ECONOMIC EVALUATION OF THE NPS MEDICINEWISE PROGRAM IMAGING FOR ACUTE LOW BACK PAIN

Cost-Benefit Analysis Report

June 2016

Independent, not-for-profit and evidence based, NPS MedicineWise enables better decisions about medicines and medical tests.

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EXECUTIVE SUMMARY

In 2013 NPS MedicineWise ran the *Imaging for acute low back pain* (IALBP) program. The IALBP program was selected based on evidence of high use of diagnostic imaging for low back pain outside of guideline recommendations resulting in unnecessary cost to the Australian health system and for patients, and avoidable exposure to radiation. The IALBP program aimed to decrease the volume of unnecessary computer tomography (CT) scans for acute low back pain, and reduce potential cancer risk associated with radiation from unnecessary CT scans.

The 2013 NPS MedicineWise IALBP program was relatively low cost. It built on a prior NPS MedicineWise program and materials developed in collaboration with the George Institute. The 2013 IALBP program involved sending a personalised MBS data feedback report to 19,997 practicing Australian general practitioners (GPs) for the purposes of self-reflection. Each GP was also provided with links to a symptomatic management pad and the online back pain choices decision support tool.

The objective of this economic evaluation is to identify in monetary terms, the costs and benefits of the 2013 IALBP program and the cost-effectiveness of the program at achieving the anticipated outcomes.

The study was conducted in two stages. Stage one involved an impact evaluation to identify the effect of the program on CT scan utilisation and to estimate cancer risk associated with unnecessary radiation. Stage two involved cost-benefit and cost-effectiveness analysis.

In stage one, Time Series analysis was used to measure the impact of the program on provider level reimbursement data for CT scan of the spine: lumbosacral region (MBS: 56223). This data was obtained from the Commonwealth Department of Human Services (DHS) for the period May 2010 to February 2015. In the period following the NPS MedicineWise program, the GP referrals for CT scan decreased relatively by 10.85% from the predicted trend without the NPS MedicineWise program. This corresponds to an estimated mean CT scan referral reduction, attributable to the NPS MedicineWise program, of 50,186 scans (95% posterior interval 3,919 - 96,476) from July 2013 to February 2015 and a savings of $11,600,898 to the MBS.

The impact of the CT scan reduction on population cancer risk was estimated using the protocol specific organ dose from a sample of 5 Western Australian public hospital CT scanners, the estimated averted CT scan per age and gender group, and the BEIR VII risk model to calculate the excess lifetime cancer incidence risk averted. Using the mean protocol specific organ dose for Hospital 4 (median), the model estimated an averted excess lifetime risk of 36 incident cancers. The risk model estimates an averted excess lifetime cancer risk of 11 colon cancers, 4 bladder cancers, 3 stomach cancers and 3 incidences of leukaemia.

The results from the stage one impact evaluation and program costs data collected from NPS MedicineWise finance and project management systems were used to conduct the stage two cost-benefit and cost-effectiveness analysis. Impact on CT scan referral was discounted at an annual rate of 5%, calculated monthly after the first year. All program costs were adjusted to 2015 currency using Australia CPI published by the Australian Bureau of Statistics. The net benefit of the program was $11,434,285, this is the difference between the savings resulting from averted CT scans and the costs of the NPS MedicineWise 2013 IALBP program. The benefit to cost ratio was 82.01, indicating that for every dollar spent on the program, $82 was gained in monetary benefit.

For the outcomes of CT scans averted and excess lifetime cancer incidence risk averted, an incremental cost effectiveness ratio (ICER) was calculated for the program with the alternative of no program. For every $2.82 spent on the NPS MedicineWise IALBP program, one CT scan was averted. This cost is offset by the savings to the MBS from the averted CT scan of $231 on average. For every excess lifetime cancer risk incidence the program averted there was a savings of $312,241.

The sensitivity analysis showed the results were most dependent on the program's estimated impact on CT scans, and there was a high level of confidence in dominance of the program. The NPS MedicineWise IALBP program is referred to as dominating the no-program option – that is, implementing the NPS MedicineWise IALBP program cost less and produced more favourable outcomes compared to not having implemented the program.

Unnecessary use of CT scans can have significant adverse effects on the health care system and consumers in terms of monetary costs and serious detrimental health outcomes. The evaluation of the NPS MedicineWise IALBP program found that in the right context, low cost programs can provide significant savings to the health care system and avert health risks to the population.

The NPS MedicineWise IALBP program produced a net benefit of $11,434,285 in monetary terms and averted an estimated excess lifetime risk of 36 incident cancers.

REPORT STRUCTURE

- The **Introduction** section provides an overview of the program being evaluated and background information.
- The **Stage one: Program effectiveness** section includes the methods and results for the impact evaluation. This section reports on the impact of the IALBP program on MBS utilisation and the associated averted excess cancer risk.
- The **Stage two: Economic evaluation** section includes the methods and results for the economic evaluation of the IALBP program. This section reports on the program and outcome costs, a cost benefit analysis and a cost-effectiveness analysis of CT scans averted and excess cancer risk averted.
- The **Discussion** section provides context to the results from stage one and two, discusses the strengths and weaknesses of this and outlines some learning for NPS MedicineWise resulting from this evaluation.
- **The Appendices** hold additional reference and technical information that is referred to in the body of the report.

INTRODUCTION

In 2013 NPS MedicineWise ran the *Imaging for acute low back pain* (IALBP) program. Through this program NPS MedicineWise aimed to decrease the volume of unnecessary computer tomography (CT) scans for acute low back pain, and reduce potential cancer risk associated with radiation from unnecessary CT scans.

Objectives of this report

The objective of this report is to present an economic evaluation of the 2013 IALBP program, which identifies, in monetary terms, the costs and benefits of the IALBP program and the cost-effectiveness of the program at achieving the anticipated outcomes.

This evaluation consists of two stages:

- Stage one evaluates the program effectiveness through:
  - a time series analysis of administrative data from the Australian Medical Benefits Scheme (MBS)
  - a linked evidence analysis of the estimated averted cancer risk
- Stage two involves cost-benefit and cost-effectiveness analysis

The NPS MedicineWise IALBP program

Rationale for the program

Since 2009 NPS MedicineWise has sought to provide accurate, balanced, evidence-based information and services to health professionals and the community on quality use of diagnostics. NPS MedicineWise systematically targets educational interventions for health professionals and consumers where uncertainties or controversy exist in relation to appropriate diagnostic testing and where inappropriate referrals may result in suboptimal health outcomes and/or increased costs. Imaging for acute low back pain was identified as an area in which the gap between evidence and practice may result in adverse outcomes for the health system and consumers.

In Australia it is estimated that four out of every five people will have an episode of low back pain at some point in their lives. It is a common condition that people seek treatment for in the primary and acute care settings.[1] Serious causes of low back pain are rare and can generally be identified via clinical examination and history taking. Radiological features identified via diagnostic imaging technologies are poorly correlated with symptoms and pathology in low back pain. In most cases acute low back pain is non-specific as the anatomical source cannot be identified.[2, 3]

For over a decade, evidence-based guidelines have advised against imaging in routine evaluation of patients with acute low back pain in the absence of “red flag” indicators of potentially serious underlying conditions. There is no evidence that imaging without a red flag reason improves patient outcomes or alters clinical decision making.[2] Despite this, a 2010 Australian study indicated that more than a quarter of patients presenting to GPs with a new episode of low back pain were referred for a diagnostic imaging test.[4]

The high use of diagnostic imaging for low back pain outside of guideline recommendations results in unnecessary cost to the Australian health system and for patients, and avoidable exposure to radiation.

Overview of the program

In June 2013 NPS MedicineWise sent a personalised MBS data feedback report to 19,997 practicing Australian GPs. The MBS feedback report gave each GP an opportunity to reflect on their referral data

for three MBS diagnostic imaging items for low back and how this compared to similar GPs. The MBS items were for CT scan of the lumbosacral region and two lumbar x-ray items. The report also contained educational messages about current guidelines and evidence based practice related to the investigation of acute low back pain in general practice. Each GP received links to two GP-led patient resources developed by NPS MedicineWise – 1) a symptomatic management pad, 2) the online back pain choices decision support tool. A copy of the MBS data feedback report is available in Appendix 1.

The 2013 IALBP program built on previous work NPS MedicineWise conducted to promote the appropriate use of imaging for acute low back pain. NPS MedicineWise first launched a program about imaging use for acute low back pain in 2010. This initial multifaceted program included a case study for GPs, interactive educational workshops run by pain specialists and facilitated by NPS MedicineWise, an MBS GP data feedback report intervention and the production and distribution of symptomatic management leaflets for GPs to provide to consumers.

In 2011 an online educational awareness campaign on low back pain, run in partnership with Prevention Magazine Australia, was developed for consumers.

In 2012 a second, smaller scale, program on acute low back pain was run. This program included interactive workshops for GPs run by physiotherapists and the launch of an online decision support tool for GPs called Back Pain Choices. This tool was developed in collaboration with the George Institute and built on an algorithm for best practice diagnostics and advice for low back pain cases in primary care.

The 2013 IALBP program utilised relevant work done during previous NPS MedicineWise programs. The MBS Feedback used previously developed indicators and key messages, and the symptomatic management pad and online decision support tool were used again. Work on problem definition and the syntheses of evidence undertaken for the previous program also contributed to the 2013 program. The methods section of Stage two outlines how the costing of the 2013 program for this economic evaluation accounts, where possible, for the use of previously developed materials. Note that the 2010 program was evaluated independently and found to have financial impact on the MBS of $5.4 million from reduced expenditure on CT scans for the spine for the period December 2010 to December 2011.[5] The scope of this economic evaluation is the costs associated with running the 2013 IALBP program and the impact of this phase.

Key program objectives and messages

The primary objectives of the NPS MedicineWise 2013 IALBP program were to educate consumers and health professionals about acute low back pain in terms of appropriate management and use of imaging tests (Table 1).

TABLE 1: KEY EDUCATIONAL MESSAGES OF THE NPS MEDICINEWISE ACUTE ALBP PROGRAM

Heath practitioner key messages	▷ Undertake a thorough history and examination to assess for the presence of serious clinical conditions (‘red flags’) ▷ Use lower lumbar imaging only in patients found to have ‘red flags’ ▷ Reassure patients that low back pain is rarely serious, most pain settles quickly and imaging does not often explain the reason for pain ▷ Provide adequate analgesia using regular paracetamol and heat/cold packs for short term symptom relief
Consumer key messages	▷ There are many effective, often simple ways to relieve low back pain ▷ X-rays and CT scans are unlikely to help identify the cause of your pain ▷ Taking more than the recommended dose of a pain reliever does not achieve better pain relief and has risks

Expected program outcomes

The expected outcomes of the program, based on the key messages and current referral patterns, was a reduction in referrals for diagnostic imaging of the low back.

Acute low back pain, CT scans and radiation

Epidemiology of conditions associated with acute low back pain

In the primary care setting it is estimated that between 1% and 5% of all patients who present with low back pain will have a serious underlying spinal pathology which requires further assessment and specific treatment.[6] The most common of these underlying spinal pathologies is vertebral fracture, followed by malignancy, infection and inflammatory disease.

In the Australian context, a prospective cohort study of 1,173 consecutive patients presenting with acute low back pain in a Sydney based primary care clinic identified 11 cases of serious pathology (0.9%), 8 of which were fractures.[7] See Table 2 below for a summary of study findings.

A 2013 Cochrane review of red flags to screen for vertebral fractures in patients with acute low back pain found a primary care prevalence of vertebral fractures of 0.7%-4.5%.[6] Another 2013 Cochrane review of red flags to screen for malignancy in patients with acute low back pain, found a primary care prevalence of spinal malignancy of 0%-0.66%.[8] Of these, approximately 10% were new primary cases.

TABLE 2: RESULTS FROM HENSCHKE 2009 STUDY: PREVALENCE OF SERIOUS SPINAL PATHOLOGY AMONG THE 1,172 PATIENTS WITH ACUTE LOW BACK PAIN PRESENTING TO A PRIMARY CARE SETTING[7]

Pathology	No. of cases of confirmed pathology	Prevalence (95% CI)*
Spinal fracture	8	0.7 (0.4–1.3)
Cancer	0	0.0 (0.0–0.3)
Infection	0	0.0 (0.0–0.3)
Cauda equina syndrome	1	0.1 (0.0–0.5)
Inflammatory disorder	2	0.2 (0.1–0.6)
Total	11	0.9 (0.5–1.7)

While the vast majority of primary care presentations for acute low back pain are non-specific in cause and are self-limiting in nature, the seriousness of potential rare underlying conditions means the accurate identification of these is important. Australian guidelines have published a list of alerting features (‘red flags’) of serious conditions associated with acute low back pain, to be used to indicate an increased likelihood of an underlying condition which warrants further investigation. See Table 3 for details of the NHMRC list of ‘red flags’ which was referenced in the NPS MedicineWise program materials.

TABLE 3: NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL. EVIDENCE-BASED MANAGEMENT OF ACUTE MUSCULOSKELETAL PAIN. 2003: ALERTING FEATURES ('RED FLAGS') OF SERIOUS CONDITIONS ASSOCIATED WITH ACUTE LOW BACK PAIN

Feature or Risk Factor	Condition
Symptoms and signs of infection (e.g. fever)	Infection
Risk factors for infection (e.g. underlying disease process, immunosuppression, penetrating wound)	
History of trauma	Fracture
Minor trauma (if > 50 years, history of osteoporosis and taking corticosteroids)	
Past history of malignancy	Tumour
Age > 50 years	
Failure to improve with treatment	
Unexplained weight loss	
Pain at multiple sites	
Pain at rest	
Absence of aggravating features	Aortic aneurysm

Identified 'red flags' indicators vary in their predictive value, and in many cases have high false positive rates. Cochrane literature reviews found that a previous history of cancer is very useful to predict an increased probability of malignancy[8] and significant trauma, older age and corticosteroid use are useful to predict an increased probability of fracture.[6] Other factors such as age greater than 50, no prior history of back pain and failure to improve after a month, when taken individually, would still result in high levels of over-testing for malignancy and therefore are most likely useful when combined.[8] The review of red flags for fracture also found that combinations of 'red flag' indicators in the primary care setting were more specific than when taken individually and maintained a good sensitivity.[6]

The NPS MedicineWise promotion of the guideline based recommendation against the routine use of imaging for patients with acute low back pain without red flags, was predicted to reduce the unnecessary use of diagnostic imaging in cases with low pre-test probability of a serious underlying spinal pathology while still capturing those at risk for diagnostic and appropriate treatment.

CT scan radiation and cancer risk

CT scans represent the largest manmade source of population exposure to ionising radiation. Australia is following the worldwide trend of increasing frequency of diagnostic x-ray use. MBS data in Australia have shown a 36% increase in the number of CT scans between 2006/07 to 2011/12.[9] The use of CT scans represents significant diagnostic value but also potential risk.

The prevailing theory of health risk from radiation exposure is the linear-no-threshold model.[10] This is the theory that there is no minimum safe level of radiation at which the relationship between radiation and health risk does not apply. While heavily debated, recent cohort studies among British[11] and Australian[12] children and adolescents have demonstrated a positive association between exposure to CT scans and cancer risk. The Australian study used linked data for a cohort of 10.9 million Australian children and adolescents.[12] The mean duration of follow up from exposure to CT scan was 9.5 years. The overall cancer incidence was 24% greater in the population exposed to CT scans compared to those not exposed, after accounting for age, sex and year of birth. The study reported an excess of 608 cancers in people exposed to CT scans and an absolute excess incidence rate of 9.38 per

100000 person years at risk. The dose-response relationship identified in the study was similar to that reported in the National Research Council's BEIR VII - Phase 2 report.[9] The causal relation was further supported by a correlation observed between the site of the CT scan and the site of the cancer.[12]

Research into the link between CT scanning and cancer had focused on children as the younger the individual the greater the risk from radiation exposure. In addition, females are at greater risk of cancer than males, across all ages. A recent Australian retrospective cohort study reported that women and younger adults had a disproportionate risk burden from CT scanning.[9] This study, using MBS data from 2006/07 to 2011/12, found females were 11% more likely to receive a CT scan than males. From the 55% share of CT scans, females were attributed 61% of incident cancers and cancer-related mortality. People aged 15-44 years accounted for 26% of CT scans and were attributed 37% of incidence cancers and 30% of cancer related mortality.[9]

The risks and benefits of CT scanning depend on the population, the anatomic region being scanned and the diagnostic value. The minimal diagnostics value of CT scans for people with acute low back pain and no red flags make the risks associated with excess and unnecessary radiation important to consider.

STAGE ONE: PROGRAM EFFECTIVENESS

Method

Evaluation design

The impact of the NPS MedicineWise IALBP program on the utilisation of CT scans of the lumbosacral region was evaluated using time series analysis on MBS referral data. MBS reimbursement data was used to estimate the costs or savings to the MBS associated with any change in utilisation.

To estimate the reduced exposure to CT scans by age and gender, the relative decrease attributable to the program estimated through the time series analysis was applied to the MBS post program trend data for the relevant age and gender groups. A linked evidence approach was then used to project estimated lifetime excess cancer risk averted due to the program. This approach used radiation dose data independently collected from sample CT machines, and estimated cancer incidence risk using BEIR VII age and gender specific lifetime attributable risk weights, based on work previously published by Moorin (2014).[13]

Data sources

The provider level reimbursement data for CT scan of the spine: lumbosacral region (MBS: 56223) were obtained from the Commonwealth Department of Human Services (DHS). The data provided covered the period from May 2010 to February 2015. The key variables in the datasets were scrambled provider code, date of service (year, month), patient sex, provider major speciality, Medicare item number, number of services and amount of benefit paid by Medicare.

The age and sex demographics of patients receiving CT scan of the spine: lumbosacral region (MBS: 56223) from publically available MBS online data was used to supplement MBS data received from DHS.[14]

Technical data collected by Moorin and colleagues[13] as part of a NHMRC funded study evaluating radiation dosimetry from CT scanning was used to estimate the dose of radiation exposure associated with the CT scan item for the lumbosacral region. This technical data was collected from CT machines from 5 public hospital located in Western Australia in 2011. A random sample of cases from specific adult diagnostic CT scanning protocols, including CT of the spine lumbar, were selected via the Picture Archiving Communication System (PACS). Between 10 and 20 cases of the spinal lumbar protocol were selected per hospital, depending on variation found. Organ and whole body radiation dose were calculated using ImPACT Monte Carlo simulation software. See Moorin 2014 for more details.[13] Age and gender specific lifetime attributable risk weights were taken from the BEIR VII-Phase 2 report TABLE 12D-1.[10]

Time series analysis

The analysis was based on the Bayesian Hierarchical Time Series Model (BHTSM). A time series data set is a series of observations or data points collected over time, in which the observations closer in time to each other are more correlated than those further away in time. This is true of the MBS data set. Time series modelling captures the correlation between data points with respect to their relation in time.

The data obtained for this analysis allowed for GP referrals to be distinguished from referrals made by other health professionals (non-GP). This separation was valuable in evaluating the impact of the NPS MedicineWise MBS feedback intervention which targeted only GPs.

Where the pre-intervention trends for GPs and other health professionals followed similar patterns, data from other health professionals could be used to model the predicted trend of GP referrals without the NPS MedicineWise intervention, using a BHTSM. This technique helps the model to

account for any concurrent environmental factors that may have influenced the referral behaviour of all health professionals, such as mainstream or health professional media pieces on the area of interest.

We selected non-GP as a quasi-experimental control group due to the ability to separate GPs from non-GPs in the dataset and because the intervention targeted changing the diagnostic referral behaviour of GPs only. We assume that the stationary relationship between the GP referral (intervention) and the non-GP referral (control) groups existed prior to the intervention, and both groups could be affected by external events. However, after delivering the MBS feedback intervention to GPs, the relationship between the two groups is no longer assumed to be similar.

We adopted a BHTSM, and used the package "Causal Impact"[15] in the statistical software R[16] for our primary analysis. See Appendix 2 for details of the BHTSM.

After the predicted trajectory with the NPS MedicineWise MBS feedback intervention is estimated, the intervention's impact can be calculated by subtracting the mean forecasted post-intervention data from the observed GP referral series during the post intervention period. 95% posterior intervals were also calculated and summarised in the results.

Cancer risk modelling

To estimate the averted CT scan exposure and excess lifetime cancer incidence risk within age and gender groups, we used the demographic distribution of patients receiving CT scans from publically available MBS online data[14] for the post-intervention period. The CT scan volume reduction each month, as estimated from the time series analysis, was assumed to be distributed in proportion to the age and sex distribution of those who received a CT scan in that month. This method assumed that the intervention effect was equally applied across all groups. If the program messages were followed as intended it is likely that the effect would be more weighted towards the younger age groups. The method was selected to produce a conservative estimate, using available data.

The age and gender specific lifetime attributable risk was inferred from a single exposure using the mean protocol specific organ dose for each sample hospital and the age/sex-specific risk coefficients from tables 12D-1 and 12D-2 of the BEIR VII report.[10] The lifetime attributable risk calculated from BEIR VII weighting factors by yearly age were averaged to created values for the 10 year age groups evaluated.

The risk rate for each hospital was multiplied by the estimated number of CT scans averted in the MBS data population group, with the exception of people aged 0-14 years and over 75 years. These groups were excluded from the analysis as the use of CT scans of ALBP in these groups is more likely to be appropriate based on guidelines thus a utilisation based on program messages would not be expected. In addition, there was a lack of data about organ dose radiation exposure data for the younger age group and radiation dose in children is hugely varied because of the differences in body size and therefore protocol used, necessitating prospective capture of dose by age. The lifetime cancer risk for the older age would be negligible.

Results

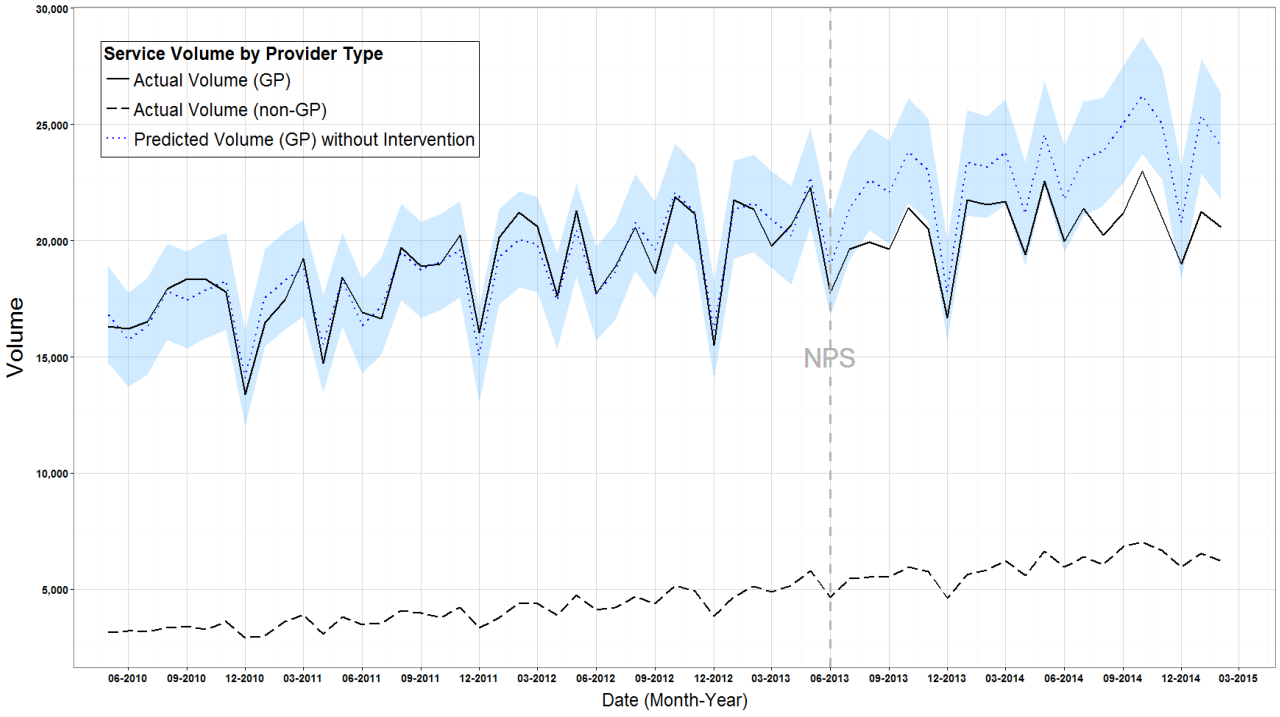
MBS utilisation

The NPS MedicineWise IALBP program was associated with a statistically significant reduction in GP referrals for CT scan of the lumbosacral region (MBS: 56223) and significant reduction in MBS expenditure.

In the period following the NPS MedicineWise program, GP referrals decreased relatively by 10.85% from predicted trend without the NPS MedicineWise program. This corresponds to an estimated mean CT scan referral reduction attributable to the NPS MedicineWise intervention of 50,186 scans (95% posterior interval 3,919 - 96,476) from July 2013 to February 2015.

Figure 1 shows that, in the post MBS feedback intervention period, the divergence between the observed referral rate (solid line) and the predicted referral rate without the NPS MedicineWise (blue dotted line) was significantly greater than in the pre-intervention period. The predicted referral trend without the MBS feedback intervention is modelled using the referral trend of other health professionals (broken line) because referral trends for these two groups are closely correlated in the pre-intervention period.

FIGURE 1: TIME SERIES ANALYSIS OF MONTH COUNT OF CT-SCAN REFERRALS (ITEM NUMBER 56223), MAY 2010-FEBRUARY 2015

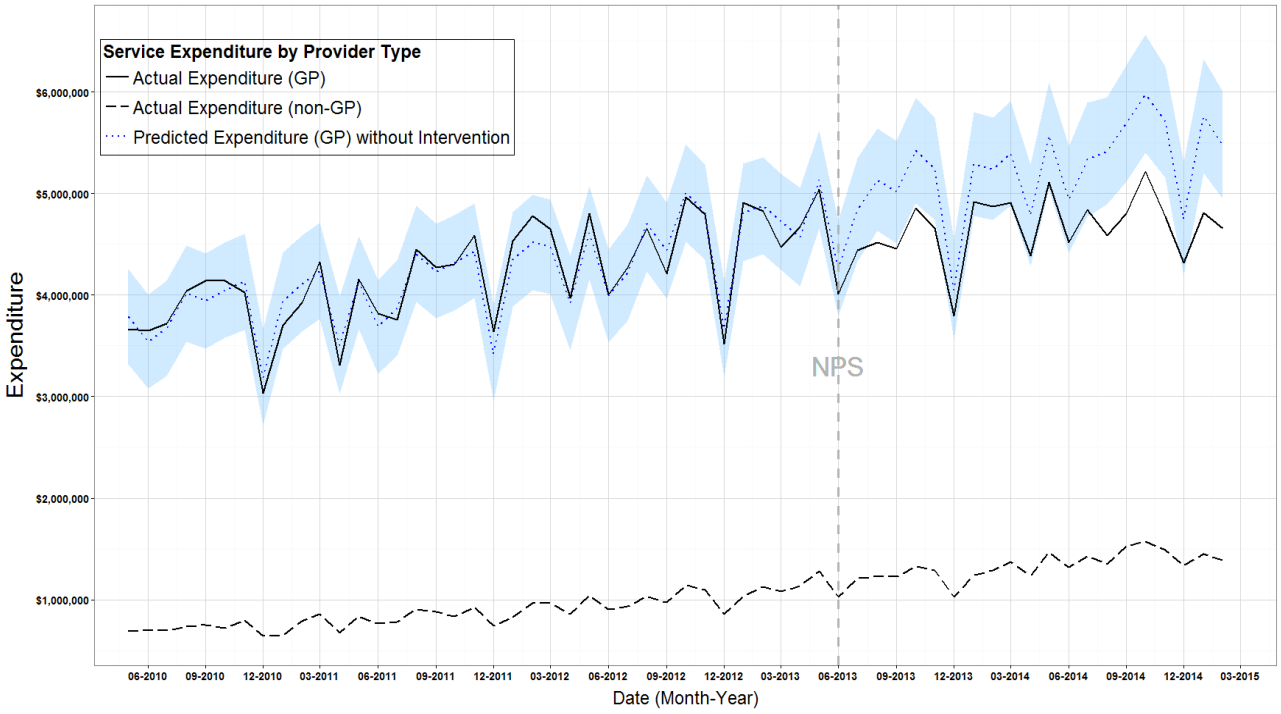


Savings estimate attributable to the NPS MedicineWise program

Figure 2 shows the observed and predicted trends in reimbursement data for the targeted CT-scan item referred by GPs. The cost savings estimate is calculated from the difference between the predicted reimbursement costs without the intervention (blue dotted line), which is modelled on the reimbursement trend of other health professionals (broken line), and the observed reimbursement cost with the intervention (black solid line) for the post-intervention period.

The estimated mean savings attributable to the NPS MedicineWise feedback intervention was $11,600,898 (an estimated 11.05% reduction in reimbursement) during the 20 months period following intervention (July 2013 – February 2015).

FIGURE 2: TIME SERIES ANALSIS OF MONTH COUNT OF CT-SCAN REIMBURSEMENT (ITEM NUMBER 56223), MAY 2010-FEBRUARY 2015



Impact of CT scan reduction on population cancer risk

Table 4 shows the estimated averted CT scans of the lumbosacral region by population group for the 20 months following the NPS MedicineWise MBS feedback intervention. The mean protocol specific organ dose for each sample hospital was put into the BEIR VII risk model to calculate the excess lifetime cancer incidence risk. This rate was then applied to the estimated averted CT scans to calculate the averted excess lifetime cancer incidence risk for each hospital.

The result from the five hospitals are presented in Table 4. Using the mean protocol specific organ dose for Hospital 4 (median), the model estimated an averted excess lifetime risk of 36 incident cancers. Data from sample hospitals gave a range from averted excess lifetime risk of 20 incident cancers to 44 incidence cancers.

The median was selected as the point estimate as risk values for the 5 hospitals were not normally distributed. The median value (36.62) of the positively skewed data was similar to the mean of the four remaining hospitals when the lowest values was excluded (37.46).

TABLE 4: ESTIMATED AVERTED CT SCAN BY POPULATION GROUP AND AVERTED EXCESS LIFETIME CANCER INCIDENCE RISK MODELLED

		Averted excess lifetime cancer risk (incidence)				
Age and gender group	Estimated averted CT scans (Jul 2013 - Feb 2015	Hospital 1	Hospital 2 Min	Hospital 3 Max	Hospital 4 Median	Hospital 5
Males 15-24 years	567	0.99	0.53	1.12	0.92	0.74
Females 15-24 years	818	1.44	0.78	1.65	1.36	1.10
Males 25-34 years	2343	2.99	1.59	3.38	2.78	2.24
Females 25-34 years	2063	2.60	1.41	2.99	2.46	1.98
Males 35-44 years	3441	3.96	2.10	4.45	3.67	2.95
Females 35-44 years	3490	3.86	2.09	4.43	3.65	2.94
Males 45-54 years	4009	4.24	2.24	4.75	3.91	3.14
Females 45-54 years	4929	4.89	2.63	5.58	4.59	3.70
Males 55-64 years	4431	3.86	2.03	4.32	3.56	2.86
Females 55-64 years	5661	4.59	2.45	5.21	4.29	3.46
Males 65-74 years	4188	2.54	1.34	2.86	2.35	1.89
Females 64-74 years	5703	3.30	1.75	3.73	3.07	2.47
Total	**41642**	**39.27**	**20.93**	**44.46**	**36.62**	**29.48**

Table 5 presents the averted excess lifetime cancer incidence risk by cancer type for the hospital with the median radiation dose values. Radiation from CT scans of the lumbar spine most greatly increases the risk of colon and bladder cancers. The risk model using data from hospital 4 estimates an averted excess lifetime cancer risk of 11 colon cancers, 4 bladder cancers, 3 stomach cancers and 3 incidences of leukaemia. A greater excess cancer risk was averted in females than males.

TABLE 5: AVERTED EXCESS LIFETIME CANCER INCIDENCE RISK BY CANCER TYPE, MODELLED ON MEAN PROTOCOL SPECIFIC ORGAN DOSE FOR HOSPITAL 4

Cancer type	Females	Males	Total averted excess lifetime cancer incidence risk
Stomach	2.10	1.37	3.47
Colon	5.07	6.58	11.65
Liver	0.42	0.74	1.16
Lung	0.71	0.26	0.97
Prostate	-	0.82	0.82
Breast	0.10	-	0.10
Uterus	0.94	-	0.94
Ovary	1.81	-	1.81
Bladder	2.31	2.00	4.31
Other	4.30	3.48	7.77
Thyroid	0.00	0.00	0.00
All solid	**17.77**	**15.25**	**33.02**
Leukaemia	1.66	1.94	3.60
All cancer	**19.43**	**17.19**	**36.62**

STAGE TWO: ECONOMIC EVALUATION

Method

Evaluation design

A *cost benefit analysis* was used to compare the cost and effects of the NPS MedicineWise 2013 IALBP program expressed in monetary terms. The measures used in this analysis are:

- The **cost** of the resources required to deliver the 2013 program (outlined in Table 6)
- The **benefits** of the program expressed as the monetary value of the effects generated by the program. In this analysis the benefits are restricted to the direct savings associated with the reduction in MBS benefit paid for CT scan for the lumbosacral region (MBS: 56223).

Other economic benefits are likely to be associated with the avoidance of excess cancer risk. These have been excluded from the analysis due to limitations in available micro level data and uncertainty regarding when these saved costs would have occurred. This is discussed further in the discussion section of the report.

The cost-benefit analysis was conducted by calculating the program net benefit and the benefit-cost ratio. The *net benefit* is calculated as the difference between the benefits and the costs. Values higher than zero indicate that the benefits exceed the costs, and thus the program represents an efficient use of public resources. The *benefit-cost ratio* is calculated as the ratio of benefits to costs. Values higher than one indicate that the benefits exceed the costs.

Two *cost-effectiveness analyses* were undertaken to compare the nets costs and effects of running the NPS MedicineWise IALBP program against the alternative of not running the program.

- The **net cost** takes into account both the **cost** of delivering the program and the **benefits** of the program as a monetary value.
- The **effects** of the MBS feedback intervention on the incidence of diagnostic CT scan referral and radiation related cancer risk expressed in natural units (excess lifetime cancer incidence risk).

The cost-effectiveness was conducted by calculating incremental cost effectiveness ratio (ICER) for the program effect on CT scans and excess lifetime cancer risk incidence. The ICER is calculated using the formula below.[17]

$$ICER = \frac{Cost_a - Cost_b}{Effect_a - Effect_b} = \frac{\Delta\, Cost}{\Delta\, Effect}$$

Time frame

The timeframe for the evaluation of program effectiveness and benefit was the 20 months post-program, July 2013 to February 2015. This timeframe was used for the economic evaluation, with the exception of the measure of averted excess lifetime cancer incidence risk.

Discounting and cost standardisation

Impact on CT scan referral was discounted at an annual rate of 5%, calculated monthly after the first year. No discounting was applied to lifetime cancer risk given the uncertainty regarding the timeframe for the occurrence. All program costs were adjusted to 2015 currency using Australia CPI published by the ABS.[18]

Decision tree

A simple decision tree was created in TreeAge Pro (TreeAge Software, 2016) with the costs, benefits and effects associated with the NPS intervention compared to no NPS intervention. See Figures 3 and 4 below.

FIGURE 3: DECISION TREE FOR CT SCANS AVERTED COST-EFFECTIVENESS ANALYSIS

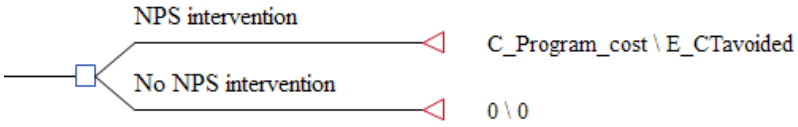
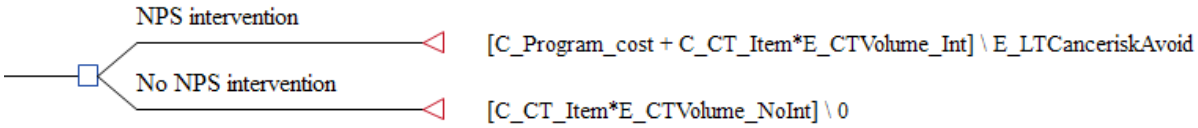


FIGURE 4: DECISION TREE FOR EXCESS LIFETIME CANCER RISK AVERTED COST-EFFECTIVENESS ANALYSIS



Decision tree variables	Description
C_program_cost	The cost of implementing the program
C_CT_item	Average MBS benefit paid per CT scan item ($231.16)
E_CTVolume_In	Observed referral rate with NPS MedicineWise intervention
E_CTVolume_NoIn	Predicted referral rate without the NPS MedicineWise intervention
E_CTAvoided	Number of CT scans averted due to the NPS MedicineWise intervention (E_CTVolume_NoIn - E_CTVolume_In = E_CTAvoided)
E_LTCancerriskAvoid	Modelled excess lifetime cancer incidence risk avoided due to the NPS MedicineWise intervention

Uncertainty

Sensitivity analysis was conducted for the cost-benefit analysis by calculating the net benefit and cost-benefit ratio for the four possible combinations of estimated maximum and minimum cost and benefit.

For the cost-effectiveness analysis, uni-variant and probabilistic sensitivity analyses were conducted using TreeAge software.

Data Sources

The economic evaluation is based on the program effectiveness results presented in Stage one of this report and program cost data collected from NPS MedicineWise organisational records.

Table 6 presents the NPS MedicineWise program costs and the source and year of these costs. All costs have been adjusted to 2015 equivalent value for the base case, using Australian CPI values published by the ABS.[18]

NPS MedicineWise human resources costs for the program could not be measured directly as the current timesheet recording system was not established until 2014. To estimate the human resource costs for the MBS feedback activity we used timesheet data for a MBS feedback intervention of a

recent quality use of imaging topic, the 2015 imaging for abdominal pain program. The 2013 IALBP MBS feedback intervention would have taken less staff resources as it was substantially based on the 2011 MBS feedback intervention. These costs reflect the effort for the production of this type of product for a new topic at NPS MedicineWise. While this is an over estimate of costs for this particular program it provides a more conservative estimate of the cost-benefit of providing this type of intervention.

The NPS MedicineWise costs associated with the 2012 online decision aid, Back Pain Choices[19] are included in this economic evaluation. While the development of the tool occurred as part of a previous program of work, the resource was advertised on the 2013 IALBP MBS feedback intervention and was considered a part of the behaviour change program. The cost to The George Institute to develop the diagnostic algorithm on which the decision tool was based has not been included. This decision was made based on the perspective that all educational programs are built on an existing evidence base, such as guidelines for best practices. This is part of the context in which the program was developed rather than a stage in the program development.

Estimated variation included in Table 6, is presented to illustrate the likely range that a product of this type would cost. Where available, actual cost data was collected from similar products to calculate this range. Where this data was not available, a conservative estimate was applied of 50% higher or lower. In the variation data based on actuals, the maximum value was 40% higher than the minimum value. As we do not know where in the range the cost of the products for this program sit, a defined variation of 50% higher or lower was used as a conservative estimate.

The cost of the 2010 program is not included in this analysis. While including these cost would make the analysis more comprehensive, information was not available to develop accurate estimates of these costs. This analysis is restricted in scope to the cost and benefits of the 2013 phase of the program, acknowledging both that the program was built on extensive existing work by NPS MedicineWise and that this prior work was associated with a financial impact on the MBS of $5.4 million from reduced expenditure on CT scans for the spine for the period December 2010 to December 2011.[5]

TABLE 6: NPS MEDICINEWISE PROGRAM COSTS

Activity	Cost type	Raw value	Source and year	Adjusted to 2015 (base case)	Variation	
MBS feedback Program costs including: design, production, data, printing and distribution	Invoiced costs $	$37,998	*Invoice record, 2013*	$39,687	$11,912-$39,687	Variation (min-max) of previous 5 similar products Source: invoice data*
	NPS MedicineWise human resources costs	$17,654	*Estimated from timesheet data for equivalent product, 2015*	$17,654	$17,654-$30,777	Variation (min-max) of previous 5 similar products Source: timesheet data*
	Total	$55,652		$57,341		
Symptomatic management pad	Invoiced costs $	$5,647	*Invoice record, 2013*	$5,898	$2949-$8847	Estimated 50% higher or lower
Online Decision aid (Back pain choices)	Invoiced costs $ (year)	$2,325 $12, 245	*Invoice record, 2011* *Invoice record, 2012*	$15,629	$7,815-$23,443	Estimated 50% higher or lower
	NPS MedicineWise human resources costs	$42,300	*Estimated from project management forecasting documents. 2015 salary data used*	$42,300	$21,150-$63,450	Estimated 50% higher or lower
	Total			$57,929		
Subtotal	Invoiced costs			$61,214	$22,676-$71,977	
	NPS MedicineWise human resources costs			$59,954	$38,804-$94,227	
	Infrastructure, support services (25%) of human resources costs			$19,985	$12,254-$29,756	
Total				$141,154	$73,734- $195,960	

* The product represented the greatest invoiced costs and lowest staff costs of similar products. This is due to a change in work distribution between NPS MedicineWise and the Department of Human Services. Variation for total product cost was $33,737-$57,341.

Table 7 presents the results from stage one evaluation on program effectiveness that will be used in the stage two economic evaluation.

TABLE 7: PROGRAM EFFECTIVIENSS DATA SUMMARY TABLE

Outcome	Raw value	Adjusted (base case)	Variation
Number of CT scans averted	50,186 95% posterior interval 3,919 - 96,476	50,076 Discounted at annual rate of 5% after year one, calculated monthly.	3,910 – 96,266
Cost of CT scans averted	$11,600,898 95% posterior interval $1,093,011 - $22,100,313	$11,575,439 Discounted at annual rate of 5% after year one, calculated monthly.	$1,090,612 – $22,051,813
Excess lifetime cancer risk averted (incidence)	36.62 (median)	36.62 (not discounted)	Min = 20.93 Max = 44.46

Results

Cost-benefit analysis

The NPS MedicineWise IALBP program aimed to reduce cost to the Australian health system via reduction in unnecessary CT scans. The extent to which this aim was achieved was evaluated using cost-benefit analysis. Table 8 presents the results of the cost-benefit analysis of the NPS MedicineWise IALBP program. The net benefit and benefit to cost ratio are used to compare the cost of the program to the benefit gained from savings to the MBS from averted CT scans.

TABLE 8: COST-BENEFIT ANALYSIS OF NPS MEDICINEWISE IMAGING FOR ACUTE LOW BACK PAIN 2013 PROGRAM

Parameter	Benefit: Savings from averted CT scans	Cost of program
Total cost of intervention	$11,575,439	$141,154
Net Benefit	$11,575,439 - $141,154 = **$11,434,285**	
Benefit to cost ratio	$11,575,439 / $141,154 = **82.01**	

The *net benefit* is the difference in the cost of averted CT scans and the costs of the NPS MedicineWise IALBP program. $11,575,439 - $141,154 = **$11,434,285**

The *benefit to cost ratio* is calculated by dividing the estimated cost of averted CT scans by the cost of the NPS MedicineWise MBS feedback intervention. Benefit to cost ratio = $11,575,439 / $141,154 = **82.01**. Values higher than one indicate that the benefits exceed the costs. The value of 82.01 indicates that for every dollar spent on the program, $82 was gained in monetary benefit.

Cost effectiveness analysis

Another goal of the NPS MedicineWise IALBP program was to reduce unnecessary exposure to medical radiation and the health risk associated with this exposure. A cost effectiveness analysis was used to assess the relationship between the program costs and benefit, and the effects of the program on these two outcomes.

An incremental cost effectiveness ratio (ICER) was calculated for the program (a) with the alternative of no program (b).

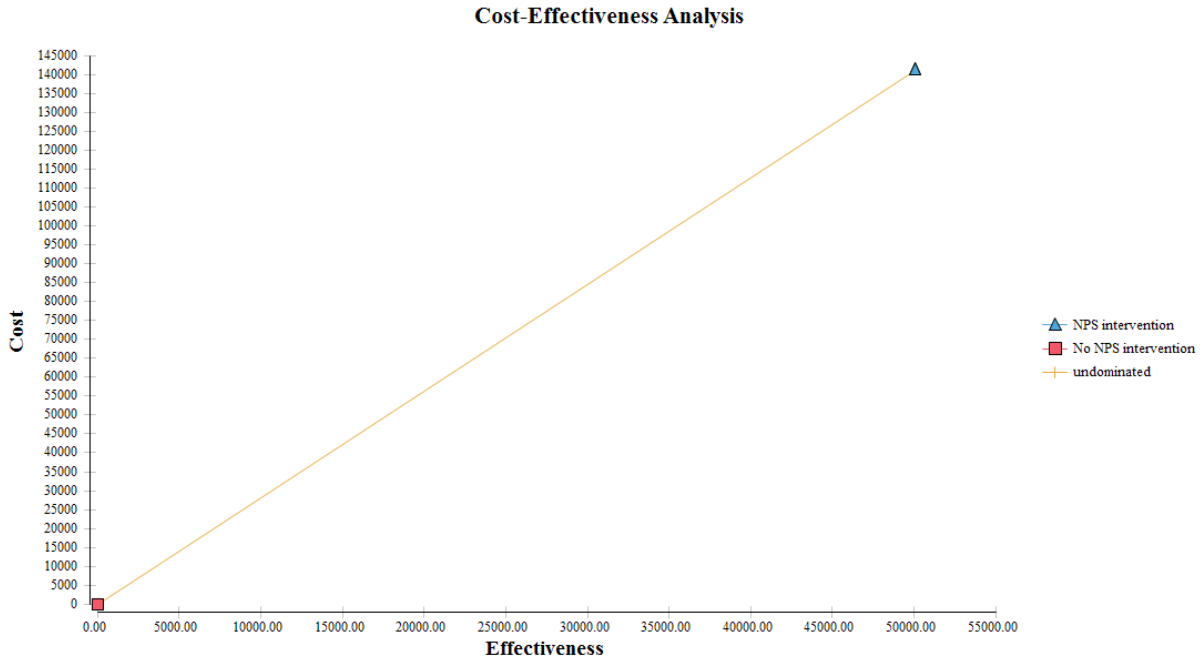
$$ICER = \frac{Cost_a - Cost_b}{Effect_a - Effect_b} = \frac{\Delta\, Cost}{\Delta\, Effect}$$

For the outcome of CT scans averted:

$$ICER = \frac{141{,}154}{50{,}076}$$

The ICER for CT averted is 2.82. For every $2.82 spent on the program, one CT scan was averted. This cost is offset by the savings to the MBS from the averted CT scan, which was on average $231. Figure 5 shows the comparison of the costs and effectiveness (in CT scan averted) of the program (blue triangle) with the alternative of no program (red square).

FIGURE 5: COST-EFFECTIVENESS ANALYSIS CHART FOR OUTCOME OF CT SCANS AVERTED



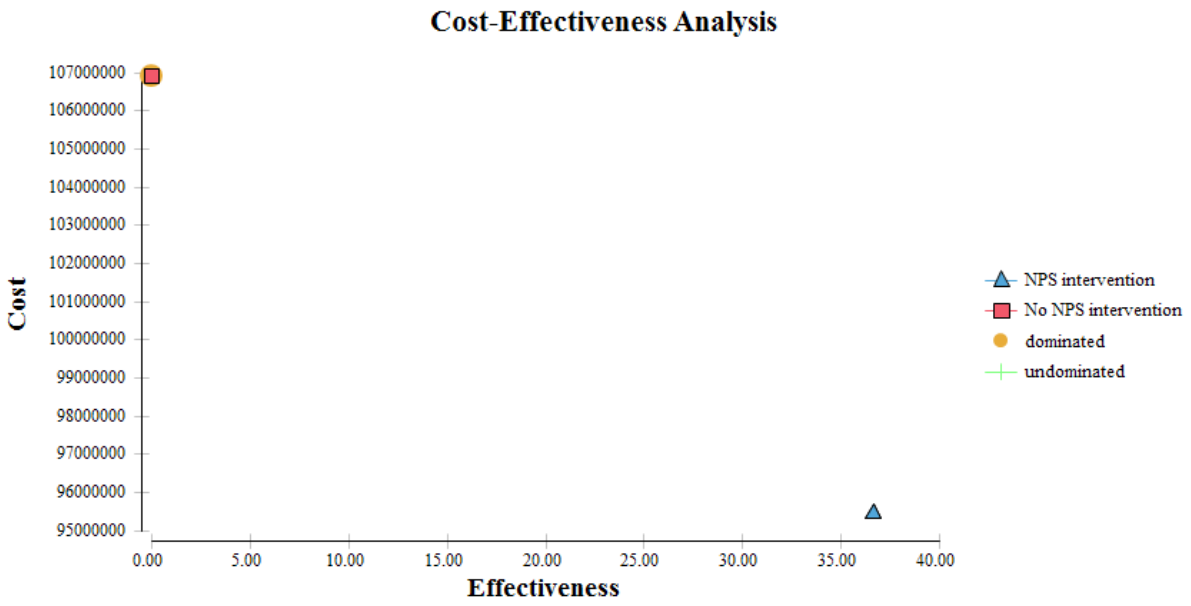
For the outcome of excess lifetime cancer incidence risk averted:

$$ICER = \frac{-11{,}434{,}285}{36.62}$$

The ICER for excess lifetime cancer risk incidence averted is -312,241. The negative value indicates that there was a savings rather than a cost associated with each additional unit of outcome. This is due to the inclusion of the savings to the MBS, which exceeded the cost of the program.

For every excess lifetime cancer risk the program averted there was a savings of $312,241. The intervention is referred to as dominating the non-intervention option, as it both costed less and produced more favourable outcomes. Figure 6 shows the comparison of the costs and effectiveness (in excess lifetime cancer risk averted) of the program (blue triangle) with the alternative of no program (red square). If the savings to the MBS are excluded from the analysis, the cost of the program per excess lifetime cancer incidence risk averted was approximately $3865.

FIGURE 6: COST-EFFECTIVENESS ANALYSIS CHART FOR OUTCOME OF EXCESS LIFETIME CANCER RISK (INCIDENCE) AVERTED



Sensitivity analysis

Cost benefit analysis

Table 9 below presents uncertainty around the net benefit and benefit to cost ratio by using four different scenarios based on estimated maximum and minimum values for program cost and benefit. In the most favourable scenario, in which the minimum program costs and the maximum benefit was used, the net benefit was $22,051,813 and the benefit to cost ratio was 299.07. In the least favourable scenario, in which the maximum program costs and the minimum benefit was used, the net benefit was $894,652.00 and the benefit to cost ratio was 5.57. Within the ranges selected as plausible or statistically probable, the benefit of the program is consistently higher than the cost.

TABLE 9: SENSITIVITY ANALYSIS FOR COST BENEFIT ANALYSIS

	Scenario 1 (Max)	Scenario 2 (Min)	Scenario 3 (least favourable)	Scenario 4 (most favourable)
Cost of program variation	Max: $195,960	Min: $73,734	Max: $195,960	Min: $73,734
Benefit: savings from averted CT scans variation	Max: $22,051,813	Min: $1,090,612	Min: $1,090,612	Max: $22,051,813
Net Benefit	$ 21,855,853.00	$1,016,878.00	$894,652.00	$21,978,079.00
Benefit to cost ratio	112.53	14.79	5.57	299.07

Cost-effectiveness analysis

One-way sensitivity analysis was performed in TreeAge to explore the effects of variation in the program costs, program effect size and average radiation dose between hospitals sampled, on the

cost-effectiveness analysis for the outcomes of CT scans averted and excess lifetime cancer risk averted. See results in Table 10; charts are available in Appendix 4.

TABLE 10: ONE-WAY SENSITIVITY ANALYSIS FOR COST-EFFECTIVENESS ANALYSIS

		ICER CT Scans Averted ($ per outcome)	ICER Cancer Risk Averted ($ per outcome)
	Base-case	2.82	-312,241
Program Cost	**Max: $195960**	3.91	-310750
	Min: $73734	1.47	-314087
Effectiveness (reducing CT scan utilisation)	**Max: 96266**	1.47	-314099
	Min: 3910	36.10	-266737
Cancer risk per CT scan*	**Max (0.001067)**	-	-257096
	Min (0.00050)	-	-545884

* Variation due to difference in average radiation dose between hospitals sampled.

The program costs per CT scan averted range from $1.47 to $36.10. This range of costs are all under the threshold of $231, which is offset by the savings to the MBS from each CT scan averted.

The negative value for each ICER for cancer risk averted in Table 10 indicates that there is savings rather than a cost associated with each additional unit of outcome for all scenarios tested.

When program costs are increased to the maximum value, the program cost per CT scan averted increases from $2.82 to $3.91. When the program costs are reduced to the minimum value the cost per CT scan averted decreases to $1.47. The savings per lifetime cancer risk averted varied from $314,087 (for minimum program cost) to $310,750 (for maximum program cost).

Variation in the effective size of the intervention on reducing CT scan utilisation had the largest impact on the cost per CT scan averted ($36.10 for minimum effect size and $1.47 for maximum effect size). Figure 8 in Appendix 4 shows that the greatest impact was seen at the lowest end of the range.

Variation in cancer risk per CT scan due to the difference in average radiation dose between hospitals sampled had the largest impact on the ICER for cancer risk averted. The savings per cancer risk averted was $545,884 for the lowest cancer risk per CT scan and $257,096 for the greatest cancer risk per CT scan. The lower the average radiation dose, the lower the cancer risk per CT scan, resulting in less cancer risk averted by the program. As the savings of the program is only due to savings to the MBS from averted CT scans, fewer cancers mean the savings per cancer risk averted is greater. If we remove MBS savings and include only program expenses, the program cost per cancer risk averted was $6739 for the lowest cancer risk per CT scan and $3174 for the greatest cancer risk per CT scan.

The results from the probabilistic sensitivity analysis can be found in Appendix 4.

DISCUSSION

The economic evaluation of the NPS MedicineWise IALBP program found that:

- The NPS MedicineWise 2013 program was effective at reducing MBS referrals for CT scans of the lumbosacral region by general practitioners by 10.85%. In the 20 months post program there was an estimated 50,186 fewer scans than predicted had the NPS MedicineWise program not occurred. This corresponded to an estimated mean savings to the MBS of $11,600,898.
- The reduction in radiation from the averted CT scans was linked to an estimated averted excess lifetime cancer incidence risk of 36.62 cancers.
- The NPS MedicineWise program had a cost-benefit ratio of 82.01, with a direct net benefit of $11,434,285.
- Cost-effectiveness analysis was undertaken as the outcomes of radiation from CT scans and lifetime cancer risk are linked to detrimental health outcomes independent of opportunity cost.
  - For every $2.82 spent on the program, one CT scan was averted. (ICER=2.82) This cost is offset by the savings to the MBS from the averted CT scan, which was on average $231 per CT scan.
  - For every excess lifetime cancer risk the program averted there was a net savings of $312,241 (ICER= -312,241).

The monetary benefit of the program used in the analysis was restricted to only direct benefit from savings to MBS from reduced CT scans. The impact of the program on lifetime cancer risk would have also led to savings to the health system. This was not included in this analysis for two reasons. The available data on the costs of specific cancers at the micro-level is limited. The risk model estimated an averted excess lifetime cancer risk of 11 colon cancers, 4 bladder cancers, 3 stomach cancers and 3 incidences of leukaemia. The best estimate of the lifetime cost of bowel cancer found was from a 2011 economic evaluation of the cost-effectiveness of screening for bowel cancer, commissioned by the Gut foundation and conducted by Deloitte Access economics.[20] This report estimated the financial lifetime costs per case of bowel cancer was $135,505, including health care costs of $36,397. These figures were inflated to 2011 prices from calculations in the 2006 Deloitte Access economics report, Cost of Cancer in NSW,[21] which are based on an Australian survey published in 1999 by Bolin et al.[25] Changes in treatments available, and the success of these, has a large impact on the cost to the health system and the community. Using old cost estimates would have introduced a degree of uncertainly had the cancer risk averted been in a short and known time frame. The uncertainty becomes very significant when the measurement of lifetime cancer risk is the outcome. As we cannot determine through this analysis when the averted cancers may have occurred, the costs of these in both financial and quality of life terms, and the appropriate discounting to apply, is unknown.

A limitation of the evaluation was the lack of measurement of the appropriateness of the behaviour change in relation to best practice evidence. As a result, the evaluation was unable to determine whether the reduction in CT scan is associated with any unintended consequences such as delayed diagnosis. We have assumed the reduction was of unnecessary CT scanning and this is consistent with a published economic evaluation of a program promoting these same guidelines.[22] It is expected that promoting materials that raise awareness and knowledge of guideline recommendations would have improved the detection of patients who would benefit from diagnostic imaging. This limitation is being addressed for evaluations of future programs. The NPS MedicineWise evaluation team is now collecting self-reported behaviour change information to evaluate the appropriateness of practice change due to personalised data feedback interventions such as MBS feedback.

Accurately quantifying historic program costs was a challenge in this economic evaluation. Improvement have been made by NPS MedicineWise including timesheet recording of staff resource costs that will improve the accuracy of program costings from 2014 onwards. To overcome this challenge the scope of the evaluation was narrowed to the 2013 phase of the program and, where necessary, used similar programs to estimate costs and likely variation ranges. A limitation of this analysis is the exclusion of the cost of the extensive existing work by NPS MedicineWise that the

program was built on and the financial impact on the MBS of this earlier work, which was estimated to be $5.4 million from reduced expenditure on CT scans for the spine for the period December 2010 to December 2011.[5] Using the informed assumption that the financial benefit of the earlier work was greater than cost of this work, the inclusion of it in this analysis would have led to a great direct net benefit, however most likely a small cost-benefit ratio. The cost-benefit ratio should therefore be considered specific to this situation and narrow program definition.

The linked evidence analysis was based on actual radiation dose data for the lumber spine CT scan protocol, using a published method[23] and with additional advice from the paper's author, Associate Professor Rachael Moorin. This is a stronger method compared to the use of radiation dose derived from survey data or collated by generic anatomical divisions. Radiation dose collected from a self-report survey has been shown to be systematically and proportionally different to data collected through random sampling of hospital electronic imaging records.[13] The calculating of risk is highly sensitive to the protocol used and the radiosensitivity of the anatomical area scanned. The use of generic anatomical divisions compared the clinical protocols has been shown to create significant differences in risk estimates.[23]

A limitation of the cancer modelling applied to population data, such as the MBS data available for this evaluation, is that the risk figures from the BEIR VII report assume independence of exposure. In the MBS data we cannot identify the relationship between scans and people. Therefore this method doesn't account for repeat scanning of individuals, which creates a bias towards a conservative estimate. However, it also doesn't account for the competing risks that people are exposed to. The finding should only be interpreted at the population level and not applied to individual cases.

The use of the MBS referral data was a valid and strong data set to use for this evaluation. The data provides a national census of funded CT scans referred by GPs, the data is not impacted by self-report bias, and NPS MedicineWise has a high level of expertise at conducting time series analysis using health administration datasets.

The findings from this evaluation demonstrated the adverse impact that unnecessary over-use of CT scans can have on costs for the health care system as well as serious detrimental health outcomes for the population.

The NPS MedicineWise 2013 IALBP program built on previous work and knowledge to deliver a relatively low cost program that combined the use of personalised data for self-reflection, passive information dissemination and the support of decision aids. The evaluation found, in the right context, low cost programs can provide significant savings to the health care system and avert health risks to the population. This evaluation will be used by NPS MedicineWise to inform the planning of programs that meet the needs of general practitioners, improve evidence based practice and are delivered in a cost-effective way.

Appendix 1. SAMPLE MBS FEEDBACK REPORT

NPS MEDICINEWISE PROFESSIONAL

IMAGING IN
LOW BACK PAIN
June 2013

⊢ 000001 000 DHS
Dr Sam Sample
123 Sample Street
SAMPLETOWN ABC 1234

21 June 2013

Dear Dr Sample,

NPS MedicineWise aims to support clinicians in professional development and continuous quality improvement activities with a focus on quality use of medicines and medical tests. The enclosed MBS feedback provides you with an opportunity to reflect on your own practice and to compare your referral patterns for imaging in low back pain with those of your peers.

We highlight that this information is confidential. NPS MedicineWise does not have access to your personal data. These data have been provided for your personal reflection only.

For over a decade, evidence-based guidelines have advised against imaging in routine evaluation of patients with acute low back pain in the absence of 'red flag' indicators of potentially serious underlying conditions. There is no evidence that imaging without a 'red flag' reason improves patient outcomes or alters clinical decision making.[1] Despite this, a recent Australian study indicates that more than a quarter of patients presenting to GPs with a new episode of low back pain are referred for a diagnostic imaging test.[2]

Reasons for the high use of diagnostic imaging for low back pain outside of guideline recommendations may reflect a variety of patient and doctor factors. For example, around three quarters of patients expect to be sent for imaging as part of their back pain management.[3-5] As well as managing these patient expectations, some health professionals have a misplaced fear of litigation if they decide not to refer.[6]

NPS MedicineWise provides free resources to support GPs in managing low back pain consultations and patient expectations.

- Low back pain symptomatic management pad www.nps.org.au/hporders
- Back pain choices, an online decision tool for the support and management of low back pain www.nps.org.au/back-pain-choices

Yours sincerely,

Janette Randall

Dr Janette Randall
Chair

Level 7/418A Elizabeth St
Surry Hills NSW 2010
PO Box 1147
Strawberry Hills NSW 2012

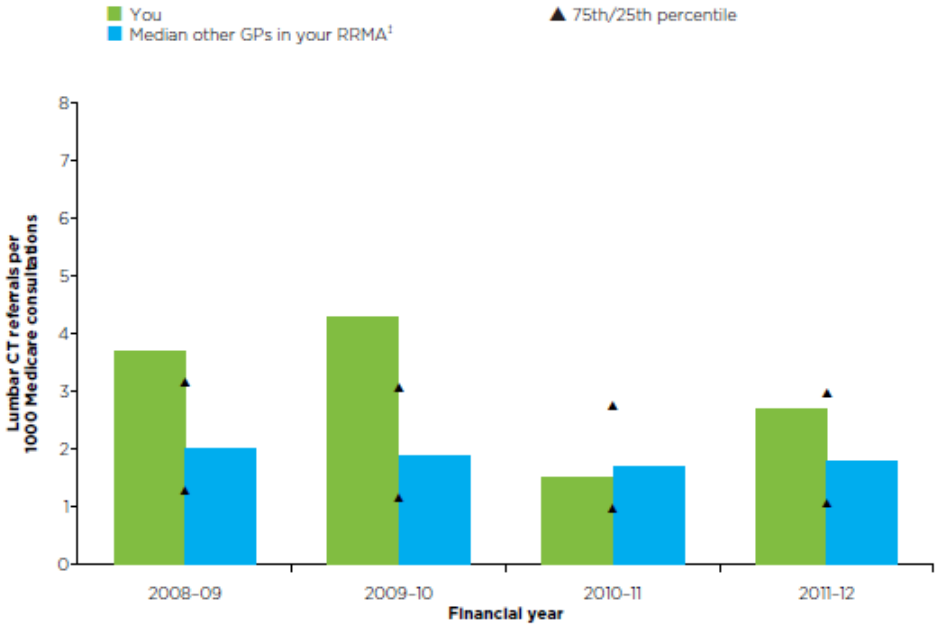
P: 02 8217 8700
F: 02 9211 7578
E: info@nps.org.au
www.nps.org.au

Dr Sam Sample Provider Number†: 999999

Your confidential referral data

The data presented from Medicare Australia include all MBS funded referrals for CT and X-rays of the lumbar spine. NPS Medicinewise provide this data for your reflection only.

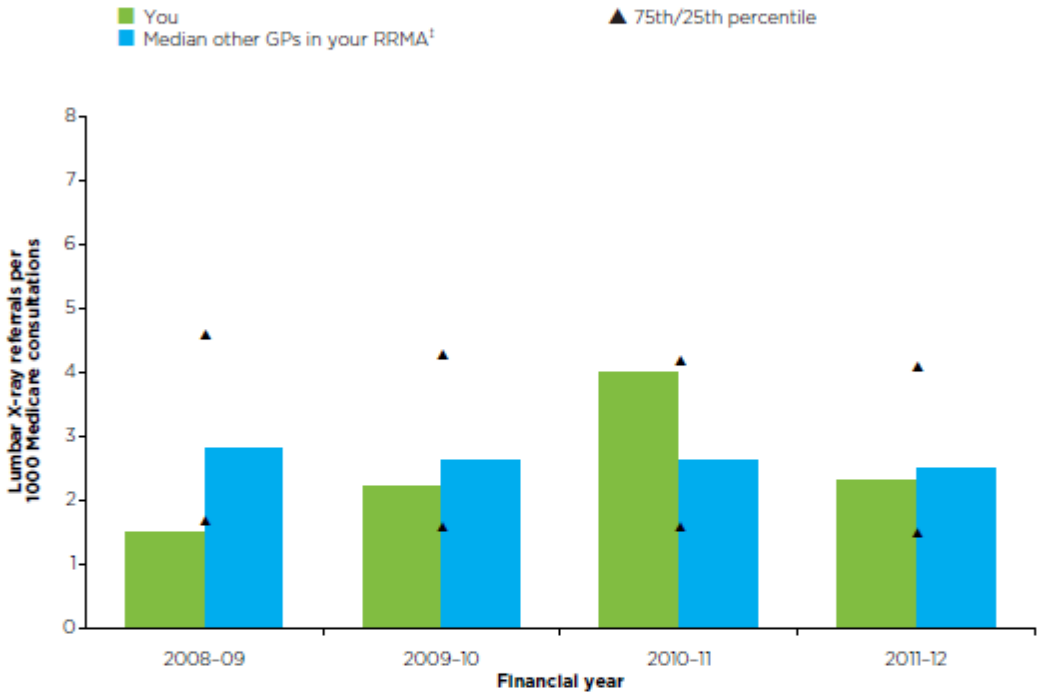
Have your requests for lumbar CT scans changed over time?



Points for reflection

- In the absence of red flag indicators, guidelines recommend against imaging in the routine evaluation of patients with acute and sub-acute low back pain (< 6-12 weeks).[1,7]
- At any one time 1 in 5 Australians have acute low back pain and around 4 out of 5 Australians will experience it at some point in their lives.[1]
- In Australia, low back pain problems are estimated to be the sixth most common reason for visiting a GP.[8]
- Serious (red flag) causes of low back pain are rare (< 5%) and can generally be excluded with careful history and examination. Most patients will recover fully within three months.[1]
- Radiological features are poorly correlated with symptoms and pathology in low back pain. In most cases acute low back pain is non-specific (i.e. an anatomical source cannot be identified).[1,9]
- Imaging and other investigations do not usually help with diagnosis or selection of therapies in acute non-specific low back pain.

Have your requests for lumbar X-rays changed over time?



Points for reflection

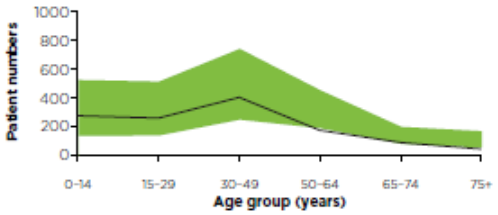
- Undertake a thorough history and examination to assess for the presence of serious clinical conditions ('red flags').[1,7]
- Reassure patients that low back pain is rarely serious, usually settles quickly and imaging rarely explains the reason for pain.[7]
- Provide adequate analgesia, including regular paracetamol as a first-line therapy for symptomatic pain relief.[7]
- Advise patients to stay active and resume normal activities, including work, as soon as possible. Adequate analgesia is important to aid mobility.[7]
- Encourage exercise interventions/programs to reduce the recurrence of back pain and where possible provide personalised written information to the patient.[1,7]

Practice profile

Data shown earlier are presented as referral rates (per 1000 Medicare consultations) to adjust for volume of service. Age profile of patients in your practice is provided to assist you to interpret your referral data.

Age profile of patients in your practice

(1 July 2011 to 30 June 2012)



The black line represents the age profile of patients in your practice. 25% to 75% of other GPs in your RRMA‡ fall within the shaded area. Your RRMA peer group is **CAPITAL**.

Medicare patients in your practice

(1 April 2012 to 30 June 2012)

Patients	You	Median other GPs in your RRMA‡
Total Medicare	670	661

Data from a 3 month period (1 April 2012 to 30 June 2012) that best represent your patient mix have been provided.

Confidentiality

NPS MedicineWise has a contract with Medicare Australia to provide your MBS referral feedback data directly to you. NPS MedicineWise does not have access to these data. The data contained in this feedback are not used for any regulatory purposes.

Discrepancies may occur between the data provided and your own referral practice. This may be due to either inaccurate recording of your provider number by the imaging provider or your referral stationery having been used by another doctor.

If you consider your individual data to be incorrect, have other data queries or general feedback please contact NPS MedicineWise on 02 8217 8700 or by email at info@nps.org.au

References

1. National Health and Medical Research Council. Evidence-based management of acute musculoskeletal pain. 2003. http://www.nhmrc.gov.au/publications/synopses/cp94syn.htm (accessed 27 March 2013).
2. Williams CM, Maher CG, Hancock MJ, et al. Low back pain and best practice care: A survey of general practice physicians. Arch Intern Med 2010;170:271–7.
3. Espeland A, Baerheim A, Albrektsen G, et al. Patients' views on importance and usefulness of plain radiography for low back pain. Spine 2001;26:1356–63.
4. Kendrick D, Fielding K, Bentley E, et al. Radiography of the lumbar spine in primary care patients with low back pain: randomised controlled trial. BMJ 2001;322:400–5.
5. Klaber Moffett JA, Newbronner E, Waddell G, et al. Public perceptions about low back pain and its management: a gap between expectations and reality? Health Expect 2000;3:161–8.
6. The Royal Australian and New Zealand College of Radiologists Quality Use of Diagnostic Imaging Program Project ES2 - Phase 1 Promoting public awareness of the appropriate use of diagnostic imaging. Melbourne: National Institute of Clinical Studies, 2006.
7. Therapeutic guidelines: rheumatology 2010 (version 2). Melbourne: Therapeutic Guidelines Ltd, 2010.
8. Australia's health 2012. Australia's health no. 13. Cat. no. AUS 156. Canberra: Australian Institute of Health and Welfare, 2012.
9. McIntosh G, Hall H. Low back pain (acute). Clin Evid (Online) 2011;pii:1102.

Notes

† Data shown are an aggregate for all your provider locations.

‡ The comparator group "other GPs in your RRMA" includes all general practitioners currently located in a similar geographical region i.e. **1.** capital cities, **2.** other metropolitan centres, **3.** large rural centres,**4.** small rural centres, **5.** other rural centres, **6.** remote centres **7.** other remote centres. **Your RRMA peer group is CAPITAL.**

▲ 25% to 75% of "other GPs in your RRMA" fall in the range shown by the triangular symbols.

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Appendix 2. BAYESIAN HIERARCHICAL TIME SERIES MODEL (BHTSM)

In the Bayesian framework, the realisations of a probability model, and all unknown parameters of interest, which can be quantified by probability distributions, are treated as random variables. Such probabilistically-quantified parameters serve as the prior information of the behaviour of true parameter values. The inference on the parameters of interest will be summarised from their posterior distributions. Given the observed data information (which condition on the unknown parameters) in terms of a likelihood function and prior information, the posterior distribution of the parameters is:

$$\text{Posterior} \propto \text{Likelihood} \times \text{Prior}$$

Bayesian hierarchical model (BHM) extend the above formulation of posterior distribution, allowing more complicated dependence structures through series of conditional distributions. A conceptual definition of BHM, proposed by Berliner (1996) [24] is adopted here, where the joint distribution of data and all unknown parameters can be factored into three levels, namely a Data Model, a Process Model and a Parameter Model, leaving the joint posterior distribution as:

$$[\text{Process},\text{Parameters} \mid \text{Data}] \propto [\text{Data} \mid \text{Process},\text{Parameters}] \times [\text{Process} \mid \text{Parameters}] \times [\text{Parameters}]$$

In the time series context, the first two levels of BHM are equivalent to the so-called state space or structural time series model. Along with the parameter model, a general BHTSM structure can be defined as

Data Model: $z_t=H_t Y_t+\varepsilon_t \quad \varepsilon_t \sim \text{Normal}(0,\sigma_t^2)$

Process Model: $Y_t=M_t Y_{(t-1)}+\eta_t \quad \eta_t \sim \text{Normal}(0,Q_t)$

Parameter Model: $[\sigma_t^2,Q_t]=[\sigma_t^2][Q_t]$

in which H_t is the observation operator that maps the process Y_t to the observations z_t and M_t is the linear model operator that maps the state process in time. Both Data Model and Process Model are assumed normally distributed with mean 0 and unknown variance σ_t^2 and variance-covariance matrix Q_t , which are to be estimated.

The hierarchical form in terms of the Data Model and the Process Model provides a unified framework for time series analyses. These include the autoregressive model (AR), the moving average model (MA) or the autoregressive and moving average model (ARMA) used in the conventional time series regression, but not limited to those autocorrelation structures.

The overall model formulation for our intervention analysis with BHM was described in Brodersen et al. (2015) [25] with a local linear trend component, a seasonality component and a non-GP referral covariate as the control series. By specifying the prior distributions for unknown quantities Y_0 σ_t^2, Q_t and β for the coefficient of non-GP covariate, a full Bayesian approach is used to infer the posterior temporal trajectory of the counterfactual GP series if without NPS intervention during the post-intervention period. The only available control group for each of the analysis is the data of other health professionals. By applying a so-called spike-and-slab prior, the model can integrate out the posterior uncertainty about the influence of each control as well as the uncertainty about which control series to include. This method will potentially be useful if, for example, interventions are delivered in ways that facilitate controlled comparisons between different regions. The prior distributions in the Parameter Model for the unknown variance parameters were assumed by inverse gamma distributions.

Appendix 3. LIFETIME CANCER RISK CALCULATIONS

Method of calculating life cancer risk averted

1. For each hospital and protocol the mean exposure data for each organ was calculated in mGy units.
   - Example: the mean exposure to the colon from a lumber CT protocol in hospital one was 29.1mGy
2. The age/sex-specific risk coefficients from tables 12D-1 and 12D-2 of the BEIR VII report were used.
   - Example: the BEIR weighting for the colon for a male aged 15 is 204.
3. The BEIR Weighting and the mean exposure organ dose were multiplied together and divided by 100 to give an estimated no of cancers per 100,000 population receiving the exposure calculated for protocol.
   - Example: 29.1mGy * 204 /100 = 59.4 cancers per 100,000 population receiving the exposure
4. This was done for all organs listed in the BEIR tables and then a total for remaining organs.
5. These rates were averaged to create a rate for the age groups in the MBS data.
   - Example: For Males 15-24years the rate of cancers per 100,000 population receiving the exposure was 51.7 (see Tables 11 and 12 below)

TABLE 11: AVERAGED CANCERS PER 100,000 POPULATION RECEIVING THE EXPOSURE - MALE

Males	15-24	25-34	35-44	45-54	55-64	65-74
Stomach	12.8	9.4	8.5	7.8	6.4	4.5
Colon	51.7	38.4	35.3	32.7	27.3	19.2
Liver	8.3	6.2	5.6	5.0	3.8	2.3
Lung	3.9	2.8	2.6	2.6	2.3	1.7
Prostate	12.6	9.5	8.9	8.3	6.6	3.8
Bladder	28.4	21.3	20.1	19.3	16.8	12.1
Other	45.3	29.6	23.8	19.6	13.9	8.3
Thyroid	0.0	0.0	0.0	0.0	0.0	0.0
All solid	163.0	117.2	104.8	95.4	77.1	51.8
Leukemia	12.0	10.6	10.4	10.3	10.0	8.9
All cancers	175.0	127.8	115.2	105.7	87.2	60.7

TABLE 12: AVERAGED CANCERS PER 100,000 POPULATION RECEIVING THE EXPOSURE - FEMALE

Females	15-24	25-34	35-44	45-54	55-64	65-74
Stomach	16.8	12.1	11.0	10.1	8.5	6.1
Colon	34.0	25.2	22.9	21.2	18.0	13.2
Liver	3.8	2.8	2.6	2.4	1.9	1.3

Females	15-24	25-34	35-44	45-54	55-64	65-74
Lung	9.1	6.6	6.1	5.8	5.1	3.8
Breast	3.5	2.1	1.2	0.6	0.3	0.1
Uterus	8.6	6.2	5.1	4.2	3.0	1.7
Ovary	15.5	10.9	9.2	7.6	5.5	3.5
Bladder	28.7	21.4	19.9	18.8	16.3	12.1
Other	46.9	30.9	25.1	20.7	15.4	9.8
Thyroid	0.1	0.0	0.0	0.0	0.0	0.0
All solid	166.9	118.1	103.0	91.5	74.1	51.6
Leukemia	8.8	7.9	7.7	7.6	7.1	6.2
All cancer	175.8	126.0	110.7	99.1	81.1	57.8

6. These rates were applied to the calculated number of CT scans averted by the NPS MedicineWise program to give an estimated lifetime cancer risk averted (Table 13).

TABLE 13: ESTIMATED NUMBER OF CT SCANS AVERTED BY THE NPS MEDICINEWISE PROGRAM

Males	15-24	25-34	35-44	45-54	55-64	65-74
Number	567	2343	3441	4009	4431	4188
Females	**15-24**	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**
Number	818	2063	3490	4929	5661	5703

TABLE 14: ESTIMATED LIFETIME CANCER RISK AVERTED DUE TO PROGRAM IMPACT - MALE

Males	15-24	25-34	35-44	45-54	55-64	65-74	Totals
Stomach	0.072759	0.219861	0.292079	0.314178	0.28216	0.187935	1.368972
Colon	0.292929	0.89917	1.213332	1.311864	1.211501	0.802566	5.731363
Liver	0.047116	0.145028	0.192386	0.20199	0.168045	0.094286	0.84885
Lung	0.022256	0.066607	0.091009	0.102485	0.099891	0.069954	0.452202
Prostate	0.07172	0.221594	0.305886	0.334575	0.293248	0.159756	1.38678
Bladder	0.160861	0.499862	0.692247	0.774347	0.74418	0.508755	3.380252
Other	0.25664	0.692733	0.819614	0.784377	0.617881	0.348235	3.51948
Thyroid	7.64E-05	0.000138	7.03E-05	2.84E-05	9.83E-06	2.89E-06	0.000325
All solid	0.924357	2.744992	3.606624	3.823844	3.416916	2.171491	16.68822

Males	15-24	25-34	35-44	45-54	55-64	65-74	Totals
Leukemia	0.068232	0.248031	0.356651	0.414568	0.445116	0.371342	1.903941
All cancers	0.99259	2.993023	3.963275	4.238412	3.862032	2.542833	18.59217

TABLE 15: **ESTIMATED LIFETIME CANCER RISK AVERTED DUE TO PROGRAM IMPACT - FEMALE**

Females	15-24	25-34	35-44	45-54	55-64	65-74	Totals
Stomach	0.137212	0.249683	0.382973	0.497682	0.48208	0.349612	2.099241
Colon	0.277937	0.519293	0.798133	1.044282	1.020487	0.752606	4.412739
Liver	0.03112	0.058606	0.092253	0.118236	0.107713	0.076419	0.484347
Lung	0.074421	0.13541	0.21261	0.287349	0.288626	0.215374	1.21379
Breast	0.028797	0.043434	0.040159	0.029699	0.015531	0.00629	0.16391
Uterus	0.069946	0.126999	0.179373	0.208425	0.168735	0.097931	0.851409
Ovary	0.126935	0.224914	0.322411	0.375147	0.313701	0.197201	1.560309
Bladder	0.23446	0.440463	0.693204	0.928777	0.924557	0.689825	3.911286
Other	0.383709	0.636748	0.87437	1.022418	0.872408	0.558296	4.347948
Thyroid	0.00059	0.000583	0.000328	0.000148	4.5E-05	1.23E-05	0.001707
All solid	1.365127	2.436135	3.595813	4.512162	4.193883	2.943565	19.04669
Leukemia	0.072351	0.163184	0.267591	0.374097	0.399213	0.355389	1.631824
All cancer	1.437478	2.599318	3.863404	4.886259	4.593096	3.298954	20.67851

7. This was completed for each of the hospitals. Table 16 below shows the summary of findings

TABLE 16: SUMMARY OF FINDINGS FOR EACH HOSPITAL – LIFETIME CANCER RISK AVERTED DUE TO PROGRAM IMPACT

	Male	Female	Total
Hospital 1	18.59217	20.67851	39.27067
Hospital 2	9.828303	11.1033	20.9316
Hospital 3	20.87146	23.59142	44.46288
Hospital 4	17.1906	19.42829	36.61889
Hospital 5	13.82343	15.6521	29.47554

Appendix 4. SENSITIVITY ANALYSIS

One-way sensitivity analysis charts

FIGURE 7: ONE-WAY SENSITIVITY ANALYSIS OF PROGRAM COSTS AGAINST ICER OF CT SCANS AVERTED

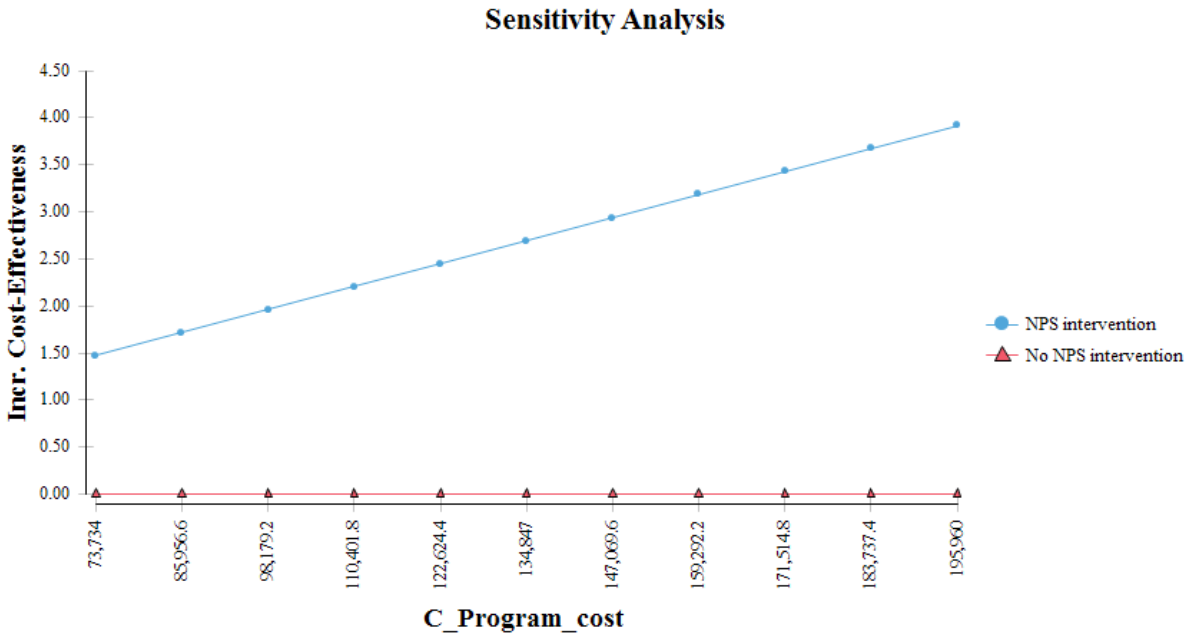


FIGURE 8: ONE-WAY SENSITIVITY ANALYSIS OF PROGRAM EFFECTIVENESS AGAINST ICER OF CT SCANS AVERTED

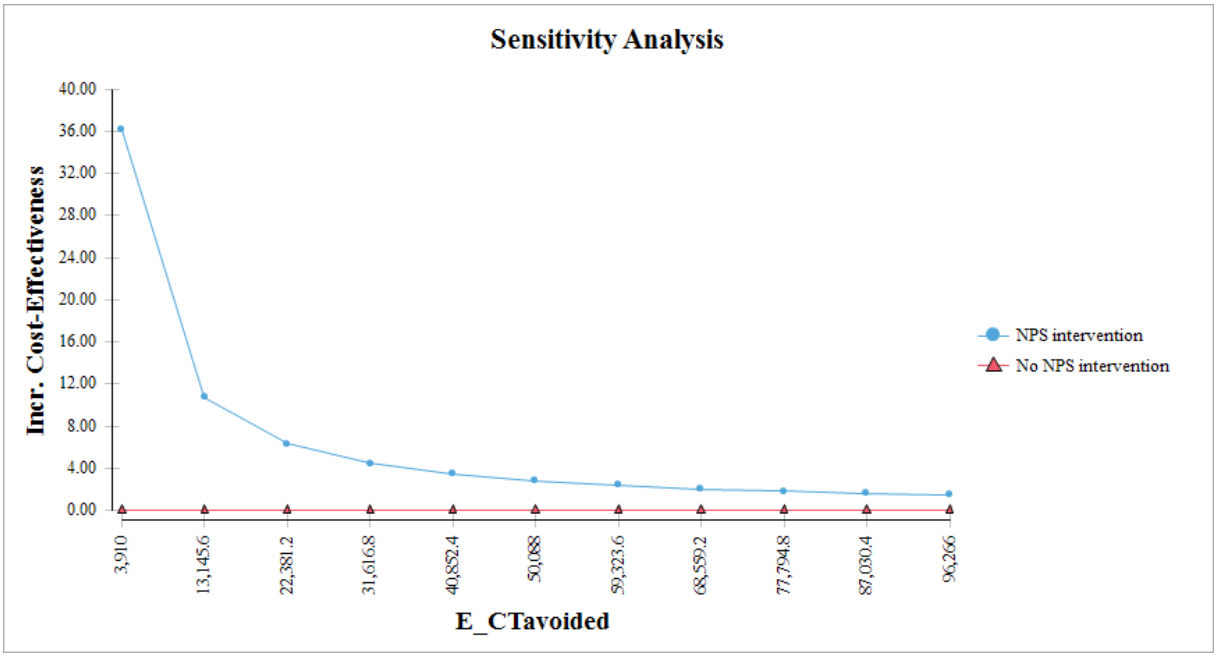


FIGURE 9: ONE-WAY SENSITIVITY ANALYSIS OF PROGRAM COSTS AGAINST ICER OF EXCESS CANCER RISK AVERTED

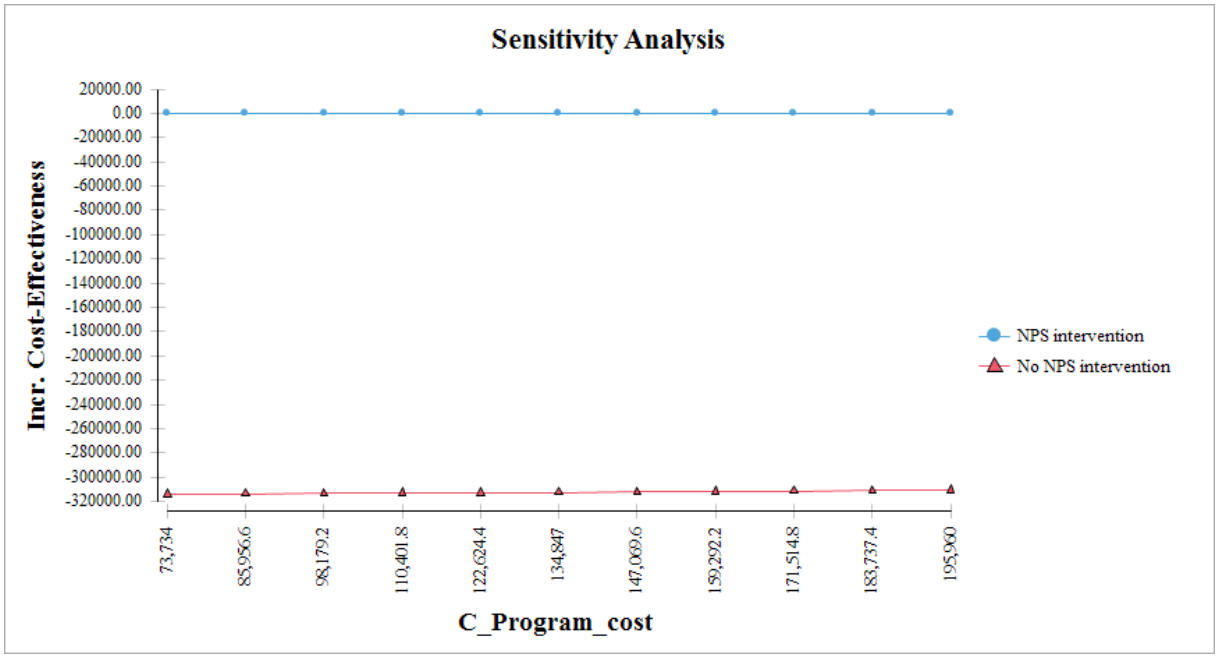


FIGURE 10: ONE-WAY SENSITIVITY ANALYSIS OF PROGRAM EFFECTIVENESS AGAINST ICER OF EXCESS CANCER RISK AVERTED

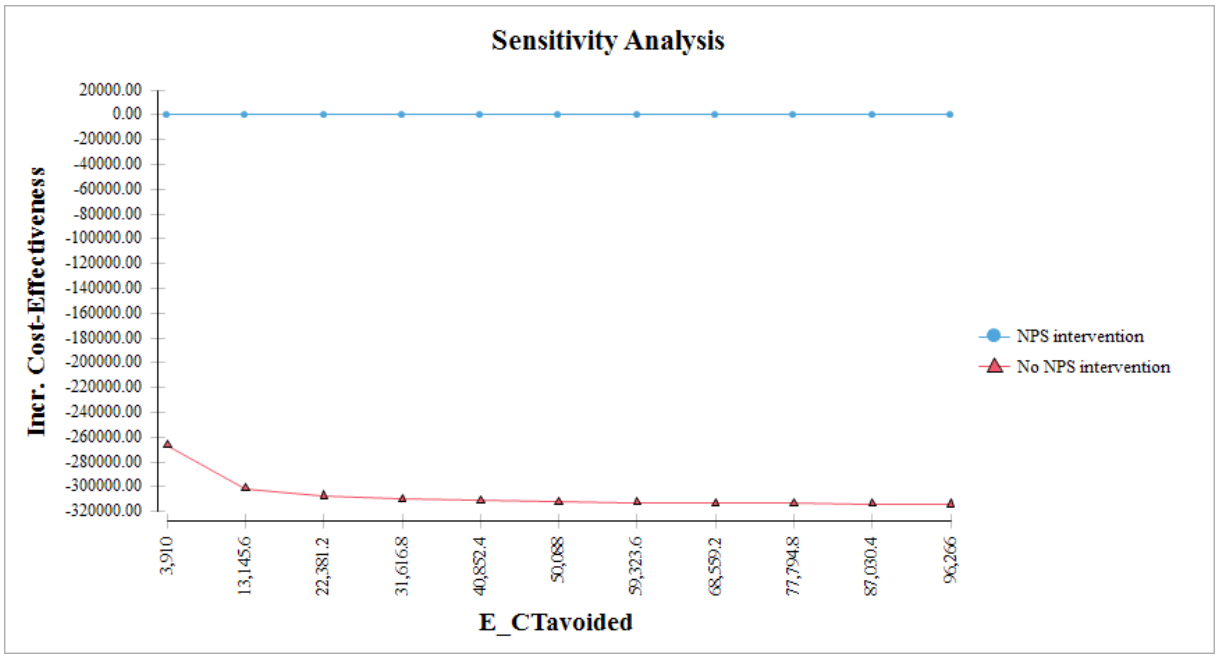
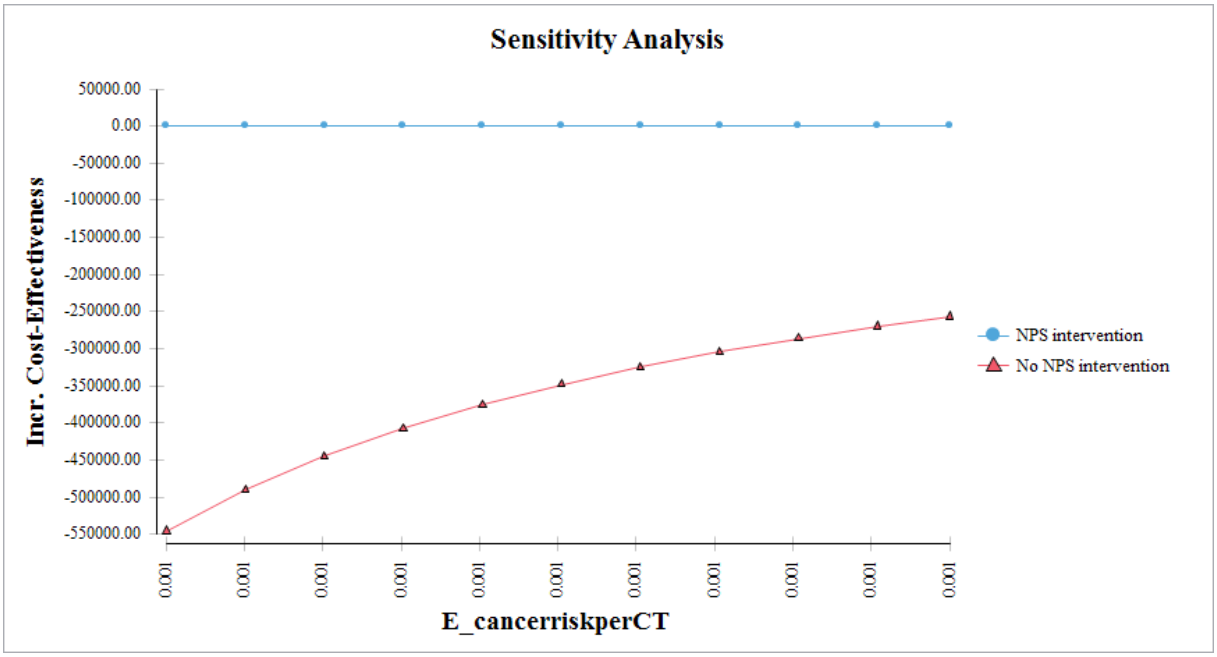


FIGURE 11: ONE-WAY SENSITIVITY ANALYSIS OF CANCER RISK PER CT SCAN AVERTED (VARIATION IN RADIATION ACROSS HOSPITAL SAMPLE) AGAINST ICER OF EXCESS CANCER RISK AVERTED



Probabilistic sensitivity analysis

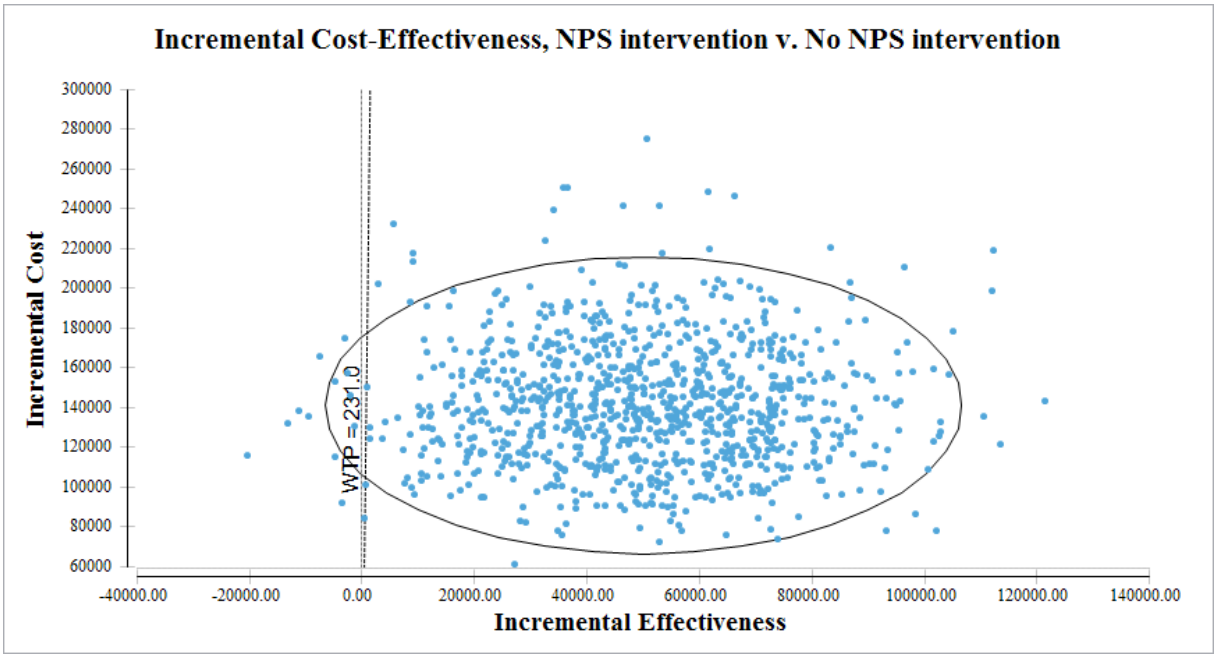
A probabilistic sensitivity analysis was performed on the cost-effectiveness analysis for the outcome of averted CT scans. Uncertainly around the program costs was included using a gamma distribution and the confidence intervals estimated from range presented in Table 6. The uncertainly around the effectiveness of the program was included using a normal distribution and confidence intervals from the time series analysis presented in Table 7.

A willingness to pay threshold of $231 was used to represent the average savings to be MBS from each CT scan averted. The probabilistic sensitivity analysis was run with 50000 samples. The results are presented in Figure 12 below and in Table 17.

TABLE 17: RESULTS FROM INCREMENTAL CE PLOT REPORT.

NPS intervention more effective, ICER less than $231	98.3% of iterations
NPS intervention more effective, ICER greater than $231	0.09% of iterations
NPS intervention inferior - less effective and greater cost	1.6% of iterations

FIGURE 12: PROBABILISTIC SENSITIVITY ANALYSIS OF CT SCANS AVERTED

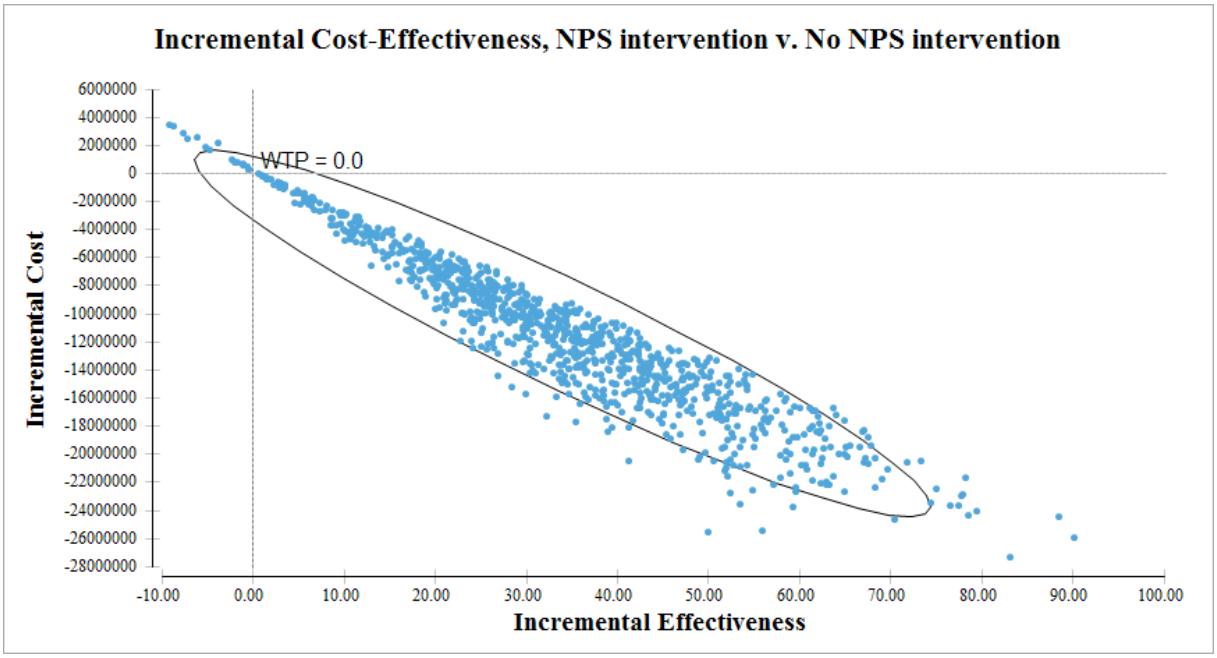


A probabilistic sensitivity analysis was performed on the cost-effectiveness analysis for the outcome of averted lifetime cancer risk. Uncertainly around the program costs and program effectiveness was included as above. Uncertainly around the radiation organ dose due to hospital variation was included using a triangular distribution using the maximum and minimum hospital values as the thresholds and the median values as the 'likeliest value'. The probabilistic sensitivity analysis was run with 50000 samples. The results are presented in Figure 13 below and in Table 18.

TABLE 18: RESULTS FROM INCREMENTAL CE PLOT REPORT.

NPS intervention superior - more effective + cost less	98.4% of iterations
NPS intervention - more effective and greater cost	0.1% of iterations
NPS intervention inferior - less effective and greater cost	1.5% of iterations

FIGURE 13: PROBABILISTIC SENSITIVITY ANALYSIS OF LIFETIME CANCER RISK AVERTED – 95% CI ELIPSE



REFERENCES

1. Kent, P.M. and J.L. Keating, *The epidemiology of low back pain in primary care.* Chiropr Osteopat, 2005. 13: p. 13.
2. National Health and Medical Research Council. *Evidence-based management of acute musculoskeletal pain.* 2002 [cited 2013 27 March].
3. McIntosh, G. and H. Hall, *Low back pain (acute).* BMJ Clin Evid, 2011. 2011.
4. Williams, C.M., C.G. Maher, M.J. Hancock, J.H. McAuley, A.J. McLachlan, H. Britt, S. Fahridin, C. Harrison, et al., *Low back pain and best practice care: A survey of general practice physicians.* Arch Intern Med, 2010. 170(3): p. 271-7.
5. NPS MedicineWise, *Financial Impact of the NPS MedicineWise Quality Use of Diagnostics Program on the MBS 2009-2013: Report to the Australia Government Department of Health*, 2013. Available:
6. Williams, C.M., N. Henschke, C.G. Maher, M.W. van Tulder, B.W. Koes, P. Macaskill and L. Irwig, *Red flags to screen for vertebral fracture in patients presenting with low-back pain.* Cochrane Database Syst Rev, 2013. 1: p. CD008643.
7. Henschke, N., C.G. Maher, K.M. Refshauge, R.D. Herbert, R.G. Cumming, J. Bleasel, J. York, A. Das, et al., *Prevalence of and screening for serious spinal pathology in patients presenting to primary care settings with acute low back pain.* Arthritis & Rheumatism, 2009. 60(10): p. 3072-80.
8. Henschke, N., C.G. Maher, R.W. Ostelo, H.C. de Vet, P. Macaskill and L. Irwig, *Red flags to screen for malignancy in patients with low-back pain.* Cochrane Database Syst Rev, 2013. 2: p. CD008686.
9. Gibson, D.A., R.E. Moorin, J. Semmens and D.J. Holman, *The disproportionate risk burden of CT scanning on females and younger adults in Australia: a retrospective cohort study.* Aust N Z J Public Health, 2014. 38(5): p. 441-8.
10. Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation, *Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII-Phase 2*, 2006, National Research Council, Division on Earth and Life Studies, Board on Radiation Effects Research. Available:
11. Pearce, M.S., J.A. Salotti, M.P. Little, K. McHugh, C. Lee, K.P. Kim, N.L. Howe, C.M. Ronckers, et al., *Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study.* Lancet, 2012. 380(9840): p. 499-505.
12. Mathews, J.D., A.V. Forsythe, Z. Brady, M.W. Butler, S.K. Goergen, G.B. Byrnes, G.G. Giles, A.B. Wallace, et al., *Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians.* BMJ, 2013. 346: p. f2360.
13. Moorin, R.E., D.A. Gibson, R.K. Forsyth, M.K. Bulsara and C.D. Holman, *Evaluating data capture methods for the establishment of diagnostic reference levels in CT scanning.* Eur J Radiol, 2014. 83(2): p. 329-37.
14. *Medicare Australia Statistics. Item reports*. 20 June 2016]; Available from: https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml.
15. Brodersen et al, *CausalImpact 1.0.3*, 2015, Annals of Applied Statistics.
16. R Core Team, *R: A language and environment for statistical computing*, 2015, R Foundation for Statistical Computing, Vienna, Austria.
17. Gray, A.M., P.M. Clark, J.L. Wolstenholme and S. Wordsworth, *Applied Methods of Cost-effectiveness Analysis in Health Care*2011, Oxford, UK: Oxford University Press.
18. Australian Bureau of Statistics. *6401.0 - Consumer Price Index, Australia*. 2016 [cited 2016 26 May]; Available from: http://www.abs.gov.au/ausstats/abs@.nsf/mf/6401.0
19. NPS MedicineWise and The George Institute. *Back Pain Choices*. 2012 [cited 2016 30 May]; Available from: http://www.nps.org.au/conditions/nervous-system-problems/pain/for-individuals/pain-conditions/low-back-pain/back-pain-acute-low/back-pain-choices.
20. Deloitte Access Economics, *Cost-effectiveness of screening for bowel cancer*, 2011. Available:
21. Access Economics Pty Limited, *Cost of Cancer in NSW*, 2007. Available: http://www.cancercouncil.com.au/wp-content/uploads/2010/11/costofcancer_summary.pdf
22. Mortimer, D., S.D. French, J.E. McKenzie, D.A. O'Connor and S.E. Green, *Economic evaluation of active implementation versus guideline dissemination for evidence-based care of acute low-back pain in a general practice setting.* PLoS One, 2013. 8(10): p. e75647.

23. Moorin, R.E., D.A. Gibson, R.K. Forsyth and R. Fox, *Demonstration of the effect of generic anatomical divisions versus clinical protocols on computed tomography dose estimates and risk burden.* PLoS One, 2014. 9(5): p. e97691.
24. Berliner, L.M., *Hierarchical Bayesian time series models.*, in *Maximum Entropy and Bayesian Methods*, K. Hanson and R. Silver, Editors. 1996, Kluwer Academic Publishers: Dordrecht, The Netherlands. p. 15-22.
25. Brodersen, K.H., F. Gallusser, J. Koehler, N. Remy and S.L. Scott, *Inferring causal impact using Bayesian structural time-series models.* Annals of Applied Statistics, 2015. 9(1): p. 247-274.