

# Cost-effectiveness Analysis of the Use of Iodixanol Compared to Iohexol in the United Kingdom

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## ABSTRACT

**OBJECTIVES:** Contrast-induced adverse drug reactions (ADRs), including contrast-induced nephropathy (renal insufficiency and diabetes), are common among high-risk patients (e.g., patients with diabetes mellitus and renal impairment). These ADRs cause extended hospital stays and additional medication use, which lead to increased costs. We examined the cost-effectiveness of the use of two contrast media in patients at high risk for contrast-induced nephropathy.

**METHODS:** A decision-analytic model was constructed to estimate the cost-effectiveness of an isosmolar contrast agent, iodixanol, compared with a low-osmolar contrast medium, iohexol, in the United Kingdom (UK). Particular emphasis of the model was to avert the incidence of severe ADRs in patients at risk of contrast-induced nephropathy. The analysis is based on a multicenter randomized controlled trial conducted in five European countries, the Nephrotoxicity in High-Risk Patients Study of Iso-Osmolar and Low-Osmolar Non-Ionic Contrast Media (NEPHRIC) trial. Patients receiving iodixanol versus iohexol experienced a statistically significant reduction in the incidence of severe ADRs in favor of iodixanol. Patients in the study were adults aged 18 years and older referred for coronary or aortofemoral angiography who had diabetes and stable serum creatinine concentrations (men: 1.5 to 3.5 mg/dL; women: 1.3 to 3.5 mg/dL). Among the ADRs considered were acute renal failure, arrhythmia, cardiovascular events, pulmonary edema, and multiple-organ failure. Resource use, including hospital days, medical visits, contrast medium, medications, laboratory tests, and hospital procedures, were obtained from the NEPHRIC clinical trial. Unit-costs data were obtained from standard UK costing sources. Costs are reported in 2006 UK pounds.

**RESULTS:** Iodixanol is cost-effective compared with iohexol; costs are lower and effects better, relating to fewer ADRs. The mean per-patient cost difference was £571.32 (£0.41 and £571.73 for iodixanol and iohexol, respectively).

**CONCLUSION:** Iodixanol results in fewer ADRs and lower ADR costs per patient for this high-risk patient population.

## INTRODUCTION

- Patients with concurrent diabetes mellitus (type 1 or 2) and renal impairment are at especially high risk for nephrotoxic events when exposed to iodine-based contrast media.<sup>1</sup>
- Although the incidence of contrast-induced nephropathy associated with iodinated contrast media in the general population is around 2%, for patients with higher-risk comorbidity (such as patients with diabetes or renal impairment) the risk can be as high as 12% to 50%.
- Acute renal failure is a clinically important adverse event that can result from the use of iodinated contrast medium,<sup>1,2,3</sup> and is in turn related to extended hospital stays and additional medication use.
- The NEPHRIC study (a randomized, prospective, double-blind, multicenter trial) compared the nephrotoxic effects of the use of iodixanol and iohexol as contrast media in high-risk patients with stable diabetes mellitus and impaired renal function who underwent coronary or aortofemoral angiography.<sup>4</sup>
- There was a significant difference in the observed incidence of contrast-induced nephropathy: 3% versus 26% in the iodixanol and iohexol groups, respectively.
- Overall, the risk of renal failure and nephropathy was estimated to be 11 times higher for iohexol compared with iodixanol.
- Understanding the economic consequences of the use of these contrast media, as well as the clinically important difference in acute renal failure rates, is important to decision makers.

## OBJECTIVES

- To assess the per-patient-level cost-effectiveness and cost savings from the use of an isosmolar contrast agent, iodixanol, compared with the use of a low-osmolar contrast medium, iohexol, in a high-risk patient cohort for the UK.
- To assess the level of cost savings that are achievable per 100 patients, based on a range of assumptions on the prevalence of high-risk patients in the cohort and uptake rates for iodixanol.

## METHODS

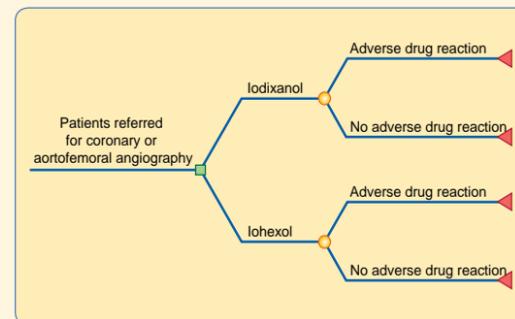
### NEPHRIC Patient Population

- The economic evaluation study was based on available patient-level data for 125 adults from the NEPHRIC study, which was conducted in 17 centers in five European countries (Denmark, France, Germany, Spain, and Sweden).
- The patients were all 18 years and over, and had been referred for coronary or aortofemoral angiography.
- The NEPHRIC study was designed to compare renal effects of a nonionic, isosmolar, dimeric contrast medium, iodixanol (320 mg of iodine per milliliter; 290 mOsm per kilogram of water) with those of the nonionic, low-osmolar, monomeric contrast medium iohexol (350 mg of iodine per milliliter; 780 mOsm per kilogram of water).
- Patients had diabetes mellitus, treated with insulin or oral antidiabetic drugs.
- Patients had stable serum creatinine concentration during the 3 months prior to enrollment, with a mean baseline of 1.49±0.53 mg/dL for patients on iodixanol and 1.60±0.52 mg/dL for patients on iohexol.
- The peak increase in serum creatinine concentration from baseline was significantly lower for iodixanol (0.13 mg/dL/11.2 micromol/liter) compared with iohexol (0.55 mg/dL/48.2 micromol/liter).

## Economic Analysis: Study Design

- The analysis was based on a simple decision-analytic framework that was developed to examine the cost-effectiveness of iodixanol compared with iohexol (Figure 1).
- The economic analysis perspective was based on that of the hospital, and was therefore centered on the direct costs associated with the treatment of ADRs related to the contrast media. The costs of general health care were not included in the analyses, nor were the costs of the contrast medium.
- Efficacy in terms of image quality was assumed to be equal as seen in a randomized, double-blind, parallel trial.<sup>5</sup> Therefore, the economic study was based on a cost-minimization approach.
- Health care resource use incurred for treating ADRs related to the use of contrast media was collected by investigators until discharge, but no later than 1 month after angiography procedure in the NEPHRIC clinical trial.
- Resource utilization included length of stay in different types of hospital wards, general practitioner follow-up visits, use of contrast medium and other medications, laboratory tests, and surgical and diagnostic procedures.
- Drug costs were limited to those drugs that were not used prior to the procedures or to drugs that had been used previously but at an increased dosage following the procedure.
- Unit costs were obtained from the British National Formulary (2006),<sup>6</sup> National Health Service (2006),<sup>7</sup> and Curtis and Netten (2006).<sup>8</sup>
- All costs are reported in 2006 UK pounds.

Figure 1: Model Structure



## RESULTS

### Average Per-Patient ADR-Related Cost Savings From the NEPHRIC Trial

- In total, 7 patients in the NEPHRIC trial experienced contrast media-related severe ADRs (iodixanol, n = 1; iohexol, n = 6), with reported data on health care resource usage.
- The economic model shows a clear difference between iodixanol and iohexol in the direct hospital-based care costs for managing ADRs related to contrast media, with an average additional cost of £571.32 per patient when using iohexol (Figure 2).
- Hospitalization is the key driver of cost difference for these patients, with patients typically cared for in an intensive care unit or a specialist nephrology or cardiology ward.
- Length of stay for hospitalized patients ranged from 5 to 21 days.
- Additional laboratory tests were present for these severely ill patients, as was additional medication related to the ADR. However, these costs were minimal when compared to the cost of hospitalization (Figure 2).

Figure 2: Average ADR Cost Differences per Patient

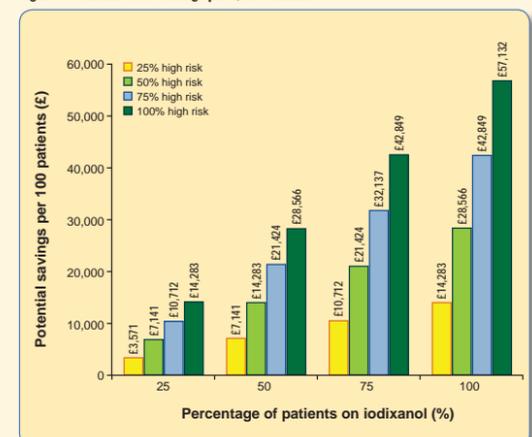
	Post-angiography procedure cost	Hospital department cost	Laboratory cost	Medication cost	Average ADR cost per patient
Iodixanol	£0.00	£0.41	£0.00	£0.00	£0.41
Iohexol	£2.76	£548.17	£7.77	£13.03	£571.73
Savings	£2.76	£547.76	£7.77	£13.03	£571.32

ADR = adverse drug reaction.

### ADR-Related Cost Savings Per 100 Patients by Uptake of Iodixanol and Prevalence of High-Risk Patients

- Cost savings from the use of iodixanol are estimated at £57,132 per 100 patients, when all patients are assumed at high risk for ADRs (as seen in the NEPHRIC patient cohort) and all patients move to iodixanol contrast media (Figure 3).
- Assuming a scenario where only a proportion of patients are at an increased risk of ADRs, the potential cost savings reduce (Figure 3). For a 50% uptake rate for iodixanol, the cost savings range from £7,141 to £28,566 per 100 patients, depending on the prevalence of high-risk patients.

Figure 3: Potential Cost Savings per 1,000 Patients



## CONCLUSIONS

- With similar image quality, the use of iodixanol results in a significant reduction in risks of contrast media-related ADRs and a lower average cost per patient in a high-risk population.
- As the percentage of high-risk patients within a hospital population increases, the potential savings to the hospital increases proportionally.
- If all patients were switched to an iodixanol-based contrast media, considerable savings could be achieved from reduced hospitalization and length of stay.

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