



ATLANTIS HEALTHCARE

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Summarized



From hospital to home: the changing therapeutic area of oncology

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Oral treatments are transforming cancer care, moving the administration of treatment from the hospital to the patient's home. This is shifting the responsibility for managing medications from healthcare professionals to patients, making adherence an important consideration.

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Executive summary

Good health outcomes for patients are dependent on a high level of adherence to oral anticancer treatments.

In 2008, cancer accounted for **13%** of all deaths worldwide.

In 2008, **12.7 million** new cases of cancer were reported worldwide.

An average non-adherence rate of **21%** has been reported to oral anticancer treatments.

New developments in cancer care are shifting the focus from treatment in a clinical setting to the patient's home. This has been reflected by the recent updates to the standards for the administration and management of chemotherapy by ASCO/ONS - where patient adherence is an important consideration.

Sub-optimal adherence compromises treatment efficacy, posing a significant threat to health and wellbeing.

Predictors of non-adherence to oral anticancer treatments include side effects, concerns about treatment, doubts about personal need for treatment and a lack of confidence in the ability to adhere long term.

Unintentional non-adherence, for example as a result of forgetting,

is also important. Influencing factors of the healthcare system may also play a role, including the physician's expertise, the consultation quality and the patient's satisfaction with their involvement in treatment decisions.

There have been few evaluations of strategies to facilitate adherence among patients taking oral anticancer treatments. However, promising interventions to improve adherence have included strategies to address the practical barriers to adherence, provision of information about treatment and side effects along with telephone follow-up.

The systematic development and evaluation of tailored interventions to address factors known to impact on adherence to oral anticancer therapies is now a priority.

In this report we look at the impact of non-adherence in cancer care, share insights from patients who have been prescribed such treatments and speak with a leading adherence researcher in oncology about findings from her latest studies. The report concludes with a summary of interventions that have been found to improve adherence to oral oncology treatments.

“Rates of non-adherence are similar to those found across many long-term illnesses, a fact that may be considered surprising given the seriousness of many cancers.”

Introduction: Adherence to cancer treatments

Cancer is a major threat to health and wellbeing. In 2008, cancer accounted for 13% of all deaths worldwide.[1] The numbers of people living with cancer continues to rise year on year. In 2008, 12.7 million new cases of cancer were reported worldwide.[1, 2] This figure is predicted to rise to 22 million new cases per year in 2030.[3]

Over the past decade, self-administered, oral treatments have become part of daily oncology practice. This trend is likely to increase as new targeted agents, currently in development, become commercialized.[4] Oral administration of anticancer treatments offers potential benefits over the intravenous route. Patients prefer oral chemotherapy, provided efficacy is not compromised. [5, 6] Reported benefits include greater convenience, being able to take treatment at home, a greater sense of control and less disruption to daily life.[5, 7] Benefits to service providers may include reduced healthcare costs resulting from fewer patient visits to outpatient clinics.[8, 9]

There are also significant challenges associated with oral anticancer therapies. As with intravenous chemotherapy, side effects are common and can be severe. Newer, targeted therapies may avoid some of the side effects associated with traditional chemotherapy and have been reported to be more tolerable by patients,[10] however these treatments have their own side effect profile. The prompt detection and management of adverse effects is therefore essential.

The increasing use of oral agents moves the administration of cancer treatments from the supervised hospital setting into patients' homes, shifting responsibility on to patients and carers. As a result, there has been increased focus on patient self-management and medication adherence in oncology.[11, 12]

Adherence is the extent to which patients take their medication in the way in which it has been prescribed. Non-adherence can occur when a patient takes more medication than recommended. This is particularly relevant when there are prescribed cycles

of X weeks on treatment and Y weeks off treatment, which is highly dangerous in oncology where the treatments can be toxic with very narrow therapeutic indexes. Non-adherence occurs when doses are missed, taken in the wrong quantity, at the wrong time [11] or without following food restrictions or requirements. Non-persistence occurs when patients do not take their medication for the full duration of its prescription.[13]

Reviews of studies reporting on non-adherence to oral anticancer treatments have found a wide variation in rates (0-84%) reflecting a variety of different definitions and measures of adherence.[11, 14] An average non-adherence rate of 21% has been identified.[15] Rates of non-adherence are similar to those found across many long-term illnesses, a fact that may be considered surprising given the seriousness of many cancers.[16] Rates of non-persistence with long-term treatments for cancer tend to increase over time. This was demonstrated in a retrospective cohort study of women with breast cancer living in Tayside, Scotland - 10% of women had discontinued tamoxifen within 1 year of treatment, rising to 51% within 5 years.[17]

A high level of adherence to oral anticancer treatments is required for success. Patients with chronic myeloid leukemia (CML) who took fewer than 85% of prescribed doses of the oral anticancer agent imatinib were less likely to achieve a complete cytogenetic response (CcyR) resulting in treatment failure.[18] The importance of a high level of adherence to tamoxifen was demonstrated in a retrospective cohort study of 1633 women with breast cancer. There was an increased risk of death among women who took less than 80% of their treatment. Increased duration of tamoxifen treatment reduced the risk of death.[17]

In addition to the impact on health and survival, non-adherence to oral anticancer treatment has been associated with increased healthcare costs, including more visits to the doctor, longer and more frequent hospital stays.[19]

Insights from patients

Some of the challenges facing patients taking oral anticancer treatments were elicited in interviews with patients receiving imatinib for the treatment of chronic myeloid leukemia (CML).^{[24]*}

Patient one:

This man described the difficulty that many patients have in accurately estimating their own adherence behaviour. Having received his medication in a container with a microchip within the lid to monitor each time the bottle was opened, the patient was able to gain an accurate assessment of his own adherence.

I've taken imatanib 600mg for a few years now. I knew I was missing days but I didn't realize how much I was missing. I asked how much I'd actually been missing. It worked out that I'd been missing 20% of the doses over a 3 month period. So it wasn't working quite as well as it could do.

Having accurate feedback on his adherence allowed him to take steps to address the difficulties he was having with his medication. The patient was able to discuss the side effects he was experiencing with his healthcare professional and find a solution.

So they said we'll bring your dose down to 400mg, make sure you take it every day. The side effects haven't been quite so bad, so it's been more manageable to do that.

Patient two:

This case study illustrates how erroneous beliefs about medicines could impact on adherence. This patient describes the misconception that missing a few doses would not make a difference.

I wouldn't have thought it would have had that major impact [to miss doses]. I believe you still have a lot of the medicine in your body system. So I think you are still topping up, keep topping up, if you've missed three, four days, then I don't know. . .

Patient three:

This patient thought that health professionals had reinforced the message that non-adherence was not a problem.

“...I am tending to miss more now, because at first I thought it was sort of life or death if you miss a tablet, but now the doctors have told me, you know, it's not a big thing if you miss one or two, so I tend to not worry about it as much as I did previously.”

Patient four:

Several patients described changes in their pattern of adherence over time.

“I think I stuck to it more rigidly at the beginning, yes, I think so... And since, when you get into cytogenetic remission and molecular remission and everything, you sort of tend to breathe a sigh of relief in some ways, because you sort of think, OK, it's working...”

Patient five:

Side effects of medication had a major impact on the lives of many of the patients interviewed. This patient describes how she altered the dose - and then temporarily stopped taking her medication - when side effects felt unbearable.

“I had a sort of fluey, buggy, thing... I was just taking [imatinib] and literally being ill... so I did try dropping the dose down, but it didn't make any odds, so I did stop taking it for about a week.”

She also described taking a 'drug holiday' to avoid experiencing side effects on her holiday.

“Because of travelling... 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, and I didn't take them for the first half of the week I was there...”

*The published patient quotes in this report (one to five) have been published in previous studies.^[24]

Insights from a leading researcher

Dr Lina Eliasson, a health psychology specialist who has conducted research with cancer patients shares insights on the challenges these individuals face when taking oral anticancer treatments.

Commitment to life-long treatment

The vast majority of patients respond to the treatment and they do really well. This means that quality of life is now an important consideration in this therapeutic area - given that patients will be taking this medication for the rest of their lives.

Side effects are a big issue and directly impact adherence

We found that the most common reason why patients chose not to take the treatment was to manage side effects. A lot of the new oral treatments have lower grade side effects than traditional chemotherapies, which means that sometimes doctors don't take them seriously enough. But actually, for a patient who has to deal with lower grade side effects like fatigue or diarrhea, this is a big issue. A key aspect in terms of supporting adherence in CML patients is to manage side effects appropriately.

Doctors inadvertently reinforce non-adherence

When people respond well to treatment they may take the occasional drug holiday. Some of them take the drugs Monday to Friday and tend to miss the weekends. This has been reinforced by doctors not emphasising how important adherence is. So the patient will call up and say 'I've just missed a dose - I don't know what to do' and the clinician will say 'don't worry about it, it doesn't really matter if you miss a dose'.

Unintentional non-adherence is common

We found that the most common reason for missing doses was simply forgetting. It is important to make patients aware of adherence aids that might be available to them, such as alarms or monitor dosing boxes.

Lack of tailored adherence support

Most hospitals do not offer patients any adherence support and are not set up with the necessary protocols to manage patients taking oral oncolytics. I guess most places have a leaflet about the importance of adherence but that's it. Patients don't have anyone that they can go and talk to.

The importance of good communication

It is essential that patients feel they can report instances of non-adherence and talk openly about the way they are managing their treatment - highlighting the acute importance of open dialogue between the patient and HCP. It's a fine line between being open and honest with patients and being realistic about the risks they face, without frightening them. HCPs need to understand how the patient is managing their treatment, especially if they are not responding well to the medication.

Unmet needs

There is a need for hospitals to establish standard protocols for managing patients on oral oncolytics. This should include monitoring and supporting patients' treatment adherence. Patients need to have ready access to support services and advice on how to better manage their treatments.

Growing awareness of the problem of non-adherence

Until now, non-adherence hasn't been a focus for HCPs and patients. But things are changing and HCPs are becoming more aware of the resulting implications of non-adherence and are eager to address the problem.

The importance of informed choice

Everyone has the right to not adhere if they don't want to, but patients have to be informed to make that decision. If they choose to adhere to their treatment, then we must provide them with the needed support to help them adhere to their treatment and consequently realize better health outcomes.

“ When people respond well to treatment they may take the occasional drug holiday.”

Predictors of non-adherence

A wide range of determinants of non-adherence and non-persistence to oral anticancer treatments have been identified in the literature.^[12] It should be noted that these studies cover a variety of different types of cancer and oral anticancer treatments. Table 1 summarises some of the key predictors of non-adherence according to the five categories suggested by the World Health Organisation.^[20]

TABLE 1:
Determinants of
non-adherence to
oral anticancer
treatments

WHO classification	Description
Patient-related	Concerns about adverse effects Doubts about necessity for treatment or adherence Forgetting or accidentally taking too much Lack of confidence in ability to adhere long-term Lack of knowledge about illness or treatment
Therapy-related	Side effects Regimen changes such as timing and dietary requirements Longer duration of treatment
Illness-related	Co-existing medical conditions Longer time since diagnosis
Healthcare system	Clinicians less cancer expertise or experience Less patient involvement in treatment decisions
Social and economic	Younger age (+45 years) and older age (+85 years) Unmarried Lower income/ higher out of pocket cost of treatment

Patients' beliefs about their treatment, including the degree to which treatment is perceived to be necessary and concerns about adverse effects are often powerful predictors of adherence to medications.^[21] The types of beliefs that have associated with non-adherence or non-persistence with oral anticancer treatments [22-28] are listed in Table 2.

Doubts about necessity	Concerns
<ul style="list-style-type: none"> ■ Doubts about necessity for treatment ■ Perceived lack of benefit from treatment ■ Negative/neutral about the value of treatment ■ Missing doses will not impact treatment efficacy 	<ul style="list-style-type: none"> ■ Experiencing distressing side effects ■ Treatment is a constant reminder of diagnosis ■ The treatment regimen is inconvenient ■ Difficulty swallowing pills

TABLE 2:
Types of beliefs associated with non-adherence to oral anticancer treatments

Promising avenues for interventions to support adherence to oral anticancer treatments

The literature exploring determinants of non-adherence to oral anticancer treatments indicates that adherence may be enhanced by:

- Implementation of strategies to detect, report and manage side effects.
- Eliciting and addressing individuals' beliefs about their treatment including concerns about adverse effects, doubts about need for treatment, and low self-efficacy for adherence.
- Education about the role of anticancer treatments in controlling disease and the rationale for maintaining a high level of adherence.
- Practical strategies such as pill boxes, reminder aids and strategies for planning around changes to daily routine, such as socialising, visiting friends or going on holiday.
- Regular assessment of adherence to proactively identify and address challenges in patients taking long-term treatment.
- Exploring challenges to adherence stemming from co-existing medical conditions.
- Involving patients in decisions about their treatment.

Interventions to improve adherence to oral anticancer treatments

FOUR PROVEN INTERVENTIONS TO ENHANCE ADHERENCE:

- 1 Educational video game [29]
- 2 Chemotherapy cycle management programme, including clinical support [30]
- 3 Pharmacist-delivered educational counselling with follow up phone consultations [32]
- 4 Training for medication taking and/or a home visit [31]

We identified four interventions that significantly enhanced adherence or persistence with oral anticancer treatments.[29-32] These included an educational video game for adolescents and young adults,[29] a chemotherapy cycle management programme, including clinical support, dose monitoring and early identification of side effects,[30] pharmacist-delivered educational counselling with follow-up telephone consultations,[32] and an educational intervention with training for medication taking and/or a home visit.[31]

Three of the interventions were tailored to individual needs.[30-32] Two included monitoring and strategies for managing side effects.[30, 32] Only one intervention was evaluated in a randomised controlled trial [29].

A systematic review across illness groups found interventions were most likely to be effective if they were multifaceted and included combinations of information, practical strategies, counseling, psychological

therapy, support, and telephone follow-up.[33] Three of the successful interventions were multifaceted.[30-32] All four included an educational component, three included practical strategies,[30-32] and two included telephone follow-up.[30, 32] Examples of the strategies adopted are shown in Table 3.

While overall the four interventions had some success in increasing adherence, results were inconsistent depending on the adherence measure used. It is also important to bear in mind that even after the interventions, adherence rates remained suboptimal. The development and evaluation of effective interventions therefore remains a priority.

Two further interventions identified did not significantly impact adherence. These included a simple intervention comparing standard packaging with a daily pill box [34] and an intervention utilising a symptom management toolkit and automated voice response system, with additional support strategies focused on side effects or adherence.[35]

TABLE 3:
Components of successful interventions to enhance adherence to oral anticancer treatments

Intervention component	Mode of delivery
Practical strategies	Written dosing schedule Training for pill training Integrating pill taking to individual routine
Information about cancer, treatment and side effects	Slide presentation Direct consultation Printed materials Video game
Support and follow-up	Telephone consultation (nurse/pharmacist) Home visit

Concluding statements

The recent rise in the use of oral anticancer treatments has moved the administration of treatment from the hospital to the patient's home, placing responsibility for managing treatment on patients and their carers. Consequently there is a growing focus on treatment adherence in oncology.

A high level of adherence to oral anticancer treatments is required for treatment success. Consequences of non-adherence include reduced efficacy, negative health consequences and increased healthcare costs.

Rates of non-adherence to oral anticancer treatments vary widely between studies. The average rate of 21% is lower than might be expected.

The literature reveals that the determinants of non-adherence to oral anticancer treatments are multifaceted, indicating the need for complex, tailored interventions to

support patients taking these treatments.

Interventions to improve adherence should take account of both intentional non-adherence (such as missing doses to manage side effects) and unintentional non-adherence (such as forgetting).

Side effects are consistently associated with non-adherence, highlighting the need for early detection and appropriate management.

The impact of emotional factors on adherence has received very little attention, yet depression is highly prevalent among people with cancer and is known to limit adherence in other illness groups.

While some interventions have shown promise, there remains a need to systematically develop and evaluate evidence-based interventions to support patients and improve adherence to oral anticancer treatments.

“The impact of emotional factors on adherence has received very little attention, yet depression is highly prevalent among people with cancer and is known to limit adherence in other illness groups.”



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