456 noted that work became important part of life and aided them to detach themselves from the illness itself.
 457 ^{28,30}
 458

459 (e) Healthcare associated medicine burden

460 Challenges associated with the complexity of the healthcare system were identified. Healthcare
 461 professional-patient relationships,^{29,30} patient-patient relationships,²⁹ healthcare support^{29,30} and provision
 462 of information³⁰ were commonly described. Cancer patients looked for professionalism and traits such as
 463 empathy, respect and good support from healthcare professionals. The support offered by healthcare
 464 professionals was overall rated as positive.^{29,30} *“Well the important thing is of course how they care for
 465 you, and not that it has to be so incredibly professional so that, that...Empathy is alpha and omega. And I
 466 think they are good and I always tell them that when they ask.”*³⁰ Provision of good quality information

467 from healthcare professionals delivered at the appropriate time was considered to be important and made
468 a positive effect in the patients' experiences. In fact, patients felt the large amount of information
469 delivered, especially during the meeting when the oncologist broke the news about their diagnosis, as
470 very "stressful".^{29,30,32} Patients described that healthcare professionals should consider each patient to
471 know nothing about the disease and the treatment and fulfil their information needs with plain, correct
472 and clear material.³⁰

473 Cancer patients identified transportation, distance to hospital for multiple visits, hospital waiting time,
474 companionship with caregivers to treatment and financial burden as barriers to treatment. These
475 difficulties decreased the patients' enthusiasm to continue long-term maintenance treatment with
476 antineoplastic maintenance.^{29,33} *"I live alone as well, and every time I come for chemo or transfusions I
477 have to have someone bring me. So that would—if I had to come real frequently that would put a
478 hardship on."*³³ Patients commented on the lack of tranquil hospital environment and individualised
479 support by hospital staff. Although the patients receiving oral antineoplastic treatment in the comfort of
480 their own home was considered to be a major advantage, they complained of insecurity about not
481 receiving professional counselling and support at home.^{29,35}

482
483 Some patients felt that other patients may offer companionship and moral support particularly when they
484 accompany one another during treatment cycles. During the chemotherapy outpatient clinic, cancer
485 patients interacted with each other and also served as a network of support. They would transmit to each
486 other positivism, strength and a feeling of unity.^{28,30} *"Yes, it is very important to have someone to share
487 this with because other people do not know what you're talking about. You can explain but they do not
488 know what chemotherapy treatment is."*³⁰ Whilst being an in-patient to receive parenteral treatment, one
489 patient even praised the consideration of healthcare professionals who ensured patients of similar age and
490 treatment share the same hospital room. However others mentioned the negative psychological impact in
491 the announcement that a patient in their group is suffering from a terminal disease which will reasonably
492 result into death within a short period of time. *"For the first treatment I was placed in a four-bed room
493 and I remembered that I thought it was so hard, really hard; for one thing, I had just found out my
494 diagnosis...and then you just see old people and it gets so obvious what am I doing here. You know it was
495 absolute, I didn't want to be there with all the drainage bags they had, and it was hard. But since then it
496 has been so nice because I was able to change rooms and she (another patient) is the same age as me; we
497 do the treatment together and I think it's great that they have scheduled us together and that we can share
498 a room."*²⁹

499
500 Patients enquired about the lack of available treatments despite the ongoing research in oncology.^{31,33} A
501 cancer patient made reference to fluorouracil, a standard antineoplastic medicine which has been available
502 for the past 20 years and is still in use; hence can be considered as quite an old drug. He considered this as
503 a bad thing in the light that continuous research is being conducted in this field and remarked, *"Surely we
504 can do better than that!"*³¹

505 Discussion

506 The systematic review indicates that none of the published papers provided a standard definition of the
507 patients' lived experience with medicine. The systematic review showed that PLEM is a highly subjective
508 and complex concept, with a lot of considerations. Hence this systematic review supports the model
509 which offers a better framework for PLEM. The model developed by Mohammed *et al.* (2016) is
510 comprehensive and encapsulates the important aspects in PLEM. This systematic review identified lack of
511 studies with none of the identified studies making use of the PLEM model. Despite the inclusion of a
512 small number of studies in this systematic review, this has captured all the themes related to medicine-
513 related beliefs, medicine-taking practice and medicine-related burden mentioned in the model by
514 Mohammed *et al.* (2016). Hence, this model is likely to be transferable to the oncology setting with slight
515 modifications.¹⁷

516
517 Collectively researchers provided an extensive account on beliefs, practice and burden of patients
518 receiving different antineoplastic medicines. Patients considered this treatment either as hope or worse
519 than the illness itself. This systematic review showed that patients' treatment decision was highly
520 influenced by the healthcare providers' and carers' preferences. Patients should be informed about all
521 treatment options and be part of the treatment decision in order to be recognised as equal partners in the
522 healthcare team.^{38,39}

523 The introduction of oral antineoplastic agents has altered the outlook of provision of cancer treatment
524 from a controlled monitored procedure in hospital for parenteral treatment to individualised responsibility
525 in the patient's home. This created a major shift in the roles of healthcare professionals mostly doctors,
526 nurses and pharmacists onto patients and carers.⁴⁰ Experienced patients who had received different
527 antineoplastic treatments argued that intravenous chemotherapy necessitates an autonomous behaviour
528 solely for managing side effects. On the other hand, the medicine-taking practice together with the
529 monitoring of adverse effects of oral antineoplastic is more dependent on the patient's autonomy. This
530 systematic review showed that patients voiced their concern that information about treatment was given
531 by healthcare professionals at a time when they were not able to fully comprehend and pose the necessary
532 questions. Hence patients expressed their need of treatment-specific education in a consistent and
533 practical manner for the complex antineoplastic treatment regimens.⁴¹

534
535 Research showed that patient adherence to long term treatment was no more than 50% but seems to be
536 higher in case of antineoplastic treatment. Although there are multiple reasons for this, it is highly
537 associated with the perceived fatal implications of cancer.⁴² This was consistent with our systematic
538 review where patients were noted to be highly adherent to treatment. Patients noted that forgetting to take
539 the treatment was often due to an alteration in their daily routine such as going on vacation or visiting
540 friends. They also described of being in doubt whether they had taken the right amount of tablets or
541 whether they had failed to take the treatment at the exact time.^{32,35} Patients who had received various
542 antineoplastic treatments had a risk of developing more secondary effects which may result in lack of
543 adherence and poor concordance to the current prescribed treatment. Therefore, the patients necessitate
544 specific advice when changing from one medicine to another.³²

545
546 This systematic review identified misconceptions that patients had about treatment especially in relation
547 to efficacy. From a biomedical perspective, chemotherapy in oral formulation has similar efficacy as
548 parenteral and hence is certainly not associated to treat less 'serious' cancers. Other patients believed that
549 they were suffering from a milder cancer compared to other patients as they were receiving oral
550 chemotherapy.³¹ Patients did not always understand or were provided with the rationale behind certain
551 requirements of the treatment. For instance, breaks between treatments were either medically prescribed
552 interruptions according to treatment protocol or due to the occurrence of adverse effects. Patients
553 associated these breaks as periods of relief and freedom from constraints to the medicine plan such as
554 'holidays' or as burdensome periods with worsening of adverse effects and fear of recurrence.^{33,35} This
555 emphasised the importance of involving patients in decision making about their treatment and the
556 explanation of treatment.³²

557
558 During the treatment journey patients are not only experiencing physical effects but also psychological
559 effects with a myriad of emotions. As a result of fear of modification or discontinuation of treatment,
560 patients delay in reporting adverse effects to healthcare professionals.^{32,35} However, patients who
561 experienced minimal adverse effects thought that their treatment was not effective. This induced
562 unnecessary concern and stress to the patients.^{28,30}

563
564 Consistent with other studies, nausea and vomiting are the most common adverse drug reactions
565 experienced by patients. Studies showed that patients required increased doses of anti-emetic treatment in

566 order to manage these symptoms. Due to the common occurrence of adverse effects with antineoplastic
567 medicine, it is vital that patients would be able to identify these toxicities and be advised on what
568 measures to follow.^{29,36,41} Reasons provided by patients about lack of reporting of adverse effects were
569 uncertainty about severity of adverse effects, fear of withholding treatment and waiting for the next
570 appointment rather than contacting the healthcare professional immediately. Delayed reporting of adverse
571 effects to healthcare professionals may lead to a detrimental effect to the patients themselves.³²

572 Cancer treatment transformed and dominated the patient's social and family life. The patients
573 acknowledged support from family members, peers, support groups and healthcare professionals during
574 their treatment and also their need to develop coping skills.^{29,30,33,35,36} This will identify the importance of
575 the provision of holistic care to the patients with cancer at all stages of the treatment journey, taking into
576 consideration their physical, psychological, social and spiritual well-being. This systematic review will
577 empower healthcare professionals to consider all the aspects of PLEM in their practice in the area of
578 cancer treatment in order to help patients achieve a better quality of life during the treatment journey. The
579 complexity of cancer treatment necessitates more patient involvement. Interprofessional collaboration
580 between healthcare professionals in primary and tertiary settings together with the carer are needed to
581 ensure services that meet the patient's needs. Educational and motivational strategies adapted and re-
582 enforced at different time-points during the treatment are necessary to address issues particularly related
583 to aspects of burden.

584
585 Future research should focus on interventions that may be practiced by healthcare professionals to
586 enhance patient's empowerment and encourage patients to take more active role in their cancer treatment.
587 Studies should also be conducted on patients refusing to initiate or discontinue treatment with
588 antineoplastic medicines to understand their beliefs, perceptions and attitudes.

589 **Limitations**

590 This systematic review followed a comprehensive search strategy in six databases since their respective
591 inception. Identification of studies and data extraction was performed by 2 independent reviewers so as to
592 reduce bias and improve the rigour. However this systematic review has its limitations. The included
593 studies had to focus on the whole concept of PLEM, which means that all 3 themes of medicine-related
594 burden, medicine-taking practice and medicine-related beliefs had to be discussed in the same
595 publication. This is due to the overwhelming amount of publications focusing on one particular aspect and
596 to offer researchers a broad complete picture of the inter-relationship between the 3 themes in a particular
597 setting experienced by the patient. Studies that assess adherence to antineoplastic agents have been
598 conducted but this systematic review included only those studies that also involved medicine-related
599 beliefs and medicine-related burden. Therefore adherence to antineoplastic medicines is being discussed
600 in relation to a holistic aspect of the patients' lived experience with medicines. This systematic review
601 relied on secondary data and combined data from different methodologies and of different quality. Hence
602 this resulted in the provision of limited detail to the authors and increased the element of bias in the
603 interpretation of the results. The review only included studies published in English, which might have
604 resulted in publication bias. In addition, grey literature including conference abstracts was not included in
605 this review. Since the review included studies conducted in different countries and settings, patients
606 provided their experiences based on their healthcare systems which may vary from country to country.
607 Although all patients were suffering from solid tumours and receiving antineoplastic medicines, different
608 cancer types may require diverse treatment regimens which vary in complexity. This may lead to
609 increased heterogeneity of the review results. Various confounding factors such as patient characteristics,
610 comorbidities, environmental factors and time-points in the treatment journey when the study was
611 conducted may have affected the findings.

612 **Conclusion**

613 This systematic review elicits a comprehensive assessment of the patients' needs which is crucial for
 614 patient-centred care. The adapted model of PLEM for patients with solid tumours receiving antineoplastic
 615 medicines explains the dynamic processes and socio-cultural influences that affect medicine-related
 616 beliefs, medicine-taking practice and medicine-related burden. It shows that patients undergo a
 617 continuous process of reinterpretations of the phenomenon along the treatment journey.

618
 619 Patients are experts by experience as they provide a unique perspective on their disease state and required
 620 care. The understanding of the patients' experience with the antineoplastic medicines sheds light on the
 621 patients' needs and support services needed during this journey. This will ultimately lead to better health
 622 outcomes and improved quality of healthcare services.

623
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Table 1 Information about the studies included in the systematic review arranged in chronological order

Study [Authors, year, country]	Stated aim(s) and objective(s)	Setting and number of respondents	Study design	Method of data collection	Data analysis	Key findings
Yokoyama dos Anjos and Zago, 2005, Brazil	To understand the meaning of the chemotherapy from the patient's point of view	Oncology hospital and patient's home, n=1	Qualitative ethnographic case study	<ul style="list-style-type: none"> • Semi-structured interviews • non-structured observations • patient's field diary 	Interpretative anthropology	<p>Seven unities of meaning were identified:</p> <ol style="list-style-type: none"> 1. discovery of cancer and search for assistance, 2. knowledge about cancer, 3. trajectory of chemotherapy, 4. networks of support, 5. lack of control of one's life, 6. uncertainty about the future, 7. expectation in the future. <p>The patient's view on her experience with cancer chemotherapy as "the loss of the control over one's life" were summarised. The study emphasised the need for nurse care to follow up the patient throughout the whole process and offer resources to the patient to resume control of her life during this critical period.</p>
Bergkvist and Wengstrom, 2006, Sweden	To acquire a deeper understanding of cancer patients' symptom experiences with focus on nausea and vomiting during chemotherapy treatment and the consequences these have on daily life	Oncology hospital, n=9	Qualitative study	Semi-structured interviews	Content analysis	<p>Five main categories in the experience of chemotherapy treatment were identified:</p> <ol style="list-style-type: none"> 1. before cancer diagnosis, 2. being ill—consequences on daily life, 3. going through chemotherapy treatment, 4. coping with treatment, 5. after treatment—looking forward to a normal life. <p>The study describes that the experience of receiving chemotherapy is a process that evolves over time. The findings suggest that experiences of nausea and vomiting during chemotherapy treatment have a profound effect on the cancer experience and thus may influence future decisions relating to new treatment.</p>
Browall, Gaston-	To describe the experience of postmenopausal women	Oncology hospital and	Qualitative study	Narrative interviews	Content analysis	Four themes were identified:

Johansson and Danielson, 2006, Sweden	with breast cancer who undergo adjuvant chemotherapy treatment	patient's home, n=20		with one open question		<ol style="list-style-type: none"> 1. the fear of the unknown, 2. affects on body and mind, 3. to get by, 4. a transformed life. <p>The participants described feelings of imbalance in their relationships due to lack of support from those close to them. The support from healthcare professionals was experienced both positively and negatively; with most of the participants revealing variations in the healthcare professionals' attitude, knowledge, and empathy. Women who decided not to work during the treatment felt pressure from society and healthcare professionals to get back to work as soon as possible. The participants expressed a feeling of not being afraid of dying but wanted more time to prepare themselves.</p>
Bell, 2009, Canada	To explore patients' perceptions of adjuvant chemotherapy	Cancer support group, n=8	Ethnography	<ul style="list-style-type: none"> • Semi-structured interviews • participant observation at the support group meetings 	Thematic analysis	<p>Three themes were identified:</p> <ol style="list-style-type: none"> 1. Hurting the good cells & really hurting cancer cells, 2. Getting a "full dose", 3. Oral vs intravenous chemotherapy. <p>A cultural model of chemotherapy was noted which stressed the value of suffering and pain as means of monitoring treatment effectiveness and even the possibility of cure. This framework differs from biomedical understanding of treatment in various aspects, with implications on anxiety levels experienced by the patients and the risk of recurrence.</p>
Regnier Denois, Poirson, Nourissat, Jacquin, Guastalla and Chauvin, 2011, France	To describe and understand existing practice for capecitabine and to evaluate the perceptions and descriptions of patients and oncologist about the prescription of capecitabine	2 oncology hospitals, n=45	Qualitative study	<ul style="list-style-type: none"> • Semi-directive interview technique to patients and oncologists • observational phase with patients • focus group interviews with patients 	Content analysis	<p>Adherence, which in this study was defined as being against not taking their treatment, generally seemed satisfactory. Results showed a wide diversity in the prescribers' practices, who often made decisions based on their experience of practice guidelines for intravenous chemotherapies. Although the results for the patients do not suggest deliberate non-adherence, they show poor observance of the dose schedule. The study identified the patient's inability to recognise and report important signs of harmful toxicity.</p>

Gerber, Hamann, Rasco, Woodruff and Craddock Lee, 2012, United States	To gain insight into patient perceptions of maintenance chemotherapy for advanced non-small cell lung cancer	Hospital (inpatient), n=47	Qualitative study	Focus group	Thematic content analysis	Five themes were identified: 1. survival benefits, disease control, and “buying time”, 2. the importance of “doing something”, 3. quality of life concerns, 4. the role of provider opinion/preference, 5. the importance of logistics.
Timmers, Boons, Moes-ten Hove, Smit, van de Ven, Aerts, Swart, Boven and Hugtenburg, 2015, Netherlands	To assess adherence to erlotinib treatment and evaluate experiences of patients as well as the relationship between medicine adherence, erlotinib exposure and symptoms	12 hospitals, n=62	Prospective observational cohort study	<ul style="list-style-type: none"> • Patients reported questionnaires • patients’ medical file • adherence measured with medication event monitoring system (MEMS) • blood samples 	Mann–Whitney test, Fisher exact test	According to the Belief about Medicines Questionnaire (BMQ), 40% (n=25) of patients were classified as “accepting” treatment with erlotinib. 55% (n=34) of patients who had started their treatment with erlotinib, considered their treatment to be of high necessity and high concern. MEMS data of 55 patients revealed a mean adherence of 96.8 ± 4.0 %. Over one-third of patients had an adherence rate <95 %. At 1 month, 21 % of patients did not always correctly take erlotinib without food. Associated risk factors were older age, suboptimal adherence, ocular symptoms and stomatitis (all $p < 0.05$). After 1 month of treatment, fatigue (91%) and rash (86%) were the most common symptoms reported. AUCs of erlotinib was higher in patients with rash and patients with moderate–severe anorexia (both $p < 0.05$).
Gassmann, Kolbe and Brenner, 2016, Switzerland	To explore the experiences of patients undergoing oral chemotherapy and investigate the impact of oral chemotherapy on their daily life	Outpatients clinic of an urban hospital, n=6	Grounded theory	Open interviews	Constant comparison coding and categorising in line with paradigm model	Participants reported physical and emotional reluctance towards oral chemotherapy as well as toxic side effects. Feeling responsible emerged as a core phenomenon with influences from context and intervening conditions. All participants intended to adhere to treatment despite being a challenging task due to complex treatment regimen. Belief in the effectiveness of the therapy was a strengthening factor. Participants struggled between the necessity of adhering to oral chemotherapy and the practicality as well as emotional difficulties of daily life. Hence, patients developed coping strategies during the treatment journey. In consequence, oral chemotherapy was found to be

						omnipresent by determining the participants' thoughts and daily life.
Komatsu, Yagasaki, Yamauchi and Yamauchi, 2016, Japan	To explore the experiences of patients with breast cancer who had received chemotherapy to understand how they perceived the impact of the treatment on their daily lives	Outpatients of breast or oncology centre clinic in a hospital, n=17	Grounded theory	Semi-structured interviews	Analysis of transcripts by first coding and then labelling the meanings. Subcategories were identified to lead categories. Core categories emerged by connecting categories and subcategories.	Patients created personal safety nets for physical, emotional and social contexts during chemotherapy, even though they found everyday life to be more challenging because of the disease and side effects. Through their safety nets, the participants felt more confident and in control of their lives and were willing to take a positive approach towards making their lives meaningful. In anticipation of side effects of chemotherapy, participants "hibernated" and consumed minimal amount of energy. They also created a protective inner space in which they were able to tolerate fear and anxiety and exert self-control. In maintaining their daily routines, patients felt more confident to balance their lives and illness and helped them to tolerate uncertainty.
Timmers, Boons, Mangnus, van de Ven, Van den Berg, Aart B, Swart, Honeywell, Peters, Boven, Hugtenburg, 2016, Netherlands	To get insight into patients' experiences with the use of capecitabine in daily practice and the various aspects that govern adherence	10 hospitals, n=92	Prospective observational cohort study	<ul style="list-style-type: none"> • Adherence assessed using a pill count, pharmacy data and dosing information obtained from the patients' medical file (PPP method) • self-reported adherence measured using the Medication Adherence Report Scale. • patients reported questionnaires • blood samples 	X ² -test, Fisher's exact test, Logistic regression	Most patients (91%) had an adherence rate of ≥ 95 and ≤ 105 %. Symptoms were frequently reported and the dosing regimen was adjusted by the physician at least once in 62% of patients (n=57). According to BMQ, 50% (n=46) of patients were classified as "accepting" capecitabine. These patients were associating their medicine with a high necessity and low concern prior to initiation of treatment. 44% (n=40) patients who had started their treatment with capecitabine considered their treatment to be of high necessity and high concern. According to the Brief Illness Perception Questionnaire (IPQ), patients were found to believe that treatment with capecitabine will help their illness and achieve treatment control. This is evidenced by the mean value which improved from baseline (7.8 \pm 1.8) to cycle 5 (8.0 \pm 1.6).

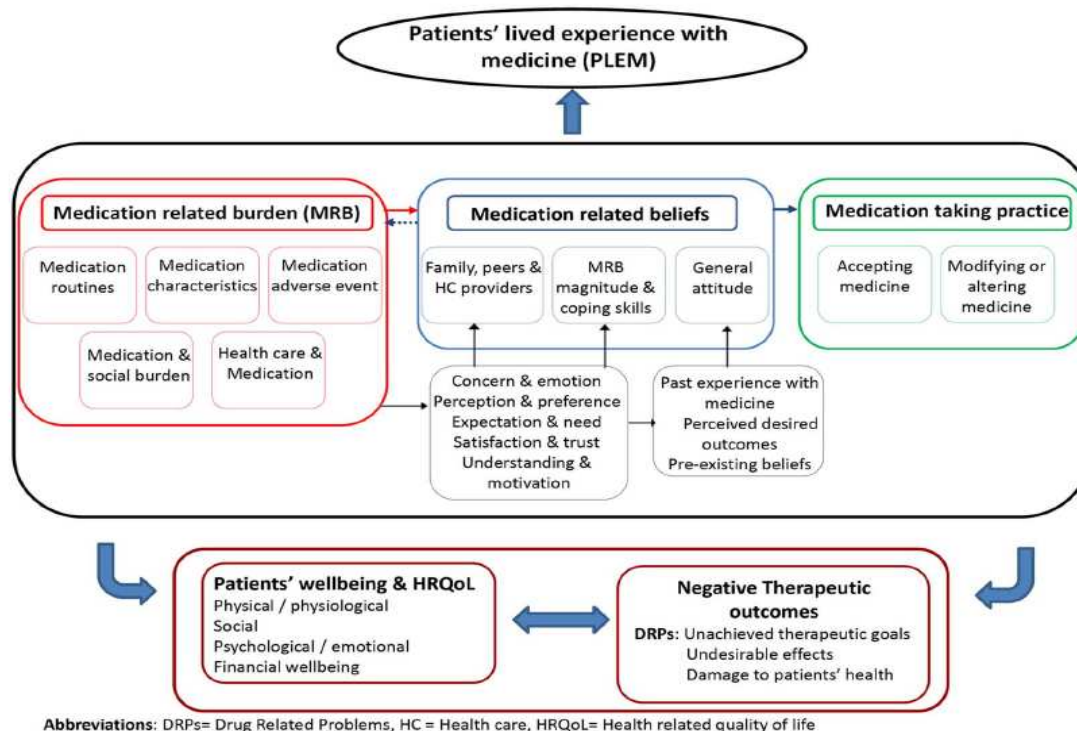


Figure 1 Conceptual model of the patients' lived experience with medicine (PLEM) as developed by Mohammed *et al.* (2016). The model shows the complexity of PLEM and an inter-relationship between medicine related burden, medicine related beliefs, medicine taking practice.

Adopted from: Mohammed MA, Moles RJ, Chen TF. Medication-related burden and patients' lived experience with medicine: a systematic review and metasynthesis of qualitative studies. *BMJ Open.* 2016;6:e010035.

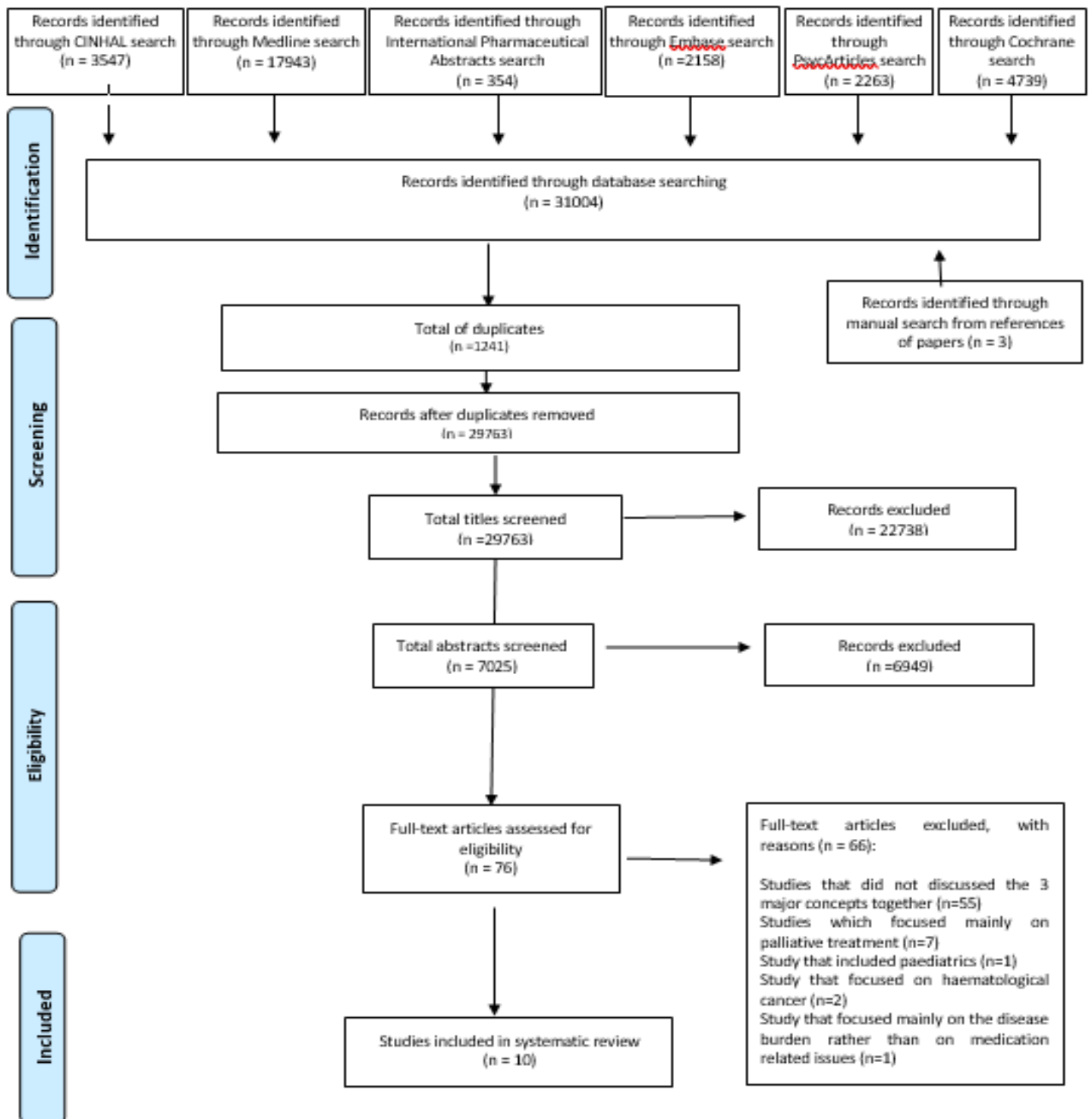


Figure 2 Prisma flow diagram showing the inclusion and exclusion of studies identified for the systematic review. Reasons for the studies being excluded are also provided. Adapted from Prisma 2009 flow diagram.²⁷

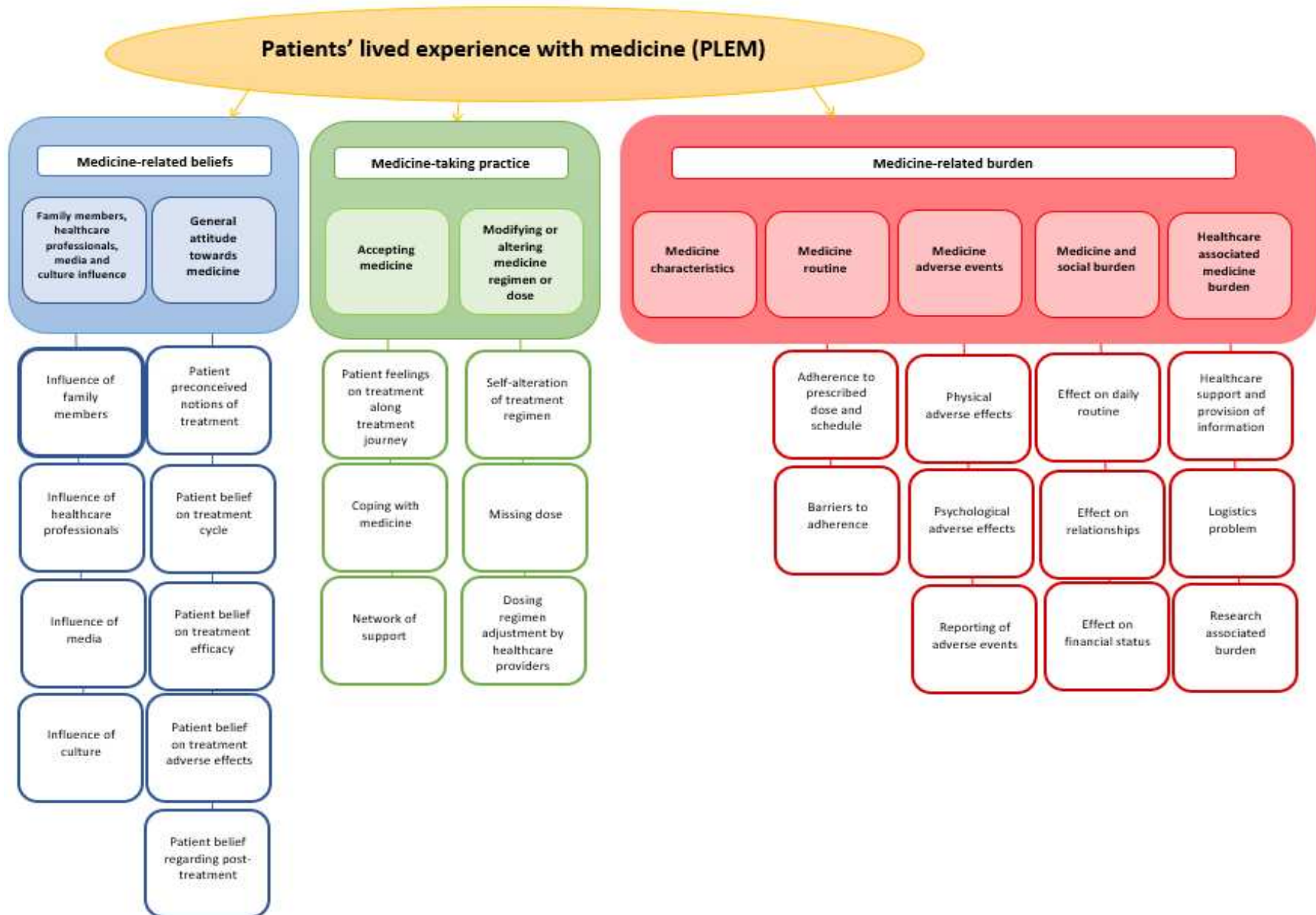


Figure 3 An adapted model of PLEM for patients with solid tumours receiving antineoplastic medicines