

# Adherence with Oral Chemotherapy in a Cancer Unit in Northern Ireland

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## Abstract

### *Title*

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### *Introduction*

Studies in Chronic Myeloid Leukaemia (CML) have shown that adherence to oral chemotherapy is fundamental in achieving good responses where better adherence (>90%) is critical in achieving a major molecular response. The aims of this study were to establish the level of adherence to oral chemotherapy of patients with malignancy, to determine how patients feel about the level of support they are provided with at the start of and during their therapy and their knowledge and beliefs regarding their treatment.

### *Method*

The Morisky 8-item questionnaire was initially used to measure adherence in 21 oncology and haematology patients. Patients then subsequently indicated their beliefs and knowledge of their medication through an interview.

Twenty one were included in the study. Patients had a diagnosis of breast cancer, colorectal cancer or myeloma and were receiving oral chemotherapy for this indication.

### *Results*

One hundred per cent of patients had median or high levels of adherence and there was no significant difference in levels of high adherence between genders or disease groups.

### *Conclusion*

The data from the interviews suggest that patients and relatives are satisfied with the information provided to them from healthcare professionals. Patients are knowledgeable regarding the aims of treatments, dosing and side effects. However, many patients rely on their relatives to remind them to take their medication, thus, patients who lack this support may benefit from further pharmacy input to ensure that they take their medication appropriately.

**Keywords:** non-adherence, Morisky Scale, questionnaire, interview, patients.

## Introduction

Over the past decade, there has been a large increase in the use of oral chemotherapy agents to treat malignancies. Over 50% of novel anti-cancer agents are available as an oral formulation.<sup>1</sup> Oral therapies are more convenient for patients; they reduce the incidence of extravasation, allow for greater flexibility, help with capacity planning and are associated with a better quality of life. The two main disadvantages are cost and patients' adherence to therapy.<sup>2</sup>

Adherence is influenced by many factors. The World Health Organisation<sup>3</sup> divides these factors into five groups, including condition/disease and patient related.

Adherence is defined as the extent to which a patient achieved in accordance with the prescribed interval and dose of a drug regimen.<sup>4</sup> Optimal adherence is when patients do not miss doses, nor include extra doses but take the correct quantity at the correct time of day.

Several reports have been published endeavouring to improve adherence. For example, the National Collaborating Centre for Primary Care (NCCPC) published a Medicines Adherence report in 2009 where suggestions included increasing patient involvement in the decision making process regarding treatment and understanding patients' knowledge, beliefs and concerns about medicines.<sup>5</sup>

A review by Partridge et al illustrates varying degrees of adherence rates in respect of cancer patients including 53-98% in breast cancer and 17-27% in haematological malignancies.<sup>6</sup>

Adherence levels can range anywhere from 20 to 50% in chronic disease<sup>7</sup> but it is thought that adherence is higher in cancer patients due to the consequences of non-adherence or poor adherence. Poor adherence is associated with poorer response to therapy within cancer; this has been observed mainly in chronic myeloid leukaemia (CML) where good adherence is critical in achieving a molecular response.<sup>8</sup>

One study investigating adherence in myeloma found that approximately one third of over 300 patients being treated with thalidomide or lenalidomide for induction were non-adherent; with thalidomide having a slightly higher percentage (37% vs 33%).<sup>9</sup>

A Spanish study found adherence levels with capecitabine for oncological malignancies of 93%<sup>10</sup> even with the complex dosing and directions for patients. Non-adherence was linked to forgetting to take medication and/or side effects. Partridge et al found adherence of 78% to capecitabine in breast cancer patients.<sup>6</sup> Patients with the less aggressive node negative disease and mastectomy were more likely to be non-adherent. Age and disease-related properties did not predict adherence.<sup>11</sup>

Another concern associated with oral chemotherapy is over-adherence, which can lead to increased toxicities especially of grade III or IV that may subsequently lead to dose reductions or cessation of treatment. In a phase II study comparing capecitabine to capecitabine in combination with sunitinib for metastatic oesophageal cancer, 75% of patients described adherence as 'always or almost always' even though they were experiencing grade III+ toxicities.<sup>12</sup>

The management of adverse effects can have a crucial impact on adherence. Decker et al studied symptom management strategies and reported a 23% non-adherence rate to oral chemotherapy due to forgetting to take the medicines or due to side effect symptoms (N = 30).<sup>13</sup>

A pivotal study of adherence to oral chemotherapy in oncology and haematology was the 'Happy Club' concept for patients treated with imatinib for CML.<sup>14</sup> Patients randomised to the Happy Club had comprehensive counselling which included the importance of adhering to medication, quality of life and regular BCR-ABL and cytogenetic monitoring. This arm was also given periodic telephone counselling. Patients in the Happy Club arm of the study were more compliant when compared with patients who did not receive the intervention (P=0.001).

No study has been undertaken which has looked at adherence to oral chemotherapy in Northern Ireland. Patient opinion on the support provided to them or their views on how healthcare professionals could help them with their adherence has been reported.

## **Aims**

The aims of the study were to investigate the level of adherence to oral chemotherapy of Northern Health and Social Care Trust patients diagnosed with malignancy, determine how patients feel about the level of support and information they are given at the start of and during their treatment and establish if patients believe that there are any further interventions which could improve adherence levels in cancer patients in the Trust.

## **Methods**

### *Study Design*

The different methods for measuring adherence can be sub-classified into direct or indirect. No method is considered to be the gold standard measurement and all have their own individual advantages and disadvantages. Direct methods include directly observed administration whilst indirect methods include questionnaires and self-reporting.<sup>15</sup>

The Morisky Scale is a widely used convenient tool to measure adherence. It was first developed in 1986 where four simple questions were used to assist in measuring adherence.<sup>16</sup> The test was trialled in essential hypertension and patients who scored higher (better adherence) had their blood pressure under significantly better control at 2 and 5 years ( $P < 0.01$ ).

Qualitative research was used in this project as the opinions of patients on the support that they believe they get from the healthcare professionals within the department and their views and beliefs on taking medication were sought.

#### *Patients and recruitment*

The study was conducted between March and May 2014 in Laurel House Chemotherapy Unit, Antrim Hospital. Each patient's consultant was asked by Conor Doyle to confirm if the patient was a suitable participant for the study and if they agreed, the patient was asked to participate. Approval for the study was obtained from the Trust's Research Governance department as a service evaluation project. No patient refused to participate in the study and no patient was deemed unsuitable for the study.

Interviews used open non-leading questions and these were developed from a review of the literature and study aim. Subsequent questions were added to clarify or explore the responses given. Interviews were transcribed verbatim.

Patients participating in the study included those:

- diagnosed with adjuvant or metastatic colorectal cancer and receiving capecitabine which may be in conjunction with intravenous chemotherapy
- diagnosed with metastatic breast cancer and receiving capecitabine
- diagnosed with Multiple Myeloma and receiving thalidomide or lenalidomide.

All other patients were not eligible for inclusion.

#### *Data collection*

Each patient's level of adherence was measured using the Morisky 8 item questionnaire (MMAS-8). Patients' attitudes and beliefs on the aims of their treatment, views and opinions on support and education given to them, side effects from these medicines and methods which they would consider useful to improve adherence were then discussed using a semi-structured interview with the patient and their relatives, if applicable. The first part of the interview focused upon their views on the support they were given at initiation and throughout their treatment time. The second part of the interview considered the patients' knowledge of their therapy, for example, aim of therapy, knowledge of medicines they take and administration directions. The last part focused on how they remember to take their medicines; for example, do they have any method of remembering to take them?

Interviews were conducted by Conor Doyle and data was collected until saturation.

#### *Data analysis (Morisky questionnaires)*

Relevant statistical analysis was performed on the data to compare:

- low, medium and high adherence
- high adherence between males and females
- high adherence between the 3 different disease groups.

#### *Interviews and thematic analysis*

After collation of the data, analysis was carried out using the 6 phase process described by Clarke and Braun.<sup>17</sup>

## **Results**

### Demographics

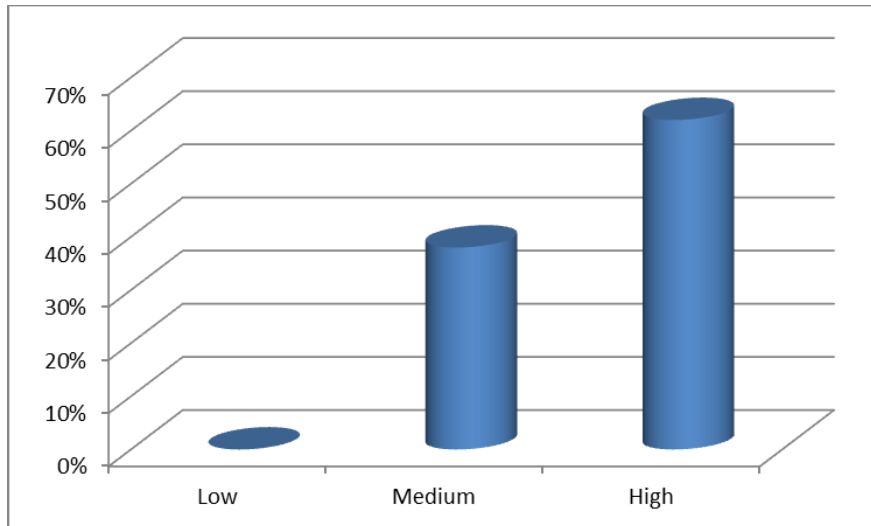
A total of 21 patients were included in the study. The median age was 68 years, (range 48- 85 years) and the mean total length of time for each introduction, questionnaire and interview was 24 minutes.

All patients were white and of Northern Irish background. Nine (43%) were male and twelve (57%) were female.

Six patients (29 %) had a diagnosis of colorectal cancer, six patients (29 %) had a diagnosis of metastatic breast cancer and nine patients (42 %) had a diagnosis of myeloma.

For the purposes of data analysis, it was assumed that  $\alpha = 0.05$  throughout. Low adherence was defined as MMAS-8 = 0-5, medium adherence as MMAS-8 = 6-7 and high as MMAS-8 = 8.

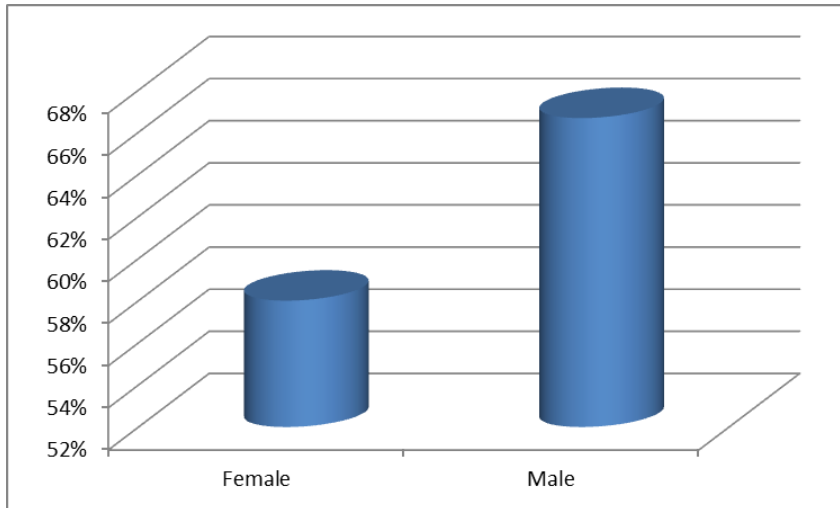
Using the Morisky 8-item Medication Adherence Questionnaire, the majority of patients (n= 13; 62%) had high adherence whilst 38% (n=8) recorded a score in the medium adherence range. No patients had low adherence scores. See Figure 1.



**Figure 1: Comparison of levels of adherence in all patients (P=0.19)**

### Gender

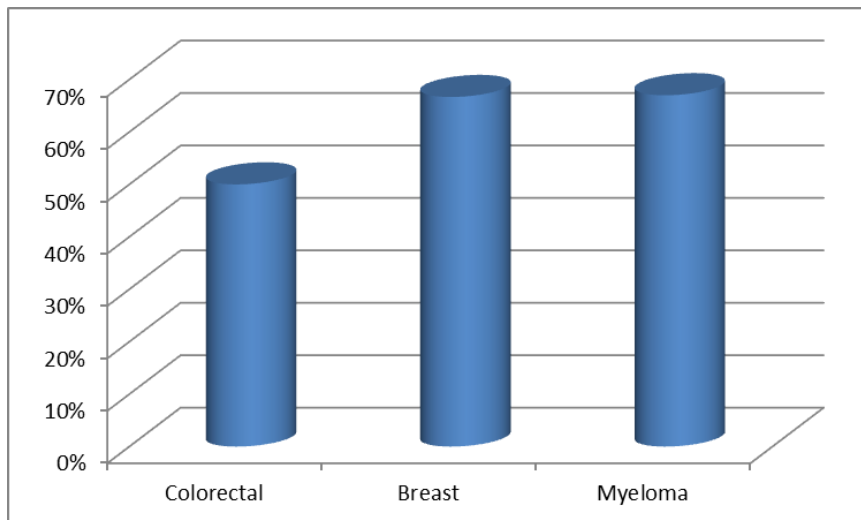
Seven female (58%) patients had high adherence scores whilst 6 male (66.67%) had high adherence scores. See Figure 2.



**Figure 2: High adherence comparison between genders (P =0 .87)**

*Type of treatment/diagnosis*

Fifty per cent (n= 6) of colorectal cancer patients had high adherence scores whilst 66.67% (n=6) of breast cancer patients and 66.67% (n=9) of Myeloma patients also had high adherence scores.



**Figure 3: High adherence comparison between diseases (P= 0.97)**

*Themes from Interviews*

At the outset, seven main themes emerged from the interviews and these are discussed below.

*\* Theme 1 - Explanations/Information/Support*

All patients were satisfied with the support, counselling and information that they were given when they commenced treatment and on subsequent occasions if required. Only one patient said that the amount of information was too much at the start of treatment but they did admit that they felt frightened commencing treatment and the written information was beneficial for domiciliary use.

*"I found the information provided by the nurse to be very useful. She explained it very well too."*

*\* Theme 2 - Knowledge and aims of treatment*

Patients were aware of the goal of their specific treatment. Many of the patients receiving thalidomide used the word 'remission' when discussing the aim of treatment for them whilst patients receiving lenalidomide were aware that the main aim was stable disease. All patients with metastatic breast cancer knew that the treatment objective was to prolong their life rather than cure them. The relevant colorectal cancer patients who were receiving capecitabine after successful surgery were also aware of this. Patients were also aware of the dosing and directions for their medication:

*"With my chemotherapy tablet, I take it for 2 weeks then have a week break before I come back up here..... I take it after breakfast and dinner."*

*\* Theme 3 - Beliefs*

Two patients receiving capecitabine for colorectal cancer were receiving the therapy following successful surgery and the treatment was to err on the side of caution. Both patients had high adherence and they stated that although the medication was more of a preventative treatment, they still took it as prescribed as they wanted to make sure that they were doing the best for themselves and that the consultants advised that they have the treatment:

*"I take all my tablets religiously. It's probably a generation thing."*

*\* Theme 4 - Experiences*

Two patients were able to associate their diagnosis and need for chemotherapy to a past/recent experience with a relative. For example, one lady remarked that her father was able to go about his normal daily living whilst on treatment. A female patient receiving capecitabine for metastatic breast cancer who had numerous lines of therapy did remark that she preferred intravenous to oral chemotherapy as she experienced less side effects with the former:

*"My dad had chemo a few years and just got on with it so I'm trying to do the same."*

*\* Theme 5 - How to remember to take chemotherapy medicines*

In this study, 'remembering' could be subdivided into:

- habit
- family support
- reminder tools (various methods).

Many patients relied heavily on family support to remind them to take their medicines:

*"If I wasn't here, he would never remember to take them."* [patient's wife]

*\* Theme 6 - Preferences*

Patients did not want to get involved in the decision-making regarding their treatment. Many commented that they trusted their consultant's decision as they are the 'experts'. With regards to the form of chemotherapy, most patients expressed the view that they preferred oral tablets/capsules as they considered it to be more convenient:

*"I get my tablets and go straight home."*

*\* Theme 7 - Extra support and suggestions*

No patient thought that support telephone calls from healthcare professionals would be beneficial to them. Patients commented that they are fully aware that they can contact the unit if they have any issues and they are all given contact details when treatment was initiated. The daughter of one patient who lives with her mother and organises her medicines stated that reviews would be a "waste of resources", she would rather "nurses were doing their jobs of treating patients." However, this service may be beneficial for low adherers or patients with no/ little domestic support. It may also help manage and identify toxicities.<sup>16</sup>

One carer suggested that technology will be useful for reminding patients to take their medicines in future generations as the current elderly population in Northern Ireland is not as 'au fait' with technology when compared with younger generations.

Another male patient stated that he would prefer to see the same clinician at each visit as this person knows him and his disease:

*"I prefer to see Dr X each time as he knows all about me."*

## **Discussion**

*Morisky questionnaires*

This was a relatively small study that indicated that patient adherence in these patients was generally good. There was no difference in the level of high adherence between genders or disease groups.

The results on adherence in myeloma patients (haematological malignancy) contradict those found by Partridge et al<sup>6</sup> as the results described above show that patients with a haematological malignancy are as adherent as their oncological counterparts whereas Partridge et al found that adherence in that group to be only 17-27%. The results on breast cancer adherence are similar to those found by Partridge et al.

From the quantitative part of the project, it would have been useful to have had more patients participating.

Only three groups of patients were included in the project; a larger study including patients with more diagnosis could be considered.

The project was single centre and did not take into consideration socioeconomic background. All patients were of Northern Irish descent so no comparison between ethnicities was possible. Further, patients with no domestic support were not identified during the duration of the project.

### *Interviews*

Patients generally reported that the information and support that they were given at the start of treatment was appropriate. They were all given the opportunity to ask questions if they had any concerns and a number commented on the usefulness of the written information provided for home use.

Patients were aware of the directions for taking their medicines including dosing and dietary or time of day recommendations. They were also conscious of the aim of treatment including female patients receiving capecitabine for metastatic breast cancer who were mindful that their disease was now at an incurable stage.

Regarding beliefs associated with taking medicines, the views in this study are similar to patients prescribed medicines to prevent cardiovascular disease where most patients trusted the judgement of their physician due to their knowledge of health and the relevant disease.<sup>18</sup>

Much of the literature regarding methods used to assist patients to remember to take their medicines concerns Medi-dose boxes. MacLaughlin et al reviewed the different technological aids to help patients (based upon elderly group) to take their medicines.<sup>19</sup> The authors comment that trials are required to assess and compare the different aids.

Patients also retain much of the information that they are given by their consultant and nurse at the start. The use of the terms 'remission' and 'written information' is language used within the department by healthcare professions.

## **Conclusion**

Cancer patients in Antrim Hospital treated with oral chemotherapy appear to demonstrate good or high levels of adherence.

The duration of treatment had no impact on adherence and patients who receive treatment until disease progression were still aware that they need to take their medicines as prescribed. Adherence was higher in patients receiving capecitabine for metastatic breast cancer (treat until disease progression) in comparison to those receiving it for colorectal cancer (finite number of treatment cycles).

There was no significant difference in the level of adherence between males and females and the three disease groups analysed.

The patients felt that the support, information and advice they were given was acceptable and the written leaflets supplied supplemented what they were told by the various healthcare professionals.

Patients were also aware of who to contact when they experience any difficulties, the aims of their treatment and many have their own novel way of remembering to take their medicines or the support of family helps many.

All patients take their oral chemotherapy as they follow the advice of their consultant and trust their expertise; this decision is not influenced by stage or type of disease.

A larger study comparing adherence levels with oral chemotherapy in all malignant diseases is a potential next step. Again, as there is a heavy reliance on family/relatives to remind patients; another potential project is to investigate levels of adherence in patients who live on their own and methods which may assist those with adherence issues to take their medicines appropriately.

## **Declaration of interests**

The authors declare no competing interests.

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## **Note**

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