Coroners Act 1996
[Section 26(1)]

Western  *Australia*

RECORD OF INVESTIGATION INTO DEATH

Ref: 13 /17

I, Sarah Helen Linton, Coroner, having investigated the death of ***Marjorie Joy JARICK*** *with an inquest held at the* ***Perth Coroner's Court, Court 51, CLC Building, 501 Hay Street, Perth*** *on* ***8 March 2017*** *find that the identity of the deceased person was* ***Marjorie Joy JARICK*** *and that death occurred on* ***10 July 2013*** *at* ***Rockingham Kwinana District Hospital*** *as a result of* ***opioid toxicity (predominantly fentanyl)****:*

Counsel Appearing:

Ms F Allen assisting the Coroner.
Ms F Vernon (Sarah Harper Avant Law Pty Ltd) appearing on behalf of Dr Yip.
Mr D Brand (MDA National Legal) appearing on behalf of Dr Holthouse.

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INTRODUCTION

1. Marjorie Joy Jarick (the deceased) was a patient at Waikiki Private Hospital when she was found unresponsive by nursing staff shortly after midnight on 10 July 2013. Resuscitation was attempted and she was taken by ambulance to Rockingham Kwinana District Hospital, where resuscitation efforts were continued but she could not be revived. Her death was declared at 1.28 am that same morning.[1]

2. A post mortem examination concluded the circumstances of the death were consistent with opioid toxicity (predominantly fentanyl). Given the deceased was in hospital at the time of her death and had been prescribed fentanyl in the post-operative setting, it was determined that an inquest should be held into the circumstances of the death.

3. I held an inquest at the Perth Coroner's Court on 8 March 2017.

4. The documentary evidence comprised a comprehensive report prepared by the Western Australia Police.[2] Oral evidence was heard from two doctors involved in the deceased's medical care prior to her death, as well as an expert witness in the field of pharmacology/toxicology, Professor David Joyce, and an expert pain specialist, Professor Stephen Schug.

5. The inquest focused primarily on the medical care provided to the deceased in Waikiki Hospital prior to her death, with a focus on the administration of fentanyl and its inherent dangers as a powerful opioid.

THE DECEASED

6. The deceased was born on 22 September 1958 and was the youngest of ten children.

7. The deceased was married to her husband Graham for 35 years and they had three children together. The deceased worked in restaurants, waitressing and on check-out, before she had her children.

MEDICAL HISTORY

8. The deceased was a heavy smoker, smoking 10 – 15 cigarettes a day for approximately 30 years.[3] She did not drink alcohol.[4]

9. There was a family history of diabetes and the deceased was diagnosed with Type 2 Diabetes Mellitus in 2010.[5]

[1] Exhibit 1, Tab 3.
[2] Exhibit 1.
[3] Exhibit 1, Tab 2, pp. 2, 4 and Tab 7 and Tab 9, Statement [19].
[4] Exhibit 1, Tab 9 [19].
[5] Exhibit 1, Tab, p. 4 and Tab 7.

10. The deceased had undergone a number of past surgeries, including:

- Breast reduction;
- Bilateral hernia repair;
- Hysterectomy;
- Tonsillectomy;
- Appendectomy; and
- Caesarean section.[6]

11. The deceased had also had a number of previous washout procedures in relation to abscesses in her groin area.[7]

12. The deceased was on a number of regular medications:

- Insulin (for diabetes);
- Crestor (for high cholesterol);
- Dilzem (for angina);
- Metformin (for diabetes);
- Minocycline (for recurrent infections); and
- Pantoprazole (for gastro-oesophageal reflux).[8]

13. The deceased was known to be allergic to morphine, oxycodone, Panadeine Forte and tramadol.

14. Shortly prior to her death the deceased had been recorded as weighing just under 100 kg, but after her death she weighed 111 kg and had a BMI of 38.4.[9] There is no clear explanation for the weight discrepancy, although on either recording the deceased had an above average body size that may have predisposed her to sleep apnoea.[10]

ADMISSION TO WAIKIKI PRIVATE HOSPITAL

15. The deceased was admitted to Waikiki Private Hospital on 24 June 2013 under the care of surgeon Mr Hairul Ahmad for management of a recurrent infection and cellulitis in her groin area. A CT scan showed extensive inflammatory changes in the labia and surrounding tissues, consistent with an infection. She was treated initially with analgesics (pregabalin, pethidine and Mersyndol Forte) and commenced on intravenous antibiotics.[11]

16. During her admission her observations were reported to be normal and her blood sugar levels were maintained between 4 and 17 mmol.[12]

17. Pain control was an ongoing issue and the deceased's pain was worse when ambulating. On 1 July 2013 Dr Ahmad reported that the deceased was

[6] Exhibit 1, Tab 7.
[7] Exhibit 1, Tab 7 and Tab 9, Statement [15].
[8] Exhibit 1, Tab 14.
[9] Exhibit 1, Tab 5.
[10] Exhibit 1, Tabs 13 and 13A.
[11] Exhibit 1, Tab 7.
[12] Exhibit 1, Tab 7.

"trying to get off the Pethidine." Pain control was difficult due to her multiple allergies. Dr Ahmad requested a review by a chronic pain management specialist.

18. At Dr Ahmad's request, the deceased was reviewed by a Consultant Neurosurgeon who specialises in the area of pain management, Dr David Holthouse. Dr Holthouse explained that this involves dealing with patients with chronic pain and he manages all aspects of pain-related practice. He is currently a consultant at Hollywood Private Hospital.[13]

19. Dr Ahmad had asked Dr Holthouse for some suggestions about possible options to manage the deceased's pain given her previous history of intolerance to oral opioids (nausea and vomiting). Dr Holthouse explained to Dr Ahmad that he was unable to be involved in her ongoing care as he only attended Waikiki Private Hospital once a week for a day. However, he was able to provide some advice regarding her analgesia and indicated Dr Ahmad could telephone him if he needed further advice.[14]

20. Dr Holthouse saw the deceased on 3 July 2013. At that time he was aware the deceased was on treatment for skin lesions and had undergone surgery, but he was not aware that any more surgery was being anticipated at that time. Therefore, Dr Holthouse understood that he was giving advice for chronic pain management, as opposed to any preoperative management of pain.[15]

21. In reviewing the deceased Dr Holthouse primarily took a pain history, in terms of what type of pain symptoms she had. He noted she had a lot of neuropathic or nerve pain symptoms, which she described as shooting pains. Dr Holthouse explained that this type of pain is more insidious and difficult to control than the usual, localised somatic type of pain.[16] The deceased rated her pain as 8 out of 10. She described receiving some relief from fentanyl patches, although the relief was incomplete.[17] Dr Holthouse felt that the fentanyl was controlling her somatic pain but not the neuropathic component of her pain.[18]

22. Dr Holthouse understood that the deceased had been treated with fentanyl patches during this hospital admission prior to his review, although this is incorrect. The deceased had, however, used fentanyl patches during a hospital admission between 8 and 15 May 2013.[19] Dr Holthouse was aware that the deceased had experienced vomiting when on a higher dose of fentanyl previously.[20] Dr Holthouse was concerned that the deceased still had significant pain despite being on the fentanyl. He did not believe that fentanyl was a good long term option for her as he did not favour the use of fentanyl patches for chronic pain.[21] Dr Holthouse also noted that fentanyl

[13] T 4.
[14] Exhibit 1, Tab 8.
[15] T 5 – 6.
[16] T 9.
[17] T 5.
[18] T 9.
[19] Exhibit 1, Tab 13A, p. 4.
[20] T 5.
[21] T 6; Exhibit 1, Tab 8.

can cause a condition called hyperalgesia, which means that they get more pain sensitivity and it can make their pain worse, especially when they have a nerve pain component. He considered this might apply in her case.[22]

23. Dr Holthouse took a history of the deceased's previous opioid use, which precluded many of the medications that are commonly used for chronic pain, due to her gastrointestinal reaction to them. He noted the deceased had never been tried on methadone. The only other possible option was another patch, such as Norspan (buprenorphine), but he was concerned she might have a reaction to it and that she wouldn't transition smoothly to it as it is not a very strong opioid and would likely have caused her to have withdrawals.[23]

24. Dr Holthouse suggested rotating fentanyl to Physeptone (methadone) with Maxalon (for nausea) to reduce the chance of side-effects. Dr Holthouse was aware that the deceased was also on Lyrica, Naprosyn and amitriptyline. He considered the combination of her other medications and the physeptone would be the optimal regime for the deceased.[24] Dr Holthouse recommended the deceased be commenced on Physeptone at a dose of 5mg twice a day and once established then any fentanyl should be ceased. Dr Holthouse advised that proper opioid observations should be undertaken whilst doing this process.[25] As it was, the deceased was not on fentanyl so she was able to commence physeptone immediately.

25. Dr Holthouse explained that his primary plan, consistent with his usual practice to wean patients off opioids wherever possible, was to eradicate all the other opioids and have the deceased only on methadone. Later, she might then be able to be changed to buprenorphine, a less strong opioid.[26]

26. Dr Holthouse explained in his evidence that he has inherited patients on very high doses of opioids before and when he does he tries very hard to get them off the opioids, but it takes some transitioning steps to do so.[27]

27. Dr Holthouse was not contacted again after 3 July 2013 in relation to the deceased.[28] He dictated a letter to Dr Ahmad explaining his advice. In his letter he stated that, "Fentanyl provides another possible option but because it is a rapidly acting opioid it is more likely to cause side effects in the longer term."[29] Dr Holthouse advised in his report to the court that the side effects he was concerned about were hyperalgesia (especially since the deceased seemed to have a neuropathic component to her pain) and dose accumulation.[30]

[22] T 9 – 10.
[23] T 5 – 6.
[24] Exhibit 1, Tab 8.
[25] Exhbit 1, Tab 8.
[26] T 6. 11.
[27] T 8.
[28] Exhibit 1, Tab 7.
[29] Exhibit 1, Tab 8.
[30] Exhibit 1, Tab 8.

28. On 4 July 2013 the deceased had a superficial dehiscence of the right groin wound with some wound discharge and surgery was planned for 8 July 2013.[31]

29. On 5 July 2013 the deceased complained of swelling of the lower legs. This prompted a Doppler ultrasound to exclude deep vein thrombosis. No evidence of deep vein thrombosis was found.[32] The deceased was allowed home for the weekend. She returned to hospital on 7 July 2013 in preparation for surgery the following morning.

THE SURGERY & ANAESTHESIA

30. Anaesthetist Dr Cheng B. Yip met and examined the deceased at around 7.30 am on the morning of the planned surgery, being 8 July 2013. Dr Yip is a consultant in Anaesthesia, Pain Medicine and Intensive Care. She has been working as a consultant anaesthetist at Royal Perth Hospital since June 2013 and also works as a visiting medical officer at various facilities in Western Australia, including with surgeon Dr Ahmad at Waikiki Private Hospital in 2013.[33]

31. Dr Ahmad would usually tell Dr Yip in advance of any potential issues with patients on the surgical list. Dr Yip was not notified by Dr Ahmad of any issues concerning the deceased. However, on the morning of the surgery, just prior to seeing the deceased, Dr Yip was told by the Clinical Nurse Manager that the deceased was a chronic pain patient and had been in the hospital before.[34]

32. Dr Yip recalled the deceased was a lovely, bubbly patient with no signs of shortness of breath.[35] After confirming what operation she was having and making sure her consent form was correct, Dr Yip ran through the deceased's surgical history and then enquired about any issues or allergies, while also noting allergies had been listed on the anaesthetic chart. It was recorded that the deceased had reactions to morphine, oxycodone, Panadeine Forte, tramadol and cephalexin. The reactions included nausea and vomiting, severe abdominal cramps and a generalised rash.[36]

33. The deceased denied any history of cardiac or respiratory disease and did not have any symptoms suggestive of sleep apnoea, except for occasional snoring.[37]

34. Dr Yip then examined the deceased and became very concerned when she saw the deceased's groin and extremely swollen lower limbs. The deceased advised that the swelling had started after the groin issues developed, but indicated that the swelling had become worse over the past week. Dr Yip

[31] Exhibit 1, Tab 7.
[32] Exhibit 1, Tab 7.
[33] T 20; Exhibit 1, Tab 9, Statement [1] – [6].
[34] T 24; Exhibit 1, Tab 9, Statement [9] – [12].
[35] Exhibit 1, Tab 9, Email.
[36] T 21; Exhibit 1, Tab 9, Statement [15] – [16].
[37] Exhibit 1, Tab 9, Email and Statement.

tried to ascertain the cause of the lower limb swelling. The main possibilities were the groin infection, deep vein thrombosis or congestive heart failure. The deceased advised a scan had been recently done, which did not find anything significant, so DVT was unlikely. The deceased's ECG did not show any right or left ventricular strain changes that would have indicated heart failure and there were no other signs of heart failure.[38] After excluding the other options, Dr Yip concluded the swelling was most likely related to the groin infection. Dr Yip considered that there was no evidence from the examination to warrant a chest x-ray.[39]

35. Dr Yip asked the deceased to rate her pain, which she scored as 7 out of 10.[40] The deceased's observations were recorded in the chart as normal and her weight had been taken by the nurses that morning and was just under 100 kg.[41]

36. Dr Yip noted the deceased's body habitus, report of moderately severe pain from the groin despite the amounts of analgesics already prescribed and the additional leg swelling, which limited her mobility and thereby increased her risk of DVT, pulmonary embolism. She considered these factors "made adequate pain control dire in her situation."[42]

37. For the surgery, Dr Yip planned a general anaesthetic, which she discussed with her.[43] Dr Yip then discussed the post-operative pain control plan with the deceased. Dr Yip initially recommended a patient controlled analgesia (PCA) but the deceased expressed concern as she had used one after a previous surgery and experienced severe stomach cramps and vomiting. Given her past experience, the deceased indicated she didn't want a PCA on this occasion. The deceased then told Dr Yip that she had used '50' fentanyl patches a month earlier, which had given her the best pain relief without any adverse reaction. The deceased also expressed her apprehension about having more pain after this surgery, as she had been informed that this was a possibility.[44]

38. Dr Yip assumed the deceased's reference to '50' fentanyl patches was to 50mcg/hr fentanyl patches and initially thought it must have been prescribed for her current groin infection. However, Dr Yip reviewed the current pain control and medication chart and noted there was no record of a prescription for a fentanyl patch and no sign that she was wearing one.[45]

39. Dr Yip does not usually use fentanyl patches for immediate post-operative pain control as it is difficult to titrate the dose for acute pain. Indeed, she gave evidence at the inquest that this was the first, and only, time that she did so.[46] Dr Yip's primary concern was the inadequate control of the deceased's chronic pain, rather than the acute immediate post-operative

[38] Exhibit 1, Tab 9, Email and Statement.
[39] Exhibit 1, Tab 9, Email.
[40] Exhibit 1, Tab 9, Statement [23].
[41] T 23.
[42] Exhibit 1, Tab 9, Email.
[43] Exhibit 1, Tab 9, Statement [26].
[44] Exhibit 1, Tab 9, Statement [27].
[45] T 23.
[46] T 24.

pain she would experience, which appeared to be less of a concern. Dr Yip also indicated she was very concerned about achieving good pain control for the deceased as the resulting immobility caused by the pain was related to the swelling in her legs, which increased the risk of DVT and pulmonary embolism. She hoped that by managing her pain it would increase the deceased's mobility and reduce the risk of deep vein thrombosis and pulmonary embolism.[47]

40. Taking into account the deceased's history of severe vomiting in reaction to most commonly used oral analgesics (other than the ones she was already prescribed) and the limited options available at that particular hospital, Dr Yip chose to prescribe a fentanyl patch as she considered it provided an alternative route of administration. Dr Yip also considered this would provide the deceased with round-the-clock pain control, avoiding the peaks and troughs of other intramuscular or subcutaneous modes of administration.[48]

41. Dr Yip indicated that if she had been in a tertiary hospital, such as Royal Perth Hospital, there would have been a lot of other different medication options available, but given it was a much smaller hospital, those options weren't available at Waikiki Private Hospital.[49]

42. Dr Yip was not aware at the time of making this decision that the deceased had been seen by Dr Holthouse, and she did not read his entry in the progress notes.[50] Dr Yip did later note that another doctor had prescribed the physeptone and Maxalon, but did not recognise the signature.[51] Dr Yip gave evidence that if she had been aware that Dr Holthouse had seen the deceased as a chronic pain patient then she would have given him a phone call to ask him what he would have done and at least discussed the perioperative plan with him. However, she did not get that opportunity.[52]

43. In determining the appropriate fentanyl dose, Dr Yip took into account that the deceased had said that her pain had been much worse since she had gone home, so she based her opioid requirement on the time the deceased was admitted in hospital. Dr Yip indicated there were two main factors to consider: first, her recent baseline requirement and second, the additional requirement after surgical intervention. Dr Yip did some calculations based upon the deceased's current opioid medications, converting them all to equivalent doses of oral morphine, to determine what the deceased would require during the operation and post-operatively. She then looked on the internet at the product information's table for conversion of oral morphine to patch and concluded that a 75mcg/hr fentanyl patch would replace the deceased's current analgesia, given the deceased was not opioid naive.[53] Dr Yip considered this to be "a conservative calculation for [the deceased], judging from her clinical response."[54] Dr Yip placed particular emphasis on

[47] T 23, 29; Exhibit 1, Tab 9, Email and Statement [30] – [34], [42].
[48] T 24; Exhibit 1, Tab 9, Email and Statement [30] – [33].
[49] T 25.
[50] T 24; Exhibit 1, Tab 9, Statement [35] – [36].
[51] Exhibit 1, Tab 9, Statement [50].
[52] T 45.
[53] Exhibit 1, Tab 9, Email and Statement [44].
[54] Exhibit 1, Tab 9.

the pethidine the deceased had received over the previous two weeks while in hospital.[55]

44. The deceased would also have pethidine available to her for her acute post-operative pain, if the need arose.[56]

45. The deceased underwent an excision of lesion in the supravagina area and exploration of the right groin at around 11.00 am. She was in theatre from 11.00 am to 12.05 pm. At the induction of anaesthesia Dr Yip had to give the deceased 150mcg of intravenous fentanyl, which is double what she would normally give for a similar procedure. Dr Yip had asked the deceased whether she had felt any difference after administering the usual 75mcg and the deceased had said no, which prompted the second 75mcg dose. Dr Yip had then proceeded to anaesthetise the deceased for surgery. The surgery itself was uneventful.

46. While the deceased was anaesthetised Dr Yip discussed with Dr Ahmad her concerns for DVT due to the deceased's lower limb swelling and pain issues. He confirmed there was no evidence of deep vein thrombosis in the ultrasound findings taken earlier. Nevertheless, Dr Yip ensured the deceased was given DVT prophylaxis immediately and this continued in the post-operative period.[57]

47. The deceased was in recovery from 12.10 to 12.45 pm. At 12.20 pm she reported a high pain score and required additional intravenous fentanyl. She was given three x 30mcg doses to control her pain. In total, during her intraoperative and recovery period, the deceased was given 240mcg of intravenous fentanyl within a 1.5 hour period. Other than her pain, the deceased's post-operative observations were generally reassuring.[58] She returned to the ward at 1.00 pm. At that time she had a sedation score of 2 (mild-occasionally drowsy, easy to rouse) and her observations were stable.

48. The deceased's daughter last spoke to the deceased at 4.00 pm on 8 July 2013. The deceased was on oxygen and appeared to have problems breathing. The deceased's family were aware that she didn't normally respond well to anaesthetic and it would usually take her a day to fully recover.[59]

49. The deceased was commenced on her first fentanyl patch 75mcg/hr at 7.00 pm on 8 July 2013 (although Dr Yip seemed to think that it had been given at 5.00 pm in her statement).[60] Dr Yip had previously explained to the deceased the safe use of the patch, including avoiding hot showers and not applying heat or hot water bottles close to the patch. Dr Yip also explained that if further patches were required, the site of application must be a new site and should be in the torso or upper arm. Dr Yip had warned the deceased to advise the hospital staff if she experienced any adverse reactions

[55] T 44 – 45.
[56] Exhibit 1, Tab 9, Statement [43].
[57] Exhibit 1, Tab 7 and Tab 9.
[58] Exhibit 1, Tab 9, Statement [52].
[59] Exhibit 1, Tab 2, p. 4.
[60] Exhibit 1, Tab 9, Statement [53].

and assured her that since she was an in-patient, she would be monitored closely.[61]

50. An entry at 8.50 pm noted that the deceased was comfortable, her wound remained intact, medications were given as prescribed and she was tolerating food and fluids.

51. The deceased was reviewed by Dr Ahmad at midday on 9 July 2013 and the deceased reported that her pain was much better and she was "in a much better place than two days ago." She was able to walk outside the ward unassisted for her cigarette smoking.[62]

52. The deceased's husband visited her at about 3.00 pm that day and she appeared to be recovering from her surgery.[63]

53. According to the medication chart the deceased was given 50mg of pethidine at 5.25 pm. At 8.45 pm on 9 July 2013 a nursing entry indicated that the deceased had slept most of the day.

54. An entry by the night staff recorded that the deceased was seen returning to her room at about 8.40 pm after going out to have a cigarette. A short time afterwards she rang her call bell as she had vomited up her medications (Mersyndol Forte, methadone and amitriptyline), all of which she had been given at 8.30 pm. Her observations at 9.40 pm recorded a BP of 105/58, a heart rate of 90, oxygen saturations of 94%, respiratory rate of 16 and a pain score of 5/10.

55. Dr Ahmad was telephoned at 10.30 pm by the night duty nurse to discuss pain relief. Dr Ahmad advised that the deceased should be re-administered Mersyndol Forte, methadone 5mg and amitriptyline 100mg, which were then given at 11.00 pm. The deceased was told that staff would return at midnight with her intravenous antibiotics and was left watching television with her door closed.

56. Dr Yip was not consulted when the deceased vomited. She gave evidence that she would have preferred to be consulted when that occurred, but unfortunately she was not. If she had been consulted, Dr Yip's evidence was that she would have asked the nursing staff to repeat the vital signs and check her oxygen saturation. If she had been told that the oxygen saturation was 94%, she would have asked them to supplement the deceased's oxygen. Dr Yip said she would certainly not have repeated the opioids dose as there was no witness to the vomiting event, and only the deceased's account that this had occurred, which would have made Dr Yip cautious in accepting it. Dr Yip stated she would have attended and assessed the deceased herself at that time to make sure that the deceased wasn't in any kind of respiratory depression because of the opioids, and also to ascertain whether the vomiting was due to toxicity from the opioids. Dr Yip said she always made herself available to the nursing staff and told them if there were any

[61] Exhibit 1, Tab 9, Statement [34].
[62] Exhibit 1, Tab 7.
[63] Exhibit 1, Tab 4.

problems at all (whether due to the anaesthetic or not) and they can't contact the surgeon, they can contact her.[64]

57. Dr Yip was not sure why on this night the nursing staff contacted Dr Ahmad rather than her, but acknowledged there was an option to contact either of them in the circumstances. Dr Yip's evidence was that usually Dr Ahmad would discuss the matter with her if there were any issues pertaining to the anaesthetic, rather than surgical alone, but unfortunately on this night Dr Ahmad did not call her.[65]

58. A torchlight check between 11.00 pm and midnight reported no concerns.

59. At 12.20 am on 10 July 2013 a nurse entered the deceased's room, which was in darkness, to administer her antibiotics. The nurse turned on the lights and found the deceased unresponsive. A Guedel airway was inserted and full CPR was commenced. The deceased was given naloxone 400 µg, which had no effect. Paramedics arrived at 12.34 am.[66] The deceased was in cardiac arrest so she was given adrenaline and two shocks were delivered, which achieved return of spontaneous circulation but no physical signs of life. The deceased was taken by ambulance to Rockingham Hospital. Further resuscitation efforts were unsuccessful and she was certified life extinct at 1.28 am on 10 July 2013.

60. Dr Yip had not seen the deceased following her surgery. She had been planning to review the deceased on 10 July 2013 but was advised of her death.[67]

CAUSE OF DEATH

61. A post mortem examination was performed on 12 July 2013 by a forensic pathologist, Dr D.M. Moss. There was evidence of recent surgery to the groin/lower abdomen/external genitalia with no evidence of significant local complications. There was focal severe hardening and narrowing of the blood vessels over the surface of the heart (coronary artery atherosclerosis) and the lungs contained excess fluid (marked pulmonary oedema and congestion). There was possible swelling of the soft tissues of the larynx.

62. Microscopy examination confirmed the presence of coronary artery atherosclerosis. The lungs were congested but showed no definite evidence of bronchopneumonia. Swelling of the tissue of the larynx was not confirmed. A blood test to look for anaphylaxis (mast cell tryptase) was not significantly raised.[68]

63. Microbiology testing of the lungs showed post mortem contaminants but no evidence of pathogenic organisms.[69]

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[64] T 30.
[65] T 30 – 31.
[66] Exhibit 1, Tab 10.
[67] Exhibit 1, Tab 9, Statement [54].
[68] Exhibit 1, Tab 5.
[69] Exhibit 1, Tab 5.

64. Toxicology showed the presence of multiple prescribed type medication, including multiple opioid drugs.[70] Professor David Joyce was requested to undertake a review of the case.

65. Based on the initial results of the toxicology analysis, Professor Joyce stated that the important drugs to consider in relation to the death of the deceased are codeine, morphine, amitriptyline, methadone, fentanyl and pethidine, although he considered the amitriptyline to be of the least concern.[71] After the initial toxicological analysis, Professor Joyce asked for a targeted analysis for fentanyl. Professor Joyce asked for this analysis as the post-mortem findings were consistent with an opioid death, which commonly involves increased lung weight and lung congestion. The hospital notes, while not describing anything particularly extraordinary about the patient's post-operative condition, also included signs which, in retrospect, might have been pointers towards opiate toxicity, such as sleeping all day, the drop in oxygen saturation and vomiting. For that reason, Professor Joyce directed the chemistry centre "to go looking for the particularly potent opioid, fentanyl, which we had seen in a number of previous cases had been a significant contributor to death, even when it had not been detected on the first screening analyses."[72]

66. Professor Joyce noted after the second round of testing that the toxicological analysis found methadone, pethidine and fentanyl in the deceased's liver. Professor Joyce explained that there is a lot of information available to him in relation to methadone and pethidine, and he was able to say that the levels of these drugs found in the deceased's liver looked like the levels found in people who were on conventional therapy with those two drugs.[73]

67. Professor Joyce noted in his report that the fentanyl level recorded in the deceased (approximately 12mcg/litre, was within the concentration range that has been associated with people dying from fentanyl, but was low in the broad range reported in fentanyl deaths.[74] However, he also noted there is no information of fentanyl levels in liver or fentanyl-treated individuals dying from unrelated causes, and it is well recognised that the distinction between lethal and therapeutic levels of opioids is blurred by tolerance. Therefore, Professor Joyce suspected that there might be a lot of people who have come to absolutely no harm from fentanyl in concentrations in the range found in the deceased. Therefore, it was consistent with a contribution to opioid death, but considered on its own, Professor Joyce did not find the level of fentanyl found to be a convincing piece of evidence.[75]

68. However, Professor Joyce performed some calculations of the opioids the deceased had been receiving prior to her exposure to the fentanyl patch, to see whether she had gained a reasonable tolerance to opioids at that time. Based on his calculations, Professor Joyce concluded that the use of a

[70] Exhibit 1, Tab 6.
[71] T 50.
[72] T 50.
[73] T 53.
[74] T 52 – 53; Exhibit 1, Tab 13A, p. 3.
[75] T 53.

75mcg fentanyl patch was "a very substantial increase in opioid exposure"[76] for the deceased.

69. Professor Joyce gave evidence that it was more likely to be the combination of opioids, put together in a person who had not developed the kind of tolerance needed to live with that fentanyl dose of 12mcg that came from a 75mcg patch.[77] Put in that context, in Professor Joyce's expert opinion it "represented a fairly compelling description of a death from opioid toxicity,"[78] with the thing that would give the additional degree of confidence being the presence of an additional opioid drug (fentanyl) within a concentration which has been associated with lethality, at least in multiple drug intoxication.[79] In that sense, Professor Joyce concluded that "without the fentanyl, the death could not be ascribed to opioid toxicity."[80] Professor Joyce indicated that the fentanyl given during the operation would have been well gone, so it was only the fentanyl that was delivered by the patch that was in issue.[81]

70. Dr Holthouse also agreed that, in his experience, the fentanyl would have contributed probably the most of all the medications, just because of its mechanism of action and how quick it is.[82]

71. Professor Joyce also noted that the liver concentration of fentanyl found was consistent with the patch releasing the dose it was supposed to do, which would suggest that contributors to toxicity such as fever or application of heat are probably not relevant in this case.[83]

72. Relying upon the reports provided by Professor Joyce, Dr Moss concluded the cause of death was consistent with opioid toxicity (predominantly fentanyl).[84]

73. Dr Yip accepted that it could not be disregarded that the deceased was on a significant opiate dose at the time of her death, including fentanyl, and that Dr Moss' opinion as to the cause of death was a possible cause. She also agreed that the fentanyl was a likely tipping point in the opioid dose and the vomiting and 94% saturation could be indicators of opioid toxicity.[85] However, Dr Yip also suggested that the deceased had a lot of other issues that could also not be disregarded as possibly contributing to her death. For example, Dr Yip referred to the deceased's documented regional wall abnormality and history of coronary spasms, as well as the evidence of developing coronary atherosclerosis and the fact that she was a diabetic and continued to smoke.[86]

74. Cardiologist Dr Xiao-Fang Xu provided a report, dated 23 December 2014, in relation to the deceased's cardiac status. Dr Xu had not met the deceased

[76] T 54.
[77] T 53 – 54.
[78] T 57.
[79] T 57.
[80] T 56.
[81] T 58.
[82] T 19.
[83] T 59.
[84] Exhibit 1, Tab 5.
[85] T 40.
[86] T 40 – 41.

but reported on her stress echocardiogram, which was ordered by her general practitioner after she had attended hospital with chest pain. The test was undertaken on 16 May 2011. The test was abnormal and suggestive of possible circumflex or diagonal coronary artery ischaemia or a myopathic process. However, subsequent diagnostic coronary angiography performed by Dr Xu's colleague, Dr Latchem, was reported as normal. This occurred after the deceased presented to hospital again with chest pains on 23 May 2011. Dr Latchem suggested at that time that the deceased's symptoms may have been due to coronary spasm, possibly related to her smoking, and he urged her to cease smoking. In addition to these two reports from 2011, Dr Xu was provided with the deceased's recent medical history. After reviewing the materials, Dr Xu expressed the opinion there was no obvious cardiac aetiology to explain the deceased's death.[87]

75. Taking into account all the evidence before me, I accept and adopt the conclusion of Dr Moss, relying substantially on the expert opinion of Professor Joyce, as to the cause of death. However, I also accept that the cause of death must be viewed in the context of the deceased's pre-existing health conditions, including her body habitus, although their contribution was not considered to be significant enough to form part of the established cause of death.

MANNER OF DEATH

76. The deceased had a number of significant health conditions, and was being treated in hospital at the time of her death for a recurrent infection in the groin area that had required surgical excision. The deceased was prescribed opioids, including fentanyl, to manage both her pain immediately after the surgery and to manage her chronic pain. The prescribing of opioids in those circumstances was standard medical management and had been part of the deceased's medical treatment in the past. The use of fentanyl patches for acute pain after surgery was not necessarily standard medical practice, but in this case it was noted to have been prescribed to manage the deceased's chronic pain rather than acute pain, even though prescribed for the post-operative period.

77. The deceased did have previous opioid drug exposure, which allowed her to tolerate a certain level of opioids. The problem arose in this case because the deceased did not have the level of opioid tolerance that was anticipated by Dr Yip, based upon her calculations of the morphine equivalence of the other opioid medications she had been exposed to prior to the surgery. The most significant addition in this case was the fentanyl patch. There was also an issue of an additional dose of some of her medications being administered as she had reported vomiting, which may have added to the opioid load, but it would not have been expected to cause respiratory depression on its own even if the deceased had absorbed the original doses.[88] There is no suggestion the deceased took any medications other than those prescribed to her and administered by hospital staff.

[87] Exhibit 1, Tab 11, Tab 12 and Tab 14.
[88] Exhibit 1, Tab 13, p. 10.

78. In the circumstances, I find that the death occurred by way of misadventure.

COMMENTS ON MEDICAL CARE AND FENTANYL

79. Under s 25(2) of the *Coroners Act 1996* (WA), a coroner may comment on any matter connected with the death, including public health or safety or the administration of justice. The circumstances of the deceased's death particularly raised public health issues in relation to the safe use of fentanyl patches.

Fentanyl

80. Fentanyl is a drug which is like morphine, but a lot more potent, so it can achieve morphine's analgesic effects at low doses. Unlike morphine, which is an opiate derived from opium, fentanyl is a synthetic opioid.[89] It has been described as being 50 to 100 times more potent than morphine and its analogues, which are designed to mimic the pharmacological effects of the original drug, may be as much as 10,000 times more potent than morphine.[90]

81. Professor Joyce explained that fentanyl's most conventional use is in the management of acute pain.[91] It can be used during anaesthesia for controlling the pain component of anaesthesia. It is usually administered by intravenous administration at the start of surgery and will wear off quickly after the operation.[92] Professor Joyce indicated in his own practice he has occasional use for it in the management of acute pain, but only in that context.[93] It was described as "a relatively easy opioid to use safely for acute pain relief" during anaesthesia and no concern has been raised about its use in that context in this inquest.[94]

82. It is not a new drug, having first been synthesized more than fifty years ago, but the use of fentanyl in the form of patches is more recent.[95] It is the use of fentanyl in patch form that is seen to be problematic and fentanyl patches have been associated with opioid deaths and "are more highly represented than they should be for the drug itself."[96]

83. The United Nations Office on Drug and Crime has noted that an increasing number of deaths have been associated with the use of fentanyl and its analogues, particularly in North America, although the problem appears to relate to illicitly manufactured fentanyl and its analogues rather than the

[89] T 51.
[90] United Nations Office on Drugs and Crime, Global Smart Update, Volume 17, "Fentanyl and its analogues – 50 years on."
[91] T 51.
[92] T 34 – 35, 51, 58.
[93] T 51.
[94] T 52.
[95] T 51 – 52;
[96] T 52.

legally manufactured product.[97] According to the United Nations Office on Drug and Crime, Australia has been experiencing a growing trend in deaths resulting from use of diverted fentanyl, with at least 123 fentanyl-associated deaths reported between 2000 and 2012 from misuse of the drug.

84. Within the Coroner's Court of Western Australia, some research has recently been undertaken in relation to reportable deaths involving fentanyl. A number of local cases involving unintentional overdose on fentanyl or one of its analogues were identified. Information from the National Coronial Information System indicated there were approximately 550 fentanyl related deaths nationally since from 2010 to 2017, with the majority determined to be unintentional deaths arising from the use or misuse of the transdermal patches.[98] Of those deaths, 66 were Western Australian deaths. Of the Western Australian deaths, just under half (45.5%) had been prescribed the drug, with the prescription status of another 21.2% unknown.[99]

85. I will return to discussion of the practice of prescribing fentanyl patches in Western Australia below, in the context of the expert evidence received during this inquest.

Use of Fentanyl in this instance

86. The choice of analgesia was difficult in the deceased's case, due to the deceased's intolerance to a large range of analgesia medications. She had experienced severe side effects when using many of the standard opioid medications in the past, which had led her doctors to try various alternatives to the standard options.

87. According to her general practitioner, the deceased was not taking any opioid drugs at her last consultation at the Parmelia Medical Centre on 7 June 2013, 13 days before her death. She started receiving pethidine on the day of her hospital admission on 25 June 2013 and Mersyndol Forte was also prescribed from that time. It appears that the deceased's prior history of intolerance to certain opioids was a key reason why Dr Ahmad requested a pain specialist's opinion, which led to her review by Dr Holthouse.[100]

88. When Dr Holthouse reviewed the deceased he mistakenly thought she was already on fentanyl patches at this time. The deceased had used fentanyl patches during an admission at Waikiki Private Hospital between 8 and 15 May 2013 after surgery for the same issue of groin infection, but had not used them during this admission. During the previous admission the deceased had tolerated the patches relatively well until the dose was increased to 100mcg/hr on 15 May 2013. This dose was not tolerated and the deceased experienced vomiting. Her vomiting had settled by the following day after removal of the patch.[101]

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[97] United Nations Office on Drugs and Crime, Global Smart Update, Volume 17, "Fentanyl and its analogues – 50 years on."
[98] NCIS Coronial Report CR17-28, Fentanyl-Related Fatalities in Australia, 2010 – 2017.
[99] NCIS Coronial Report CR17-28, Fentanyl-Related Fatalities in Australia, 2010 – 2017.
[100] Exhibit 1, Tab 8, p. 1.
[101] Exhibit 1, Tab 13A, p. 4.

89. Believing the deceased was prescribed a fentanyl patch at the time, Dr Holthouse elected to replace that opioid with methadone. Dr Holthouse expressed the opinion that the use of a fentanyl patch was not, per se, wrong in this case, but it did increase the risks.[102] Dr Holthouse stated more broadly that "the use of fentanyl as a drug is not wrong, but the … problem is it comes with a price."[103] In his view, it was better to change to methadone as he did not consider fentanyl a good long-term option for the deceased. Dr Holthouse was not aware that the deceased was to undergo surgery when he reviewed the deceased.

90. After finding out later that the deceased had undergone surgery, Dr Holthouse indicated that he would have liked to have been consulted about the deceased's perioperative management as he believes patients on high opioids are a special sub-group of patients and they need special considerations. Further, opioid patients that have a degree of obesity also constitute a special group of risk. He explained that obesity is also often associated with sleep apnoea and undiagnosed sleep apnoea, which can pose a very significant risk. Dr Holthouse believed it might have been better to have moved the deceased to a larger institution than Waikiki Private Hospital, as she may have required very special perioperative care and more intensive monitoring post-operatively.[104] It would require close monitoring of oxygen saturations hourly for the first 48 hours and generally half-hourly observations for the first 24 hours and then hourly or every second hour.[105]

91. Dr Yip gave evidence at the inquest after hearing Dr Holthouse's evidence. Dr Yip indicated that she absolutely agreed with Dr Holthouse's "opinion and exactly his sentiments about not using fentanyl patches in the perioperative setting and especially in the postoperative setting." As noted above, she had never used it before and this was the only occasion that she ever prescribed one.[106] Dr Yip said in evidence that she thought it was "because of the circumstances that led me to use the fentanyl patch on that day,"[107] referring to the deceased's allergies to opioids in particular. Also, Dr Yip agreed that the deceased's suggestion of a fentanyl patch probably did influence her to choose the fentanyl patches as an option.[108]

92. Dr Yip acknowledged that in hindsight another option may have been to increase the physeptone (methadone) rather than using the fentanyl patch. However, she was not very familiar with using physeptone, which is why she didn't go down that path.[109] As noted above, she was also swayed by the deceased's suggestion that a fentanyl patch had worked for her in the past.

93. Professor Stephen Schug is currently the Chair of Anaesthesiology at the University of Western Australia and the Director of Pain Medicine at Royal Perth Hospital. Professor Schug's particular area of research interest is opioids. Professor Schug was involved in the original development of fentanyl

[102] T 18.
[103] T 19.
[104] T 7 – 8.
[105] T 9.
[106] T 25.
[107] T 24.
[108] T 24.
[109] T 25.

patches when he was in Germany in the early 1980's and was working in one of the first centres to test the patches.[110] Professor Schug noted that despite some early efforts to promote the patches for acute pain relief, the early experience made it clear that the patches were not suitable solely for acute post-operative pain relief as there was a high risk of overdose because the patient had no background tolerance.

94. However, Professor Schug acknowledged in this case that Dr Yip was not prescribing the patch for acute post-operative pain relief, but rather to address the deceased's underlying chronic pain condition. In the context of the deceased's history of vomiting and inability to tolerate oral intake, her pre-existing opioid requirements before the operation and her refusal to use a PCA pump, Professor Schug expressed the opinion that Dr Yip's decision to prescribe a fentanyl patch was a reasonable choice in the circumstances.[111]

95. Professor Schug went on to explain that the case of the deceased would fit within that limited category when he would make use of a fentanyl patch in a perioperative setting, and whilst Professor Schug acknowledged that this then carried some risk of overdose, it is a case of balancing the benefits for the patient versus the risks. Professor Schug also noted that there are equally risks associated with methadone overdose.

Opiate Equivalence Conversion – establishing the correct dose

96. The deceased received her first, and only, fentanyl patch during this hospital admission on 8 July 2013. It was a 75mcg/hr patch.[112] The patch takes some time to reach maximal dose, usually at about 24 hours after application, which was only a few hours prior to her death.[113]

97. Dr Yip gave evidence that in deciding upon the 75mcg/hr fentanyl patch, she had used an equianalgesic conversion chart that varied slightly from that used by Professor Joyce, but the variation was not drastic.[114] Dr Yip indicated she based all her calculations on the equivalent dose of subcutaneous morphine, whereas Professor Joyce based his calculations on oral morphine.[115] The difference in calculations meant that on Professor Joyce's conversion rate it equated to a fentanyl patch of 50mcg/hr as opposed to 75mcg/hr.[116]

98. Professor Joyce had heard Dr Yip's evidence about her calculations, and the reasons why she may have reached a different conclusion to Professor Joyce. In his evidence Professor Joyce indicated that he wouldn't concur with Dr Yip's method of accounting, but he did concur with the proposition that a doctor may have read the medical charts to gain that impression (that a higher level of opioid tolerance had been reached, warranting a greater potency of patch).[117] This was particularly so given the time and information

[110] T 72.
[111] T 71 – 73.
[112] Exhibit 1, Tab 13A, p. 5 and Tab 14.
[113] Exhibit 1, Tab 13A, p. 3, Figure 1.
[114] T 27.
[115] T 28.
[116] T 34.
[117] T 55.

Dr Yip had available to her to do those calculations, compared to the length of time, information and expertise available to Professor Joyce to do his calculations. In essence, Professor Joyce maintained his calculations were correct, but acknowledged it was not unreasonable for Dr Yip to reach her conclusion at the time.[118]

99. Professor Joyce also noted that whilst there might have been some difference in survivability if Dr Yip had elected to use a 50 mcg/hr patch instead, it might still have had the same lethal potential as the 75 mcg/hr patch that was used.[119]

Monitoring and observations

100. The deceased was being monitored while in hospital, but the level of monitoring and recording of observations varied, with the interval increasing as the length of time following surgery increased.

101. Dr Holthouse referred to the observation charts and noted the reduced oxygen saturations and the extended gaps between the saturations taken on 9 July 2013, with a long gap between the reading of 94% taken at 12.50 pm, and 94% taken at 9.00 pm. Dr Holthouse observed that if they were retrying to titrate opioids, he would have thought that the observations should have been more frequent, at least two hourly. However, he acknowledged that a reading of 94% was not disturbingly low and it might depend upon her normal saturation levels.[120] Dr Holthouse also noted that in his practice, as part of that close monitoring, he generally would confine the patient to the ward. In this case, where the deceased was a long-term smoker, he would have strongly encouraged her to use a nicotine patch rather than leave the ward and have a cigarette.[121]

102. Dr Holthouse suggested that, with the benefit of hindsight, the deceased's reduced oxygen saturations and the fact that she had vomited, could have suggested opioid toxicity, and to then give another dose of physeptone on top of that without being sure whether the first dose of medications was absorbed, should have prompted more frequent observations.[122] Dr Holthouse suggested this was the type of thing that would need to be addressed at a hospital policy level as part of a protocol for perioperative opioid management.[123]

103. Dr Holthouse indicated that if he, as a pain specialist, had been told that the saturations were at 94% and she had vomited, that would have prompted him to get in the car and go in to the hospital and have a look at her. But he acknowledged that as a pain specialist he is 'hyper' about opioid analgesia and overdoses.[124]

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[118] T 56.
[119] T 66.
[120] T 17.
[121] T 9.
[122] T 18, 20.
[123] T 18 – 19.
[124] T 19.

104. Dr Yip noted that in a person with the deceased's body habitus and who was a chronic smoker, a saturation of 94% on room air is not very uncommon. Further, the observation chart did not indicate that a recording of 94% oxygen saturation should prompt any action. However, in hindsight, putting the oxygen saturation together with the vomiting, Dr Yip agreed with Dr Holthouse that at that stage the deceased should have been put on oxygen and put under continuous observation. Dr Yip acknowledged that it would not necessarily have been obvious to the nursing staff that this was what was required, although Dr Yip would have given them that instruction if she had been called.[125] For that reason, like Dr Holthouse, Dr Yip's evidence was that if she had been called, she would have attended the hospital to assess the deceased.[126]

105. Dr Yip also acknowledged that both the nursing staff and Dr Ahmad may have been misdirected by the fact that the deceased was still complaining of pain at the time she was vomiting, which was why the doses were repeated, as it may have appeared that she had not gained the benefit of those medications. For this reason, they would also not have been thinking it was necessary to remove the fentanyl patch. The deceased's history of vomiting on opioids may also have caused them to have less concern about this symptom, and Dr Yip explained that it is also not uncommon for many patients to vomit up to one or two weeks after surgery.[127] However, Dr Yip would have been particularly concerned about the possibility of respiratory depression as she did not normally prescribe a fentanyl patch.[128]

106. Professor Schug expressed the view the observations recorded would not cause any alarm about respiratory depression, noting "the level of consciousness, the intensity of pain and the respiratory rate are all contradicting that this patient was, at that point in time, at least, under the influence of a …too-high dose of opioid."[129] In his experience, you would expect the deceased to have become very drowsy and sedated first, which was not apparent in this case, although I note Professor Joyce did point to the fact that the deceased had been sleeping most of the day as a possible sign of sedation.

107. In Professor Schug's opinion the oxygen saturations were a less helpful guide and indicated that they train their team to look for a drop in the level of consciousness as the primary indicator of respiratory depression, which was not present here.[130] Professor Schug also did not think the repeated dose of methadone was of great significance, in comparison to the other opioids the deceased was on.[131]

108. Professor Joyce's evidence was that, like Dr Holthouse and Dr Yip, he also would have ensured closer monitoring of the deceased after she was readministered the dose of methadone and other drugs, noting that he works

[125] T 31 – 32.
[126] T 30.
[127] T 32 – 33.
[128] T 31 – 32.
[129] T 78.
[130] T 79 – 81.
[131] T 78.

in a teaching hospital with ready access to resident medical officers to perform that task, unlike at Waikiki Hospital.[132]

109. The evidence of Professor Joyce was that the deceased was recoverable right up until the time she expired, so closer monitoring may well have saved her life.[133] If it had been identified that the deceased was experiencing opioid toxicity, there were steps that could have been taken, including removing the fentanyl patch, stopping all opioids, monitoring the deceased more closely and administering naloxone.[134]

Prescription and use of Fentanyl Patches generally

110. Professor Joyce gave evidence that a lot of his clinical practice involves relatively old people and a proportion of those, in the vicinity of two or three a year, will come to hospital in a state of confusion or very, very sick and ultimately it will be revealed that they have a fentanyl patch on them that is the source.[135]

111. Dr Holthouse gave evidence that he does not advocate the use of fentanyl in ongoing management of pain patients and indicated his belief that all of the pain physicians in Western Australia would hold a similar view. Dr Holthouse explained that fentanyl has a number of problems, including dose accumulation, variable absorption in some people, unpredictable absorption if people are febrile (raised temperature) and people can develop a tolerance to it.[136] Dr Holthouse stated "it's a drug which I have really never been impressed with"[137] and his general approach with fentanyl patches is to try and remove people from them.[138]

112. In particular, Dr Holthouse does not tend to advocate fentanyl patches for use in the community and he remarked that "they're really a hospital based drug as far as I'm concerned."[139] Dr Holthouse explained that the potential for fentanyl to cause opioid induced hyperalgesia was one reason for this, as in a short term setting in hospital that is unlikely to occur, but in the longer term they can interfere with the treatment of the pain by making the patient more sensitive to pain.[140]

113. Dr Holthouse expressed his personal view that fentanyl patches should only be used in the community for palliative patches, and similarly he believes fentanyl patches should only be used in hospitals for palliative patients. He indicated that he has expressed this view numerous times in the past, so it is a long held view on his part and not something simply arising from the

[132] T 64.
[133] T 64 – 65.
[134] T 19 – 20.
[135] T 52.
[136] T 6 – 7.
[137] T 7.
[138] T 7.
[139] T 10.
[140] T 10.

events in this case.[141] He also believes that many of his colleagues would share his view.[142]

114. Dr Holthouse explained that fentanyl patches can pose a major risk in the opioid naïve patient, so he believes there shouldn't be an opportunity for a general practitioner to write a script for them to a patient who has never been on them. Dr Holthouse has in the past found them on 80 year old ladies, which makes him "very nervous"[143] because the elderly have an impaired ability to deal with opioids. However, his greatest concern is the variable rates of absorption. Dr Holthouse explained that if somebody puts them on a different area of the body, it can alter absorption. If they take a warm shower, it can also alter absorption. If they have a fever or infection, again it can alter absorption. Dr Holthouse stated that "the problem is you've got an agent which can accumulate" and it is also "really potent." For example, it is so potent that it is used as an anaesthetic. Dr Holthouse described fentanyl as a very good drug for rapid pain control after surgery (as was initially used for the deceased), so it is not this use of fentanyl that concerns him. Rather, it is the need to move them quickly from that situation straight after surgery to a long-acting drug.[144]

115. Dr Holthouse also explained the issue of dose accumulation. With a fentanyl patch the actual dose takes some time to equilibrate in the body. Dr Holthouse indicated that the effect can then slowly build up and accumulate. Dr Holthouse observed that with opioids, you can have really good pain control and then just a little bit more is enough to tip them into toxicity, and this is a recurrent thing he has seen occur with fentanyl patches. He recalled having seen a couple of cases where people have been on fentanyl patches for a few months and then been hospitalised with a lot of side effects as they are on the borderline between toxicity and therapeutic value.[145]

116. It is for these reasons that Dr Holthouse does not consider it to be a suitable drug to be used in a community setting unless the patient has a condition requiring palliative care.

117. In the hospital setting, although Dr Holthouse's preference is also for only palliative patients to use fentanyl patches, he explained that sometimes patients are admitted who are already prescribed them, which presents a difficulty. In those circumstances, it is necessary to manage the patients with what they are on, although Dr Holthouse indicated that down the track he would still be trying to get the patient onto a different type of opioid, although fentanyl is so potent that it requires a replacement with something else potent, like methadone.[146]

118. In conclusion, Dr Holthouse described fentanyl patches as "a very difficult drug to manage" and said that "even for pain specialists we find them

[141] T 12 – 13.
[142] T 13.
[143] T 13.
[144] T 13 – 16.
[145] T 14.
[146] T 13 – 14.

difficult." He believes they have a definite risk of causing problems, which is why he holds the opinion they should not be available outside the palliative setting.[147]

119. Dr Yip indicated that she does not normally use fentanyl patches as she deals primarily with post-operative pain and fentanyl patches cannot achieve good acute pain control as they take can take up to 72 hours to reach maximal level.[148] Consistent with this view, the product information for the fentanyl transdermal patches available in Australia indicates that they should not be used in the management of acute or post-operative pain as there is no opportunity for dose titration during short term use.[149]

120. Dr Yip has obviously reflected at great length on the death of the deceased. Dr Yip gave evidence that the deceased's death has taught her many things, particularly about chronic pain. Dr Yip is on the medical advisory committee at Waikiki Private Hospital and the things she has learnt from the deceased's death have prompted her to implement an in-hospital opiate observation chart at Waikiki Private Hospital that sets very strict guidelines as to the observations of a patient receiving opiates, as well as specific warnings to consider for anyone intending to start prescribing a fentanyl patch. In effect, the warning indicates that fentanyl patches should not be used in a perioperative period and should be prescribed solely for palliative care patients.[150] This is consistent with the view of Dr Holthouse as to fentanyl patches being appropriate only for palliative care.

121. As to the use of fentanyl patches generally by the medical profession, Professor Schug expressed a similar view to Dr Holthouse that "the fentanyl patches are widely used in Australia now and we think overused for chronic pain treatment and we have made multiple attempts to educate GP's and the general medical public about possibly the inappropriateness of fentanyl in many situations."[151] Professor Schug acknowledged that there are indications for a fentanyl patch to be used, and they are used at Royal Perth Hospital for patients with a background of chronic pain who may have nausea and vomiting or a requirement to fast post-operatively and a fentanyl patch is an elegant way to provide background analgesia to control most of the pain. However, that is the only time when they would use a patch in a perioperative setting and they will often initially use a PCA pump with fentanyl over 24 hours to try to ascertain an appropriate dose for the patch.[152]

122. Professor Schug also indicated that at Royal Perth Hospital fentanyl patches cannot be started by every doctor in the hospital. They can only be started by the anaesthesia pain team or palliative care team doctors, because of the potential risks. Professor Schug explained that they had experienced problems at Royal Perth Hospital with other teams starting fentanyl patches, which had brought about the change and they now have strict rules in place

[147] T 14.
[148] T 35.
[149] Exhibit 1, Tab 13A, Attachment – Durogesic Transdermal System Product Information.
[150] T 46 – 47; Exhibit 3.
[151] T 73.
[152] T 73 – 75.

for the prescribing of the patches. The same strict rules also apply to methadone, due to the potential risks.[153]

123. Professor Schug also referred to the problem that fentanyl patches are now a source of abuse in the community, where people boil them up, or smoke them, or put them in their cheeks so the drug is absorbed through the mucosa. Professor Schug described fentanyl patches as a "risky drug' and one needs to be aware of that and put precautions in place.[154] I note the product information specifically refers to the possibility that the patches may be retried and potentially abused, and the need to dispose of them carefully and return unused patches to the pharmacy.[155] However, the product information does not explain that accidental exposure to fentanyl can occur from handling the patches with bare skin.

124. Professor Joyce included information in his report that the fentanyl "patches have a notable reputation of post-operative toxicity and opioid death in similar situations. The risk prompted a warning from the United States Food and Drug Administration in 2005, updated in 2007, that fentanyl patches are contraindicated in the management of post-operative pain,"[156] and as I have set out above, similar information is provided in Australia through the Therapeutic Goods Administration (TGA) product information for the fentanyl transdermal patches. Professor Joyce explained that the product information can be taken as a set of directions as to how to use the product.[157] Professor Joyce noted that while the product information is not an absolute proscription on that use, he described it as "fairly strong wording"[158] and noted one would have to have fairly good reason to practice in a manner contrary to that recommendation.[159]

125. Professor Joyce noted in his report that "patch formulations are beguiling to a prescriber because everything about them seems benign."[160] Professor Joyce explained that his concern was that the patches' beguiling appearance (tiny bits of skin colour plastic) and the preconceptions we have about the skin's ability to prevent toxins getting across (as opposed to directly injecting a drug into the veins or introducing it into the gut) provides, in effect, a false reassurance that they are benign.[161] This applies to both prescribing doctors and patients.[162] Professor Joyce also noted that patients are quite accepting of them as a treatment as they have a naturopathic quality of a poultice being applied and can also have a strong emotional effect on patients as the patches are a constantly present reminder that they are being treated.[163]

126. In addition to the beguiling nature of the patches, Professor Joyce referred to the problem that the dose is in micrograms, which sounds very little but is because fentanyl is so potent.

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[153] T 81.
[154] T 82;
[155] Exhibit 1, Tab 13A, Attachment - Durogesic Transdermal System Product Information, p. 20.
[156] T 60; Exhibit 1, Tab 13A, p. 6.
[157] T 60; Exhibit 1, Tab 13A, Attachment.
[158] T 61.
[159] T 60 – 62.
[160] Exhibit 1, Tab 13A, p. 7.
[161] T 62.
[162] T 66.
[163] T 66.

127. Professor Joyce commented that opioid deaths are still the commonest drug toxicity deaths that he sees and many of those seem to involve doses of opioids which are not all that much greater than what the individual is accustomed to. It can also involve the introduction of some other drug, most commonly a benzodiazepine, which can be the tipping point.[164]

128. Professor Joyce noted that there needs to be an appreciation that tolerance to opioids is lost almost as quickly as it's gained, so that people who have been able to tolerate high concentrations of opioids may within a week or two have lost practically all of that tolerance.[165] Therefore, while everyone can tolerate a modest dose of opioid, before a person is put on a high dose their opioid history requires more scrutiny rather than simply taking reassurance from the fact that a person has tolerated a similar dose in the past.[166]

129. I asked Professor Joyce whether he believes the risks of fentanyl patches are well known in the profession in terms of the inherent risks that they carry. Professor Joyce's response was that the risks are better known now than they were in 2013 at the time of this death. Professor Joyce recalled that between about 2009 and 2013 he was asked about a number of fentanyl patch related deaths and over that time he was also seeing more patients who were coming in with fentanyl toxicity. However, although the risks are better known now, Professor Joyce also indicated he didn't know whether the risks were *well enough* known even now. Professor Joyce commented that he thinks that the "patches just have too good a reputation and that it hasn't been sullied enough by fact yet."[167]

130. In conclusion, the expert evidence consistently supported some limitation on the use of fentanyl patches in the community other than for palliative care, with a strong preference for restriction on the ability of general practitioners to prescribe fentanyl patches in Western Australia. The fact that even within Royal Perth Hospital where Professor Schug practices, the prescribing of fentanyl patches is limited to the anaesthesia pain team or palliative care team doctors because of the potential risks, supports this conclusion. From a coronial perspective, limiting access to fentanyl patches in the community to only those patients for whom it is recommended by an anaesthetist or pain specialist would be likely to have the additional benefit of reducing the potential for misuse of the patches in the community.

131. Accordingly, I make a recommendation, as set out below, to limit the ability to prescribe fentanyl transdermal patches to appropriate specialists.

132. I will also arrange for a copy of this finding to be provided to the Therapeutic Goods Administration so that they are aware of my recommendation arising out of the death of the deceased, as well as the other concerns raised in this case in relation to the use and disposal of fentanyl transdermal patches in the community.

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[164] T 63.
[165] T 63.
[166] T 64.
[167] T 65.

RECOMMENDATION

I recommend that the Department of Health amend the Department of Health *Schedule 8 Medicines Prescribing Code* to limit the authorisation to prescribe fentanyl transdermal patches to approved specialists for the treatment of pain, as set out in 2.5.8 of the current Schedule (2017). The current system in place for methadone, as set out in 2.5.3, might provide a helpful guide.

CONCLUSION

133. The deceased was a 54 year old woman who had a number of significant health conditions, and was being treated in hospital for a recurrent infection in the groin area that had required surgical excision. The deceased was prescribed opioids, including fentanyl, to manage both her pain immediately after the surgery and to manage her chronic pain. The prescribing of opioids in those circumstances was standard medical management and had been part of the deceased's medical treatment in the past. The use of fentanyl patches for acute pain after surgery was not necessarily standard medical practice, but in this case it was noted to have been prescribed to manage the deceased's chronic pain rather than acute pain, even though prescribed for the post-operative period. This was reasonable in the circumstances.

134. The deceased did have previous opioid drug exposure, which allowed her to tolerate a certain level of opioids. The problem arose in this case because the deceased did not have the level of opioid tolerance that was anticipated by Dr Yip, who prescribed the fentanyl patch, based upon her calculations of the morphine equivalence of the other opioid medications the deceased had been exposed to prior to the surgery. The most significant addition in this case was the fentanyl patch. There was also an issue of an additional dose of some of her medications being administered as she had reported vomiting, which may have added to the opioid load, but it would not have been expected to cause respiratory depression on its own even if the deceased had absorbed the original doses.[168] There is no suggestion the deceased took any medications other than those prescribed to her and administered by hospital staff.

135. On the evening of 9 July 2013 the deceased succumbed to respiratory depression due to the combined dose of opioids she was receiving. Closer monitoring and observations might have identified that this was occurring, but the signs had been subtle and it was not clear to the nursing staff that the deceased was affected by opioid toxicity until it was too late. The

[168] Exhibit 1, Tab 13, p. 10.

deceased was found unresponsive shortly after midnight on 10 July 2013 and she could not be resuscitated.

136. In the circumstances, I find that the death occurred by way of misadventure.

137. This case demonstrates the inherent dangers of opioid use, and the particular dangers arising from the use of fentanyl patches, which has prompted my recommendation, as set out above, for greater restriction on their prescription and use in Western Australia.

S H Linton
Coroner
23 August 2017