Waikato District Health Board

A District Health Board

A Report by the

Health and Disability Commissioner

(Case 14HDC01771)

Health and Disability Commissioner
Te Toihau Hauora, Hauātanga

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Executive summary

1. In 2012, (in Month1)[1] Mrs A (then aged 51 years) was diagnosed with ovarian cancer. At that time she weighed 84kg. She was seen by oncologist Dr B at Waikato DHB (Hospital 1). Mrs A agreed to receive neo-adjuvant chemotherapy[2] with paclitaxel[3] and carboplatin.[4]

2. As Mrs A did not live in the Waikato DHB region, she travelled to her nearest public hospital's (Hospital 2) oncology clinic chemotherapy unit for her treatment. An oncologist from Waikato DHB attended there twice a month.

3. The dose of carboplatin[5] is based on an assessment of the level of the patient's kidney function. Waikato DHB uses a computer based calculator, the Aesculapius programme, which calculates the carboplatin dose based on the patient's weight and serum creatinine level.

4. At the time of Mrs A's treatment, Hospital 2 chemotherapy staff nurses documented the patient's height and weight only at the initial visit, and did not note the weight again. When the patient was seen in the oncology clinic, the oncologist noted the weight in the clinical file but, as the Aesculapius programme was not readily available to the consultant while at Hospital 2, the input into the computer system depended on the oncologist entering the information when he or she returned to Hospital 1.

5. Mrs A had one cycle of paclitaxel/carboplatin, which was poorly tolerated. On 24 Month4 she underwent a total abdominal hysterectomy[6] and bilateral salpingo-oophorectomy.[7] The surgery was uneventful.

6. On 14 Month5 Mrs A's weight was 70.8kg. Dr B planned to resume chemotherapy with paclitaxel and carboplatin. A CT scan was performed, which showed no evidence of disease, and Mrs A then declined further chemotherapy. It was decided to monitor her progress and not administer further chemotherapy at that time.

7. On 1 Month11 Mrs A's weight was 72.9kg. She had a CT scan, which showed further progression of the disease.

8. Mrs A was treated with oral low-dose etoposide[8] from Month13 until 11 Month24.

[1] Relevant dates are referred to as Months 1-37 to protect privacy.
[2] Treatment given as a first step to shrink a tumour before the main treatment, which is usually surgery, is given.
[3] A drug used to treat ovarian, breast, lung, pancreatic and other cancers.
[4] A drug used to treat ovarian cancer.
[5] Carboplatin is used alone or with other drugs to treat advanced ovarian cancer. It is used with other chemotherapy as first-line treatment. It is used alone (single agent carboplatin) as palliative treatment for disease that has recurred after earlier chemotherapy.
[6] Surgical removal of the uterus through an incision in the lower abdomen.
[7] Removal of both ovaries and fallopian tubes.
[8] Cytotoxic anticancer drug.

9. By 11 Month24, Mrs A's weight was 65.6kg, and further disease progression was evident on a CT scan. Dr B advised Mrs A to stop etoposide and try single agent carboplatin treatment.

10. Dr B calculated Mrs A's first dose of single agent carboplatin. The Aesculapius prescription form shows that the calculation of the dose of 600mg was based on her levels from 2012, which were prepopulated into the Aesculapius programme (weight of 84kg and creatinine of 90mmol/L). Mrs A received her first dose on 8 Month25. Further doses of 600mg single agent carboplatin were administered on 5 Month26 and 25 Month26. At Mrs A's next consultation on 4 Month27, Dr B recorded that the effect of the carboplatin seemed to be favourable. Further doses of 600mg carboplatin were administered on 16 Month27 and 6 Month28.

11. On 5 Month29 Mrs A was due for her next cycle of carboplatin, but her blood counts were too low, so she did not receive it. Mrs A was experiencing pain and fatigue. Dr B recommended a change to gemcitabine. He calculated a dose of 1950mg of gemcitabine based on a weight of 84kg. The prescription noted that Mrs A's creatinine was then 66mmol/L.

12. Around 8 Month30, a chemotherapy nurse noticed that Mrs A had been receiving chemotherapy based on a weight of 84kg, some 20kg more than her then actual weight of 65kg.

13. Dr B directed that Mrs A's dose of gemcitabine be reduced to 75% of the dose she had been receiving because of the difficulty she was having with cytopenia.[9] Dr B planned to send a new order sheet for chemotherapy with the updated weight. There are no clinical notes from Dr B about the change in dosage.

14. Over the next months Mrs A's condition deteriorated, and she died on 13 Month37.

Findings

Waikato DHB

15. The following factors contributed to Mrs A receiving a dose of carboplatin calculated on the basis of her measurements from 2012, rather than 2014, owing to systemic issues at Waikato DHB:

- Changes in patient information, on which prescriptions for chemotherapy treatment were based (such as weight and creatinine levels), could be recorded only in the chemotherapy treatment computer system at Hospital 1, where it was based, and not by oncologists working at off-site clinics.

- There were insufficient safeguards to identify the use of historic data, and whether the weight and creatinine levels on the day of delivery differed from that data. The oncologists were unable to update patient details remotely, and the patient's weight was not displayed prominently (or consistently) in the clinical file, which

[9] Cytopenia is a reduction in the number of blood cells.

meant that it was not necessarily brought to the clinician's attention at clinic appointments.

16. Accordingly, Waikato DHB did not provide services to Mrs A with reasonable care and skill and breached Right 4(1)[10] of the Code of Health and Disability Services Consumers' Rights (the Code).

17. Adverse comment is made about the frequency with which Mrs A was reviewed by a specialist while receiving chemotherapy.

Dr B

18. Adverse comment is made about Dr B not ensuring that the calculations for treatment, which he signed off, were correct. Dr B was aware that Mrs A's weight was decreasing; however, he failed to ensure that the Aesculapius programme was updated when further doses of carboplatin were calculated.

DHB2

19. Adverse comment is made about the lack of systems in place at DHB2 to check that the data relied on was correct, prior to administering chemotherapy treatment.

Recommendations

20. The Commissioner recommended that Waikato DHB:

a) Provide a written apology to Mr A for its breach of the Code.

b) Report to HDC with a detailed update on the effectiveness of the changes made as a result of this case, including:

i. how clinicians' ability to access the Aesculapius programme remotely is affecting their service delivery;
ii. the results of the review of Waikato and DHB2's models of service, and
iii. an assessment of the effectiveness of the changes made to its service delivery following the review.

21. The Commissioner recommended that Dr B report to HDC on how the ability to access the prescribing software remotely has affected his practice.

22. The Commissioner recommended that DHB2 report to HDC on the effectiveness of the changes it has made, including the new practice by Hospital 2 chemotherapy staff of weighing patients prior to treatment, and notifying a clinician at Hospital 1 if a discrepancy is detected against the script. The update should also provide details on the changes made to Aesculapius, whether an onsite physician has been appointed for the outreach clinics, and whether clinicians at those clinics have adequate access to electronic databases, including the Aesculapius programme.

[10] Right 4(1) states: "Every consumer has the right to have services provided with reasonable care and skill."

Complaint and investigation

23. The Commissioner received a complaint from Mrs A about the services provided to her by Waikato District Health Board and DHB2. The following issues were identified for investigation:

- *The appropriateness of the care provided to Mrs A (dec) by Waikato District Health Board.*
- *The appropriateness of the care provided to Mrs A (dec) by DHB2.*

24. An investigation was commenced on 29 September 2015.

25. The parties directly involved in the investigation were:

Mrs A	Consumer/complainant
Mr A	Complainant's husband
Waikato District Health Board	Provider
DHB2	Provider
Dr B	Consultant medical oncologist

26. Information was received from the above parties, and also from general practitioner Dr C.

27. Independent expert advice was obtained from a medical oncologist, Dr Richard Isaacs (**Appendix A**).

Information gathered during investigation

Background

28. In Month1 Mrs A (then aged 51 years) was experiencing abdominal pain. On 29 Month1 she underwent a computerised tomography (CT) scan at Hospital 1's oncology department, which showed a 15cm x 15cm mass in her pelvis, extending into her right abdomen. The medical oncology registrar recorded her impression as: "Stage III[11] serious primary ovarian malignancy."

29. On 6 Month2 a multidisciplinary meeting (MDM) was held at Hospital 1, where "extensive peritoneal disease" was noted. The MDM recommended that Mrs A undergo an ultrasound-guided biopsy of her right adnexal mass and, "[i]f [positive] for carcinoma [to be] refer[red] to Medical Oncology in [Hospital 1]". As the biopsy was positive for carcinoma, Mrs A was referred to the Medical Oncology department for follow-up.

[11] Progression of ovarian cancer is categorised into four stages in order of seriousness.

30. On 25 Month2 Mrs A saw consultant medical oncologist Dr B at a medical oncology clinic at Hospital 1. Dr B assessed Mrs A and recorded her symptoms, which included shortness of breath, decreased appetite, and constipation. Dr B recorded his impression as: "Stage three primary serious ovarian malignancy." The following day her case was discussed at a gynaecology MDM, which recommended that Mrs A proceed to chemotherapy, with consideration of debulking surgery[12] if she had a good response to chemotherapy.

31. On 28 Month2 Dr B discussed the MDM findings with Mrs A and her husband. Mrs A said that at the appointment her height and weight were measured by a nurse and, at that time, she weighed 84kg.

32. Dr B advised Mrs A's GP, Dr C, that Mrs A should receive chemotherapy and consider debulking surgery. After further discussion, Mrs A agreed to receive neo-adjuvant chemotherapy[13] with paclitaxel[14] and carboplatin.[15] She was to receive carboplatin every three weeks and paclitaxel weekly.

Systems for administration of chemotherapy

33. Mrs A travelled to Hospital 2 to receive chemotherapy treatment. Waikato DHB told HDC that the Hospital 2 oncology clinic chemotherapy unit is an outlying one, and that an oncologist from Waikato DHB attends there twice a month.

34. Waikato DHB stated that if a patient is on a three-week treatment schedule, the frequency with which he or she would be reviewed by the consultant in person could vary from immediately before a treatment, to a review occurring during one of the two weeks after a treatment. Dr B stated:

> "Because of the nature of the scheduling when dealing with a remote clinic like this, it is **not** possible or feasible to physically review the patient prior to each treatment. However, patients **are** seen by an oncology nurse prior to each treatment and calls are made to me, the physician, as required according to the individual and particular case." (Emphasis in original.)

DHB2 process

35. DHB2 provides satellite services to the Waikato DHB cancer treatment service (CTS). DHB2 stated that it has staff trained and updated by the CTS, and the process for providing chemotherapy at Hospital 2 is as follows:

- The patient is seen by the medical oncologist at Hospital 1's Oncology Department.

[12] Removal of part of a malignant tumour that cannot be excised completely, so as to enhance the effectiveness of radiation therapy or chemotherapy.
[13] Treatment given as a first step to shrink a tumour before the main treatment, which is usually surgery, is given.
[14] A drug used to treat ovarian, breast, lung, pancreatic and other cancers.
[15] A drug used to treat ovarian cancer. Carboplatin is used alone or with other drugs to treat advanced ovarian cancer. It is used with other chemotherapy as first-line treatment. It is also used alone (single agent carboplatin) as palliative treatment for disease that has recurred after earlier chemotherapy.

- A referral for the delivery of chemotherapy at the Hospital 2 Chemotherapy Unit is generated by either the oncologist or his/her registrar at Hospital 1 and sent through to the Clinical Nurse Manager (CNM) at Hospital 2.
- The CNM receives the referral via a telephone call, email or occasionally a visit from the oncologist when he or she is at Hospital 2 doing a clinic.
- The CNM then makes an appointment for the patient and contacts the patient via a telephone call or letter.
- The chemotherapy regimen is decided upon by the medical oncologist and charted onto a Hospital 1 specific chemotherapy drug chart (prescription).
- The drug chart (prescription) is sent from Hospital 1 via the mail system, and the same script is faxed to the Hospital 2 Chemotherapy Unit. A copy is made by the chemotherapy staff and given to the pharmacy to enable the dispensing of the drugs. If the original script does not arrive before the patient receives the first dose, the administration record is signed on the faxed copy, and subsequent doses are signed for on the original script.
- When the chemotherapy drug regimen is changed to another drug regimen, the prescription charts are returned to Hospital 1's Oncology Unit to be filed in the patient's Hospital 1 file. A new drug chart is then sent to Hospital 2.
- If there are any issues regarding the patient's treatment, the chemotherapy staff at Hospital 2 telephone the medical oncologist or his/her registrar at Hospital 1, and the patient is given an appointment for the next available clinic. This may be at Hospital 2 or Hospital 1 depending on the appointment availability.
- On average, patients see the oncologist every two to three months during their treatment.

36. DHB2 is responsible for administering the Hospital 2 Chemotherapy Unit.

Carboplatin dosage calculation

37. Dr B advised that the dose of carboplatin is based on the patient's glomerular filtration rate (GFR), an assessment of the level of the patient's kidney function. An estimate of a patient's GFR is calculated from the patient's serum creatinine level.[16]

38. Dr B said that the computer-based calculator used at Hospital 1, the Aesculapius programme, has a calculator that determines the creatinine clearance based on the patient's weight and serum creatinine level, and then directly calculates the carboplatin dose using the Calvert formula.[17]

[16] Creatinine is a normal waste product from the breakdown of protein in muscles. Creatinine is removed from the body by the kidneys. The creatinine clearance rate is a measurement of the ability of the kidneys to clear creatinine from the blood. This measurement helps to estimate the GFR — the rate of blood flow through the kidneys.

[17] In 1989 the "Calvert formula"was developed as a simple calculation that allows doctors to calculate the correct dose of carboplatin.

39. Dr B advised that the Aesculapius chemotherapy order sheet has a specific place for recording the patient's height and weight, and the sheet has instructions not to give the chemotherapy if the measured height and weight deviate beyond specified values. He stated that in Mrs A's case, "it appears that the height and weight were not recorded on the chemotherapy order sheet, and the fact there was a deviation from the initial height and weight was not noted".

40. DHB2 told HDC that at the time of Mrs A's treatment, Hospital 2 chemotherapy staff nurses documented the patient's height and weight only at the initial visit, and the nurses did not note the weight again. DHB2 said that when Mrs A was seen in the oncology clinic at Hospital 2, the oncologist noted her weight in the clinical file but, as the Aesculapius programme was not readily available to the consultant while at Hospital 2, the input into the computer system depended on the consultant entering the information when he or she returned to Hospital 1.

Preoperative chemotherapy

41. Mrs A had one cycle of paclitaxel/carboplatin prior to surgery. Three infusions were given weekly during the cycle (carboplatin and paclitaxel on day #1, paclitaxel on day #8, and paclitaxel on day #15).

42. Mrs A had her first infusion of paclitaxel and carboplatin on 3 Month3. The treatment was poorly tolerated owing to cytopenia.[18] Shortly after the treatment, Mrs A experienced episodes of fainting and unsteadiness on her feet, thought to be related to vaginal bleeding.

43. Mrs A had been receiving Clexane[19] because of a suspected thrombus in her right external iliac vein. On 9 Month3 she was admitted to Hospital 2 because of unsteadiness, fainting and vaginal bleeding. She was discharged on 10 Month3.

44. On 13 Month3, when she was due for her infusion of paclitaxel, Mrs A saw Dr B at a clinic appointment. Dr B noted:

> "At this time it is too early to conclude how the treatment is proceeding and how [Mrs A's] tumour is responding. I have encouraged [Mrs A] to continue forward with treatment. I would like to give [Mrs A] a second cycle after this one is concluded … Then we will re-evaluate and assuming she is showing a therapeutic response, I would like to give [Mrs A] a total of four cycles at the most then consider her for surgical debulking. At this time I would say hold the Clexane in view of the fact of her vaginal bleeding."

45. On 16 Month4 Mrs A underwent a CT scan to re-evaluate her disease. The scan showed no change in the complex pelvic mass. In response to the provisional opinion, Mr A said that he was told that the initial CT scan indicated that "the tumours were multiple and inoperable and surgery was not an option".

[18] A reduction in the number of blood cells. Cancer patients frequently develop cytopenia, which may be caused by chemotherapy or radiation treatment.
[19] Medication used to treat blood clots and prevent blood clots forming.

46. On 17 Month4 Mrs A was seen for follow-up at the medical oncology clinic in Hospital 1. Dr B noted that since her first treatment on 3 Month3, Mrs A had had "lingering leukopenia[20] which in essence [had] prevented the second cycle being given three weeks later". Because the neo-adjuvant therapy had had little positive benefit, Dr B asked an obstetrician and gynaecologist consultant to review Mrs A. The consultant advised that debulking surgery should be attempted. Mrs A agreed, and the consultant arranged for Mrs A to proceed to surgery at Hospital 1.

47. In response to the provisional opinion, Mr A told HDC that surgery was offered after Mrs A became so ill that she could not go to the bathroom, and it was considered that surgery would alleviate that problem.

Surgery 24 Month4 and follow-up

48. On 24 Month4 Mrs A underwent a total abdominal hysterectomy[21] with bilateral salpingo-oophorectomy.[22] The surgery was uneventful. In response to the provisional opinion, Mr A told HDC that the surgery revealed a single mass rather than multiple tumours.

49. On 4 Month5 an MDM was held at Hospital 1, and it was recommended that Mrs A have further chemotherapy. The consultant noted in his letter to a gynaecologist at Hospital 2 that "[t]he histology on both ovarian masses showed carcinosarcoma[23]", and that Mrs A's first follow-up should be at six weeks' post surgery.

50. Mrs A saw Dr C for follow-up, and he wrote to Dr B on 6 Month5 and advised that "[Mrs A was] doing remarkabl[y] well physically", and that her weight was "stable at 70.4kg". Mrs A stopped taking Clexane at that time.

51. On 14 Month5, at her first oncology consultation following surgery, Dr B noted that Mrs A's weight was 70.8kg, which was a reduction from her weight of 84kg prior to starting adjuvant chemotherapy in Month2. Dr B indicated that postoperative chemotherapy was required, and recorded in the clinical notes that he planned to resume chemotherapy with paclitaxel and carboplatin. A CT scan was performed, which showed no evidence of disease.

52. Mrs A then declined further chemotherapy, and it was decided to monitor her progress and not administer further chemotherapy at that time.

53. On 19 Month6 Mrs A was seen by Dr B and an oncology registrar. The clinical record states:

> "It is highly likely that [Mrs A's] disease will recur in the future. [Mrs A] made clear that she does not wish any chemotherapy at this point in time. [Dr B] …

[20] A reduction in the number of white cells in the blood.
[21] A surgical procedure that removes the uterus through an incision in the lower abdomen.
[22] Removal of the ovaries and fallopian tubes.
[23] A malignant tumour that consists of a mixture of carcinoma and sarcoma. Carcinosarcomas are rare tumours, and can arise in various organs.

advised [Mrs A] regarding the need to closely monitor her disease and treat [Mrs A] with palliative chemotherapy, when the disease relapses."

54. On 14 Month8 Mrs A saw Dr B for follow-up. At that time she was generally well and had returned to work. Her CA 125[24] was within the normal range.

55. Mrs A continued to see Dr B for regular review. During the period between Month8 and Month13 Dr B recorded a rising CA 125 (which was noted as indicative of malignancy), and recommended instigation of gradual palliative care.

Treatment with etoposide

56. On 1 Month11 Dr B recorded Mrs A's weight as 72.9kg. On 10 Month13 Mrs A was seen by an oncology registrar who noted that her symptoms were increasing. A CT scan was arranged, and she was booked to see Dr B on 30 Month13. The scan showed further progression of the disease.

57. Dr B told HDC that Mrs A was being treated for relapse and progression of her ovarian cancer. However, Mrs A was still active and working, and did not want a treatment with toxic side effects. He stated that oral low-dose etoposide[25] was selected because it is easy to tolerate and there was a possibility that the tumour would respond to it. In response to the provisional opinion, Dr B said that Mrs A did not want a potentially more toxic regimen, and it was felt that oral etoposide would be "very easily tolerated while at the same time offering a significant palliative response".

58. Mr A told HDC in response to the provisional opinion that Mrs A researched the use of etoposide as a means of controlling her ongoing and "extremely debilitating" ascites,[26] and asked Dr B if this was an option to consider. Mr A said that etoposide was prescribed at Mrs A's request.

59. Oral etoposide 50mg per day was administered to Mrs A from Month13 until 11 Month24. Dr B told HDC that during that period Mrs A did not have cytopenia.

60. On 28 Month14 Dr B recorded Mrs A's weight as 66kg. In Month18 Dr B recorded that Mrs A's symptoms had improved with the use of etoposide. Mrs A told HDC that the treatment provided "tremendous relief" from the ascites she had developed in Month13.

61. Mrs A next saw Dr B on 4 Month18. Her pain had increased and she was started on a fentanyl patch.[27] Dr B saw Mrs A next on 17 Month21. The disease was recorded to be "minimally progressing, if at all" on the etoposide regimen. However, at the next appointment on 11 Month24, Dr B recorded that the cancer had started to worsen. At this appointment Dr B recorded Mrs A's weight as 65.6kg, and noted that it had been

[24] A test that measures the amount of the protein CA 125 (cancer antigen 125) in the blood. A CA 125 test may be used to monitor certain cancers during and after treatment.
[25] A cytotoxic anticancer drug.
[26] Accumulation of fluid in the peritoneal cavity, causing abdominal swelling.
[27] A transdermal system (patch) that provides continuous systemic delivery of fentanyl, a potent opioid analgesic.

67kg at her last visit. Further disease progression was evident on a CT scan, and Dr B advised Mrs A to stop etoposide and try single-agent carboplatin treatment. Mrs A agreed with the plan.

Treatment with single-agent carboplatin[28]

62. Mrs A's treatment was delayed because she was admitted to another hospital with neutropenic sepsis[29] following her treatment with oral etoposide. She was commenced on oral antibiotics and given granulocyte-colony stimulating factor[30] (G-CSF) support. She recovered well and, a week later, received her first dose of single-agent carboplatin. In response to the provisional opinion, Mr A told HDC that administering G-CSF nightly to his wife was "extremely traumatic", which added to their stress.

63. Just prior to treatment, Dr B calculated Mrs A's first dose of single-agent carboplatin. The Aesculapius prescription form shows that the calculation of the dose of 600mg was based on Mrs A's weight (84kg) and creatinine level (90mmol/L) from 2012, which had been prepopulated into Aesculapius. Mrs A received her first dose on 8 Month25.

64. At the first follow-up appointment on 15 Month25, Dr B recorded that Mrs A had tolerated the treatment well with few side effects. Dr B recorded that Mrs A felt happy with progress and was keen to continue the chemotherapy. Mrs A's weight was recorded as 60.8kg.

65. Further carboplatin was planned to be given in three-weekly cycles. Waikato DHB said that DHB2 oncology nurses contacted Dr B to tell him Mrs A's white blood count (WBC) prior to each treatment.

66. Further doses of 600mg single-agent carboplatin were administered on 5 Month26 and 25 Month26. At Mrs A's next consultation on 4 Month27, Dr B recorded that the effect of the carboplatin seemed to be favourable. Further doses of 600mg carboplatin were administered on 16 Month27 and 6 Month28. The dose rate continued to be based on Mrs A's previously recorded weight of 84kg and creatinine level of 90mmol/L.

67. On 5 Month29, when Mrs A was due for her next cycle of carboplatin, Dr B noted that her blood counts were too low, so she did not receive it. Mrs A was experiencing pain and fatigue. Dr B noted that it would be difficult to continue with further chemotherapy because of the problems with cytopenia. He noted:

> "On examination [Mrs A's] weight is at 66.8 kilograms which is a significant drop since she was started on carboplatin, when it was 84 kilograms. She appears in no discomfort."

[28] Used for the treatment of recurrent ovarian cancer.
[29] Sepsis caused by neutropenia (an abnormally low number of white blood cells (neutrophils) in the blood).
[30] A glycoprotein that stimulates the bone marrow to produce granulocytes and stem cells and release them into the bloodstream.

68. Dr B ordered a CT scan and arranged to see Mrs A again on 9 Month29. The CT scan showed stable findings; however, Dr B noted that it was not advisable to continue with the carboplatin, which was "simply giving her myelosuppression[31]". Dr B decided to start Mrs A on gemcitabine,[32] and noted that she should continue to use the G-CSF as she had done in the past. In relation to the prescription for gemcitabine (which is usually given weekly for three weeks, followed by a break on the fourth week, with the cycle repeated every four weeks), Dr B recorded: "In [Mrs A's] case her marrow may be unable to handle that degree of marrow suppression and the schedule may have to be modified …" Dr B calculated a dose of 1950mg of gemcitabine based on a weight of 84kg. The prescription noted that Mrs A's creatinine was then 66mmol/L.

69. On 24 Month29 Mrs A was given education on receiving gemcitabine by a chemotherapy nurse, and received her first dose that day. When Mrs A was given her second dose on 1 Month30, a nurse noted: "Managing minimal side effects well."

Weight difference

70. Around 8 Month30, Mrs A asked a chemotherapy nurse what the "84" on the medication bag meant. The nurse then noticed that Mrs A had been receiving chemotherapy based on a weight of 84kg, some 20kg more than her then actual weight of 65kg. Mrs A told HDC that she believed she had received a 30% overdose of carboplatin for four months, which increased the side effects she experienced.

71. Waikato DHB said that the chemotherapy nurse told Dr B about the incorrect weight. The nursing notes record that Dr B directed that Mrs A be administered a dose of 75% of the gemcitabine she had been receiving. Waikato DHB said that the reduced dose was prescribed in view of the difficulty Mrs A was having with cytopenia, and that Dr B planned to send a new order sheet for chemotherapy with the updated weight. There are no clinical notes from Dr B about the change in dosage.

72. Mrs A's next appointment with Dr B was on 30 Month30. Dr B recorded that gemcitabine had not been effective in reducing Mrs A's palpable lesions, which were "noticeably slightly larger". Following discussion of her clinical options, Mrs A's treatment was changed to a weekly dose of paclitaxel, which was first administered on 4 Month31.

73. On 14 Month31 Mrs A saw Dr B, who recorded that she was "very stable and therefore further weekly Paclitaxel will be given". Mrs A saw Dr B again one month later, when it was noted that she was tolerating the paclitaxel well, and that the masses in her abdomen were palpable, but not prominent.

74. On the advice of Dr B, Mrs A was referred for radiation therapy to try to minimise the likelihood of the mass in the suprapubic area breaking through the skin and forming an ulcer. On 12 Month33, a consultant radiation oncologist reported to Dr B that Mrs

[31] A condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets. Myelosuppression is a side effect of some cancer treatments.
[32] Gemcitabine is used in combination with other chemotherapy drugs to treat cancer of the ovaries.

A should commence palliative radiotherapy, and she underwent a CT scan to determine the depth of the subcutaneous lesion. On 16 Month33 Mrs A had a single fraction of radiation therapy, which made the lesion "less threatening".

75. Dr B reported to Dr C on 29 Month33 that Mrs A was continuing with "weekly Paclitaxel treatments which she [was] tolerating extremely well" and "appeared to be stable", although her CA 125 showed a "continued rise from 174 on [6 Month33] to now 275". Dr B wrote to Dr C again on 5 Month34, noting that Mrs A's CA 125 was rising and was by then 280. Dr B concluded that weekly paclitaxel was "not doing the job". Mrs A was given a trial of vinorelbine.[33]

76. On 9 Month34 Mrs A was admitted to the Emergency Department at Hospital 2 for drainage of ascites, which was causing pain. Mrs A received further scheduled vinorelbine on 10 Month34.

77. On 19 Month34 Mrs A received a transfusion of two units of red blood cells and experienced no adverse effects.

78. A CT scan of Mrs A's chest, abdomen and pelvis was taken on 26 Month34. On 27 Month34 the vinorelbine was ceased because it was deemed to be no longer effective.

79. From Month35 Mrs A developed malignant ascites, which required drainage. On 13 Month36 it is recorded that Mrs A had end-stage ovarian cancer with recurrent ascites, and was "pale and chronically ill appearing". Sadly, Mrs A died thereafter.

Further information — Waikato DHB

80. Waikato DHB told HDC that at the time of these events the Aesculapius programme used to calculate dosing of chemotherapy agents (including single-agent carboplatin) could be accessed only at Hospital 1, where it is based, or within the Waikato DHB IT network.

81. The Aesculapius programme could not be accessed remotely, which meant that the prescribing system was not readily available to the consultant at Hospital 2 to review or update patient information during clinic visits. If a patient's weight changed, it was up to the oncologist to make a "definite and determined" entry into the programme when he or she returned to Hospital 1, which could be several days later.

82. Waikato DHB said that this system relied on the treating clinician to record and enter the relevant clinical data for each patient. The latest patient data was therefore not available at DHB2's hospitals, introducing the risk of medication error if the database was not updated by the treating clinician.

83. Waikato DHB said that Mrs A's recorded weight on the Aesculapius programme was not corrected during her treatment as her weight changed.

[33] A chemotherapy medication used to treat a number of types of cancer.

84. Waikato DHB stated that the process used by the nursing staff to administer carboplatin was the same standard process followed to administer chemotherapy, using the Lippincott procedure manual.[34]

85. Waikato DHB told HDC that a patient's weight was sometimes, but not always, dictated into the oncologist's clinic appointment notes, and the transcription became available a week later. It said that it had considered how it could prevent an error in respect of a process reliant on one person's memory, and observed that it would have been easier to update Mrs A's weight if:

- the weight had been displayed prominently on the front page of the clinical notes each time Mrs A was seen in the clinic, rather than on the back page, which was not easy to find; and

- there had been a connection between the computer programme system at DHB2 and the Aesculapius programme at Waikato DHB, so that the information could have been accessible in real time.

86. Waikato DHB told HDC that Mrs A had "at most two cycles between [clinic] visits", and "was not seen infrequently" during the time she received carboplatin. It said that Mrs A was seen infrequently when she was on oral etoposide "because she was doing very well and did not require such frequent visits". In response to the provisional opinion, Mr A told HDC that Mrs A was doing well because of her own research on the effects of natural remedies and a strict diet, removing any toxins that could have enabled the cancer.

87. Waikato DHB told HDC that it had recommended to DHB2 that it appoint an onsite physician for oncology patients. Waikato DHB also said that it is reviewing the model of service used at DHB2, and has requested that a clinician with interest in oncology/chemotherapy be appointed to DHB2 staff to provide clinic oversight.

Further information — Dr B

88. Dr B accepted that he failed to make the changes in the Aesculapius programme when he returned to Hospital 1. This meant that the Aesculapius programme was not updated and Mrs A's carboplatin dosage did take into account her reduced weight and changed creatinine level. Dr B said that "it is [his] fault entirely" that Mrs A's weight was not updated at Hospital 1.

89. Dr B also told HDC:

> "[Mrs A] specifically expressed to me that she had no problem with my management of her case whatsoever from the standpoint of the doctor–patient relationship. …"

90. In response to the provisional opinion, Dr B said that he told Mrs A that he accepted responsibility for the failure to update her weight and that they spoke at length about

[34] A point-of-care procedure guide to help clinical and nursing staff provide safe and effective care.

this and that she said she considered him "to be as much a victim of the system failure as was she". Dr B also said:

> "[Mrs A] told me personally that she had no complaint or concern with my management of her case [or] otherwise. She had me review her complaint [to HDC] and approve it prior to her submitting it. Her purpose in submitting the complaint was solely and entirely that the 'system' could be improved …"

Further information — DHB2

91. DHB2 stated that it provides satellite services to Waikato DHB cancer treatment service (CTS). DHB2 staff are trained by the CTS staff, who work with the consultants at the clinics situated at either of the DHB2 hospitals. DHB2 is responsible for administering the outreach clinics.

92. DHB2 told HDC that at the time of Mrs A's treatment, the Hospital 2 chemotherapy staff nurses documented the height and weight of the patient only at the patient's initial visit, and did not check the weight again. When the patient was seen in the oncology clinic by the consultant, the weight was noted in the clinical file. However, because the Aesculapius programme was not "readily available", it relied on the consultant entering the information after returning to Hospital 1.

Subsequent events

93. Waikato DHB and Dr B told HDC that medical oncologists are now able to access the Aesculapius programme remotely, and that they can make appropriate modifications to patient data while onsite at Hospital 2.

94. Waikato DHB said that it has reiterated to its consultants its current process with regard to weight recording, which is that "patients' weight will be recorded on the patient notes in a specific location". It said that the consultant will ensure that "any information that needs to be loaded into the Aesculapius programme for the purpose of calculating the dose will be done … at [Hospital 1]".

95. DHB2 advised that Hospital 2 chemotherapy staff now weigh patients at the start of every treatment, and document this in the patient's notes. The new weight is then checked to see if it is consistent with the weight documented on the script. If a discrepancy is noted, the oncologist/registrar at Hospital 1 is notified before the drug is given.

96. DHB2 stated that when the medical oncologist holds a clinic at Hospital 2, a DHB2 chemotherapy nurse attends with the patient, so each outpatient clinic has both Hospital 1 and Hospital 2 staff involved.

DHB2 policies

97. DHB2 provided HDC with a copy of the Lippincott Procedures, which state, in particular, that before recalculating a chemotherapeutic drug, the patient's "vital signs and current weight" should be obtained.

New policy introduced

98. In mid 2015 DHB2 introduced a Medication Management Policy[35] (the policy) which states, in particular, that where the medication regimen is altered (ie, a change in dose), the prescriber must:

- cross through the medication order and administration section for that order;
- sign, date and time it in the appropriate box on the chart;
- re-prescribe the medicine on a new line; and
- notify the nursing/midwifery staff of changes made.

99. The policy also states that medicines requiring a mathematical calculation to ascertain the correct dose "must be independently checked by a second health professional", and that the health professionals checking medicines and administering medicines are "directly accountable" when the prescription is not clearly understood or followed, or if the checking procedures have not been followed.

Response to provisional opinion

100. Mr A's response has been incorporated into the opinion where appropriate.

101. Mr A told HDC that Mrs A did not have any issues with her doctor–patient relationship with Dr B.

102. Waikato DHB told HDC:

> "As a result of this complaint, Waikato DHB ensured all SMOs [senior medical officers] had access to the Aesculapius programme. This has now been in place for several months and is working effectively for all SMOs."

103. Waikato DHB also said that an external body is currently undertaking a review of DHB2's model of service, and that discussions are ongoing with both DHBs. It agreed to provide an update on this to HDC.

104. Dr B's response has been incorporated into the opinion where appropriate.

Opinion: Waikato District Health Board

Introduction

105. Waikato DHB, DHB2, and the staff involved in Mrs A's care had a responsibility to take all reasonable steps to ensure that services were provided to Mrs A with reasonable care and skill. District health boards are responsible for the services they operate, and are responsible for any service failures. Dr B, who provided care to Mrs A, bears some responsibility for the failure to enter the correct information to

[35] Procedure, Protocol and Guidelines Manual, document number 39083.

calculate the dosage of her medication. However, I am of the view that, overall, this deficiency was a result of systemic issues at Waikato DHB.

Calculation of chemotherapy dosage — Breach

106. In 2012 Mrs A was diagnosed with ovarian cancer. At an MDM, it was recommended that she commence chemotherapy, with consideration of debulking surgery if she had a good response to the chemotherapy. On 28 Month2 Dr B discussed the MDM findings with Mrs A and her husband. Mrs A agreed to receive neo-adjuvant chemotherapy with paclitaxel and carboplatin. She had one cycle of paclitaxel/carboplatin prior to surgery. Three infusions were given weekly during the cycle (carboplatin and paclitaxel on day #1, paclitaxel on day #8, and paclitaxel on day #15).

107. Mrs A's first cycle of paclitaxel and carboplatin was poorly tolerated, and she had leukopenia, which prevented the second cycle being given three weeks later. In Month4 Mrs A underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy.

108. Dr B planned to resume chemotherapy with paclitaxel and carboplatin. However, a CT scan showed no evidence of disease, and Mrs A declined further chemotherapy, so it was decided to monitor her progress.

109. By Month13 Mrs A's symptoms were increasing, and a CT scan showed further progression of the disease. Mrs A was still active and working, and did not want a treatment with toxic side effects, so Dr B prescribed oral low-dose etoposide. Oral etoposide 50mg per day was administered from Month13 until 11 Month24 and, during that period, Mrs A did not have cytopenia.

110. In Month24 the cancer began to worsen. By then, Mrs A's weight was 65.6kg compared with 84kg in 2012. Dr B advised Mrs A to begin a course of single-agent carboplatin.

111. Blood tests on 29 Month24 showed a creatinine level of 64mmol/L, which was written on the chemotherapy prescription.

112. Dr B calculated Mrs A's first dose of single-agent carboplatin. The Aesculapius prescription form shows that the calculation was based on levels from 2012, prepopulated into the Aesculapius programme. These were a weight of 84kg and a creatinine level of 90mmol/L. Mrs A received her first dose of 600mg of single-agent carboplatin on 8 Month25.

113. Further doses of 600mg of single-agent carboplatin were administered on 5 Month26, 25 Month26, 16 Month27 and 6 Month28, at which stage the carboplatin was discontinued because of myelosuppression, and Mrs A was commenced on gemcitabine and remained on G-CSF support.

114. On 8 Month30 a chemotherapy nurse noticed that Mrs A had been receiving gemcitabine based on a weight of 84kg, some 20kg more than her actual weight of 65kg.

115. Dr B directed that Mrs A be administered a dose of 75% of the gemcitabine she had been receiving because of her cytopenia. On 30 Month30 Dr B noted that gemcitabine had not been effective in reducing Mrs A's palpable lesions, which were larger. Following discussion of her clinical options, Mrs A's treatment was changed to a weekly dose of paclitaxel, which was administered from 4 Month31 until 23 Month32.

116. Mrs A remained relatively stable until Month34, when her condition began to deteriorate, and she died a few months later.

117. The carboplatin dosage was calculated by the Aesculapius programme using data entered by Dr B. A weight of 84kg and creatinine level of 90mmol/L were entered when Mrs A's adjuvant chemotherapy was first ordered on 3 Month3. Dr B told HDC that using a weight of 84kg he calculated a carboplatin dose of 607mg, and the Aesculapius calculator determined that Mrs A be given 600mg, which is what Dr B signed off.

118. Mrs A's creatinine of 64mmol/L was handwritten into the Aesculapius script from 29 Month24. However, the calculation of carboplatin was still based on the historical data above. Mrs A believed that this error resulted in her receiving an overdose of chemotherapy drugs.

119. My expert advisor, oncologist Dr Richard Isaacs, advised: "There was a moderate deviation in the standard of care in calculating the initial dose [of single-agent carboplatin] …". Dr Isaacs calculated a dose of 668mg based on a weight of 84kg and creatinine of 90mmol/L. This meant that Mrs A was prescribed a lower dose than she should have been, although based on measurements from 2012, not 2014. Therefore, Mrs A was "ultimately not over-dosed … although the wrong weight and creatinine were used in calculating the dose", because her renal function had improved.

120. Dr Isaacs advised that, while Mrs A did not receive an excessive initial dose of carboplatin, "an error was made in using historic clinical data to calculate the dose. While there was human error in not using the current measurements, other contributing factors highlight this as a systems error …"

121. Dr Isaacs identified the contributing factors to Mrs A receiving an incorrect dose as being:

- An inability to enter clinical data immediately at the clinic visit; and
- A failure of safeguards to identify the use of historical data in the Aesculapius programme and to highlight the fact that the creatinine typed on the initial prescription differed significantly from the creatinine on the day of delivery.

122. The Aesculapius programme could be accessed only at Hospital 1, not directly from the outreach clinics. The system therefore relied on the consultant entering the updated patient information (such as a change in weight or creatinine level) when he or she returned to Hospital 1, or arranging for it to be done by someone else there. Based on the updated information, the oncologist at Hospital 1 would generate a referral to the clinical nurse manager in Hospital 2, who would arrange for the delivery of chemotherapy. The oncologist would chart the drug into a prescription form using the Aesculapius programme, and then the prescription would be sent from Hospital 1 to the Hospital 2 chemotherapy unit. The Aesculapius operating system meant that the latest data was not available at Hospital 2, which introduced the risk of medication error if the database was not updated.

123. In addition, Waikato DHB advised that Mrs A's weight was displayed on the back page of her clinical notes.

124. In my view, it was fortunate that Mrs A's renal function had improved, as this meant that she was not overdosed despite her weight loss. However, I consider that it was suboptimal to have a system that was dependent on clinicians updating the data on the Aesculapius programme some time after the relevant clinic. Dr Isaacs said that the miscalculation of the dose of carboplatin was a moderate deviation from the standard of care, and this was a systems error. I agree with Dr Isaacs.

Conclusion

125. The following systemic factors contributed to Mrs A receiving a dose of carboplatin calculated on the basis of her measurements from 2012 rather than 2014, and were, in my view, the responsibility of Waikato DHB:

- Changes in patient information, on which prescriptions for chemotherapy treatment were based (such as weight and creatinine levels), could be recorded only in the chemotherapy treatment computer system based at Hospital 1, and not by oncologists directly from off-site clinics.
- There were insufficient safeguards to identify the use of historic data, and that the weight and creatinine levels on the day of delivery differed from that data. Not only were oncologists unable to update patient details remotely, the patient's weight was not displayed prominently (or consistently) in the clinical file, which meant that it was not necessarily brought to the clinician's immediate attention at clinic appointments.

126. Accordingly, I find that Waikato DHB failed to provide services to Mrs A with reasonable care and skill and breached Right 4(1) of the Code.

Specialist review — Adverse comment

127. Dr B said that the time at which a patient would be seen by an oncologist could vary from just before a treatment to up to two weeks' post treatment. According to Dr B's notes, over the course of her single-agent carboplatin treatment (Month25–Month28), Mrs A was reviewed in Month25, Month27, and Month29. Dr B said that Mrs A had, at most, two cycles of treatment between visits.

128. Dr Isaacs criticised the infrequency of specialist clinical review of patients receiving chemotherapy at the outreach clinic. He said:

> "In my opinion, patients should have medical or nurse specialist review after each cycle of treatment to identify and manage toxicities, particularly those who have already experienced significant side effects."

129. Dr Isaacs said that there is a significant clinical risk if patients are reviewed with insufficient frequency. He observed that in the absence of more frequent review by the specialist team, "there should be an appointed local clinician with responsibility for patients on treatment, who is available to review patients prior to each cycle of treatment".

130. In my view, patients should have specialist review as soon as possible after each cycle of treatment, in order to identify and manage toxicities. This is particularly important for patients experiencing significant side effects. Although Mrs A was recorded as not being in discomfort from the treatment, she had, in Month25, been given G-CSF treatment due to neutropenic sepsis following her treatment with oral etoposide, which, according to Dr Isaacs, "clearly indicated she was at risk of subsequent myelosuppression". This risk alone, in my view, indicated the need for more regular review.

131. However, I accept that patients are seen by an oncology nurse prior to each treatment, and the oncologist is available by telephone if concerns arise. I also accept the limitations resulting from the operation of a remote clinic, which must be balanced against the benefit to patients of not having to travel to Hospital 1 for treatment.

Opinion: Dr B — Adverse comment

132. From Month1 to Month34 Mrs A consulted Dr B in respect of her ovarian cancer. Dr B signed off prescriptions for the chemotherapy treatment that Mrs A received, and approved the dosages calculated by the Aesculapius programme.

133. Dr B accepts that he was responsible for failing to update Mrs A's weight in Aesculapius. However, I note that Dr Isaacs was asked whether he would be critical of Dr B for not having his own system in place for updating patients' weight in the system, given the importance of weight in the calculation, and the fact that he knew that he could not do so remotely. Dr Isaacs advised:

> "I am sure he attempted to do so, but with a busy practice and dissociation of the measurement and site of prescription there will always be risks of omission due to distraction and human error."

134. As Mrs A's responsible clinician, Dr B was required to ensure that the calculations for treatment, which he signed off, were correct. Dr B recorded Mrs A's weight regularly.

He was therefore aware that her weight was decreasing; however, he failed to ensure that the Aesculapius programme was updated when further doses of carboplatin were calculated. I am critical that Dr B repeatedly signed off incorrect doses of carboplatin because of using incorrect information in making those calculations, despite the correct information being available to him. I am also critical that Dr B did not record the change in dosage he directed when the calculation error was brought to his attention.

135. I note that Dr B was aware of the system within which he worked, and it was open to him to have taken precautionary steps — such as having a system to remind himself to update the data when patient data entered in the Aesculapius programme was incorrect. I am critical of Dr B in that he failed to set up a back-up system, given the issues with the system in which he worked.

Opinion: DHB2 — Adverse comment

136. DHB2 provides satellite services to Waikato DHB cancer treatment service. DHB2 staff are trained by the CTS staff, who work with the consultants at the Hospital 2 Chemotherapy Unit. DHB2 is responsible for administering the outreach clinics.

137. DHB2 told HDC that, at the time of Mrs A's treatment, Hospital 2 chemotherapy staff nurses documented the height and weight of a patient only at the patient's initial visit, and did not check the weight again. When the patient was seen in the oncology clinic by the consultant, the weight was noted in the clinical file. However, because Aesculapius was not "readily available", it relied on the consultant entering the information when he or she returned to Hospital 1.

138. Dr Isaacs advised me that there were potential safeguards that could have been put in place, including the role of the clinical pharmacy team in checking doses, particularly for first dose administration, and the nursing staff administering the drug ensuring that the weight and creatinine stated on the prescription matched current levels.

139. I agree with this advice and am critical that DHB2 did not have adequate systems in place to check that the data relied on was correct, prior to administering chemotherapy treatment.

Recommendations

140. I recommend that Waikato DHB:

a) Provide a written apology to Mr A for its breach of the Code. The apology should be sent to HDC within three weeks of the date of this report, for forwarding to Mr A.

b) Report to HDC, within three months of the date of this report, with a detailed update on the effectiveness of the changes made as a result of this case, including:

- how clinicians' ability to access the Aesculapius programme remotely is affecting their service delivery;
- the results of the review of Waikato DHB and DHB2's models of service; and
- an assessment of the effectiveness of the changes made to its service delivery following the review .

141. I recommend that Dr B report to HDC, within three months of the date of this report, on how the ability to access the prescribing software remotely has affected his practice.

142. I recommend that DHB2 report to HDC, within three months of the date of this report, on the effectiveness of the changes it has made, including the new practice by Hospital 2 chemotherapy staff of weighing patients prior to treatment, and notifying a clinician at Hospital 1 if a discrepancy is detected against the script. The update should also provide details on the changes made to Aesculapius, whether an onsite physician has been appointed for the outreach clinics, and whether clinicians at those clinics have adequate access to electronic databases, including the Aesculapius programme.

Follow-up actions

143. An anonymised copy of this report, with details identifying the parties removed except Waikato DHB and the expert who advised on this case, will be sent to the Royal Australasian College of Physicians (RACP), the Health Quality & Safety Commission, and the New Zealand Pharmacovigilance Centre, and placed on the Health and Disability Commissioner website, www.hdc.org.nz, for educational purposes.

Appendix A: Independent advice to the Commissioner

The following expert advice was obtained from medical oncologist Dr Richard Isaacs:

"Thank you for inviting me to provide advice to the Health and Disability Commissioner on the care provided by [Dr B] and the [CTS] to [Mrs A] between 5 [Month26] and 24 [Month29].

I confirm I have read and agree to follow the guidelines for independent advisors to the Health & Disability Commissioner.

I am a Medical Oncologist with 19 years of Consultant experience, holding the Fellowship of the Royal Australasian College of Physicians since 1995. I am currently Head of Medical Oncology at the MidCentral Regional Cancer Treatment Service in Palmerston North and have held leadership roles in Medical Oncology and General Physician training in New Zealand. I am responsible for chemotherapy administration not only in the Manawatu, but also supervise an outreach service in New Plymouth.

You have asked me to comment not only on the quality of care provided to [Mrs A], but also the systems put in place to ensure appropriate care and whether the complications identified by [Mrs A] are directly attributable to the increased chemotherapy dose she stated she received.

Case Summary

I would first like to review the facts as provided to me, by summarising her clinical history from my perspective.

[Mrs A] was diagnosed in [Month1], at the age of 51, with bulky Stage III serous cystadenocarcinoma of the ovary with extensive pelvic and peritoneal disease. She was treated with 3 infusions of paclitaxel and carboplatin as primary therapy from [Month3] and I understand had significant myelosuppression with that treatment. She was able to proceed with surgical debulking in [Month4], leaving her with small volume residual disease. [Dr B] states further chemotherapy was offered, but declined.

In [Month13] [Mrs A] developed abdominal swelling with ascites and a decision was made to commence her on continuous, low dose daily oral etoposide, which was continued with clinical benefit until [Month23]. Her disease then progressed and in [Month26] she commenced single agent carboplatin, with her prescription stating this was given at a calculated dose factor of AUC6. She received an initial dose of 600mg. The calculated dose at that time, however, was based on levels of weight and creatinine from [Month2], rather than the 2014 levels, and [Mrs A] states that, as a consequence, she received a 30% overdose of chemotherapy, as her weight had fallen in 2014.

Following further treatments with the same dose of carboplatin, [Mrs A] had significant myelosuppression, with a fall not only in white cells, but also in her red

cell and subsequently platelet count. This myelosuppression was initially managed with the use of Granulocyte Colony Stimulating Factor (G-CSF), to avoid delays, rather than dose reduction. During this time [Mrs A] required repeated blood transfusion, receiving 2 units of resuspended red cells on three separate occasions (21 [Month27], 26 [Month28] and 31 [Month30]).

[Mrs A] asserts that there was a systems failure in her initial dose calculation, as the electronic database Aesculapius, which is based in Hospital 1, could not be accessed in 'real time' at [DHB2] Hospitals, preventing immediate transfer of clinical data to this electronic prescribing system. Treatments were prescribed in Hospital 1, on the return of clinicians from peripheral clinics, and changing data, such as weight, needed to be manually entered on the return of the clinician to Hospital 1, introducing the risk of error if this data was not added to the database. [Mrs A] feels that this is a 'systems error', rather than individual consultant responsibility, and advocates for an improvement in systems. [CTS] has subsequently upgraded their system to allow real time transfer of information between the different DHB Hospitals.

Assessment

Was the care provided to [Mrs A] by [Dr B] reasonable?

To provide my opinion on this question I must review the management process in further detail.

Initial management and calculation of carboplatin dose

[Dr B] reports [Mrs A] had significant myelosuppression with her initial 3-weekly chemotherapy regimen of carboplatin/paclitaxel chemotherapy in 2012. Significant (grade 3–4) myelosuppression occurs in 25–29% of patients receiving that combination, but would not usually preclude further treatment, which was being given with curative intent at that stage. I agree with [Dr B's] recommendation that she should have had further post-operative chemotherapy, to achieve maximal disease-free and overall survival, but am told this was declined. I have no doubt this would have followed full discussion at that time.

When [Mrs A's] disease recurred in [Month13], the management focus would have been on disease control rather than cure. Single agent carboplatin would usually be considered at that time, as [Mrs A] had 'platinum-sensitive' disease (defined by a platinum free interval of >6 months), and suboptimal exposure to this drug previously. [Mrs A] was apparently reluctant to receive the drugs which generated toxicity previously, however, and instead she received continuous oral etoposide 50mg daily, with documented clinical review by the specialist team 3 monthly. Oral etoposide is recognized as a second line treatment for advanced ovarian cancer, but carries risks of myelosuppression, which can be detected by regular monitoring of blood counts. [DHB2] only provided me with two FBC results during the period [Mrs A] was on this drug, which demonstrated mild, but progressive anaemia.

In [Month24], [Mrs A's] disease had again progressed and [Dr B] recommended she start on carboplatin. [Mrs A's] initial carboplatin was delayed, however, due to an episode of febrile neutropenia, following her prolonged course of oral etoposide. This clearly indicated she was at risk of subsequent myelosuppression.

The dose calculations for carboplatin are unique, in that they are dependent on the glomerular filtration rate (GFR), as drug levels are highly dependent on renal function. Dosing is based upon an estimate of the GFR and the desired level of drug exposure, according to the 'area under the curve' (AUC) of concentration x time (AUC, mg/mL x min). GFR should be estimated using the Cockroft-Gault equation. Using the desired target AUC (which typically varies between 5 and 7 mg/mL x min) and the estimated GFR, the dose of carboplatin is then calculated by use of the Calvert formula: Total carboplatin dose in mg = Target AUC x (estimated creatinine clearance + 25). Because of potential changes in weight or renal function, this calculation should be repeated prior to each administered course of carboplatin, if there is significant change in the variables of weight and serum creatinine levels.

[Mrs A's] weight of 65.6kg was recorded in [Dr B's] clinic letter of 11 [Month24] and her creatinine was manually annotated as 64mmol/l on the chemotherapy prescription sheet from 29 [Month24]. Calculations to define dose, however, were based on levels from 2012, when she had a weight of 84kg and creatinine of 90mmol/l. This error was the primary driver of [Mrs A's] complaint. Using the AUC factor of 6 to calculate dose, with a weight of [84]kg and creatinine 90mmol/l, my calculations predicted an actual dose of 668mg. [Mrs A] was thus prescribed 8% lower than that dose, but still based on measurements from 2012. Most importantly, if the dose was calculated using the actual measurements of [Month24], the planned dose would have been higher at 701 mg, because her renal function had improved. [Mrs A] thus had a 15% dose reduction, if an AUC of 6 was to be used, and she was ultimately **not over-dosed** as claimed, although the wrong weight and creatinine were used in calculating the dose.

Care during administration of carboplatin

Despite the initial carboplatin dose being reasonable, [Mrs A] did have significant toxicity from ongoing use of carboplatin. She received carboplatin 600mg on 8 [Month25], which as noted above was not an excessive dose.

My opinion on the care [Mrs A] received during this period is based on the provided written clinical notes. I have been provided with no record of further planned clinical reviews, or of verbal or email communication between the staff at [DHB2] and the [CTS] on [Mrs A's] situation. If this communication occurred, it is my opinion that it should have been documented in the clinical record and been available for review.

[Mrs A] was reviewed a week after starting carboplatin by the Waikato DHB team on 15 [Month25], when her weight was recorded at 60.8kg. She was clinically well and a plan was then made to review her after a further 3 cycles of

chemotherapy. The next record is from 4 [Month27] when it was noted that [Mrs A] had a clinical response to treatment. However, her second cycle had been delayed due to neutropenia and to enable treatment on schedule for her 3rd cycle she received G-CSF. She continued to receive this agent for subsequent cycles, receiving subcutaneous injections for 5 days, commencing the day after chemotherapy. There was no discussion of dose reduction in the provided clinical record.

The next medical review by [Dr B] was on 5 [Month29] when it was noted that [Mrs A] had suffered marked myelosuppression, having a haemoglobin of 60 g/l (normal 115–150), neutrophils 0.5 (normal 1.5–8 x 10^9/l) and platelets of 29 x 10^9/l (normal 150–400) on 29.8.14, resulting in cessation of carboplatin chemotherapy. [Mrs A] had a further blood transfusion as noted above and was subsequently treated with different chemotherapy, although CT staging indicated her disease was stable at that time.

Opinion and recommendations

My opinions on the quality of care provided to [Mrs A] relate to the time she received carboplatin from [Month25] until [Month29]. (The period is longer than that requested, but I believe the whole treatment period must be considered).

Carboplatin overdose

[Mrs A] did not receive an excessive initial dose of carboplatin, but an error was made in using historic clinical data to calculate the dose. While there was human error in not using the current measurements, other contributing factors highlight this as a systems error, as suggested by [Mrs A].

Those contributing factors included:

The inability to immediately enter clinical data at the clinic visit.

A failure of safeguards to identify the use of historical data and to highlight the fact that the creatinine typed on the initial prescription differed significantly from the creatinine on the day of delivery (7 [Month25]).

Potential safeguards included the Clinical Pharmacy team, who have a role in checking doses, particularly for first dose administration, and the nursing staff administering the drug, who should ensure that the weight and creatinine stated on the prescription are matched to current levels.

My opinion is that there was **a moderate deviation in the standard of care in calculating the initial dose**, despite the final result being lower and thus less toxic than the accurate calculated dose. This was a systems error.

Access to Aesculapius at peripheral clinics should significantly reduce the likelihood of further errors, but I also recommend that all first doses of chemotherapy are recalculated by the Clinical Pharmacy staff and that nurses

administering the chemotherapy ensure that the weight and creatinine measurements are current before they administer the drug. The e-prescribing system should also 'red flag' when there are significant changes in weight or creatinine levels e.g. a variance of >10%, as a further safeguard.

Frequency of Specialist review

The complications described after receiving carboplatin relate to [Mrs A] being at clear risk of myelosuppression, with significant toxicity seen at the time of initial chemotherapy in 2012, and again at the end of her treatment with oral etoposide.

From the information provided, it appears that after early assessment one week after cycle 1, subsequent clinical review by the specialist team was planned only after every 3 cycles, without planned and documented intercurrent review by a local clinician. There was evidence of nursing review with documentation of blood results and patient side effect questionnaires during chemotherapy, but no documentation of planned clinical assessment was provided.

There are no New Zealand guidelines that I know of, but in my opinion patients should have medical or nurse specialist review after **each** cycle of treatment to identify and manage toxicities, particularly in those who have already experienced significant side effects. If such interactions occur, they must be documented and readily accessible in the clinical record, including any verbal or email discussion about decisions to treat and dose changes.

Without such documentation, I can only conclude that there was infrequent specialist review in this case, which in my opinion is a **moderate deviation** from an acceptable standard of care and carries significant clinical risk.

If the specialist team does not have the capacity to personally review patients more frequently, then there should be an appointed local clinician with responsibility for patients on treatment, who is available to review patients prior to each cycle of treatment. This could be a Medical Officer of Special Scale (MOSS) or a local Physician with an interest in malignancy, such as occurs at peripheral sites served by other Regional Cancer Treatment Services, including my service. If a Nurse specialist model is preferred, then there should be clear documentation of all interactions.

The use of G-CSF to maintain dose in palliative chemotherapy

G-CSF is used to maintain dose intensity in curative treatment and is used in selected patients on palliative therapy who have isolated neutropenia. However, [Mrs A] had toxicity not only in the neutrophil line (where G-CSF has activity), but also in the red cell and platelet lines, which would not have been reduced by this agent. [Mrs A] also describes bone discomfort related to G-CSF use, which further limited her quality of life. In a patient with a clear history of limited marrow reserve, it is my opinion that dose modification should be considered as a primary intervention when treatment is given with palliative intent and G-CSF should only be considered in highly selected patients in this setting.

In my opinion the continued use of G-CSF was a **mild deviation** from an acceptable standard of care, as its continued use was impacted on by infrequent clinical review as described above.

Do the systems put in place by the [CTS] … adequately support appropriate care? Were [Dr B's] responsibilities in relation to management of Aesculapius reasonable?

The concerns raised by [Mrs A] have directly resulted in Aesculapius being available to clinicians on site in remote clinics and should enable real time recording of weight and blood results, potentially adjusting doses as identified in this case. At all times dose calculations must be accurate, using current data and accepted formulae. If eprescribing is used with a database such as Aesculapius, there must be warnings to clinicians if blood levels or weights change significantly from pre-defined limits and doses must be adjusted during a treatment course. I agree with [Mrs A] that the requirement of clinicians to enter new data at a different time in [Hospital 1] carried some risk and could be considered a systems failure. I am told this particular issue has now been resolved with real time access to Aesculapius at [DHB2] sites. One of the main safety advantages of the eprescribing function is that systems provide a series of warnings that alert clinicians to the need for dose reviews e.g. if weight or critical blood levels change by a pre-specified percentage. Provided these functions are now in place, then the possibility of further such errors is unlikely, but further checks by the Pharmacist and Nursing and nursing teams must occur.

In my opinion the failure to access the prescribing software from outreach clinics was a further **moderate deviation** from the standard of care. These concerns have now been addressed and thus a similar situation is much less likely to occur.

Can the complications identified by [Mrs A] be attributed to the increased chemotherapy dose she received?

As discussed above, [Mrs A] did not receive an initial increased carboplatin dose, but did demonstrate intolerance of the prescribed dose of chemotherapy and dose reduction should have been considered. More frequent clinical review and early dose reduction would potentially have attenuated the toxicity [Mrs A] endured.

Yours sincerely

Dr Richard Isaacs MNZM MBChB D.Phil (Oxon) FRACP
Medical Head
Medical Oncology
MidCentral Regional Cancer Treatment Service
Palmerston North Hospital"

On 10 February 2016 further advice from Dr Isaacs was obtained in response to the following questions:

> **Whether you are aware of the systems used at comparable sized DHBs to calculate carboplatin. If you are, would the system deficiencies identified in this case be likely to occur at other DHBs?**
>
> "[Those hospitals that use e-prescribing] calculate Carboplatin doses from weight measured before each treatment. This is usually prescribed at the site the treatment is delivered. When using hard copy the weight is also measured before each treatment and dose adjustments made as needed."
>
> **Would you be critical of [Dr B] for not having his own system in place for updating patients' weight in the system, given the importance of weight in the calculation and the fact that he knew that he could not do so remotely?**
>
> "I am sure he attempted to do so, but with a busy practice and dissociation of the measurement and site of prescription there will always be risks of omission due to distraction and human error."

On 3 May 2016 Dr Isaacs provided the following amendment to his advice:

> "When I recalculate the actual dose with a weight of 84kg (correct) and creatinine 90mmol/l for a 51[-year-old] woman the dose would be 668mg."