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# Exploring perceptions and experiences of oral chemotherapy in people with cancer

Ana Costa, Caroline McGraw

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**Correspondence**
caroline.mcgraw.1@city.ac.uk

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## Abstract

The increasing use of oral chemotherapy treatment for cancer offers benefits in terms of care closer to home. However, these formulations are associated with a significant number of adverse events. One source of error is patient non-adherence, resulting in treatment resistance, increased toxicity, disease progression and even death. This literature review explores how people with cancer perceive and experience adherence to oral chemotherapy. Thematic analysis identified four main themes: my own way of doing things, understanding how oral chemotherapy works, not being alone and things beyond my control. Barriers to adherence included health beliefs, medication side effects and lack of access to ongoing advice and support. The authors argue that adherence to oral chemotherapy is a complex and multifaceted phenomenon. They recommend that healthcare practitioners should provide personalised counselling at the point of prescription and review, as well as accessible support between appointments.

## Author details

**Ana Costa, haemato-oncology nurse, cancer services, Barts Health NHS Trust, London, England; Caroline McGraw, lecturer (public health), City University London School of Health Sciences, Health Service Research and Management, London, England**

## Keywords

**adherence, cancer, cancer nursing practice, chemotherapy, literature review, drug administration**

## Background

Treatment options for people with cancer have developed significantly over the past 20 years (Department of Health 2011, NHS England 2014), and developments in drug delivery include oral chemotherapy. While chemotherapy has traditionally been administered intravenously (IV), more than 20% of drugs can now be given orally (Findlay et al 2008). Unlike IV drugs, which need to be administered in clinical settings, oral chemotherapy can be self-administered at home (Gater et al 2012, Wood 2012), which offers several advantages, such as allowing care closer to home and improved cost-effectiveness (Oakley 2010). Consequently, clinical commissioning groups are encouraged to develop safe models for the dispensing and supply of oral chemotherapy in primary care settings (Williamson 2011). It is estimated that 50% of chemotherapy formulations being developed are for oral administration (Given et al 2011, Bassan et al 2014).

Despite these developments, oral chemotherapy is associated with a significant number of adverse events, in primary and secondary care (Medicines and Healthcare Products Regulatory Agency 2008).

In primary care, one source of error is patient non-adherence. Adherence is the extent to which patients can follow recommendations for prescribed treatments. Non-adherence can be intentional or non-intentional. In relation to oral chemotherapy it can result in treatment resistance, increased toxicity, disease progression and even death (Moore 2009, Mitchell et al 2014). It is also associated with increased hospital admissions, longer hospital stays and additional visits to the GP (McCue et al 2014). Despite the gravity of a cancer diagnosis and expectations that patients will be highly motivated to take their medication as prescribed, Hohneker et al (2011) found adherence to oral chemotherapy was similar to adherence to long-term medication for non-cancerous disease, with rates ranging between 50% and 70%.

The aim of this literature review is to explore how patients with cancer experience and perceive adherence in the context of self-administration of oral chemotherapy. This will be of interest to nurse prescribers who might review patients' prescribed oral chemotherapy and assess their suitability for continued therapy, and practitioners and managers

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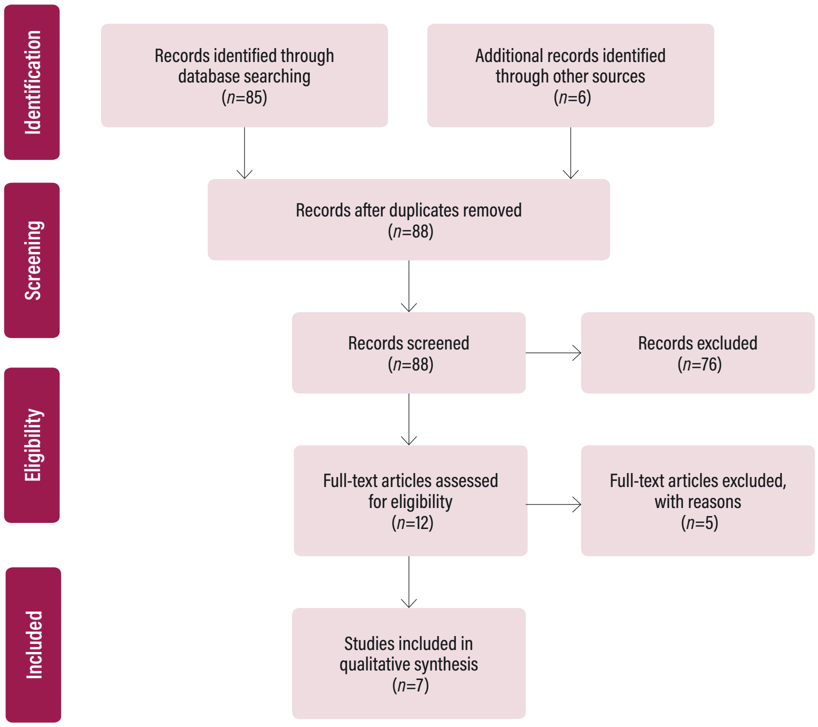
looking to develop personalised care and support services for people treated at home with oral chemotherapy.

## Literature review

The review included only qualitative studies that explored the experience of people with cancer. Studies that adopted a purely quantitative approach were excluded and only qualitative data from mixed methods research were included. Participants had to be adults with a cancer diagnosis who were self-administering oral chemotherapy at home. Studies that sampled patients, healthcare providers and/or family caregivers were included if patient-reported experiences could be extracted from the analysis.

Keywords were developed to describe the sample (patients with cancer), phenomenon of interest (adherence to oral chemotherapy), design (qualitative interviews and focus groups), evaluation (experiences, perceptions and attitudes) and research type (qualitative studies). Four electronic databases – Academic Search Complete, CINAHL, MEDLINE and EMBASE – were searched from January 2000 week 1 to May 2016 week 4. Searches were limited to studies published in English, with no restriction on location. The titles and abstracts generated by each search were reviewed and potentially relevant full-text articles were obtained. The reference lists of retrieved articles were also scrutinised to identify other appropriate studies. Figure 1 depicts the flow of information through the review.

Figure 1. Flow of information through literature review



Seven papers addressed the aim of the literature review (Table 1), and only qualitative data collected from patients were included, in line with the inclusion criteria. Participant characteristics are summarised in Table 2.

## Findings

Findings from the collective research were synthesised using a thematic approach to qualitative synthesis, which involved familiarisation with the data, coding the data, searching for themes, reviewing themes, and defining and naming themes (Braun and Clarke 2006). Four themes were identified: my own way of doing things, understanding how oral chemotherapy works, not being alone and things beyond my control. These are explored below with selected explanatory quotes provided in Table 3. Two studies did not include direct patient quotes (Regnier Denois et al 2010, Bourmaud et al 2015).

### My own way of doing things

Participants expressed feelings of responsibility with regard to taking their medication as prescribed, and often devised unique ways of remembering to take it (Simchowitz et al 2010, Eliasson et al 2011, Regnier Denois et al 2011, Wu et al 2015, Bourmand et al 2015, Gassmann et al 2016) and managing the negative effects (Simchowitz et al 2010, Eliasson et al 2011, Regnier Denois et al 2011, Wu et al 2015). In relation to the former, participants described various strategies, such as using calendars and diaries to keep track of treatment cycles, programming alarms on mobile phones, counting pills and leaving tablets in a visible location. Establishing routines was very important for some patients, who made their administration of treatment automatic to a large extent. However, with this came the risk that changes in their daily routine could cause medicines to be forgotten.

Side effects had a major influence on quality of life and many participants reported problems such as diarrhoea, constipation, nausea, fatigue, skin changes and loss of appetite. Some participants sometimes delayed or avoided discussing these with their clinicians, because they did not want to bother them or they feared treatment might be withdrawn. Others did not mention side effects to their healthcare practitioners because they felt able to manage them using a combination of willpower, over-the-counter treatments and complementary medicines. Other coping strategies included changing the timing of doses or intentionally omitting them to enjoy some respite from the symptoms. A minority of participants found symptoms so intolerable that they decided to stop taking the oral chemotherapy.

Participants reported that the way they managed their treatment changed over time. One study developed a typology to describe patients depending on what they were focusing on at any one time – those whose focus was on survival or quality of life, or on a balance between the two (Verbrugghe et al 2016). While oral chemotherapy dominated the lives of all participants, this typology helps to understand the ways in which patients manage their treatment at different times in their cancer journey. For example, patients whose primary focus was survival gave treatment the highest priority, and adopted strategies to support adherence, but also tended to under-report side effects. Patients whose focus was on quality of life were more willing to omit or delay treatment doses to reduce the impact of side effects on their daily lives.

## Key points

- Increasing use of oral chemotherapy at home offers a number of benefits
- Adherance to oral chemotherapy is a complex and multi-faceted phenomenon
- These formulations can be associated with patient non-adherance in primary care
- To resolve this issue, health practitioners should provide personalised counselling and accessible support between appointments

**Table 1. Studies included in the literature review**

| Authors and year of publication | Aim | Methods | Location and study population | Data collection |
|---|---|---|---|---|
| Bourmaud et al (2015) | To identify patient adherence profiles in relation to (oral chemotherapy) | Mixed methods | Lyon, France<br>16 adult patients | In-depth interviews using a topic guide |
| Eliasson et al (2011) | To explore the experiences of adherence to (oral chemotherapy) | Qualitative | London, England<br>21 adult patients | In-depth interviews using a topic guide |
| Gassmann et al (2016) | To explore the experience of patients undergoing oral chemotherapy | Qualitative | Switzerland<br>6 adult patients | Autobiographical narrative interviews |
| Regnier Denois et al (2010) | To describe and understand existing practice for (oral chemotherapy) in metastatic breast and colon cancer | Qualitative | Rhône-Alps region, France<br>42 adult patients | In-depth interviews using a topic guide and focus group interviews |
| Simchowitz et al (2010) | To better understand how patients and their caregivers manage oral chemotherapy | Qualitative | Boston, US<br>15 adult patients and 3 parents | Focus groups |
| Verbrugghe et al (2016) | To gain insight into (non) adherence behaviour in patients taking oral (chemotherapy) | Qualitative | Belgium<br>30 adult patients | In-depth interviews using a topic guide |
| Wu et al (2015) | To understand patients' experiences of chronic myeloid leukaemia (and oral chemotherapy), including identified barriers to adherence | Qualitative | Melbourne, Australia<br>16 adult patients | In-depth interviews using a topic guide |

**Table 2. Participant Characteristics**

| Author(s) and year of publication | Age range (years) | Oral chemotherapy drug prescribed | Diagnosis |
|---|---|---|---|
| Bourmaud et al (2015) | 59 (average) | Capecitabine | Breast or colon cancer |
| Eliasson et al (2011) | 26-70 | Imatinib | Chronic myeloid leukaemia |
| Gassmann et al (2016) | 36-77 | Vemurafenib, capecitabine, abiraterone, erlotinib | Lung, colon or prostate cancer |
| Regnier Denois et al (2010) | 65.4 (mean) 45-87 | Capecitabine | Breast or colon cancer |

**Table 3. Selected explanatory quotes for main themes**

| | |
|---|---|
| **My own way of doing things** | |
| Remembering to take medication | But the tablets, no, I don’t forget. It’s part of my daily routine, like cleaning your teeth or combing your hair. (Eliasson et al 2011) |
| | It gets tedious, that you HAVE TO. Also if you don’t have other plans you have to get up at 7am so that you can take the pills at 8am. If you get out of the normal rhythm, for example if I go out or want to go for a visit, I have to remember to take them [the pills] with me. (Gassmann et al 2016) |
| Managing side effects | The oncologist said that surgery was not an option any more, that they only could give medication. And then I thought: ‘I have to make sure that the tumour will shrink’... Even when side effects are so intense, I wait to report them to the hospital until I really can’t hold on any more. (Verbrugghe et al 2016) |
| | I thought there was no way I was going [on holiday] and being tired. So I did actually stop taking the tablets for a week before I went. (Eliasson et al 2011) |
| **Understanding how chemotherapy works** | |
| The significance of taking doses at the right time | All I know is that... my medical oncologist prescribed it for me and because I have confidence and I’m not educated in the medical field... I’m taking it. (Simchowitz et al 2010) |
| | I wouldn’t have thought it would have had that major impact [to miss doses]. I believe you still have a lot of medicine in your body system. So I think you are still topping up, keep topping up. (Eliasson et al 2011) |
| | I said I missed one and they said ‘Yeah, don’t worry about it too much, just try and take them as soon as you can’. So I’m not too worried about missing one. (Wu et al 2015: PT10) |
| Side effects | I don’t think that they, you know, prepared us for what kind of journey we are gonna go on. (Simchowitz et al 2010) |
| | Sometimes when you’re talking to the GPs or even chemists, like you know more about CML [chronic myeloid leukaemia] than they do. (Wu et al 2015) |
| **Not being alone** | |
| The importance of family and friends | You’ve got to absorb so much... when you hear some of the news. So when you have that secondary person there, they can absorb something. (Verbrugghe et al 2016) |
| | My wife is quite good at nagging me in terms of taking the medication, so that is quite a good prompt. (Eliasson et al 2011) |
| | Yeah, you feel a bit like a sack of potatoes sometimes. You sit around and see your wife having stress with the kids, but you can’t just jump up and do something. (Gassmann et al 2016) |
| Regular reviews with healthcare practitioners and access to advice and support | I do feel guilty ringing the doctor direct when it might be something that I consider small like... when I’m fasting, how am I going to take my drug? (Wu et al 2015) |
| | It depends on me to get in touch with them. I would much prefer somebody to call me every one or two weeks, a nurse practitioner, and say ‘Tell me what’s going on’. Rather than me trying to determine ‘Well... am I just imagining this damned thing? Is it a side effect? I’m gonna call these people again?’ (Simchowitz et al 2010) |
| | When I vomited, the information wasn’t there; do I take another dose, don’t I, will I overdose? (Wu et al 2015) |
| | If you have any questions, they are there. You never feel alone. I think that’s very important to many patients. You do not have the feeling to be just one of many and if you have any questions, you also get the chance to talk about it. (Verbrugghe et al 2016) |
| **Things beyond my control** | |
| Dispensing delays | They would say, like, ‘We can only give you half of it today. We ran out’. So, sometimes I would have to come back like two or three times a week to get the full medication. But... that’s not happening as much, thank God. (Simchowitz et al 2010) |
| | The pharmacy had no medication for me, so I went for nearly a week with no medication. (Eliasson et al 2011) |
| Forgetfulness | And sometimes you just forget. It’s very strange. It’s almost a surprise when you don’t take it. (Eliasson et al 2011) |
| | I suppose it’s all into routine like and that’s where sometimes if I’m distracted I can forget. (Wu et al 2015) |

Lastly, patients whose focus was achieving a balance between survival and quality of life engaged with healthcare providers and negotiated changes to their regimen (Verbrugghe et al 2016).

### Understanding how chemotherapy works

Participants in the studies reviewed discussed their chemotherapy schedules. One important issue in relation to how chemotherapy works was understanding the significance of taking doses at the right time (Simchowitz et al 2010, Eliasson et al 2011, Regnier Denois et al 2011). Oral chemotherapy doses are set to ensure sustained and mild plasma concentrations. Some participants understood the need to take their medication at the right time to avoid toxicity while ensuring the treatment was effective. Others suggested they always took their medication at the right time because they were conformist by nature.

In contrast, a number of participants missed doses or took them at the wrong time. Some became very anxious about missing a dose, but most felt occasional departures from the regimen were unlikely to have negative effects. In general, changes to the regimen were not reported routinely to healthcare practitioners, and when they were reported, pre-existing perceptions about the limited significance of this were often reinforced by clinicians who minimised the consequences. Perceptions were further enforced by the absence of immediate consequences, such as feeling more unwell, or in the medium term in blood test results.

Another issue in relation to knowing how oral chemotherapy works was understanding the significance of side effects (Simchowitz et al 2010, Regnier Denois et al 2011, Verbrugghe et al 2016). Some participants perceived these as a sign that the treatment was working, but many felt that they were not given sufficient information about it. Some also complained that when they approached community pharmacists and GPs the information they were given was insufficient. As previously stated, side effects were often endured or self-managed, though they can be an indicator of harmful levels of toxicity, and some participants wanted more information to help them differentiate between common side effects and red flag signs and symptoms.

### Not being alone

The ability to deliver oral chemotherapy at home afforded participants greater freedom than regimens administered in hospital. However, this required the involvement of family and friends in care provision, scheduling regular reviews with healthcare practitioners, and access to ongoing medical advice and support.

The importance of social support was emphasised in nearly all the studies (Simchowitz et al 2010, Eliasson et al 2011, Regnier Denois et al 2011, Bourmaud et al 2015, Wu et al 2015, Gassmann et al 2016). During periods of fatigue, participants described how family and friends helped them with everyday activities. Family and friends also helped synthesise complex information and supported adherence by prompting them to take medication. Participants without close family and friends talked about shouldering the burden of their illness and treatment alone.

The value of regular reviews with healthcare practitioners, and access to ongoing advice and support, was highlighted by participants in a number of studies (Simchowitz et al 2010, Regnier Denois et al 2011, Wu et al 2015, Verbrugghe et al 2016).

Most participants reported seeing a doctor or nurse regularly, although the intervals between appointments varied. Appointments were typically used for tests or procedures, and were an opportunity to discuss treatment issues. Participants said they were always instructed to contact their healthcare practitioners if problems arose between appointments. Some participants felt comfortable contacting their providers, who they found accessible and quick to respond, but others were unsure whether their problems warranted contact, and wanted their healthcare practitioners to take the lead and check in with them between appointments. Additional information and advice was often sought from the internet, including cancer blogs, bulletin boards and cancer organisations.

### Things beyond my control

Participants in two studies recalled encountering problems in having oral chemotherapy dispensed in community settings (Simchowitz et al 2010, Eliasson et al 2011). These included delays in dispensing because chemotherapy was not a stock item.

**Table 4. Factors that influence adherence to medication**

| Patient-related factors | Therapy-related factors | Healthcare team-related factors | System-related factors |
|---|---|---|---|
| » Health beliefs<br>» Social support<br>» Forgetfulness | » Regimen complexity<br>» Medication side effects | Access to specialist knowledge | Dispensing delays |

Occasional forgetfulness was also reported as unavoidable and mainly related to changes in routine, such as going out of town or going on holiday. However, even without these disruptions, and despite efforts to remember, some patients occasionally forgot to take a dose.

## Discussion

The aim of this review is to understand how people with cancer experience and perceive adherence in the context of the self-administration of oral chemotherapy. Findings confirm earlier studies (Moore 2009, Hohneker et al 2011, Mitchell et al 2014) that suggested people with cancer can experience problems achieving adherence.

The World Health Organization (2003) argued that adherence to medication is a multidimensional phenomenon, determined by the interplay of four sets of factors – patient, therapy, healthcare team and system – and this review identified all four factors and subcomponents (Table 4). This section discusses three subcomponents – health beliefs, medication side effects and access to ongoing specialist knowledge – and the implications for supporting patients in clinical practice.

### Health beliefs

This is a subcomponent of patient factors. It is defined as personal convictions that influence health behaviours (Partridge et al 2002). None of the participants in the studies in the literature review questioned the necessity of their prescribed medication, but some missed doses or took them at the wrong time. The rationale given by those who intentionally failed to adhere was a desire for respite from side effects. Some of these participants are likely to have been aware of the implications of non-adherence, and chose a behaviour they believed maximised their quality of life. Other participants believed that missing occasional doses was not especially significant. It is unclear from the data whether they were poorly informed or in denial.

Health beliefs founded on inadequate knowledge are amenable to educational interventions involving individually tailored information provision and discussion (National Institute for Health and Care Excellence 2009). Healthcare practitioners should make every contact count (Public Health England 2016), and proactively seek opportunities to discuss adherence issues with patients. Exploring how oral chemotherapy affects patients' daily routines helps practitioners to identify conflicts, challenges and coping strategies, and to ensure that recommendations for improving adherence are grounded in reality. Listening to patients and acknowledging their experiences is crucial (King's Fund 2005). If denial is encountered, the literature suggests that practitioners should intervene by exploring emotional reactions, respond with empathy and gently challenge inconsistencies in patients' narratives (Sheahan and Kissane 2017).

### Medication side effects and access to ongoing support and advice

Medication side effects is a subcomponent of therapy factors, while access to ongoing support and advice is a subcomponent of healthcare team factors. Participants in the studies included in the literature review discussed unpleasant side effects associated with treatment. Some participants wanted more information about side effects, while others tolerated them beyond what was reasonable, and chose not to alert their healthcare practitioners because they feared treatment might be discontinued. In relation to the latter, some participants were at risk of severe toxicity, since some signs and symptoms, although not those reported in the studies reviewed, should be categorised as a red flag, including fever, chest pains and breathing difficulties, and require urgent treatment.

While medication side effects are discussed routinely with patients at the point of prescription and at review, there is growing interest in interventions intended to improve the management of side effects, and reduce the risk of adverse events between appointments. Some interventions are simple check-in phone calls by a nurse or pharmacist, while others are more complex and involve digital technologies. For example, Agboola et al (2014) described the development of ChemOtheRapy Assistant, a personalised mobile phone-based self-management application that helps patients to recognise signs and symptoms at an early stage, assess their severity and act appropriately.

## Conclusion

This literature review demonstrates the complexity of the factors involved in adherence to oral chemotherapy. People with cancer are not a homogeneous group in terms of their perceptions and experience of adherence to oral chemotherapy. As cancer care moves closer to home, much of the burden of care shifts to patients. In addition to personalised counselling at the point of prescription and review, it is imperative that healthcare practitioners provide accessible support to patients between appointments.

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