Senate Community Affairs Legislation Committee

ANSWERS TO QUESTIONS ON NOTICE

HEALTH PORTFOLIO

Therapeutic Goods Amendment (2016 Measures No.1) Bill 2016

17 March 2017

Question no: 1

Topic: Review

Type of Question: Hansard, page 24, 17 March 2017

Senator: Senator Watt

Question:

Senator WATT: So did that 2014 review reveal similar sorts of levels of risk?
Dr Kelly: It revealed that kind of risk. I cannot recall the exact quantum of risk that we found in the general review that we did. We did publish the review of the website, so it is up there for everybody to see. Whether or not it is the same magnitude of risk in the same patient populations, I would have to go back and look in more detail.
Senator WATT: Could you take that on notice for us?
Dr Kelly: Sure.

Answer:

The recent Danish study by Sondergaard et al, published in the European Heart Journal, looked at 29,000 patients who experienced an out-of-hospital cardiac arrest, and then looked at whether or not they had been prescribed an NSAID in the 30 days prior to cardiac arrest. The study found that people prescribed ibuprofen had a 31% higher risk of suffering an out-of-hospital cardiac arrest, whilst people prescribed diclofenac had a 50% risk. It should be noted that these results relate to use of prescription ibuprofen and diclofenac, which are given under medical supervision at higher doses compared to products available over-the-counter. It should also be noted that this was an 'observational' study, not a randomised controlled trial. Observational studies have a number of limitations and generally do not provide adequate evidence to definitively prove that a medicine is responsible for an adverse outcome.

The Therapeutic Goods Administration's (TGA) 2014 NSAIDs review did not specifically examine the risk of cardiac arrest, but rather examined cardiovascular risk, including risk of myocardial infarction or related coronary syndromes, which can be causes of cardiac arrest. It also examined the risk of stroke. It should be noted that comparing results between different studies can be difficult, due to differences in study populations and methodology. Whilst single studies may provide some evidence of an association between a medicine and an adverse outcome, studies often have conflicting results. Pooling the results of multiple studies using robust statistical methods (known as a 'meta-analysis') generally provides better evidence.

The studies examined in the 2014 review identified the following levels of risk of myocardial infarction or related coronary syndromes for ibuprofen and diclofenac:

Ibuprofen

- Substantial differences in the estimates of risk were found, with some studies finding no increase in the risk of myocardial infarction whilst other studies found an increased risk.
- For the studies showing an increased risk, the increased risk ranged from 24-80%.
- When the results of all the publications were pooled together in a meta-analysis, the overall increased risk of myocardial infarction was 15% higher for patients taking ibuprofen.

Diclofenac

- Estimates of cardiovascular risk varied depending on the study design and whether the included patients had a prior history of coronary heart disease.
- Three meta-analyses were examined as part of the review, and these identified an increased risk of cardiovascular events ranging from 38-63%.

Overall, the results of the recently published Danish study do not alter the conclusions of the TGA's 2014 review, which concluded that the benefit-risk profile for NSAIDs remains positive, but there is a need to raise awareness among consumers and health professionals of the cardiovascular risks associated with NSAIDs. Similar reviews have also been carried out by the US FDA and the European Medicines Agency and their conclusions have been similar.

Following completion of the NSAIDs review, the TGA has worked with sponsors of prescription NSAIDs to update the product information to reflect the review findings. Prescription NSAIDs carry warnings in the product information regarding cardiovascular risk including heart attack and stroke. The precautions further mention that the risk may increase with dose or duration of use and therefore the lowest dose should be used for the shortest possible duration.

The TGA has also mandated the following new advisory statement to appear on the product labels for oral over-the-counter NSAIDs containing diclofenac, ibuprofen, flurbiprofen, ketoprofen, mefenamic acid or naproxen:

> *"Do not use for more than a few days at a time unless a doctor has told you to. Do not exceed the recommended dose. Excessive use can be harmful and increase the risk of heart attack, stroke and liver damage".*

In keeping with our usual practice for safety issues, the TGA has kept consumers and health professionals informed through web statements. The TGA continues to liaise with NPS MedicineWise concerning additional communication activities.

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ANSWERS TO QUESTIONS ON NOTICE

HEALTH PORTFOLIO

Therapeutic Goods Amendment (2016 Measures No.1) Bill 2016

17 March 2017

Question no: 2

Topic: Studies on the overuse of NSAIDs

Type of Question: Hansard, page 24, 17 March 2017

Senator: Senator Watt

Question:

Senator WATT: Are you aware of any other studies that have been conducted, say, in the last two or three years, into the overuse of NSAIDs—anti-inflammatories, essentially—and any connection with stomach ulcers, or liver or kidney problems? That seems to have come up today as well.
Dr Kelly: I will take that on notice as well. There have been occasional reports that we have become aware of. Whether there have been any systematic studies, I would have to go back and check.

Answer:

It has long been known that misuse of NSAIDs, specifically use of NSAIDs at higher doses and/or for longer periods than recommended, can be associated with a range of problems, including stomach ulcers and kidney problems. New evidence regarding the safety of NSAIDs emerges all the time, and the Therapeutic Goods Administration (TGA) monitors the scientific literature on an ongoing basis.

In addition to the new warning statement mandated by the TGA following the NSAIDs review, over-the-counter NSAIDs including diclofenac, ibuprofen, flurbiprofen, ketoprofen, mefenamic acid or naproxen are also required to carry the following warnings:

- Do not use [this product/insert name of product] if you have a stomach ulcer.
- Do not use if you have impaired kidney function.
- Do not use if you have heart failure.

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ANSWERS TO QUESTIONS ON NOTICE

HEALTH PORTFOLIO

Therapeutic Goods Amendment (2016 Measures No.1) Bill 2016

17 March 2017

Question no: 3

Topic: Sansom Review

Type of Question: Hansard, page 34, 17 March 2017

Senator: Senator Watt

Question:

Senator WATT: In the 2016-17 budget the government allocated $20.4 million over four years to implement the Sansom review. Do you know how much of that is for post-market monitoring?
Dr Skerritt: I would have to take the question on notice. I would remind you that that is $20.4 million from our reserves—of our industry cost-recovered funding. But it is, in law, government funding, because as soon as you make a payment to the government. We would take that question on notice but I would account that it is a significant amount. As you will see with these papers that Dr Kelly was talking about, there is a rather detailed paper on post-market monitoring, which we expect to be published for public consultation on Monday or Tuesday. But we will take that figure on notice.

Answer:

As noted, $20.4 million over four years has been set aside from the Therapeutic Goods Administration (TGA) reserves for reforms to the therapeutic goods regulatory framework arising from the Review of Medicines and Medical Devices Regulation.

This figure, published in the 2016-17 Budget Paper No.2, includes implementation costs and the commencement of ongoing costs and associated cost recovery. Implementation costs are estimated at $19.33 million across the estimates period, which includes an estimated $4.7 million for post market reforms[1]. Implementation costs also includes $1 million for cross-cutting work and initiatives that are attributable to both pre and post market functions. This includes work such as the establishment of support for small and medium sized enterprises, the development of guidance material, and changes to fees and charges required by the reforms.

The $4.7 million for post market reforms includes $2.09 million for IT capital.

Based on activity based costing data 35%, or approximately $51 million, of TGA's total operating budget is attributable to post market work, on a pre and post market split basis.

1 Please note that a number of projects include both pre and post market components and estimations of staff effort against each category have been necessary to arrive at a total post market figure.

This includes direct costs as well as the allocation of indirect costs. Post market activity includes pharmacovigilance, compliance and laboratory testing. Functions such as variations to an entry on the Australian Register of Therapeutic Goods, although these may occur post registration, listing or inclusion of the original good, have been included in pre-market costs.

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ANSWERS TO QUESTIONS ON NOTICE

HEALTH PORTFOLIO

Therapeutic Goods Amendment (2016 Measures No.1) Bill 2016

17 March 2017

Question no: 4

Topic: Post market arrangements

Type of Question: Hansard, page 34, 17 March 2017

Senator: Senator Watt

Question:

Dr Kelly: Enhancing our current post-market arrangements. We already have a suite of post-market arrangements in place. The paper talks about enhancing those things. So, as we move to priority pathways, provisional pathways, as we look to see what other regulators do, this is an opportunity to revamp to enhance our current suite of post-market tools.
Senator WATT: But it would be fair to say that some of the budget allocation is going to go towards post-market monitoring?
Dr Skerritt: More than some. I would say many millions, but be will give you the figure as a question on notice—but it is many millions of it.

Answer:

Refer to response to Question 3

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ANSWERS TO QUESTIONS ON NOTICE

HEALTH PORTFOLIO

Therapeutic Goods Amendment (2016 Measures No.1) Bill 2016

17 March 2017

Question no: 5

Topic: Clinical registries

Type of Question: Hansard, page 35, 17 March 2017

Senator: Senator Watt

Question:

Senator WATT: I have a few questions about clinical registries. How many clinical registries are there currently in Australia?
Dr Skerritt: I would have to take that question on notice. They are scattered throughout the place. I have heard there are well over 30.

Answer:

It is estimated that there are at least 40 clinical quality registries (CQRs) in Australia. The exact number is unknown.

Note: A large number of registries used in clinical settings are not considered CQRs. CQRs are defined by the provision of benchmarked feedback on practice and outcomes directly to clinicians, hospitals, the Therapeutic Goods Administration, device manufacturers and state/territory governments, where relevant. CQRs must also have a policy and procedure to manage the identification and reporting to clinicians, and other relevant stakeholders, of data that significantly varies from benchmarks (outliers).

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HEALTH PORTFOLIO

Therapeutic Goods Amendment (2016 Measures No.1) Bill 2016

17 March 2017

Question no: 6

Topic: Clinical quality registries

Type of Question: Hansard, page 35, 17 March 2017

Senator: Senator Watt

Question:

Dr Skerritt: There is a number of full clinical quality registries but there are others that might, for example, not look at the full clinical experience but they might look at which patients have had the product fail and have had to have the operation done again. That is euphemistically called 'revision', but it is a bit harder than the revision I had to do when I was at primary school.
Senator WATT: Could you take the number on notice, but I would be interesting in finding out—if it is easy enough—where they are, who they are, and that kind of thing?
Dr Skerritt: A recent study was done—I think it is now in the public domain—by our colleagues at the Australian Commission on Safety and Quality in Health Care. If it is a public document we would certainly be happy to provide that. They did do a review of registries not long ago.

Answer:

The Department of Health administers contracts for service or funding agreements in relation to four CQRs:

- Bariatric Surgery Registry: managed/hosted by Monash University, based in Victoria.
- Australian Breast Device Registry: managed/hosted by Monash University, based in Victoria.
- Cardiac Devices Registry: managed by the Australasian Cardiac Outcomes Registry (Cardiac Society of Australia and New Zealand), based in Sydney, and hosted by the South Australian Health and Medical Research Institute, based in Adelaide.
- National Joint Replacement Registry: managed by the Australian Orthopaedic Association, based in Sydney, and hosted by the South Australian Health and Medical Research Institute, based in Adelaide.

In December 2016, the Prime Minister announced a Commonwealth contribution to the Australian Trauma Registry.to be jointly funded by the Department of Health and the Department of Infrastructure and Regional Development. The Australian Trauma Registry is managed by Alfred Health, based in Victoria, and hosted by Monash University, based in Victoria.

Monash University and the South Australian Health and Medical Research Institute host/manage a number of other registries, some of which are CQRs. Registry lists and links to the web pages are provided at Attachment A.

Other CQRs are managed by a number of individual organisations.

Attachment A

Monash University

http://www.med.monash.edu.au/sphpm/depts-centres-units/registries/

Those indicated with "*" fit into more than one category.

Clinical	Condition/disease	Drug/device
Australian and New Zealand Massive Transfusion Registry (ANZ-MTR)	Australian Cystic Fibrosis Data Registry (ACFDR)	Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS)*
Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS)*	Haemoglobinopathy Registry (HbR)	Australian Rheumatology Association Database (ARAD)
Australian Rheumatology Association Database (ARAD)	Lymphoma and Related Diseases Registry (LaRDR)	Bariatric Surgery Registry (BSR)*
Australian Trauma Registry (ATR)	Myeloma and Related Diseases Registry (MRDR)	Australian Breast Device Registry (ABDR)*
Burns Registry of Australia and New Zealand (BRANZ)	Neonatal Alloimmune Thrombocytopenia (NAIT)	Melbourne Interventional Group Registry (MIG)*
Melbourne Interventional Group Registry (MIG)*	Registry of Kidney Diseases (ROKD)	
Prostate Cancer Outcome Registry Australia and New Zealand (PCOR-ANZ)	Thrombotic Thrombocytopenia Purpura (TTP)/Thrombotic Microangiopathies (TMA) registry	
Upper Gastrointestinal Cancer Registry (UGICR)	Venous Thromboembolism cohort study (VTE)	
Victorian Cardiac Outcomes Registry (VCOR)	Victorian Lung Cancer Registry (VLCR)*	
Victorian Lung Cancer Registry (VLCR)*		
Victorian Orthopaedic Trauma Outcomes Registry (VOTOR)		
Victorian Prostate Cancer Clinical Registry (PCR)		
Victorian State Trauma Registry (VSTORM)		

South Australian Institute of Health and Medical Research

https://www.sahmriresearch.org/our-research/adelaide-registry-consortium-3

Australian and New Zealand Audit of Surgical Mortality
Australian and New Zealand Dialysis and Transplant Registry
Australian and New Zealand Ophthalmic Surveillance Unit
Australian Spinal Cord Injury Register
Australian Corneal Graft Registry
ACOR Cardiac Procedures Registry
BreastSurgANZ Quality Audit (formerly known as the National Breast Cancer Audit)
Australian and New Zealand Gastric and Oesophageal Surgery Association (ANZGOSA) Audit
SA Birth Defects Register/SA Cerebral Palsy Register
SA Prostate Cancer Clinical Outcomes Collaborative (SA-PCCOC)
ACOR Cardiac Devices Registry