

# Oral chemotherapy safety practices at US cancer centres: questionnaire survey

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## ABSTRACT

**Objective** To characterise current safety practices for the use of oral chemotherapy.

**Design** Written questionnaire survey of pharmacy directors of cancer centres.

**Setting** Comprehensive cancer centres in the United States.

**Results** Respondents from 42 (78%) of 54 eligible centres completed the survey, after consulting with 89 colleagues. Clinicians at 29 centres used handwritten prescriptions, two used preprinted paper prescriptions, and six used electronic systems for most oral chemotherapy prescribing. For six commonly used oral chemotherapies, on average 10 centres required a diagnosis on the prescription, 11 required the protocol number, four required the cycle number, nine required double checking by a second clinician, 14 required a calculation of body surface area, and 14 required a calculation of dose per square metre of body surface area. Only a third of centres requested patients' written informed consent when oral chemotherapy was given off protocol. Nearly a quarter (10) of centres had no formal process for monitoring patients' adherence. In the past year respondents at 10 centres reported at least one serious adverse drug event related to oral chemotherapy, and respondents at 13 centres reported a serious near miss.

**Conclusion** Few of the safeguards routinely used for infusion chemotherapy have been adopted for oral chemotherapy at US cancer centres. There is currently no consensus at these centres about safe medication practices for oral chemotherapy.

## INTRODUCTION

Common malignancies can be treated with oral chemotherapy.<sup>1</sup> This offers patients unprecedented convenience compared with intravenous infusion therapy.<sup>2-4</sup> Given the potential toxicities of oral chemotherapy and the importance of adherence for successful treatment, ensuring safe use of these drugs may require special safeguards.<sup>4-11</sup> The extent to which such safety practices have been introduced into clinical care is unknown.

To characterise current safety practices for oral chemotherapy we surveyed pharmacy leaders at comprehensive cancer centres in the United States. Given the relatively recent introduction of oral chemotherapies, we expected considerable variation in practice.

## METHODS

**Sample selection**—We used the internet to compile contact information for pharmacy directors at all 62 comprehensive cancer centres designated by the US National Cancer Institute. We excluded eight research centres that do not directly care for patients.

**Instrument development**—We developed a questionnaire

**Table 1** | Details of 42 respondents from US cancer centres who took part in survey of safety practices with oral chemotherapy

Job title given by respondent:	No
Pharmacy director, manager, supervisor	19
Oncology pharmacist	8
Quality or clinical outcomes manager	3
Clinical nurse specialist	2
Physician director of clinical services	1
Not specified	9
Colleagues (n=89) with whom respondent discussed survey:	
Pharmacist	28
Pharmacy director or manager	19
Nurse	13
Nurse manager or administrator	10
Nurse practitioner	6
Attending physician	5
Quality, risk, or safety director	5
Clinical fellow	2
Medical director or chief medical officer	1

that examined aspects of the use of oral chemotherapy medication. We focused on non-hormonal oral agents with risk of serious toxicity including capecitabine, cyclophosphamide, gefitinib, imatinib, oral methotrexate, and temozolomide. We circulated a draft survey among the quality directors of the Comprehensive Cancer Center Consortium for Quality Improvement and incorporated revisions into the final instrument.

**Study protocol**—We sent the questionnaire by email and post in September 2005. Non-responders received up to three follow-up telephone calls. If the pharmacy director was misidentified or unable to participate, we encouraged recipients to identify a substitute respondent who was familiar with oral chemotherapy practices.

**Data analysis**—We deleted respondents' names and organisations before analysis and tabulated responses using Stata 7.0 (StataCorp, College Station, TX).

## RESULTS

### Responses

We received 42 completed questionnaires from the 54 eligible centres. Table 1 shows the job titles of 33 respondents who reported this information. Thirty one respondents consulted with colleagues about the survey (total 89, median 2, range 0-8).

### Prescribing

Prescribing practices for oral chemotherapy varied considerably. For most oral chemotherapy prescribing clinicians at 29 centres used handwritten prescriptions. At two centres they used preprinted paper prescriptions

**Table 2** | Prescription writing for oral chemotherapy at 42 US cancer centres. Figures are numbers (percentages) of centres

	Proportion of prescriptions generated by method	
	Majority (>50%)	Minority (≤50%)
Handwritten paper prescriptions	29 (69)	13 (31)
Preprinted paper prescriptions	2 (5)	40 (95)
Electronic order entry	6 (14)	36 (86)

and at six they used electronic systems (table 2).

Organisations did not have many compulsory requirements on prescriptions. For six commonly used oral chemotherapies (see table on [bmj.com](http://bmj.com)), on average 10 centres required a diagnosis on the prescription, 11 required the protocol number (when appropriate), four required the cycle number, nine required double checking by a second clinician, 14 required a calculation of body surface area, and 14 required calculation of dose per square metre of body surface area. Over half (23) had no required element for oral chemotherapy prescriptions.

Lack of standardisation was also reflected in the use of informed consent. Only a third of centres asked patients to provide written informed consent when oral chemotherapy was given off protocol.

#### Coordination and monitoring

Respondents reported considerable variation in the methods used to coordinate oral and infusion chemotherapy among patients who received both types of treatment. Twenty five centres coordinated care by maintaining a record of oral chemotherapy in the patient's medication profile. At 26 centres, a nurse or pharmacist reviewed oral chemotherapy during infusion treatment. Seven centres reported no formal coordination.

Clinicians at most centres monitored patients' adherence to oral chemotherapy during office visits. Staff at 10 centres asked patients to bring in logbooks, and staff at nine regularly counted pills. Respondents from nine centres reported no formal process for monitoring adherence.

#### Pharmacy practices

Pharmacy services may be underused in the care of patients on oral chemotherapy. Although 33 centres offered patients a formal consultation with a pharmacist, respondents estimated that many (42%) patients declined a consultation.

Thirty four centres had an on-site pharmacy for patients receiving oral chemotherapy who were not on research protocols. Respondents estimated, however, that 38% of eligible patients did not use this facility. Failure to use an on-site pharmacy may be problematic as respondents at 17 centres rated communication between community pharmacies and cancer centres as fair or poor.

#### Education of patients

At most centres physicians shared responsibility with

other health professionals for educating patients about oral chemotherapy. Respondents at 25 (60%), 34 (81%), and 40 (95%) organisations indicated that nurse practitioners, nurses, and pharmacists, respectively, were also responsible for educating patients about use and safety. Only a third of organisations provided special training or certification for those who educate patients about these medications.

#### Safety assessment

Respondents at 10 centres reported that a "serious adverse drug event" related to oral chemotherapy had occurred in the past year, and 13 centres reported a "serious near miss." Respondents at 36 centres indicated that clinicians in their organisations were concerned about the risks of oral chemotherapy.

#### DISCUSSION

Despite the increased use of oral chemotherapy, current practices for prescribing, coordinating and monitoring, and dispensing these medications and educating patients in US cancer centres leave room for improvement. We found that most organisations had no required elements for prescribing oral chemotherapy and few requested patients' written informed consent for off protocol prescribing. Only about half of cancer centres coordinated oral with intravenous chemotherapy. Most organisations provided little infrastructure to support adherence to treatment. On-site pharmacies and consultation with a pharmacist were widely available to patients, but both were underused. Clinicians from various professions shared responsibility for educating patients about oral chemotherapy, but few centres provided clinicians with relevant formal training.

Surprisingly few of the safeguards in routine use for infusion chemotherapy at US cancer centres have been adopted for oral chemotherapy. Only one in three organisations required a clinician to note the body surface area or calculation of dose on the prescription for six commonly used oral drugs, and only one in four required the patient's diagnosis or protocol. One in five organisations required a second clinician to double check the prescription, and fewer than one in 10 required the clinician to enter the treatment cycle. Half of the centres required no safeguards around prescription writing at all.

#### Study limitations

Medication safety practices at sites that did not respond may differ from those that responded. Our results may overemphasise the perspective of pharmacy directors relative to other oncology clinicians. Similarly, respondents' characterisation of safety practices reflected their best—but potentially biased—judgments. We asked respondents to consider oral agents with considerable toxicity risks, but they may not have shared a common definition of oral chemotherapy. Finally, it may have been difficult for respondents to characterise medication practices in organisations with practice patterns that varied across clinicians and treatment regimens.

**WHAT IS ALREADY KNOWN ON THIS TOPIC**

Although oncologists prescribe oral chemotherapy for many indications, little is known about associated safety practices

**WHAT THIS STUDY ADDS**

Few of the safeguards in routine use for infusion chemotherapy have been adopted for oral chemotherapy

**Conclusions**

Our data indicate that prescribing, monitoring and coordination, pharmacy practices, and education of patients for oral chemotherapy vary substantially. Despite clinicians' concern about oral chemotherapies, there is no apparent consensus among oncology professionals about safe practices for these drugs. Safeguards used for infusion chemotherapy cannot be abandoned for oral treatment. The oncology community must define safe medication practices appropriate for oral chemotherapy, develop practice guidelines, and accelerate their adoption.

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**Contributors:** SNW, JF, AP, SB, LNS, and MC were responsible for conception and design. SNW, JF, DB, LM, and MC collected the data. SNW, AP, LNS,

and MC analysed and interpreted data. SNW, JF, DB, LM, AP, SB, LNS, and MC drafted and revised the paper. AP and SNW carried out the statistical analysis. SNW, JF, DB, LM, SB, LNS, and MC were responsible for administrative, technical, and material support. SNW and LNS supervised the study. SNW is guarantor.

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## Effect of reducing caffeine intake on birth weight and length of gestation: randomised controlled trial

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**ABSTRACT**

**Objective** To estimate the effect of reducing caffeine intake during pregnancy on birth weight and length of gestation.

**Design** Randomised double blind controlled trial.

**Setting** Denmark.

**Participants** 1207 pregnant women drinking at least three cups of coffee a day, recruited before 20 weeks' gestation.

**Interventions** Caffeinated instant coffee (568 women) or decaffeinated instant coffee (629 women).

**Main outcome measures** Birth weight and length of gestation.

**Results** Data on birth weight were obtained for 1150 liveborn singletons and on length of gestation for 1153 liveborn singletons. No significant differences were found for mean birth weight or mean length of gestation between women in the decaffeinated coffee group (whose mean caffeine intake was 182 mg lower than that of the other group) and women in the caffeinated coffee group. After adjustment for length of gestation, parity, prepregnancy body mass index, and smoking at entry to the study the mean birth weight of babies born to women in the decaffeinated group was 16 g (95% confidence interval -40 to 73) higher than those born to women in the caffeinated group. The adjusted difference (decaffeinated

group—caffeinated group) of length of gestation was -1.31 days (-2.87 to 0.25).

**Conclusion** A moderate reduction in caffeine intake in the second half of pregnancy has no effect on birth weight or length of gestation.

**Trial registration** Clinical Trials NCT00131690.

**INTRODUCTION**

Some studies have shown an association between high caffeine intake in pregnancy and an increased risk of giving birth to small for gestational age or low birth weight (<2500 g) babies.<sup>1-5</sup> Some have also shown an association between caffeine intake during pregnancy and miscarriage.<sup>6,7</sup>

We carried out a randomised double blind trial to estimate the effect of reducing caffeine intake on birth weight and length of gestation.

**METHODS**

From April 1996 to April 1998 we sent a questionnaire to all pregnant women booking for delivery at Aarhus University Hospital, to assess coffee intake. At around 16 weeks of pregnancy we contacted those who had stated a daily intake of at least three cups of coffee.