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Costs of unsafe care and cost effectiveness of patient safety programmes

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Costs of unsafe care and cost-effectiveness of patient safety programmes

Final Report

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Table of Contents

List of Tables

List of Figures

List of Abbreviations

ADE	Adverse Drug Event
AE	Adverse Event
b	Billion
BSI	Bloodstream infection
CABSI	Central-line associated bloodstream infection
CAD	Canadian Dollar
CAUTI	Catheter-associated urinary tract infection
CDI	Clostridium difficile infection
CHAFEA	The Consumers, Health, Agriculture and Food Executive Agency
CDSS	Clinical Decision Support System
CPOE	Computerized Physician Order Entry
d	Day(s)
DG SANTE	Directorate General for Health & Food Safety
EU	European Union
EUR	Euro
GBP	British Pound
HAI	Healthcare-associated infection
HE	Health Expenditure
HIC	High income countries
ICER	Incremental Cost-Effectiveness Ratio
k	Thousand
m	Million
MRSA	Methicillin-resistant Staphylococcus aureus
n	Case(s)
nMRSA	Non-Methicilin-resistant Staphylococcus aureus
OECD	Organisation for Economic Co-operation and Development
pADE	preventable Adverse Drug Event
ROI	Return on Investment
SSI	Surgical site infection
US	United States (of America)
USD	United States Dollar
UTI	Urinary tract infection

VAP	Ventilator-associated pneumonia
VRE	Vancomycin-Resistant Enterococci
y	Year(s)

Executive Summary

Given the growing importance of patient safety not only for health systems but first and foremost for patients, it is necessary to assess the impact of patient safety efforts and to develop priorities for action. In light of the recent economic crisis, the economic burden associated with unsafe patient care received more attention. Member States have set efforts to cut expenditures and to improve efficiency in their health care systems. In addition to increased cost of healthcare services, unsafe care also leads to loss of trust in health care systems by the public and diminished satisfaction by patients and health care professionals.

Patient safety programmes may prevent and reduce such adverse events which ultimately results in less harm inflicted to patients. According to the Council of the European Union, a large proportion of adverse events both in the hospital sector and in primary care are preventable. Contextual systemic factors play an important role.

The three main objectives of this study are:

- To provide a comprehensive picture of the financial impact of poor patient safety, including poor prevention and control of healthcare-associated infections, on European Union's health systems;
- To identify cost-effective patient safety programmes implemented in the EU/EEA Member States and develop an analysis identifying their success factors;
- To assess cost-effectiveness and efficiency of investment in patient safety programmes.

To answer the research questions, a mix of different methods was used. A systematic literature search as well as hand search for evidence on prevalence and costs of adverse events and cost-effective patient safety programmes was conducted. An expert panel was consulted to complement results from literature where necessary. To calculate the economic burden of adverse events and cost-effectiveness of patient safety programmes we developed computational procedures in Microsoft Excel, which can be made available for decision makers.

The literature on unsafe care clearly shows that the burden resulting from adverse events is substantial. Results show a general prevalence of adverse events in 4-17 percent of all patients. Calculations based on two European references show an economic burden for the public health care sector with direct costs of about EUR 21 billion or 1.5 percent of health expenditure for EU member-states in 2014.

Identified epidemiological studies have only limited value for answering the research questions of this study. Publications primary focuses on very specific events and give insufficient information on adverse event groups defined in this study's context. Besides that, studies with adequate information feature wide ranges in results for identical adverse events within countries, regions and cities and lack representativeness for EU member states. Most information on the occurrence of adverse events focuses on inpatient care. Considerably less information is available regarding adverse events in outpatient (primary) care.

Data availability on cost of singular adverse events is dissatisfactory and allows few statements on the exact level of costs and their variation between different member states or on the factors leading to higher or lower economic burden. Few figures on costs are available, and the small number of existing studies features a large variation in estimates. This is due to small sample sizes, differences in methods employed, cost categories included and definitions of time horizon. Many of the available studies appear to be of low quality, with low transparency on exact methodology and data sources applied and with few standards allowing the comparison of studies across settings and types of adverse events. In conclusion, the extensive review of the

literature finds that further primary studies of epidemiology and costs of adverse events are needed in order to gain a better grasp of the exact size of economic burden and factors influencing its magnitude.

The literature search on cost-effective patient safety programmes yielded a large number of publications. No studies reported inefficient programmes; only one cost-neutral study was identified. The reported interventions show that a promising programme is based on a multi-methodological approach. Efficient programmes can be developed by the organisation itself or existing programmes can be adapted for implementation. Employees of all professions have to be involved.

A basic simulation model was established to transfer information from existing cost-effective patient safety programmes to the specific setting of EU member-states. The model calculates costs, effects, cost-effectiveness ratios and savings from selected patient safety programmes on country level for member states. Calculation for three selected programmes estimate EU-wide savings of EUR 300 million for a programme to reduce several HAI, about EUR 2 billion for a programme to reduce pressure ulcers and about EUR 6 billion for implementing an electronic medication ordering system, consisting of a computerized physician order entry system with a Clinical Decision Support System to prevent adverse drug events.

This report also aims to give recommendations on the prioritisation of patient safety programmes on the basis of identified studies and calculated cost-efficiency figures. In a first step, the Council Recommendations of the European Union are reviewed and matched with the results of the identified literature. In a second step this study gives recommendations on how to choose between two or more patient safety programmes. In order to make a prioritisation on patient safety programmes a number of key indicators of programmes must be taken into consideration. These indicators are the prevalence of the adverse event, the relevance of (easily preventable) adverse events and the (established) cost-effectiveness of available patient safety practices.

Relative cost-utility would be an ideal indicator for prioritising patient safety programmes; however the application of this indicator is problematic for several reasons. Due to scant evidence on patient safety programmes' cost-utility ratios and high variability in baseline prevalence of adverse events among hospitals, this study recommends that prioritization of programmes must follow a process that includes an assessment of patient safety deficits in the specific setting, the identification of appropriate patient safety practices, a formulation of a precise implementation strategy and the incorporation of new guidelines (where appropriate) and training of staff.

In a final task, this study aims to give recommendations on further economic assessment of patient safety programmes. The best choice for cost-effectiveness and efficiency indicators depends on the nature of the adverse event that is to be prevented by the intervention.

For performing economic burden studies and cost-effectiveness analyses in patient safety it is essential to systematically collect data on patient safety related incidents, and obtain reliable cost figures for these adverse events in European countries, with a special focus on countries where such studies have not yet been performed.

Periodic monitoring of patient safety indicators can potentially assist in setting priorities for patient safety policy. However, data on prevalence of adverse events is not accurate enough to draw conclusions regarding regional differences or trends in patient-safety related indicators. These limitations need to be addressed before systematic assessment of efficiency of patient safety programmes can be performed.

We thus deem any routine/periodical evaluation of economic burden or efficiency of medical care as not feasible.

Résumé analytique

Compte tenu de l'importance grandissante de la sécurité, non seulement pour les systèmes de santé, mais d'abord et avant tout pour les patients, il est nécessaire d'évaluer l'impact des efforts de la sécurité des patients et de développer des priorités d'action. À la lumière de la récente crise économique, le fardeau économique associé aux soins dangereux a été l'objet d'une attention plus accrue. Les États membres ont fait des efforts pour réduire les dépenses et améliorer l'efficacité de leurs systèmes de soins de santé. En plus de l'augmentation du coût des services de santé, les soins dangereux conduisent également à la perte de confiance de la population par rapport aux systèmes de soins de santé et à la diminution de la satisfaction des patients et des professionnels de la santé.

Les programmes de sécurité des patients peuvent prévenir et réduire ces effets indésirables ce qui aboutira finalement à une réduction des dommages infligés aux patients. Selon le Conseil de l'Union européenne, une grande partie des effets indésirables, à la fois dans le secteur hospitalier ainsi que dans les soins primaires, sont évitables. Les facteurs systémiques contextuels jouent un rôle important.

Les trois principaux objectifs de cette étude sont:

- de fournir un tableau complet de l'impact financier de la mauvaise sécurité des patients, y compris d'une mauvaise prévention et contrôle des infections associées aux soins, sur les systèmes de santé de l'Union européenne;
- d'identifier les programmes de sécurité des patients rentables mis en œuvre dans les États membres de l'UE/EEE et de développer une analyse identifiant les facteurs de réussite;
- d'évaluer le rapport coût-efficacité et l'efficience de l'investissement dans les programmes de sécurité des patients.

Afin de répondre aux questions de recherche, un mélange de différentes méthodes a été utilisé. Une recherche méthodique ainsi qu'une recherche manuelle de la littérature ont été réalisées sur la prévalence et sur les coûts des effets indésirables ainsi que sur la rentabilité des programmes de sécurité des patients. Un groupe d'experts a été consulté afin de compléter les résultats des documents, le cas échéant. Pour calculer le fardeau économique des effets indésirables et de la rentabilité des programmes de sécurité des patients, nous avons développé des procédures de calcul dans Microsoft Excel, qui peuvent être mis à la disposition des décideurs.

La documentation sur les soins à risque montre clairement que la charge résultant d'effets indésirables n'est pas négligeable. Les résultats montrent une prévalence générale des effets indésirables sur 4-17 pour cent de tous les patients. Les calculs basés sur deux références européennes montrent un fardeau économique d'environ 21 milliards d'euros pour le secteur de la santé publique ou 1,5 pour cent des dépenses de santé pour les Etats membres de l'UE en 2014.

Les études épidémiologiques mentionnées n'ont seulement qu'une valeur limitée pour répondre aux questions de recherche de cette étude. Les publications se concentrent principalement sur des événements très spécifiques et donnent suffisamment d'information sur les groupes d'effets indésirables définis dans le contexte de cette étude. En plus de cela, des études regroupant des informations adéquates montrent de larges gammes de résultats pour les effets indésirables identiques au sein des pays, régions et villes et le manque de différenciation entre les États membres de l'UE. La plupart des informations sur la survenue des effets indésirables se concentrent sur les soins aux patients hospitalisés. En revanche, beaucoup moins d'informations sont disponibles concernant les effets indésirables dans les soins ambulatoires (primaire).

La disponibilité des données sur le coût des effets indésirables est fortement insatisfaisante et ne permet que quelques affirmations sur le niveau exact des coûts et la variation entre les différents Etats membres ou sur les facteurs conduisant à une charge économique plus ou moins élevée. Seulement peu de chiffres sur les coûts sont disponibles, et le petit nombre d'études sur le sujet montre une grande variation dans les estimations. Cela est dû à petite taille des échantillons, aux différences méthodologiques, aux catégories de coûts inclus et à la définition de l'horizon temporel. La plupart de ces études disponibles semblent être de mauvaise qualité, avec peu de transparence sur la méthodologie ou sur les sources utilisées et avec peu de normes permettant la comparaison entre les études dans tous les milieux et par types d'effets indésirables. En conclusion, l'examen approfondi de la documentation nous permet de constater que des études primaires de l'épidémiologie et des coûts des effets indésirables sont nécessaires afin d'acquérir une meilleure compréhension de la taille exacte du fardeau économique et des facteurs qui influent sur son ampleur.

La documentation sur la rentabilité des programmes de sécurité des patients montre un nombre énorme d'études. Aucune étude n'a rapporté de programmes inefficaces et seulement une étude neutre sur le plan des coûts a été identifiée. Les exemples montrent qu'un programme prometteur est basé sur une approche multi-méthodologique. Les programmes efficaces peuvent être développés par l'organisation elle-même ou les programmes existants peuvent être adaptés pour la mise en œuvre. Les employés de toutes les professions doivent être impliqués dans ces processus.

Un modèle de simulation de base a été mis en place pour transférer des informations à partir des programmes existants de rentabilité de la sécurité des patients vers les paramètres spécifiques des Etats-Membres de l'UE. Le Calcul pour les trois programmes sélectionnés montrent des économies de 300 millions d'euros à l'échelle de l'UE pour un programme de réduction de plusieurs infections associées aux soins de santé (HAI), environ 2 milliards d'euros pour un programme visant à réduire les escarres et environ 6 milliards d'euros pour la mise en œuvre d'un système électronique de commande de médicaments, comprenant un système informatisé de saisie de commande pour les médecins avec un système de soutien des décisions cliniques afin de prévenir les accidents liés à la médication.

Ce rapport vise à formuler des recommandations sur la hiérarchisation des programmes de sécurité des patients sur la base des études identifiées et des chiffres de rentabilité calculés. Dans un premier temps, les recommandations du Conseil de l'Union européenne sont examinées et comparées avec les résultats de la documentation identifiée. Dans un second temps, cette étude formule des recommandations sur la façon de choisir entre deux ou plusieurs programmes de sécurité des patients. Afin de hiérarchiser des programmes de sécurité des patients un certain nombre d'indicateurs clés des programmes doivent être pris en considération pour la définition des priorités. Ces indicateurs sont la prévalence du problème, la pertinence des effets indésirables (facilement évitables) et du coût-efficacité (établis) des pratiques de sécurité des patients.

En outre, le rapport coût-utilité serait un indicateur idéal pour hiérarchiser les programmes de sécurité des patients, mais l'application de cet indicateur est problématique pour plusieurs raisons. En raison du peu de preuves sur les rapports coût-utilité de programmes de sécurité des patients et de la forte variabilité de la prévalence de référence des effets indésirables entre les hôpitaux, cette étude recommande que la hiérarchisation des programmes doit suivre un processus qui comprend une évaluation des déficits de la sécurité des patients dans le cadre spécifique, l'identification des pratiques appropriées de sécurité des patients, la formulation d'une stratégie précise

de mise en œuvre et l'incorporation de nouvelles lignes directrices (le cas échéant) et la formation du personnel.

Enfin, une dernière tâche de cette étude a pour objectif de formuler des recommandations sur la poursuite de l'évaluation économique des programmes de sécurité des patients. En ce qui concerne les recommandations sur les indicateurs de rentabilité et d'efficacité, le meilleur choix dépend donc de la nature de l'effet indésirable qui doit être évité par l'intervention.

Pour la réalisation d'études sur le fardeau économique et l'analyse coût-efficacité en matière de sécurité du patient, il est essentiel de recueillir systématiquement des données sur les incidents liés à la sécurité des patients, et d'obtenir des données sur les coûts fiables pour ces effets indésirables dans les pays européens, avec un accent particulier sur les pays où de telles études n'ont pas encore été réalisées.

une surveillance périodique des indicateurs de sécurité des patients serait idéale pour aider à établir des priorités pour la politique de la sécurité des patients. Toutefois, les données sur la prévalence des effets indésirables ne sont pas assez précises pour tirer des conclusions sur les différences régionales ou sur les tendances des indicateurs liés la sécurité des patients. Ces limitations doivent être abordés avant que l'évaluation systématique de l'efficacité des programmes de sécurité des patients ne puisse être effectuée. Nous estimons ainsi toute évaluation de routine/périodique du fardeau économique ou de l'efficacité des soins médicaux comme non réalisable.

Zusammenfassung

Angesichts der steigenden Bedeutung von Patientensicherheit für Gesundheitssysteme und Patienten ist es notwendig den Einfluss von Patientensicherheitsmaßnahmen und deren Priorisierung zu bewerten. Angesichts der aktuellen Wirtschaftskrise erhält die Debatte um ökonomische Auswirkungen von unsicherer Pflege zusätzlichen Aufschwung. Deshalb setzen die Mitgliedstaaten der EU Maßnahmen um diese Ausgaben zu reduzieren und die Effizienz der Gesundheitssysteme zu steigern. Neben den monetären Kosten verursacht unsichere Pflege jedoch auch einen Verlust des Vertrauens der Patienten in das Gesundheitssystem und sinkende Zufriedenheit mit den Akteuren, nämlichen dem Gesundheitspersonal.

Aufeinander abgestimmte Patientensicherheitsprogramme können dazu beitragen das Aufkommen unerwünschter Ereignisse zu reduzieren oder zu verhindern, was zu einer Schadensverhinderung bei Patienten führt. Gemäß des Rats der Europäischen Kommission sind unerwünschte Ereignisse sowohl im Krankenhaus- als auch im niedergelassenen Bereich vermeidbar, wobei das Gesundheitssystem für einen großen Teil der Ereignisse verantwortlich ist.

Die drei primären Ziele dieser Arbeit sind:

- die Darstellung der finanziellen Auswirkungen unzureichender Patientensicherheit für Europäische Gesundheitssysteme,
- das Identifizieren kosteneffektiver Patientensicherheitsprogramme und deren Erfolgsfaktoren die in der EU umgesetzt werden und
- die Ermittlung der Kosteneffektivität und Effizienz von Investitionen in Patientensicherheitsprogramme.

Um diese Forschungsfragen zu beantworten kamen verschiedene Methoden zum Einsatz. Eine systematische Literaturrecherche und eine Handsuche wurden eingesetzt um Literatur zu Prävalenz und Kosten bzw. kosteneffektiven Patientensicherheitsprogrammen von unerwünschten Ereignissen zu identifizieren. Ergänzend dazu wurde eine Expertengruppe eingesetzt um die Ergebnisse der Literatursuche zu vervollständigen und zu prüfen. Die Berechnung der finanziellen Auswirkungen von unerwünschten Ereignissen und der Kosteneffektivität von Patientensicherheitsprogrammen erfolgte mittels eigener Modelle und Berechnungen.

Die Ergebnisse der Literaturrecherche zeigen eine nicht unwesentliche finanzielle Auswirkung von unerwünschten Ereignissen auf die Gesundheitssysteme der EU. Durchschnittlich 4 – 17 Prozent aller Patientinnen erfahren ein unerwünschtes Ereignis, davon sind 44 – 50 Prozent vermeidbar. Die finanzielle Last der direkten Kosten dieser Ereignisse liegt für die öffentlichen Gesundheitssysteme aller Mitgliedsstaaten bei etwa EUR 21 Mrd. oder 1.5 Prozent der Gesundheitsausgaben im Jahr 2014. Die wichtigste Erkenntnis dieser Studie ist allerding, dass Primärstudien zur Epidemiologie und Kosten von unerwünschten Ereignissen benötigt werden um aussagekräftige Ergebnisse zu liefern. Die epidemiologischen Studien untersuchen zum größten Teil nur sehr spezielle Ereignisse, was eine aggregierte Betrachtung der Thematik erschwert beziehungsweise nicht ermöglicht. Außerdem zeigen die Ergebnisse von Studien mit vergleichbaren Design einerseits große Spannen innerhalb von Ländern, Regionen und Städten, andererseits zeigen Ländervergleiche aber keine EU-weiten Unterschiede. Auch die Verfügbarkeit von Daten zu Kosten unerwünschter Ereignisse ist unzureichend und lässt daher nur sehr limitieret Aussagen zu exakten Kosten. Die geringe Anzahl an Kostendaten zeigt wie bei der Epidemiologie zum Teil enorme Variabilität der Ergebnisse. Grund dafür sind kleine Stichproben, verschiedene Methodenansätze und Kategorien sowie unterschiedliche Zeithorizonte. Dazu kommt, dass die Studienqualität oft unzureichend ist und keine genauen Angaben zu Methoden

und Quellen gemacht werden. Ein weiterer unbeantworteter Aspekt der Thematik ist die Perspektive der Kostenträgerschaft und die Frage, wer für die Kosten aufkommt. Zusammenfassend zeigt die ausführliche Analyse der Literatur, dass weitere Primärstudien zu Epidemiologie und Kosten notwendig sind um das tatsächliche Ausmaß von Kosten und Krankheitslast von unerwünschten Ereignissen zu bestimmen.

Für kosteneffektive Patientensicherheitsprogramme liefert die Literatur ausreichend Beispiele. Keine Studie berichtet über ineffiziente Programme, nur eine kostenneutrale Studie wurde identifiziert. Die identifizierten Programme zeigen, dass erfolgreiche Programme auf multiplen Methoden aufbauen. Dabei macht es keinen Unterschied ob effiziente Programme von Organisationen neu entwickelt oder bestehende adaptiert werden. Entscheidend für den Erfolg des Patientensicherheitsprogramms ist die Einbindung aller Berufsgruppen in den gesamten Prozess. Um Daten und Informationen von bestehenden Patientensicherheitsprogrammen die in einzelnen Staaten umgesetzt werden auf die gesamte EU zu übertragen, wurde ein Simulationsmodell entworfen. Das Modell berechnet Kosten, Effekte, Kosteneffektivitätswerte und die durch das umgesetzte Programm erreichte Einsparung. Die Berechnung für drei EU-weite Programme zeigen Einsparungen von EUR 300 Mio. für ein Programm zur Verhinderung diverser Infektionen, EUR 2 Mrd. für ein Programm zur Verhinderung von Druckstellen und EUR 6 Mrd. für den Einsatz von elektronischen Arzneimittelbestellsystemen.

Neben den drei Forschungsfragen verfolge diese Studie auch das Ziel auf Basis der berechneten Werte Empfehlungen für die Priorisierung von Patientensicherheitsprogrammen abzugeben. Dafür wurden in einem ersten Schritt die Empfehlungen des Rates der Europäischen Kommission zu diesem Thema analysiert und mit den Resultaten dieser Studie vergleichen. Dann wurden konkrete Empfehlungen abgegeben, wie man bei der Wahl mehrere Programme idealerweise vorzugehen hat. Um Patientensicherheitsprogramme zu priorisieren müssen deren Schlüsselindikatoren bewertet werden: die Prävalenz des Problems, die Relevanz des unerwünschten Ereignisses und die Kosteneffektivität des Patientensicherheitsprogramms. Weiters wäre der relative Nutzwert ein anstrebenswerter Indikator für die Priorisierung von Patientensicherheitsprogrammen. Diese Studie empfiehlt, dass die Priorisierung von Programmen folgendem Prozedere entspricht: Identifikation von Defiziten im Bereich der Patientensicherheit für bestimmte Bereiche oder Abteilungen, die Auswahl eines angemessenen Patientensicherheitsprogramms, die exakte Formulierung von präzisen Implementierungsstrategien, gezieltes Training des Personals und gegebenenfalls die Erarbeitung neuer Leitlinien.

In Bezug auf Empfehlungen zu Kosteneffektivitäts- und Effizienzindikatoren sollen sich Studien immer an der Art des unerwünschten Ereignissen, das es zu verhindern gilt und der jeweiligen Intervention orientieren. Für die Struktur und Richtlinien von ökonomischen Analysen generell sind die systematische Erfassung von Patientensicherheitsdaten und die Verfügbarkeit dazugehöriger Kostendaten wesentlich. Um die Machbarkeit regelmäßiger Beobachtungen auf Basis ökonomischer Studien zu bewerten, würden wiederkehrende Kontrollmaßnahmen von Patientensicherheitsprogrammen eine ideale Unterstützung von Priorisierungsmaßnahmen darstellen. Jedoch sind die derzeit erfassten Daten (regionale Unterschiede) zu unerwünschten Ereignissen nicht exakt genug um Folgerungen abzuleiten. Erst wenn diese Limitation bereinigt wurde können systematische Bewertungen zur Effizienz und Kosteneffektivität von Patientensicherheitsprogrammen vorgenommen werden.

Abstract

English

BACKGROUND & AIMS: Given the growing importance of patient safety not only for health systems but first and foremost for patients, it is necessary to assess the impact of patient safety efforts and to develop priorities for action. The three main objectives of this study are (1) to provide a comprehensive picture of the financial impact of poor patient safety, including poor prevention and control of healthcare-associated infections, on European Union's health systems; (2) to identify cost-effective patient safety programmes implemented in the EU/EEA Member States and develop an analysis identifying their success factors and (3) to assess cost-effectiveness and efficiency of investment in patient safety programmes.

METHODS: The applied mix of different methods contains a systematic and literature search by hand for identification of evidence on prevalence and costs of adverse events and cost-effective patient safety programmes. Subsidiary an expert panel was consulted to complement results from the literature review. Economic burden of adverse events and cost-effectiveness of patient safety programmes were calculated by own calculation.

RESULTS: In general, about 4–17 percent of patients experience adverse events, whereby 44–50 percent of these events are preventable. The economic burden for the public health care sector was about EUR 21 billion of direct costs or 1.5 percent of health expenditure for EU member-states in 2014. A mayor finding of this study is that primary studies of epidemiology and costs of adverse events are needed. Another question that arises with the economic burden of adverse events is the perspective of costs and who bears the costs in different systems. The literature search on cost-effective patient safety programmes identified a large number of studies. Calculation for three selected programmes suggest possible EU-wide savings of EUR 300 million for a programme to reduce several HAI, about EUR 2 billion for a programme to reduce pressure ulcers and about EUR 6 billion for implementing an electronic medication ordering system.

CONCLUSION: In order to make a prioritisation on patient safety programmes, key indicators of programmes must be taken into consideration: the prevalence of the problem, the relevance of adverse events and the cost-effectiveness of patient safety practices. Relative cost-utility would be the preferable indicator for prioritising patient safety programmes. Regarding recommendations on cost-effectiveness and efficiency indicators, the best choice for cost-effectiveness or efficiency indicators depends on the nature of the adverse event that is to be avoided by the intervention. For a framework and guidelines for performing economic burden studies and cost-effectiveness analyses it is essential to systematically collect data on patient safety related incidents, and obtain reliable cost figures for these adverse events. For a feasibility analysis on periodical surveillance based on economic burden studies and cost-effectiveness and efficiency analyses in patient safety programmes, periodic monitoring of patient safety indicators would ideally assist in setting priorities for patient safety policy. However, data on prevalence of adverse events is not accurate enough to draw conclusions regarding regional differences or trends in patient-safety related indicators. These limitations need to be addressed before systematic assessment of efficiency of patient safety programmes can be performed.

Français:

CONTEXTE ET OBJECTIFS : Compte tenu de l'importance grandissante de la sécurité, non seulement pour les systèmes de santé, mais d'abord et avant tout pour les patients, il est nécessaire d'évaluer l'impact des efforts de la sécurité des patients et de développer des priorités d'action. Les trois principaux objectifs de cette étude sont (1) de fournir un tableau complet de l'impact financier de la mauvaise sécurité des patients, y compris d'une mauvaise prévention et contrôle des infections associées aux soins, sur les systèmes de santé de l'Union européenne; (2) d'identifier les programmes de sécurité des patients rentables mis en œuvre dans les États membres de l'UE/EEE et de développer une analyse identifiant les facteurs de réussite et (3) d'évaluer le rapport coût-efficacité et l'efficience de l'investissement dans les programmes de sécurité des patients.

MÉTHODES : Ce mélange de différentes méthodes inclut une recherche documentaire manuelle et méthodique pour l'identification des éléments de preuve sur la prévalence et les coûts des effets indésirables et sur la rentabilité des programmes de sécurité des patients. De plus, un groupe d'experts a été consulté pour compléter les résultats de la documentation. Le fardeau économique des effets indésirables et le rapport coût-efficacité des programmes de sécurité des patients ont été calculés selon nos propres calculs.

RÉSULTATS : En général, environ 4-17% des patients éprouvent des effets indésirables, dont 44 à 50% sont évitables. Le fardeau économique des effets indésirables était d'environ 21 milliards d'euros pour le secteur de la santé publique ou 1,5 pour cent des dépenses de santé pour les Etats membres de l'UE en 2014. un constat majeur est que les études primaires de l'épidémiologie et les coûts des effets indésirables sont nécessaires. Une autre question qui se pose avec le fardeau économique des effets indésirables est le point de vue des coûts et qui supporte ces coûts. La documentation sur la rentabilité des programmes de sécurité des patients montre un nombre imposant d'études. Les calculs de trois programmes sélectionnés montrent à l'échelle de l'UE des économies de 300 millions d'euros pour un programme de réduction de plusieurs infections associées aux soins de santé (HAI), d'environ 2 milliards d'euros pour un programme visant à réduire les escarres et d'environ 6 milliards d'euros pour la mise en œuvre d'un système électronique de commande de médicaments.

CONCLUSION : Afin d'établir un ordre de priorité sur les programmes de sécurité des patients, des indicateurs clés de programmes doivent être pris en considération: la prévalence du problème, la pertinence des effets indésirables et le rapport coût-efficacité des pratiques de la sécurité des patients. En outre, le coût-utilité relatif serait un indicateur idéal pour hiérarchiser les programmes de sécurité des patients. En ce qui concerne les recommandations sur les indicateurs de coût-efficacité et d'efficience, le meilleur choix pour la rentabilité ou l'efficacité des indicateurs dépend de la nature de l'effet indésirable devant être évité par l'intervention. il est essentiel de recueillir des données sur les incidents liés à la sécurité des patients, et d'en obtenir sur les coûts fiables pour ces effets indésirables afin de développer un cadre et des lignes directrices pour la réalisation d'études sur le fardeau économique et sur les analyses coût-efficacité. La surveillance périodique des indicateurs de sécurité des patients serait, quant à elle, recommandée pour aider à établir des priorités pour la politique de la sécurité des patients pour l'analyse de faisabilité sur la surveillance périodique basé sur des études de fardeau économique et coût-efficacité, et l'efficacité des analyses dans les programmes de sécurité des patients. Toutefois, les données sur la prévalence des effets indésirables ne sont pas assez précises pour tirer des conclu-

sions sur les différences régionales ou les tendances des indicateurs liés à la sécurité des patients. Ces limites doivent être traitées avant que l'évaluation méthodique de l'efficacité des programmes de sécurité des patients ne puisse être effectuée.

Deutsch:

HINTERGRUND UND ZIELE: Angesichts der steigenden Bedeutung von Patientensicherheit für Gesundheitssysteme und Patienten ist es notwendig den Einfluss von Patientensicherheitsmaßnahmen und deren Priorisierung zu bewerten. Die drei primären Ziele dieser Arbeit sind (1) die Darstellung der finanziellen Auswirkungen unzureichender Patientensicherheit für Europäische Gesundheitssysteme, (2) das Identifizieren kosteneffektiver Patientensicherheitsprogramme und deren Erfolgsfaktoren die in der EU umgesetzt werden und (3) die Ermittlung der Kosteneffektivität und Effizienz von Investitionen in Patientensicherheitsprogramme.

Methoden: Ein Methodenmix aus Systematischer- und Handsuche kam für die Evidenzaufbereitung für Prävalenz und Kosten von unerwünschten Ereignissen und Patientensicherheitsprogrammen zum Einsatz. Ergänzend dazu wurde ein Expertengremium unterstützend herangezogen. Die finanzielle Last und Kosteneffektivität von Patientensicherheitsprogrammen wurden auf Basis eigener Berechnungen ermittelt.

Ergebnisse: Durchschnittlich 4 – 17 Prozent aller Patientinnen erfahren ein unerwünschtes Ereignis, davon sind 44 – 50 Prozent vermeidbar. Die finanzielle Last dieser Ereignisse lag im Jahr 2014 für die öffentlichen Gesundheitssysteme aller Mitgliedsstaaten bei etwa EUR 21 Mrd. an direkten Kosten oder 1.5 Prozent der Gesundheitsausgaben. Die wichtigste Erkenntnis dieser Studie ist allerding, dass Primärstudien zur Epidemiologie und Kosten von unerwünschten Ereignissen benötigt werden um aussagekräftige Ergebnisse zu liefern. Ein weiterer unbeantworteter Aspekt der Thematik ist die Perspektive der Kostenträgerschaft und die Frage wer dafür aufkommt. Für kosteneffektive Patientensicherheitsprogramme liefert die Literatur ausreichend Beispiele. Die Berechnung für drei EU-weite Programme zeigen Einsparungen von EUR 300 Mio. für ein Programm zur Verhinderung diverser Infektionen, EUR 2 Mrd. für ein Programm zur Verhinderung von Druckstellen und EUR 6 Mrd. für den Einsatz von elektronischen Arzneimittelbestellsystemen.

Schlussfolgerungen: Um Patientensicherheitsprogramme zu priorisieren müssen deren Schlüsselindikatoren bewertet werden: die Prävalenz des Problems, die Relevanz des unerwünschten Ereignisses und die Kosteneffektivität des Patientensicherheitsprogramms. Weiters wäre der relative Nutzwert ein anstrebenswerter Indikator für die Priorisierung von Patientensicherheitsprogrammen. In Bezug auf Empfehlungen zu Kosteneffektivitäts- und Effizienzindikatoren sollen sich Studien immer an der Art des unerwünschten Ereignissen, das es zu verhindern gilt und der jeweiligen Intervention orientieren. Für die Struktur und Richtlinien von ökonomischen Analysen generell sind die systematische Erfassung von Patientensicherheitsdaten und die Verfügbarkeit dazugehöriger Kostendaten wesentlich. Um die Machbarkeit regelmäßiger Beobachtungen auf Basis ökonomischer Studien zu bewerten, würden wiederkehrende Kontrollmaßnahmen von Patientensicherheitsprogrammen eine ideale Unterstützung von Priorisierungsmaßnahmen darstellen. Jedoch sind die derzeit erfassten Daten (regionale Unterschiede) zu unerwünschten Ereignissen nicht exakt genug um Folgerungen abzuleiten. Erst wenn diese Limitation bereinigt wurde können systematische Bewertungen zur Effizienz und Kosteneffektivität von Patientensicherheitsprogrammen vorgenommen werden.

1 Introduction

This report at hand is the final report of the request for Specific Services N° Chafea/2014/Health/08 for the implementation of Framework Contract N° Chafea/2013/Health/01 "Health economic reports - analysis and forecasting" (Lot 2) for a "Costs of unsafe care and cost-effectiveness of patient safety programmes" commissioned by CHAFEA/DG SANTE.

1.1 Background and context

Increasing importance of patient safety

'Unsafe care' or patient safety related 'adverse events' are defined as 'incidents which result in harm to a patient' [1]. Patient safety programmes may prevent and reduce adverse events, which ultimately results in less harm inflicted to patients. According to the Council of the European Union, a large proportion of adverse events, both in the hospital sector and in primary care, are preventable. Contextual systemic factors cause a large proportion of adverse events [1]. Thus, it appears as if the majority of errors or adverse events in health care that lead to harm of patients are not caused by individuals but by faulty systems, processes and conditions that lead people to commit mistakes or shortage of prevention [2]. Hence, it is expected that the economic burden faced by EU/EEA countries could be reduced through patient safety programmes.

This stands in contrast with traditional approaches to unsafe care and patient safety which assume that well-trained and conscientious health professionals would not commit errors and thus equated error with incompetence. This explains why the reporting of errors resulting in the occurrence of adverse events could not be established as a culture for a long time. Only in the 1990s it was recognized that errors of health care professionals may also result from errors in the health system such as errors in organisation, management, training and equipment. Furthermore, it was realized that information on the occurrence of adverse events can provide useful insights for their avoidance [3]. At this point there was a culture shift from a culture of punishing errors towards a new 'safety culture' which emphasized reporting and learning and aimed at reducing adverse events through systematic approaches.

In the light of growing importance of patient safety not only for health systems but first and foremost for patients, it is necessary to assess the impact of patient safety efforts and to develop priorities for action.

European efforts

Already since the early 2000s, patient safety has been a priority topic on the European policy agenda and many initiatives have been taken on national levels. While some countries used legislative measures to stimulate improvement in patient safety others considered softer solutions such as guidelines, standards, plans or campaigns as appropriate instruments. Some countries made use of contracts and agreements as well as platforms and databases. A common initiative at the national level has been the accreditation of health care services to improve patient safety [4].

The European Commission helps its member countries to coordinate these national efforts to protect and foster public health by making them share best practice and set actions to improve patient safety in Europe [5]. In 2009 the Council Recommendation on patient safety and healthcare associated infections laid down an EU-wide strategy

on patient safety, focussing on 1) policies and programmes on patient safety, 2) empowering patients, 3) reporting adverse events and learning from errors, and 4) education and training of healthcare workers [1].

Just recently - in October 2014 - the independent Expert Panel on effective ways on investing in health (EXPH), which advises the European Commission adopted its opinion on the Future EU Agenda on Patient Safety and Quality of Health Care [6]. Accordingly, all services of health care should fulfil the criteria of being effective, safe, appropriate, patient-centred, efficient and equitable in order to improve the quality of health care and patient safety.

Economic burden of adverse events

In light of the recent economic crisis, the economic burden associated with unsafe patient care received more attention. Although scarce public resources have increasingly become contested during the past decade due to the economic crisis, health systems in Europe are continuing to experience increasing expenditures in healthcare. Member States have therefore set efforts to cut expenditures and to improve efficiency in their health care systems [7]. In addition to its financial impacts, unsafe care is also costly in terms of loss of trust in health care systems by the public and diminished satisfaction by patients and health care professionals [2]. According to the Council of the European Union, poor patient safety represents both a severe public health problem as well as a high economic burden on limited health resources [1]. The prevention or reduction of unsafe care or adverse events, defined as 'incidents which result in harm to a patient' [1], does therefore not only contribute to an increase in quality of care for patients but also to a reduction of the economic burden incurred by national health systems.

Adverse events may harm health outcomes or cause increased morbidity, temporary or permanent disability or death due to a lack or low performance of health care. Adverse events are related to different types of errors. Most frequently, errors in health care occur during prevention (e.g. lack of monitoring), diagnosis (e.g. late correct diagnosis, contraindications, delay in administration etc.) or treatment (e.g. wrong-side surgery, medication errors, errors related to medical equipment, errors in nursing). Other causes are, for example, infections or bad communication among health care professionals. Furthermore, errors may occur in every place of care - in hospitals as well as primary care institutes and in specialised ambulatory care, long-term care and in transition from hospital to outpatient care [8]. Especially vulnerable populations such as pregnant women, children or elderly are often subject to suffering from adverse events. For example, falls and decubitus ulcers are widespread adverse events among the elderly population.

Reliable information on the occurrence of adverse events is more likely to be available for inpatient care, as documentation is mostly standardized. The European Commission's patient safety policy [5] estimates that 8 to 12 percent of patients admitted to hospitals suffer from adverse events, for example healthcare-associated infections, medication-related errors, surgical errors, medical device failures, errors in diagnosis or failures to act on the results of tests.

Considerably less information is available regarding adverse events in outpatient (primary) care. Errors may occur during the diagnosis stage (missed or delayed diagnosis), treatment (often related to medication) and preventive services. Process errors may be clinical (judgement, decision making, etc.), communicational (patient/physician, physician/health care provider) or administrational (insurance and government regulations) [9].

2 Objectives

According to the European Council's recommendation on patient safety, including the prevention and control of healthcare associated infections [1]and the implementation report on patient safety [7], more evidence on the cost-effectiveness of patient safety programmes is required.

The study aims to investigate costs of unsafe care and cost-effectiveness of patient safety programmes in response to adverse events.

The specific objectives are:

- To provide a comprehensive picture of the financial impact of poor patient safety, including poor prevention and control of healthcare-associated infections, on European Union's health systems;
- To identify cost-effective patient safety programmes implemented in the EU/EEA Member States and develop an analysis identifying their success factors;
- To assess cost-effectiveness and efficiency of investment in patient safety programmes.

Furthermore, clear recommendations on how to prioritize patient safety strategies to achieve an improvement in unsafe care will be presented.

Representation of adverse events

The wide range of adverse events and their occurrence across every type of care has led to specialized investigations focused on single, specific events or broader studies focusing on special groupings of adverse events. Due to a lack of comprehensive information it is considered useful to estimate the impact of adverse events on an aggregate, systematic level. The starting point and basis of this project is an aggregated list of the following adverse events:

- errors in diagnosis
- acute care adverse events/adverse events due to surgical errors
- adverse drug events
- healthcare associated infections
- medical devices adverse events
- adverse events due to unsafe blood products
- adverse events due to falls
- injury due to pressure sores and decubitus ulcers

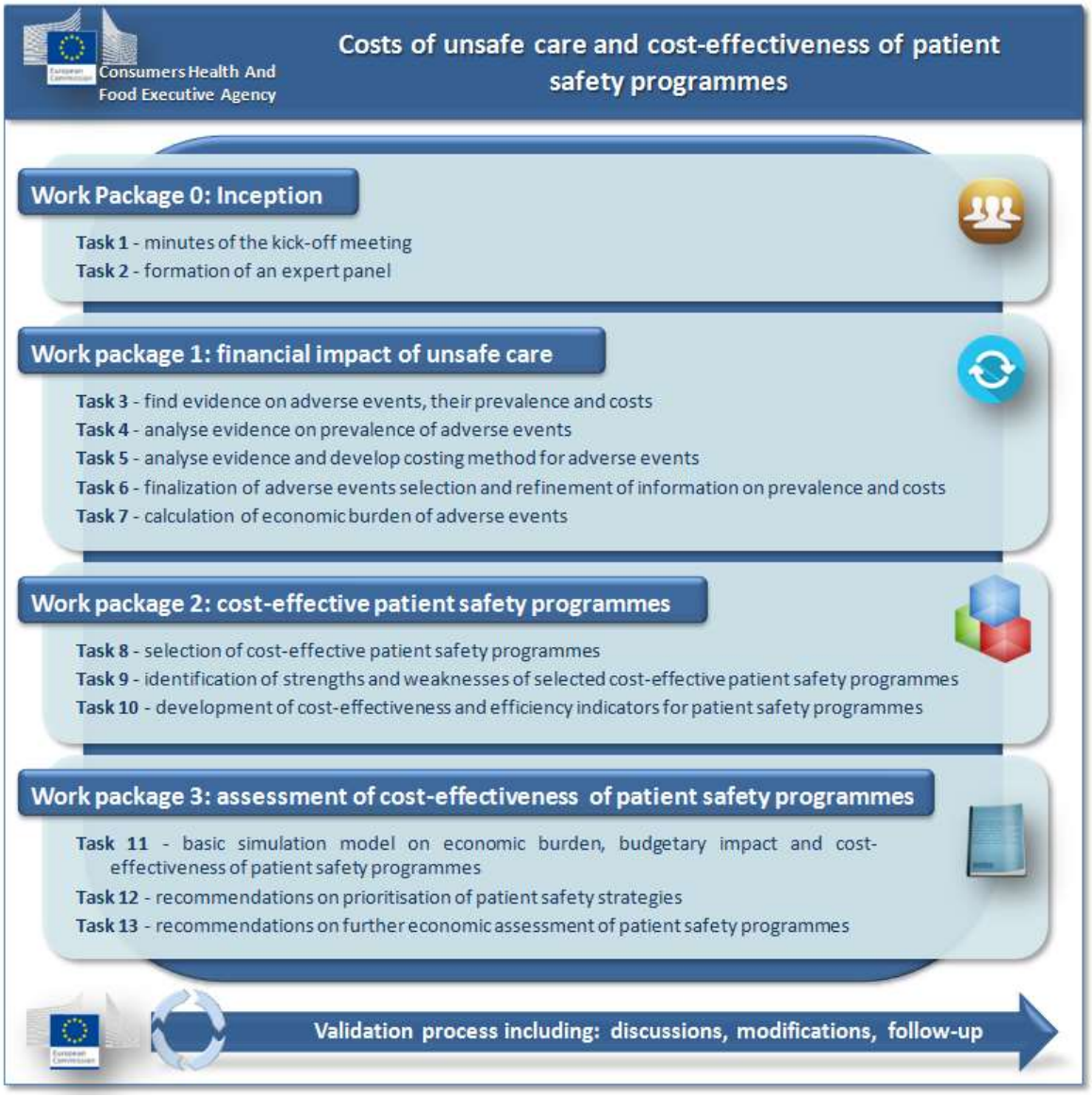
This aggregation brings the advantage of delivering a workable basis for the complex field of adverse events. A full list of all possible single adverse events would due to its complexity neither be clearly arranged nor complete. The disadvantage of an aggregation lies in double counts of adverse events and generalization of conclusions.

A final list of aggregated adverse events will be developed in the course of this project by extracted literature and expert consultations in chapter 5.3.

3 Activities and Deliverables

To reach these objectives mentioned in the previous chapter, 13 tasks are created (see Figure 1). The whole process was supported by project management activities.

Figure 1: Tasks to be implemented in this project



Source: CHAFEA

4 Expert Panel

4.1 Aim

For some tasks a consultation of experts with expertise in management of patient safety programmes or costing analysis and cost-effectiveness analysis in the health care sector was foreseen and required. The main aim of the panel was to validate results from the literature review, provide further information on publications and advise the project team in terms of the methods used.

The project team enlisted 15 experts from different EU/EEA Member States plus the WHO representing a well-balanced mix of medical, nursing, managerial and research staff. Experts have demonstrated expertise in either management of patient safety programmes with over 5 years of experience covering relevant adverse events, or in costing analysis and cost-effectiveness analysis in the health sector with at least 4 relevant peer reviewed publications in the last 10 years. The members of the panel were identified by consulting EU-wide and national patient safety organisations as well as screening the results of the literature search for adequate candidates.

4.2 Methodology

The systematic method used for interviewing was a Delphi process. Experts were presented with a questionnaire including the preliminary list of adverse events according to literature and meta-analysis. Experts were then asked to confine and complete the list by adding adverse events they believe to be missing, or eliminating events they consider less important and providing brief justifications for doing so. Further, they are asked to comment on the general adequacy of the list, for instance on aggregation and grouping of events. In the same questionnaire, experts are interviewed regarding prevalence rates, proportion of adverse event and degree of preventability of the adverse events listed. If data is available, prevalence rates are derived from literature and refined by meta-analyses and are presented and experts are able to evaluate whether they believe given figures to be correct or whether they regard them to be biased up or downwards. In the case of adverse events for which there is no prevalence rate available, experts shall provide their best estimates. Degree of preventability of adverse events was judged on a traffic light scale, asking experts for their judgement on whether certain adverse events could be easily, to an average extent, or only avoided with great difficulty.

Beside the two interviewing rounds, selected experts were consulted to provide assistance in terms of methods for calculating the economic burden of adverse events and developing cost-effectiveness and efficiency indicators of patient safety programmes.

4.3 Results

A major finding from the feedback of the experts was that their knowledge, just as the information from literature, is limited at an aggregate level of adverse events. The experts have in-depth knowledge of certain singular adverse events and cannot provide information for adverse event groups.

The results of the expert panel consultations are provided directly in the results parts below.

5 Financial impact of unsafe care

5.1 Aim

The aim was to provide a comprehensive picture of the financial impact of poor patient safety, including poor prevention and control of healthcare-associated infections, on European Union's health systems.

The following research questions will be addressed:

- What prevalence may be estimated and attributed to adverse events according to the scientific literature?
- Which costs and costing methods for adverse events are used in the scientific literature?
- What methodological approach may be used to calculate the aggregated cost of adverse events respectively the economic burden of unsafe care in Europe?
- What is the economic burden of selected adverse events in EU/EEA Member States?

5.2 Methodology

5.2.1 Find evidence on adverse events, their prevalence and costs (Task 3)

The systematic literature search for evidence on prevalence and costs of adverse events was conducted by linking different search terms regarding

- adverse events (e.g. unsafe care, adverse reaction, adverse effect, patient safety, administration/process/surgical/medical/diagnosis error, etc.),
- prevalence (e.g. epidemiology, prevalence, incidence),
- costs (e.g. cost analysis, economic burden, economic impact, economic evaluation) and
- study type (systematic reviews, meta-analysis, randomized controlled trials, comparative studies, evaluation studies, observational studies, validation studies, multicenter studies, etc.).

For the search terms subject headings (e. g. Medical Subject headings (MeSH) and free-text (e. g. truncation like adverse event* for adverse event or adverse events) were used. The search covered a period of ten years (2006-2015) and was conducted in English. Abstracts and full texts of all EU languages were included in the selection process. The detailed search strategies are outlined in Annex 1.

The following international databases were searched: Medline, Cochrane and Embase via OVID, Cinahl via EBSCOhost Research Databases and Scopus.

Furthermore, reference lists of studies identified were used for reference tracking to ensure that all relevant literature on adverse events was captured. Additionally, a thorough hand search for the identification of grey literature on the issue of patient safety, unsafe care and adverse events was conducted including a search on the internet and on websites of the international organisations (e.g. European Union, WHO, OECD).

Screening and selection of the abstracts and full texts was based on criteria defined ex ante by a minimum of two experts independently. The selection of the studies was subdivided into the first selection of publications and the second selection of full texts, both of which are described in the next section.

First selection of relevant publications

The first selection of publications was based on available abstracts and titles (if abstracts were not available) using eligible pre-defined criteria.

The inclusion/exclusion followed formal criteria, contextual criteria, criteria concerning study design, medical criteria or other inclusion criteria (see Table 1).

Table 1: First selection (abstracts)

No.	Selection aspects
1	Formal aspects (duplicates, publication date,…)
2	Geographical aspects (include EU, USA and Canada)
3	Primary focus is on unsafe care
4	One or more adverse events investigates
5	Epidemiologic or economic outcomes are analysed

Source: GÖ FP

Second selection (full texts)

For the second selection the criteria for the first selection were also applied and enhanced by quality and validity criteria and criteria for relevant endpoints. The full texts of all included abstracts were thoroughly read (in-depth review) and selected or eliminated.

Quality assessment and grade of evidence

The internal (risk of bias) and external validity (applicability of study results to patients outside the study population) of the selected studies was assessed after the second selection. The overall grading of the evidence was conducted in three steps: (1) evaluation of internal validity (risk of bias), (2) evaluation of external validity and (3) evaluation of the overall grad of evidence synthesizing the internal and external validity.

Evaluation of the internal validity (risk of bias)

To evaluate the risk of bias, quality criteria checklists were used [10]. These checklists depend on the study type (i.e. systematic literature reviews, meta-analysis, randomised controlled trials, cohort studies, etc.) of the included literature. To interpret the levels of risk of bias, the following definitions are used.

Table 2: Risk of bias - Definitions

Low risk of bias	It is unlikely that the outcome of the study is significantly distorted by confounding factors. The confidence in the correctness of the results is high.
Moderate risk of bias	It is unclear to what extent the results of the study are distorted by confounding factors. Confounders are possible and could provide the correctness of the results into question.
High risk of bias	It is very likely that the result of the study is significantly distorted by confounding factors. The confidence in the correctness of the results is very low.
Unclear risk of bias	The risk of bias cannot be evaluated because of missing information in the study.

Source: Higgins/Green 2011; presentation: GÖ FP

Evaluation of external validity

To evaluate the external validity of studies, the following criteria are used (Table 3) [11].

Table 3: Criteria for evaluation of external validity

Relevant question	Explanation
Did the study refer to populations in primary care?	Many studies are conducted in a highly specialised inpatient setting (such as university clinics) and the results are therefore not transferable to other settings such as primary care.
Were the eligibility criteria not too stringent?	The inclusion and exclusion criteria for patients of clinical trials are often very stringent (age, co-morbidities etc.) and do not reflect the actual patient population. The transferability of the results to average patients is therefore low.
Were endpoints assessed that are relevant for the patient (health outcomes)?	In clinical trials the primary endpoints are often surrogate endpoints from laboratory data that might not be relevant to the patient. Patient relevant endpoints are health outcomes that the patient can subjectively experience and feel (such as reduction of symptoms).
Were the study period and the modes of treatment clinically relevant (resembling conditions of daily living)?	The study period and mode of treatment should resemble treatment situations in real life. This means that the mode and duration should be flexible and according to patient´s behaviour in real life.
Was the sample size sufficiently large to assess minimally important differences from a patient perspective?	Statistical significance is usually ensured by a sufficiently large study population; however, this does not mean that the population is large enough to assess relevant differences that can be experienced by the patient. The minimal clinically important difference should be taken into account when calculating the necessary size of the study population.

Source: Methods Manual for Health Technology Assessment; presentation: GÖ FP

The assessment of the external validity and any identified limitations of the included studies (e.g. the applicability only to a particular subgroup, etc.) are described in the results part of this report.

Evaluation of overall grade of evidence

The overall quality grade of the obtained evidence is derived from the internal and the external validity of the studies according to Table 4 [12]:

Table 4: Evidence grade

		Internal validity			
External validity		**Low**	**Moderate**	**Unclear**	**High**
	Low	Very low	Low	Very low	Low
	Moderate	Low	Low/moderate	Unclear	Moderate/high
	Unclear	Low	Low	Unclear	Moderate
	High	Low	Moderate	Unclear	High

Source: Guyatt et al. 2008; presentation: GÖ FP

The results of the overall evidence grading can be interpreted using the following definitions (Table 5).

Table 5: Overall evidence grade - Definitions

Evidence Grade	Definition
High	It is unlikely that further research changes the confidence in the observed results.
Moderate	Further research is likely to have an impact on the confidence in the observed results and the intervention effect might change.
Low	Further research is very likely to have a significant impact on the confidence in the observed results and the intervention effect might change.
Very low	The observed intervention effect is very uncertain.

Source: Guyatt et al. 2008; presentation: GÖ FP

5.2.2 Analyse evidence on prevalence, costs and costing methods of adverse events (Task 4-6)

Data extraction and analysis

The aim of the extraction process was to find published figures for costs and prevalence as well as information on costing methods.

Costs per occurrence of adverse events are typically expressed in monetary terms, in Quality Adjusted Life Years (QALYs) or lives lost, or in days of additional hospital LOS. Figures were extracted both from review and original research articles; the majority of extracted figures are indirect citations from review articles.

Prevalence of adverse events are typically reported in prevalence rates or rations such as "per 1.000 patients/admissions/bed days". As the literature gives no hints on how many patients/admissions/bed days are recorded for the study population in total, a translation into one unit is not possible. Due to this non-comparability this study only took into account the most frequent representation of results, prevalence rates.

Regarding economic methods, if at all, a wide range of different methods for attributing and measuring costs were identified.

Studies, which meet the eligibility criteria are described in the result section (see chapter 5.3) and annex 2. The results of the different studies included are presented in annex 3.

5.2.3 Calculation of economic burden of adverse events (Task 7)

As was found in previous reviews, **many published studies on the economic burden or cost of unsafe care describe no costing methodology** or exact details on how figures have been derived [13-15]. 'Cost' is often not clearly defined, sometimes referring to direct resource consumption in health care, sometimes referring to broader concepts of 'cost of illness'. Further, details on cost components, quantity, prices, time frames and similar are often missing, making it difficult for readers to assess quality of estimates as well as judge potential application to their settings [15].

Those studies that do elaborate on costing methodology**, use a wide range in methods for attributing and measuring costs**. Indeed, different methods for cost estimation are a major factor influencing the observed cost variation [15]. Choices in costing methodology often depend, for instance, on the

- **perspective or viewpoint of a study**

  Estimated 'costs' can include resource use in the health sector, in other sectors, resources used by patients and their families as well as productivity changes (Drummond). Travel costs to the clinic are costs from a patient as well as from a society's point of view, but no when considering the viewpoint of a Ministry of Health or a public budget perspective. Similarly, if a study focuses on acute care it might be less likely to include costs after hospital discharge such as societal costs of illness [14].

- **the chosen *time horizon* in which costs are tracked** [14, 16]

- as well as **the *attribution of healthcare resources* to the adverse event versus the patient's underlying condition** [14].

  Patients with longer length of stay and more co-morbidity are associated to higher cost for management of their underlying condition, but also more likely to experience and adverse event [14]. There are several methodological possibilities to attribute healthcare resources, for instance attributing resources to the unsafe care event versus underlying condition by a clinical expert, or comparing groups of patients with and without the occurrence of adverse events [14].

In general cost information can be based either on ***gross* or *micro costing* techniques**.

- Gross costing is a top-down approach which allocates the total budget to specific services.
- Micro costing is a bottom-up approach which estimates various cost components precisely. The cost components taken into consideration can vary between studies which makes comparisons difficult [13].

Micro-costing, or quasi-micro (activity-based) costing, provides the highest level of accuracy as micro-costing attempts to measure actual resource consumption [15]. Gross-costing uses aggregated cost data to estimate typical costs. **Such data is usually more readily available from electronic datasets, however provides less precise estimates** [15]. In terms of hospital costing, for instance, levels of precision can range from (a) micro-costing to (b) case-mix group data, (c) disease-specific per diem to (d) average per diem data which is the least accurate [16]. Researchers thus face the usual trade-off between accuracy and effort and expense in data collection. Data required to conduct micro-costing analysis is often unavailable or more difficult to obtain, meaning that micro-costing studies often focus on single hospitals or smaller samples rather than broader settings.

In general, the cost estimation of adverse events is often based on the average incremental length of stay. This is then multiplied by a cost estimate as just described, for instance a disease-specific per diem rate or average per diem information. While incremental length of stay is straightforward to use, it implies excluding adverse events which do not prolong length of stay of those causing immediate death [13].

Deriving cost of unsafe care by adverse event group and EU Member country

The **choice of costing methodology applied in this report is heavily constrained by the availability of data or lack thereof**. Since most costing information identified in the literature review is provided in the form of total cost of the adverse event or adverse event group, rather than broken down in single cost components or incremental length of stay, this report is forced to use such total costing information. This means that costing methodologies might be mixed depending on available studies.

Further, the **limited number of studies** providing costing estimates, particularly for some adverse event groups, as well as the **non-transparent reporting on costing details**, allows for **no systematic selection or weighting based on quality of costing estimates**. The report thus extracts all available 'cost of adverse event' estimates and uses relevant averages of such figures to estimate costs by adverse event group and EU Member country.

Cost of adverse event data is **only available for a few countries**, most studies focusing on the US. The report uses OECD health-specific Purchasing Power Parity (PPP) estimates to approximate cost by EU Member State. Ideally, the report would use country-specific prevalence rates to adjust costing information. However, evidence on prevalence rates of adverse events is equally scarce, with again most of the few available studies stemming from the US or UK. Thus, this report will assume that prevalence rates are equal across EU Member States. Usually prevalence rates are provided as percentages of hospital patients or patients and thus such figures will be adjusted using country-specific hospitalisation figures (hospital discharges) from the OECD.

To summarize, the report aims to systematically extract cost per adverse event and prevalence rate from the available literature and subsequently calculate the **economic burden of each adverse event category for each EU Member State** along the following line:

Figure 2: Calculation of Economic Burden of Adverse Event Group per EU Member State

Source: GÖ FP

Firstly, extracted costs are normalized to the same year, the same currency and the European average price level using health-sector specific purchasing power parity information from Eurostat 2014 sector-specific PPP figures and, in the case of USA and Canada, data from the OECD 2011 PPP Benchmark [17] [18]. An average cost per case for each adverse event category is derived without being able to weight for

quality of costing information or other study details. Particular care is taken not to include the same estimation multiple times, since many publications cite the same primary studies further cost estimates. These average costs are then multiplied by prevalence rates which depend on country-specific hospitalisation or doctor consultation figures. Lastly, figures are adjusted to each country's price level by using Eurostat's health-sector specific purchasing power parity figures.

The aim is to calculate costs for each adverse event category and lastly summarize to total burden of adverse events. One limitation of such an additive approach is that certain adverse events might fall into multiple groups and thus potentially be included twice in the prevalence rates from the literature used. For instance, certain healthcare-associated infections might have also been included in acute-care adverse event studies In terms of sensitivity analysis, the report will compare overall costs derived thought this method with other studies calculating overall burden for certain countries.

5.3 Results

5.3.1 Find evidence on adverse events, their prevalence and costs (Task 3)

The first literature search for both prevalence and costs yielded approximately 5.000 results per search (9.900 total), which is not workable in the scope of this project. The analysis of random samples of the results revealed the reason for the large number of studies: the search terms (such as safety or costs) are favoured key terms in titles and abstracts, most of the identified studies did not give any information on prevalence or costs of adverse events/unsafe care. To reduce the number of results only reviews were included in the systematic literature search. To ensure that the identified reviews cover the whole scope of literature, reference lists of the identified studies were analysed. The analysis of included reviews showed two results which lead to the assumption that the chosen strategy is justified. First, all reviews refer to the same pool of primary studies. Second, the reviews cover a wide time frame with very recent studies. Studies that were published after the time horizon of the latest review were additionally covered by a hand search. An additional hand search was conducted on selected websites and institutions as well as for adverse event groups with little information from the systematic search.

The systematic literature search on **prevalence of adverse events** was conducted in Medline via OVID, Cochrane via OVID, Embase via OVID, CINAHL via EBSCO and Scopus on 22nd April 2015 (see annex 1 for search strategies). In total, 893 abstracts were delivered (duplicates were excluded). After the selection of relevant abstracts according to predefined selection criteria 183 full texts were ordered, of which all were available. The additional hand search of grey literature adds 16 relevant publications. For a detailed representation of search results see annex 2.

The systematic literature search on the **costs of adverse events** was conducted in Medline via OVID, Cochrane via OVID, Embase via OVID, CINAHL via EBSCO and Scopus on 20th April 2015 (see annex 1 for search strategies). In total, 616 abstracts were delivered (duplicates were excluded). After the selection of relevant abstracts according to predefined selection criteria 160 full texts were ordered, of which all were available. The additional hand search of grey literature adds 24 relevant publications. Publications were excluded if no such figure could be extracted. In total, figures were extracted from 45 publications. For a detailed representation of search results see annex 2.

Some publications report figures that are applicable to specific groups of patients, e.g. patients in paediatric ICUs or patients undergoing a specific type of treatment, e.g. transplantations. These figures were extracted from the publications but not used in subsequent calculations of total costs, as it is unlikely that these figures are representative for adverse events in general.

5.3.2 Analyse evidence on prevalence of adverse events (Task 4)

Prevalence

Although a large number of epidemiological studies could be identified by systematic and hand search, only a few could be incorporated in this study. Table 14 in annex 3 shows the results of the data extraction from studies with comparable designs and results. It lists ranges and figures for seven adverse event groups and adverse events in general. The table also includes rates of preventability and the region a study was conducted. Final results will be presented in chapter 5.3.4.
This project and its research questions face four major issues related to published studies: comparability of results, insufficient information on several EU member-states, wide ranges of results in-between studies and countries and level of aggregation of adverse event groups.

Comparability of study design and results

As this study seeks to calculate the overall economic burden for adverse events it is important to derive the burden of all different types and groups of adverse events. Authors of published studies don't have the need of this kind of aggregation and the way the epidemiology of adverse events is reported differs strongly, according to available data while conducting a study or the adverse event group itself. Therefore the reported epidemiology in identified studies varies from prevalence, incidence, cases per 100/1.000 admissions/bed days/patients etc. Due to a lack of information (e.g. how many admissions are recorded for a certain hospital or health care system) it is not possible to standardise these data.

No sufficient information on EU member-states

Identified studies don't give sufficient information on prevalence in different EU countries or member-states. Only single results for certain countries and adverse events are reported. Level of geographical aggregation is EU-wide, world-wide, USA, Africa, high- middle- and low-income countries or "international". Therefore the assumption has been made that adverse events have the same prevalence across Europe.

Wide ranges of results in-between studies and countries

All studies (also from European countries with only a small number of participating institutions) report wide ranges in their results (e.g. prevalence rates from 0.1-74%). This hinders a comparison of studies considerably and shows that adverse events rates vary in countries and health systems.

Level of aggregation of adverse event groups

This study aims to give an overall picture on adverse events by aggregating adverse events into subgroups. Studies on adverse events focus in most of the cases on

specific events which can be classified in different subgroups (e.g. an infection during surgery is in primary studies classified as surgical error or health care associated infection). Classification of subgroups was done in accordance with the expert panel.

5.3.3 Analyse evidence on costs of adverse events (Task 4)

The following chapter analyses the evidence on costs of adverse events. Detailed tables for these results are listed in annex 3.

Generic adverse events

11 publications address adverse events generally. They report average or regional total (e.g. national) costs of adverse events. Some publications focus on Canada (2), USA (2) or the UK (2); the others include data from several countries. Table 15 in annex 3 summarizes all data on costs of generic adverse events extracted from publications.

Total impact of adverse events

Annually, adverse events cause 44.000 to 98.000 deaths in the US [19] and 9,250 to 23,750 deaths in Canada [20]. We found no such total number for other countries.

Worldwide, 23 million DALY are lost due to adverse events, of which 78.6% is due to premature death [21].

But also the financial impact of adverse events is substantial. In general terms, adverse events are reported to be responsible for 1% (Netherlands, preventable AE only) [22] to 4–6% (USA) [19] of all healthcare expenditures.

In the UK, the costs of preventable adverse effects in terms of extra bed days alone was calculated to be a billion pounds per year [22], or in total two billion pounds per year [23].

In Canada, increased length of stay of adverse events alone causes extra costs of approximately CAD 400m [24]. In the USA, adverse events result in 2.4m extra hospital days, costing a total of USD 9.3m [25] to 37.6b [26].

Costs of episodes of adverse events

Some publications also give costs per episode of generic adverse events. Etchells [24] list references for costs per episode of adverse event between CAD 6,124 and CAD 12,648, with a typical increased LOS of 6 days. Mittmann [27] reports costs per episode of adverse event of USD 4,571 or USD 10,074.

Acute care adverse events

5 publications address acute care adverse events. However, only one publication quotes per case costs of "generic" acute care events – about 13 thousand dollars per case [28]. Rivard [29] reports costs per case, excess LOS and excess mortality for a series of postoperative conditions (see Table 16, annex 3).

Other publications report costs of specific adverse events, such as USD 55,654 per case in US transplant patients [28], AUD 5,751 per case in cardiac surgery (Austrialia) [30] or fourfold increase of in an US paediatric ICUs (17.5 days vs. 7.6 days) following failed extubation [31]. Occurrence of venous thromboembolism, a typical adverse

event caused by surgery-related bed rest, was found to be responsible for loss of 2,282 DALYs in high-income countries in 2009 [32].

The diverse nature of adverse events related to acute care impede comparability of figures. Published figures for cardiac surgery, transplant or PICU adverse events are unlikely to be representative for all acute care adverse events; publication bias would distort results if we were to extrapolate costs of acute care adverse events from these figures Table 16 summarizes all extracted data.

Adverse drug events

Since this study focuses on the consequences of unsafe care with the aim of guiding patient safety improvement priorities for healthcare organisations, publications that discuss known side effects of drugs that may very well occur in absence of any error were thus excluded.

7 publications meet these criteria. They are summarized in Table 17 in annex 3.

Total impact of adverse drug events

Adverse drug events lead to death or injury of 770k people per year in the USA [33]. 779 thousand DALYs were lost in high income countries due to ADE in 2009 [21].

In economic terms, total costs of inappropriate medication in the USA are reported to be 7.2 billion dollar [26, 33], 1.5 to 5.5 billion [33], and 2 billion (extra hospital costs) or 100 billion (total burden of disease) [34]. In Canada, total costs of ADE in patients 65 years or older are USD 35.7 million [34].

Costs per adverse drug event

Publications report costs of an ADE per case at USD 2,000 [26]; EUR 793–2380; EUR 5,505; EUR 1,329; EUR 2,116; EUR 1,887; EUR 3,725; EUR 1,000 [35]; CAD 4,028 [24]; USD 1,310 for all ADE, and 1,983 for preventable ADE; EUR 321 or 824 in two different calculation methods employed in Ireland, EUR 2,507 per episode, in Netherlands; EUR 4,844 in Spain [34].

Chiatti [34] also list costs of ADE attributable to some specific medications, such as aspirine, which causes additional costs of GBP 50 per episode of ADE or inappropriate use of proton pump inhibitors, which causes US-wide total costs of USD 233,944 (over-the-counter) plus 1,566,252 (prescribed) in USA. The use of NSAID causes extra costs of USD 117 in 1998 per application due to adverse events.

Falls

4 publications address the costs of falls. In USA, falls cause 581 thousand hospitalizations and 19.7 thousand deaths in 2008. They are responsible for costs of USD 19.2 or 28.2 billion, i.e. 0.85% to 1.5% of total health expenditures. A hip fracture costs AUD 11,991 [36] or more than USD 20 thousand [37].

The WHO [26] reports falls lead to a 61% increase in LOS, and 71% increase in inpatient costs. They are responsible for a loss of 27 thousand DALYs in high income countries [21].

Table 18 in annex 3 lists all extracted cost figures.

Unsafe blood products

Unsafe blood products are primarily a problem for low income countries. Two publications, listed in Table 19, annex 3, address this issue.

Worldwide, unsafe injections cause 1.3M early deaths, loss of 26M life years and USD 535M direct medical costs [26]. Unsafe injections alone are estimated to cost the world USD 535M in direct medical costs per year [26]. Relevance of that information to European countries is however questionable.

Diagnostic errors

Only one publication, listed in Table 20, annex 3, deals with diagnostic errors specifically. Diagnostic errors account for 40,000 – 80,000 deaths in US hospitals per year. As a specific example, suboptimal radiology processes were identified as a contribution to medical errors escalating economic costs, which are estimated at more than USD 38 thousand per year [38].

Healthcare-associated infections

With 24 publications, healthcare-associated infections are the most prominent group of adverse events among our literature search results. These publications are summarized in Table 21, annex 3.

Generic healthcare-associated infections: In general, healthcare-associated infections kill 5,000 people per year in France and the UK [26] and about 100 thousand people per year in the United States. They cause costs of about USD 800 million to several billion in each USA and Europe.

Stratifications: Publications stratify costs of HAI by pathogen, by type/location of infection, and setting.

C. difficile and multi-resistant S. aureus are the most highlighted pathogens: Types of infections most frequently covered in the literature include ventilator-associated pneumonia (VAP), central-line associated bloodstream infections (CLABSI), surgical site infections (SSI) and urinary tract infections (UTI).

Other publications report costs of infections in the ICU or the paediatric ICU: In general, most publications report cost figures of about USD 1,000 to 20,000 per case of HAI. In special settings or populations, costs can be much higher.

Decubitus ulcers

5 publications, summarized in Table 22 (annex 3), address the cost of decubitus ulcers. The total treatment cost of decubitus ulcers in the UK amounts to GBP 1.4 to 2.1 billion or 4% of health expenditures [26]. In the USA, 60 thousand patients die from decubitus ulcers per year [39]. In all high-income countries, decubitus ulcers are responsible for the loss of 134 thousand DALYs [21]. A single occurrence of decubitus ulcer causes excess mortality of 7.2%, excess costs of USD 10,845 and increased LOS of 4 days [29]. Jackson [36] reports costs per case of AUD 8,435.

Adverse events related to medical devices

Publications addressing device-related adverse events are very rare. Only one publication [36] reports costs of one type of adverse events related to medical devices

(Table 23, annex 3). Costs complications of cardiac and vascular implants excluding septicaemia at AUD 7,749 per case.

Albeit these complications are comparatively common with 2,873 cases in the database of 1,699,997 hospitalizations in two Australian provinces, it is questionable to what degree this type of adverse event can be regarded as representative for adverse events related to medical devices.

Discussion

Variation

A striking feature of cost figures for adverse events is the ***substantial variation*** among published figures. Even for a specific type of adverse event, cost figures may vary by a factor of up to 1:10. If figures of different types of adverse event of the same category (e.g. healthcare-associated infections) are compared, or specific settings ore populations are considered (e.g. paediatric ICU) the spread is even larger.

The leading causes of variation are

- **Small sample sizes of the studies**. If the sample size of a study that reports costs of adverse events is small, high variation of costs due to patient heterogeneity is to be expected. [13]
- **Difficulties of allocating inpatient costs**. A number of problems impede the attributability of costs to adverse events. Running costs of departments may be difficult to attribute to single patients with adverse events. Internal service charges, on which cost estimates obtained via activity-based costing could be based, may vary across providers. Also, it may prove difficult to uniquely identify the adverse event as single root cause for a given on-patient activity.
- **Differences in the time frames used.**
- **The economic perspective employed**, i.e. payers' perspective, hospital costs, societal perspective, etc. [16]
- **The cost categories included.** [40, 41]
- **Organizational-level variation in coding practices**. [42]
- Different costs of medical services in different countries. [43]
- **The costing method employed and the cost categories included** (see chapter 5.2.3). Unfortunately, many publications do not report the underlying costing methodology [40].

Payer

Theoretical concepts of costs of adverse events comprise monetary costs to hospitals providers, health insurance, patients, as well as non-monetary tangible and intangible costs of illness which accrue to patients and/or their relatives [16].

Only one publication lists societal costs of healthcare-associated infections [44]. Other publications refer to the (incremental) cost of treating the adverse effect or to cost figures established by malpractice litigation.

Theoretically, if hospitals shoulder the burden of additional costs due to adverse events, they should have an extra financial incentive to invest in patient safety programmes that reduce these avoidable costs.

However, even if we limit our analysis to financial costs, it is not obvious who bears them:

> *"Besides harming patients, adverse events have major financial consequences. But who bears the extra costs for treating adverse events is not well understood." [45]*

In the United States, adverse events lead to increased hospital charges via increased LOS [45]. In an analysis of adverse events in Utah and Colorado, Mello [46] find that in 1992 hospitals bear only 22% of the societal costs caused by adverse events. On average, health care costs account for only about half the costs of the adverse event. Of these costs, hospitals can externalize a substantial ratio to patients or health insurance. Only a fraction of total costs of injuries are internalized via litigation claims.

Reforms of the tort system may be the key to better internalization of the cost of adverse events [47]; however the effects of malpractice laws on medical practice is not unequivocally beneficial. Fear of litigation might cause healthcare providers to minimize litigation risk instead of choosing the optimal treatment for patients. This *defensive medicine* may cause additional costs and/or harm to patients [48].

5.3.4 Finalization of adverse events selection and refinement of information on prevalence and costs (Task 6)

The finalization of prevalence of adverse events is the result of extracted literature and interviews from the expert panel. As mentioned above the experts showed detailed information of specific events (e.g. in this case urinary tract infections) but had very limited information (in addition to the extracted literature) on adverse event groups (e.g. in this case health care associated infections).

Table 6 shows the combination of extracted literature and expert estimations per adverse event group. Preventability of events is illustrated by degree of preventability with "easy, medium or hard". Note that in contrast to the original grouping of events (see chapter 2) "Decubitus Ulcers" was incorporated into "Acute Care" due to expert recommendation.

As described in chapter 5.3.3, variation in cost figures and different types of adverse events within each adverse event groups hinder quantification of costs of adverse events at the level of adverse event groups. Table 7 compares lowest and highest estimates of costs per episode of an adverse event for three adverse event groups, all values are converted to 2014 Euro.

As can be seen in Table 16, the lowest estimate within the acute care AE group, accidental puncture, is estimated to cost only a fraction of a typical adverse event in transplants patients' acute care. Likewise, costs of healthcare-associated infections vary substantially. An episode of nosocomial urinary tract infections may be 56 times less costly than nosocomial sepsis. The spread of 1:19 in adverse drug events may be related to the fact that different types of adverse events are included in the cost figures. Therefore no reliable statements on costs of adverse events and event groups can be made.

Table 6: Final list of adverse event groups

Adverse Event Group	Prevalence	Share	Preventable
acute care adverse events/ adverse events due to surgical errors	0.3-15% of patients are affected	38%	Medium/Hard
healthcare associated infections	3.5–14.8% of patients in hospitals have infections	25%	Medium/Hard
adverse drug events/medication error	0.4–28.3% of patients experience ADE	15%	Medium/Hard
errors in diagnosis	1.4%–5.8% - rate of misdiagnosis)	10%	Medium/Hard
others	-	5%	-
adverse events due to falls	0.3-2% of patients in hospitals suffer from falls	3%	Medium
medical devices adverse events	-	2%	Easy/Medium
adverse events due to unsafe blood products & biological products	0.37% of apheresis collections lead to AE	2%	Easy/Medium

Source: GÖ FP

Table 7: Costs of adverse events by adverse event group

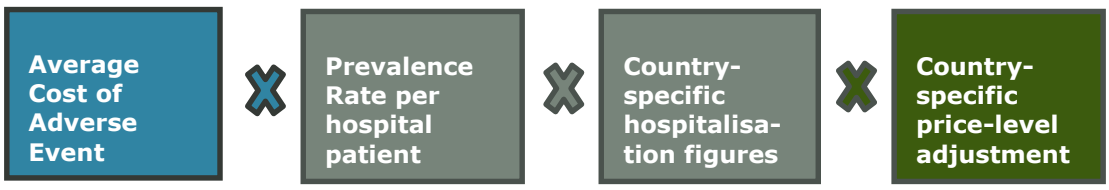
Adverse event group	lowest cost estimate	highest cost estimate	spread
acute care adverse events / adverse events due to surgical errors	EUR 3.016	EUR 43.414	1:14
healthcare-associated infections	EUR 645	EUR 36.141	1:56
adverse drug events / medication errors	EUR 294	EUR 5.689	1:19

Source: GÖ FP

5.3.5 Calculation of economic burden of adverse events (Task 7)

As outlined in Section 5.2.3, this report aims to use the extracted costing and prevalence information to derive average prevalence and cost per case figures per identified adverse event category and calculate overall economic burden of adverse events by EU Member country.

Figure 3: Calculating Economic Burden per Adverse Event Category and Member State



Source: GÖ FP

As was outlined in Section 5.2.1, estimated prevalence rates vary vastly, however a general bandwidth per adverse event category could be derived. The issue here, as described, is that **categories are likely to overlap and thus overall prevalence rates when aggregating adverse event categories might be overestimated**. For instance, certain infections might be counted both among acute care events as well as healthcare-associated infections.

In terms of costs of adverse events, aggregating the available costing information to category level is similarly problematic. The available studies generally do not cost adverse event groups, or comparable adverse event groups, but calculate costs for specific adverse events or settings. For instance, within the acute care adverse event category, one of the very few available studies estimates costs for transplant patients, surely a rather small subgroup and not necessarily representative in terms of costs for the overall category.

Deriving costs per case for each adverse event category by simply averaging over available studies thus may yield a substantial publication bias. In terms of healthcare-associated infections, the category with most available costing evidence, the most researched infections appear to be central-line associated bloodstream infection, catheter-associated urinary tract infections or non-Methicillin-resistant Staphylococcus. Without information on what fraction of overall healthcare-associated infections are such types of cases, all types of infections are weighted equally. If infections that are more costly are more likely to be studied and more likely have available costing evidence, then such publication bias will lead to larger average cost per case figures.

Due to data quality and availability problems, but also largely due to such aggregation and publication bias issues, the approach outlined in Section 5.2.3 and above in 5.3.3 proves to be problematic.

Since the outlined approach cannot be used to yield reliable values, this report has to rely on previous estimates of overall costs to provide a sensible suggestion of magnitude of the burden of adverse events.

Cost estimated for overall adverse events are available for a small selection of countries.[1] In the US, Kohn reports that total costs associated with adverse events represent USD 37.6 to 50 billion, or about 4-6 percent of health expenditure. On the other hand, Vlayen 2014 [25] estimates an annual burden of USD 9.3 million, which[19] is 0.3% of total health expenditure. For the UK, Milna 2007 [23] cites an overall burden of GBP 2 Billion, which equals around 1.5% of total national health expenditure[2]. For Canada, Milna 2007 cites estimates between CAD 300 million and CAD 1.5 billion, i.e. 0.2% to 0.8% of total health expenditure.

[1] Costing studies cited here refer to studies that aim to cost the entire adverse event burden, not merely the preventable or avoidable share of adverse events.

[2] After the literature search was conducted, a new study [49] was published with relevant data for this report in December 2015. Due to organizational and methodological reasons this study was not incorporated in this report. The results from the study support the findings in this report.

Table 8: Overall Economic Burden of Adverse Events according to Literature

Country	Source	Costs of adverse events	Costs as % of total health expenditure 2014
USA	Kohn 2000	4-6% of health expenditure	4.0-6.0%
	Vlayen 2011	USD 9.3 billion	0.3%
UK	Milna 2007	GBP 2 billion	1.5%
Canada	Milna 2007	CAD 300 million – 1.5 billion	0.2-0.8%

Source: Calculation GÖ FP; OECD Database Annual consumer price inflation; Eurostat Database GDP at current market prices and annual exchange rate 2014; World Bank Database total health expenditure as percentage of GDP

Thus, according to the scarcely available literature, estimates of the overall burden of adverse events range from about 0.2% to 6.0% of total health expenditure, confirming that the results of the previously outlined approach highly overestimate economic burden. The range suggested by the literature would imply an economic burden of adverse events within the European Union of between EUR 2.8 and EUR 84.6 billion of direct costs for the public health care sector (this value would be even higher if also indirect cost would be incorporated). The only European reference figure suggests a burden around 1.5% of health expenditure (HE) (which is confirmed by a recent publication from the Netherlands [49]).

Table 9: Estimate of overall burden of adverse events - direct costs, in Million EUR

	Bottom-range of Adverse Event Burden (0.2% of HE)	**European Reference (1.5% of HE)**	**Upper-range of Adverse Event Burden (6.0% of HE)**
Austria	72.7	545.0	2,180.1
Belgium	89.6	672.2	2,689.0
Bulgaria	6.5	48.9	195.6
Croatia	6.3	47.2	188.8
Cyprus	2.6	19.4	77.6
Czech Republic	22.4	168.1	672.6
Denmark	54.8	410.7	1,642.9
Estonia	2.3	17.1	68.6
Finland	38.6	289.3	1,157.1
France	497.4	3,730.2	14,920.8
Germany	658.8	4,940.8	19,763.2
Greece	34.9	261.6	1,046.4
Hungary	16.8	125.8	503.3
Ireland	33.7	253.0	1,012.0
Italy	293.4	2,200.7	8,802.8
Latvia	2.7	20.2	80.9
Lithuania	4.5	34.1	136.4
Luxembourg	6.9	52.1	208.2
Malta	1.4	10.4	41.6
Netherlands	170.8	1,281.0	5,124.0
Poland	54.7	410.6	1,642.5
Portugal	33.7	252.6	1,010.4
Romania	16.0	120.1	480.6
Slovakia	12.4	93.1	372.4
Slovenia	6.8	51.3	205.0
Spain	184.9	1,386.7	5,546.8
Sweden	83.6	627.2	2,509.0
UK	410.9	3,081.8	12,327.0
EU 28	2,820.2	21,151.4	84,605.5

Source: Calculation GÖ FP; World Bank Database Total Health Expenditure as % of GDP; Eurostat Database GDP at current market prices

5.3.6 Conclusions and discussion of financial impact of unsafe care

The literature on unsafe care clearly shows that the burden resulting from adverse events is not negligible. Results of the literature review show a general prevalence of adverse events in 4-17 percent of all patients [32, 50-53]. Even when using the bottom-range of estimates direct costs for the public health care sector appear to be a minimum of EUR 2.8 billion, or 0.2 percent of HE. The upper-range direct costs appear to be a maximum of 84.6 billion or 6 percent and the results from a European reference 21.2 billion or 1.5 percent of HE. As no indirect costs are incorporated in this

estimate, the overall economic burden (direct and indirect costs) is higher than the results of this report. Indirect costs are not incorporated in this report due to the following reasons:

It is difficult to quantify intangible costs associated with unsafe care. Assigning a price tag to deaths following adverse events in Europe is even more difficult. Firstly, no reviewed publication reported a number of deaths due to adverse events, all available figures refer to Northern America.

Economists refer to the concept of statistical value of life when the trade-off between monetary wealth and fatal risks are analysed. These concepts are widespread in traffic accident prevention and industrial safety, where values of lives saved need to be determined in order to justify levels of investments in safety. Economists estimate the statistical value of life using the behavioural concepts of revealed preferences – e.g. wage premiums in high-risk professions – or stated preferences – e.g. willingness to pay as determined via contingent valuation questionnaires.

Application of statistical values of life is less widespread in health policy, where cost-effectiveness analysis or cost-utility analysis prevails [54]. These methods do not assign a monetary value to a person's life.

Estimation of statistical value of saved lives through investment in patient safety face the additional challenge that patients whose lives can be saved via patient safety investments are – in contrast to potential traffic accidents – of old age and have impaired health. Here it should be noted that, strictly speaking, patient safety investments do not save lives but rather delay death; and the older and sicker a patient is, the less death can be delayed by patient safety investments. In contrast to that, findings from stated preferences studies suggest that the willingness to pay does not as anticipated decrease with older and/or sicker respondents [55].

Furthermore, estimates of statistical value of life feature substantial variance. Mrozek and Taylor [56] report that "estimates of the VSL vary substantially, from less than $100,000 to more than $25 million". However, most figures for high-income countries range between $ 7 and $ 10 million.

Identified epidemiological studies have only limited value for answering the research questions of this study. Literature primary focuses on very specific events (e.g. urinary tract infection) and gives insufficient information on adverse event groups defined in this studies context (e.g. health care associated infections). Besides that, studies with adequate information show wide ranges in results for identical adverse events within countries, regions and cities and lack of a differentiation across EU member states.

Data availability on cost of adverse events is strongly dissatisfactory and allows few further statements on the exact level of costs, variation of cost and prevalence rates between different member states and on the factors leading to higher or lower economic burden.

Few figures on costs are available, even fewer outside the US, UK or Canadian context. Further, the small number of exiting studies shows a large variation in estimates, due to small sample sizes, different methodologies, cost categories included and definition of time horizon. Many of the available studies appear to be of low quality, with low transparency on exact methodology and data sources applied and with few standards allowing the comparison of studies across settings and types of adverse events.

In conclusion, this extensive review of the literature finds that further primary studies of epidemiology and costs of adverse events are needed, to gain a better grasp of the exact size of economic burden and factors influencing its magnitude.

6 Cost-effective patient safety programmes

6.1 Aim

The aim of this chapter is to identify and select cost-effective patient safety programmes in the EU/EEA Member States. For the selected programmes success factors and potential weaknesses will be identified and cost-effectiveness and efficiency indicators developed.

The following research questions will be addressed:

- What cost-effective patient safety programmes related to a selected set of adverse events are implemented according to the literature?
- What success factors and potential weaknesses of the selected programmes can be identified?
- What are indicators for cost-effectiveness and efficiency of patient safety programmes?

6.2 Methodology

6.2.1 Selection of cost-effective patient safety programmes (Task 8)

The systematic literature search on patient safety programmes was conducted by linking different search terms regarding

- Patient safety programmes (e.g. patient safety program/project, safety management program/project, risk management program/project)
- Cost-effectiveness (e.g. cost, cost analysis, cost-benefit-analysis, program evaluation, evaluation study, etc.).

For the search terms subject headings (e. g. Medical Subject headings (MeSH) and free-text (e. g. truncation like program* for programs or programme or programmes) were used. The search covered a period of ten years (2006-2015) and was conducted in English. Abstracts and full texts of all EU languages were included in the selection process. The detailed search strategies are outlined in Annex 1.

The following international databases were searched: Medline, Cochrane and Embase via OVID, Cinahl via EBSCOhost Research Databases and Scopus.

For further details on the literature search, data extraction, quality assessment and risk of bias as well as data extraction and analysis see chapter 5.2.

6.3 Results

6.3.1 Selection of cost-effective patient safety programmes (Task 8)

The systematic literature search on **patient safety programmes** was conducted in Medline via OVID, Cochrane via OVID, Embase via OVID, CINAHL via EBSCO and Scopus on 23rd June 2015 (see annex 1 for search strategies). In total, 339 abstracts were delivered (duplicates were excluded). After the selection of relevant abstracts according to predefined selection criteria 69 full texts were ordered, of which 69 were available.

The additional hand search of grey literature adds 8 relevant publication. After the selection of the full texts, 20 publications were identified to be relevant. 6 publications were included for background and context information. For a detailed representation of search results see annex 4.

6.3.2 Identification of strengths and weaknesses of selected cost-effective patient safety programmes (Task 9)

A total of 49 abstracts and programmes were collected and analysed according to their contents. Descriptions (e.g. addresses, setting, prevalence, cost data, aim, effectiveness, etc.) were collected and transferred to an examination file. In a further step, the programmes were classified into 3 categories. The extracted abstracts had to fulfil sufficient criteria, such as exact description of the programme objectives, planned interventions, outcome description, report of the programme costs and impact on further cost reductions due to the intervention to be selected as a matching programme.

The evaluation of the programmes resulted in following findings (Table 10). Eleven out of 49 programmes met all the mentioned criteria, included cost data and were identified as efficient programmes [41, 57-66]. Twelve out of 46 programmes did not met all mentioned criteria due to the lack of cost data, but were identified as efficient programmes [23, 67-77] as these programmes include precious information and costs can be estimated if necessary. Studies with Authors, title and year of publication are listed in Annex 4.

Table 10: Selected / excluded abstracts or programmes

selected / excluded abstracts or programmes	quantity
efficient programme – cost data available	11
efficient programme – no cost data	12
study, systematic review, insufficient outcome or other reasons for exclusion	26
total	49

Source: GÖ FP

The aim of this task was to identify and select cost-effective patient safety programmes in the EU/EEA Member States. Efficient programmes with available cost data are primary based on American (7) or Canadian (1) and three European studies (3). Reasons for exclusion of studies varied, e.g. the reports contained no cost data and/or insufficient results were presented in the study or reports had methodological weaknesses. Attention is invited to the fact that no studies report weaknesses of programmes or cost-inefficient programmes (only one study reports cost-neutral results). This might be a hint on a publication bias. Sources of efficient programmes containing no cost data derive from different countries. A detailed overview is given in the following table.

Table 11: Selected / excluded abstracts or programmes

country of origin	Number of efficient programmes – no cost data
United States	6
United Kingdom	2
Spain	2
Canada	1
France	1
total	12

Source: GÖ FP

Examples of good patient safety programmes with cost data

The following section introduces three European studies on cost-effective patient safety programmes (note that the programmes are not always declared as patient safety programmes per se, but practices or interventions, but serve their purpose). The selected programmes focus on three different adverse event groups and types and represent a major burden of adverse events described in chapter 6. The studies focus on labour efforts to prevent pressure ulcers, a theory based approach to implement clinical guidelines and the introduction of electronic medication ordering systems [64-66].

As a fourth example of a cost-effective patient safety programme a Canadian study which deals with HAI is introduced, as it describes a best practice example and served as prototype for the applied simulation model [78]. For background information and incorporation in the recommendations two more programmes were included, although the studies are US based, as the information given can be transferred to the European setting [41, 58].

Mølbak et al. Are labour-intensive efforts to prevent pressure ulcers cost-effective?

The Danish Society for Patient Safety introduced the Pressure Ulcer Bundle in order to reduce hospital-acquired pressure ulcers in 2010. The objective of this study [64] was to investigate the cost-effectiveness of labour-intensive efforts to reduce pressure ulcers in the Danish Health Care Sector, comparing the Pressure Ulcer Bundle with standard care.

The results of the study show that prevention of hospital-acquired pressure ulcers by implementing labour-intensive effects according to the Pressure Ulcer Bundle was cost-saving and resulted in an improved effect compared to standard care. The incremental cost of the bundle was minus EUR 38.62. The incremental effects were a reduction of 9.3 % prevented pressure ulcers and 0.47 % prevented deaths. The analysis confirmed the incremental cost-effectiveness ratio's dominance for both prevented pressure ulcers and saved lives with the Pressure Ulcer Bundle.

The main measures of the Pressure Ulcer Bundle are:

- The Danish Society for Patient Safety developed the Pressure Ulcer Bundle to reduce the prevalence of pressure ulcers in Danish hospitals. The bundle was tested at five Danish hospitals from 2010 to 2013.
- The bundle consists of guidelines on how to optimize and secure the use of already existing tools and on structuring the preventive initiatives.
- The four major elements of the bundle are: (1) all newly hospitalized patients are assessed for the risk of developing pressure ulcers, (2) patients at risk of developing pressure ulcers are reassessed daily, (3) patients at risk should be nutrition

screened and (4) patients at risk should be mobilized optimally and decompression should be used when repositioning in accordance with guidelines.
- The four elements were adjusted and implemented in the daily routine using the Model for Improvement which aims to continuously improve and reflect on the methods used by the involved hospital staff.

Taylor et al. The clinical and cost effectiveness of a theory based approach to the implementation of a national guideline

The authors of this study tested a theory based approach in three NHS hospitals in the UK in 2011 to improve the implementation of guidelines [65]. The study adopted the Theoretical Domains Framework Implementation (TDFI) approach for supporting behaviour change required for the uptake of a national patient safety guideline to reduce the risk of feeding through misplaced nasogastric tubes. The target behaviour identified for change was to increase the use of pH testing as the first line method for checking the position of a nasogastric tube.

The results show that the TDFI approach improved the uptake of a patient safety guideline across three hospitals and is clinically and cost-effective in comparison to the usual practice. The estimated savings and costs in the first year were GBP 2.56 million and £GBP1.41 respectively, giving an ROI of 82 %, and this was projected to increase to 270 % over five years.

The main measures of the TDFI approach are:

- A behaviour change methodology for implementation is called "Theoretical Domains Framework" and it aids the identification of barriers and levers to organisational and individual behaviour change.
- The "Theoretical Domains Framework" was adapted for the implementation of clinical guidelines This TDFI approach draws on evidence based implementation principles.
- The TDFI approach is based on a six step procedure for behaviour change: (1) forming an implementation team, (2) defining a locally relevant target behaviour, (3) understanding barriers to performing the target behaviour, (4) devising intervention strategies to address identified barriers, (5) intervention implementation and (6) evaluation.
- As a bottom-up strategy, the TDFI approach aims to facilitate a collaborative team with a blend of front-line healthcare professional expertise and theoretical support to co-work through an implementation process.

Vermeulen et al. Cost-effectiveness of an electronic medication ordering system in hospitalized patients

This study [66] was conducted in two Dutch hospitals between 2005 and 2008. The aim was to study the balance between the effects and costs of an electronic medication ordering system (CPOE/CDSS) compared to the traditional paper-based medication ordering.

The results show costs of EUR 12.37 for paper-based ordering and EUR 14.91 for CPOE/CDSS per patient/day. The amount that has to be invested in order to prevent an error is EUR 3.54 for medication errors and EUR 322.70 for preventable medication errors. Electronic medication ordering systems contribute to a decreased risk of preventable harm and the extra costs of CPOE/CDSS are acceptable.

The main measures of electronic medication ordering systems are:
- The traditional medication prescribing system is paper-based and relies on hand-written prescriptions by various healthcare professionals.

- Computerized physician order entry (CPOE) systems and CPOE with a Clinical Decision Support System (CDSS) are considered to be a useful alternative to enhance patient safety
- Recent studies report a significant impact (decrease) of CPOE on medication errors.

Raschka et al. Health economic evaluation of an infection prevention and control (IPC) programme

The Vancouver Coastal Health is a regional Health Authority in British Columbia that spent more than CAD 66.3 million managing 24,937 health care-acquired infections (HAI) cases over the 4-year evaluation period [62]. Urinary tract infections, methicillin-resistant Staphylococcus aureus, and Bacteremias caused the main costs. During the four year time period a reduction of 4,739 HAI cases avoided costs of CAD 9.1 million while the infection prevention and control programme generated investments of CAD 6.7 million. The investment costs were CAD 2.4 million below the expected costs if no intervention would have been done.

Over a time period of two years several basic points were developed to control and avoid adverse events:

- establishing consistent infection prevention policies and procedures
- developing focused interventions (e.g., reduction of Bacteremias, control of methicillin-resistant Staphylococcus aureus [MRSA], a hand hygiene program, Clostridium difficile [CDI] isolation and treatment guidelines, catheter-associated urinary tract infection [UTI] prevention initiatives) in collaboration with the IPC team, medical microbiologists and senior administration
- the IPC programme was fully integrated into a quality and patient safety programme along with a number of other key programmes (e.g. accreditation, quality improvement and change management, performance monitoring, and human factors engineering)
- For five years all laboratory tests were processed centrally, facilitating data collection and integration of surveillance initiatives.

Concluding remarks on patient safety programmes

The identified examples show that a promising programme is based on a multi-method approach. Efficient programmes can be developed by the organisation itself or existing programmes can be adapted for the implementation. Employees of all professions have to be involved in relating processes.

Working programmes include the training of different occupational groups and professions for patient safety-related measures. The aim of professional trainings is to increase the awareness of their employees for patient safety. In a next step, employees will be entrusted with responsibility to avoid errors in the future. Human resources department ensure to provide resources for the agreed duties and responsibilities to fulfil the patient safety-related measures. In addition, processes and instructions for actions are defined.

Basic points of successful programmes:

- Defining objectives,
- Defining responsibilities,
- Creating structures,
- Optimizing processes,
- Monitoring and analysing results,
- Setting additional or adjusted interventions if necessary.

Hospital owners or the management of hospitals have to assume responsibilities to lead the project or programme to success. As structural and financial decisions have to be taken, the commitment of authorities is essential. The mentioned elements should all be embedded in a working quality and/or risk management. The quality management should take the role to coordinate and monitor all essential activities.

The lack of one or more basic points will presumably affect the success of patient safety programmes.

7 Assessment of cost-effectiveness of patient safety programmes

7.1 Aim

The aim of the following three tasks is to assess the cost-effectiveness and efficiency of investment in patient safety programmes and develop policy recommendations on prioritisation of patient safety strategies. Further, lessons will be drawn from the conducted analysis and areas of further research will be proposed and recommendations on methodologies and frameworks for economic analysis of patient safety programmes given. The following research questions will be addressed:

- What is the economic case for investing in patient safety?
- Which patient safety programmes are the most cost-effective?
- What recommendations can be given in terms of prioritization of different patient safety strategies?
- How should further evaluations of patient safety programmes be conducted?

7.2 Methodology

7.2.1 Basic simulation model on economic burden, budgetary impact and cost-effectiveness of patient safety programmes (Task 11)

In order to assess economic impact of patient safety programmes, a number of figures need to be calculated or extracted from publications which are then incorporated in a basic simulation model. The basic simulation model used for this report is delivered in a separate Microsoft Excel file.

First, the **cost of the programme** represents the initial financial burden of implementing the programme. Cost figures should include initial investments and running costs over a homogenous time period such that annual costs of the programme can be calculated and compared across programmes.

Second, the **effect of the programme** is measured primarily in differences in clinical parameters among the study population. In terms of patient safety programmes, this is a reduction in incidence of one or several types of specific adverse events that are targeted by the intervention. This reduction can also be expressed as a reduction in the odds of the adverse event occurring.[3] Next to changes in incidence of adverse events, mortality and hospital length of stay are often cited generic measurements of effects of patient safety interventions that are measured in natural units.

From the cost and one specific (clinical) effect of the programme, specific **cost-effectiveness ratios** can be computed. Theoretically, this allows a comparison of programmes regarding the cost per avoided case of an adverse event type in a specific

[3] Reduction in adverse events can be measured in absolute and relative numbers. For a comparison of costs and benefits of a programme, absolute figures of prevented adverse events are decisive. Relative reduction in incidence of adverse events (or a linear reduction in the odds ratio of the adverse event occurring) is crucial for generalization of effects of patient safety initiatives.

setting, or a comparison of reduction in odds of adverse effects occurring. However, most patient safety interventions address more than one specific clinical effect, such as several types of healthcare-associated infections or several common adverse events, yet cost-effectiveness ratios only allow for one-dimensional outcome indicators.

Several alternative approaches are possible. One is to generalize adverse event incidence by using other indicators in natural units such as length of stay. The other common option is to sum over several adverse event types using adverse-event specific figures for cost or monetary-equivalent burden.

These **costs of adverse events** are either extracted from other studies that try to quantify the impact of adverse events or are recorded in the evaluation of the patient safety intervention itself [40]. Different types of costs can be included in the tabulation of expenditures due to adverse events (see chapter 5.2.3). Typically, costs of adverse events in the context of patient safety interventions refer to financial expenditures of the hospital, covered by the health insurance, the patient or other public budgets (see chapter 5.3.3).

Once costs of adverse events are established, benefits of an intervention can be expressed in terms of financial savings accrued via decreased incidence of adverse events. Thus, in a (partial) cost-benefit-analysis, the difference between costs of the intervention and savings through decreased financial costs to the hospital can be expressed in a **cost-savings ratio**. Interventions that feature ratios of savings to costs above 1 are considered efficient; which means that implementation serves to reduce expenses of the hospital. If the cost of the adverse event is limited to financial costs to the hospital, this cost-benefit approach however ignores benefits in terms of gained quality of life of patients and therefore must be considered a partial analysis of benefits only. Note also that, if the effect of an intervention is expressed in an expected reduction in the odds of an event occurring, the base rate of adverse event incidence affects the cost-savings ratio of an intervention [79].

7.2.2 Recommendations on prioritisation of patient safety strategies (Task 12) and further economic assessment of patient safety programmes (Task 13)

The recommendations on prioritisation and further economic assessment are based on a combination of findings from literature and results of the simulation model.

Regarding prioritisation of patient safety programmes the study aims to give universalize suggestions, as the number of identified programmes can’t draw a complete picture of implemented patient safety programmes. Particular attention is attracted to recommendations on further economic assessments, as this study discovered several methodological and publication errors and bias in this field.

7.3 Results

7.3.1 Basic simulation model on economic burden, budgetary impact and cost-effectiveness of patient safety programmes (Task 11)

Next to the patient safety intervention that we used in the mock simulation model [78], we performed a simulation of two other patient safety interventions. These two interventions, Mølbak [64] and Vermeulen [66] were identified in a hand search of European patient safety interventions. Although Taylor et al. [65] report cost-efficient

results, this study is not suitable for the simulation model that was developed in this study.

All costs were standardized using health price level indicators (OECD) and are expressed in 2014 EUR.

Cost of the intervention

In a first step, we calculate total costs of the intervention per patient admitted to the hospital. This cost figure is then adjusted for inflation and national health PLI and multiplied by hospital admissions throughout EU countries (Eurostat Database). Scenarios allow for various degree of hospitals in EU member countries that actually implement the intervention.

Effect of the intervention and cost-effectiveness

The effect is derived from the percent change in adverse events resulting from the intervention, which is extracted from the publication. This percentage change in AE is then applied to all countries' estimate of the particular adverse effects prevalence rates that are affected by the intervention. In the base case scenario, we assume prevalence rates of the adverse event to be uniform across EU-countries, but this assumption can be relaxed in alternative scenarios.

From the cost estimates and the effect estimates, we will calculate **cost-effectiveness ratios** for this intervention if applied to all, or a subset of, hospitals in EU countries.

Accrued savings and efficiency

In a third step possible savings attributable to the intervention are identified. For this purpose we multiply price-adjusted estimates of costs of the prevented adverse events with figures of prevented adverse events. This allows assessing the financial impact of patient safety interventions on EU member state healthcare expenditures.

Sensitivity analysis explores the effect of changes in selected parameters such as prevalence rates or degree of implementation of an intervention.

7.3.1.1 Raschka et al. 2013

Raschka [78] evaluate an intervention that comprises quality and several patient safety that aim at reducing several types of hospital-acquired infections: MRSA infection and colonization, urinary tract infection, Clostridium difficile infection, VRE infection and colonization, Bacteremia, surgical site infection and central venous catheter-related bloodstream infection. The intervention was conducted in Vancouver Coastal Health, a Canadian health authority and includes a bundle of measures that were developed by the program directors in collaboration with the IPC team.

Costs

In total, costs of the intervention were CAD 6.7 million over a 4-year period. These costs were converted to costs per hospitalization in 2014-EUR adjusted for health price levels of EUR 10.44. An implementation of that intervention in all EU hospitals would thus cost EUR 844 million[4].

Effect

The effect of the intervention is given in a reduction in prevalence of selected healthcare-associated infections. Difference in prevalence pre vs. post-intervention range from 1.52 % (CDI) to 24.79 % (SSI).

In order to assess the effect of the intervention in European countries, base rate prevalence rates of the targeted HAI are crucial. However, we found no published figures on prevalence of all specific HAI mentioned in the study. Therefore, we assumed that baseline prevalence of HAI is identical in Canada and the EU.

If this assumption is made, the intervention prevents in total 1,358,490 infections at a cost of EUR 621 per adverse event.

Savings

Costs of adverse events were established in the publication and converted to price-level adjusted 2014-EUR and are given in Table 12. Savings due to the intervention are given by reduction in prevalence times cost of the adverse event. On average, the intervention prevents 15.97 % of targeted infections with attributable savings of EUR 14.10 per hospitalization. If applied to all EU hospitals, AE-related healthcare costs of 1,140 million could be prevented.

Net benefit of the intervention is thus EUR 3.67 per hospitalization or 300 million for the entire EU.

Table 12: Costs of adverse events and intervention effect

	MRSA inf.	**MRSA col.**	**UTI**	**CDI**	**VRE inf.**	**VRE col.**	**Bac-teremia**	**SSI**	**CVC-BSI**	**total**
Cost of AE, PPP standard-ized	EUR 8.533,92	EUR 809,83	EUR 440,70	EUR 1.304,73	EUR 8.277,78	EUR 3.960,72	EUR 5.392,24	EUR 7.175,51	EUR 9.251,22	**EUR 1.151,55**
prevalence of AE	0,20%	0,24%	8,04%	0,39%	0,03%	0,39%	0,49%	0,03%	0,08%	9,91%
% reduction	6,44%	6,30%	18,53%	1,52%	28,05%	2,68%	11,29%	24,79%	20,45%	**15,97%**
savings per hosp	EUR 1,10	EUR 0,12	EUR 6,57	EUR 0,08	EUR 0,68	EUR 0,42	EUR 3,00	EUR 0,54	EUR 1,59	**EUR 14,10**

Source: GÖ FP

4
Different health price levels have been accounted for in that calculation.

Sensitivity analysis

With a ratio of benefits to costs of about 1:1.36 the cost-effectiveness of the intervention heavily depends on the accuracy of input parameters, i.e. prevalence rates, cost of the adverse events and cost of the intervention. If, for example, intervention costs are increased by 20 % and costs of adverse events are decreased by 20 %, the intervention would not result in a reduction of healthcare expenditures and efficiency of the intervention would depend on the valuation of the benefits to other providers or non-monetary benefits, i.e. patient welfare.

Likewise, lower prevalence rates mean a lower absolute effect of the intervention and a less favourable cost–savings ratio. If prevalence rates are assumed 25 % lower than in the reference hospital, the net benefit of the intervention is barely positive, and it is negative if prevalence rates are assumed 26 % lower than given in the publication.

Further sensitivity analyses can be performed in the Excel tool provided as supplementary material.

7.3.1.2 Mølbak et al. 2013

Mølbak [64] use a decision analytic model to assess cost-effectiveness of an intervention to reduce decubitus ulcers. The pressure ulcer bundle (PUB) consists of evidence-based initiatives implemented by ward staff and has been found to reduce prevalence of pressure ulcers by 50 % in previous research.

Costs

Costs of the programme were established using expert-opinion regarding time spent on additional tasks as well as costs of intervention material. The prevention programme costs EUR 7.73 per patient and an additional EUR 66.66 for patients who already have developed a pressure ulcer or have tissue damage that could lead to a pressure ulcer ('stage 0 PU'), resulting in a total cost of EUR 15.55 per patient[5]. Applied to all EU discharged patients, total costs would be EUR 6,557 million.

Effect

The effect of the intervention was assumed to be a reduction of the prevalence of pressure ulcers by 50 %. The total effect of that intervention in the EU can be obtained by multiplying the base rate of pressure ulcer prevalence (18.6 %) with the reduction (50 %) and the total number of hospital discharges in the EU (85.8 million), which results in an estimated prevention of almost 8 million pressure ulcers at a cost of EUR 157 per prevented PU. Furthermore, a 5 % mortality from pressure ulcers

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Total cost of the intervention depends on the prevalence of pressure ulcers itself. We calculated adjusted costs using the publication's baseline and post-intervention prevalence rates of pressure ulcers, which resulted in per hospitalization costs between EUR 15.55 and EUR 25.36. For subsequent calculations, we made the simplifying assumptions that effect of the intervention is without delay and thus used the lower estimate for intervention cost.

means that a reduction by 50 % would save about 404,000 lives at a cost of EUR 3,108 per life saved.

These figures seem highly exaggerated. We thus performed a sensitivity analysis to test the impact of the intervention if only a subset of hospitalized patients are in fact subject to the given prevalence rate of pressure ulcers (50 %, 25 %).

Savings

Mølbak et al. calculate costs of pressure ulcer treatment from costs of a number of possible complications and respective probabilities. On average, treatment of pressure ulcers causes healthcare expenditures of standardized EUR 435.76. A reduction in prevalence from 18.6 % to 9.3 % would therefore result in savings of EUR 24.98 per hospitalization, or in EUR 2,020 million if applied EU-wide.

Sensitivity analysis

The results of this study depend heavily on the rather high numbers of pressure ulcer prevalence and mortality. We thus performed a sensitivity analysis to test the impact of the intervention if prevalence of pressure ulcers were lower. If prevalence is 8 % across all EU countries, cost of the intervention drops to EUR 9.96 per hospitalization, and savings per hospitalization to EUR 19.61, for a total net benefit (EU-wide) of EUR 604 million.

Net benefit remains positive if prevalence rate of pressure ulcers is above 3.5 %.

A lower exposure of hospitalized patients to the risk of obtaining a pressure ulcer would leave costs and savings per patient at risk unchanged but reduce the total impact of the intervention in terms of net benefit and lives saved. If only 75 % (50 %) of patients are at risk, the intervention would reduce EU-wide health expenditures by EUR 1,515 million (EUR 1,010 million) and save 303,500 (202,000) lives.

Other sensitivity analyses can be performed using the Excel tool provided.

7.3.1.3 Vermeulen et al. 2014

Vermeulen [66] evaluate an electronic medication ordering system, consisting of a computerized physician order entry (CPOE) system with a Clinical Decision Support System (CDSS) in two Dutch hospitals. The aim of this intervention is to reduce medication errors (ME) by providing dosage and drug-drug interaction alerts, and subsequently reducing preventable adverse drug events (pADE).

Costs

Costs of the intervention consist of personnel use, hard - and software and implementation costs. The cost of the CPOE/CDSS system exceeds that of the previously used paper-based medication order system by standardized EUR 2.28 per patient-day. Since the two intervention hospitals feature an average length of stay of 13 days

instead of the OECD-reported average LOS in the Netherlands of 5 days, costs of the programme has been adjusted to 5.93 per patient-day[6].

Effect

At baseline, 55 % of medication orders had at least one error, and 15.5 % of medication orders had medication orders that caused adverse drug events. 6 months after implementation of the intervention, these figures dropped to 17 % and 7.3 %, respectively.

The authors conduct a regression analysis to control for time trends in these error rates and find that there is no sufficient evidence to link the improvement in the error rates to the intervention. The time trend in the model dominates the intervention period dummy, which features and insignificant coefficient. The remainder of this chapter will however assume that the drop in the error rate and pADE rate can in fact be attributed to the intervention.

If that is the case, cost of preventing a medication error is EUR 3.18 and cost of preventing a pADE is 330,72 (ICER).

Savings

The publication does not give any costs for adverse drug events. In our literature search, we found costs of error-related adverse drug events between EUR 300 and EUR 4,800. If we assume a pADE to cost about EUR 1,500, the intervention would result in EU-wide savings of EUR 8,934 million and a total net benefit of EUR 5,796 million.

Sensitivity analysis

The authors conduct a sensitivity analysis in which they adjust both costs of CPOE/CDSS systems and paper-based systems by ±20 % in several scenarios. In the least favourable case, i.e. cheaper paper-based systems and more expensive CPOE/CDSS systems, the cost of preventing a pADE rises to about EUR 1,500. In that case, the intervention would increase net health-care spending, and any net beneficial effect of the intervention would depend on the valuation patient welfare.

In the most favourable case, CPOE/CDSS are in fact less costly than the paper-based alternative. In that case, ICER of preventing a pADE would be negative; implementing the more effective version in terms of patient safety would save money before benefits in terms of prevented adverse events are considered.

Further sensitivity analyses can be performed using the Excel tool provided.

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6 This retains patient-days as cost reference, but corrects for the fact that a higher patient turnover results in more medication orders.

7.3.2 Recommendations on prioritisation of patient safety strategies (Task 12)

The recommendations on prioritisation of patient safety strategies are assembled from general recommendations on the Council Recommendations of the European Union 'on patient safety, including the prevention and control of healthcare associated infections' [1] and findings from identified cost-effective programmes and the simulation model. The Council Recommendations serve as general recommendations on the execution of patient safety programmes. The recommendations on prioritisation give a step by step guidance on choosing from more than one programme in order to invest resources efficiently.

Council Recommendations in context with this study

The Council Recommendations of the European Union above [1] suggest their member states advancing patient safety issues on diverse levels. The ambitions to increase patient safety and to reduce adverse events should be realised by strengthening the issue at national levels. However this attempt disregards the different health care systems of its member states. The implementation of the path for implementing the recommendations in detail is not being sketched. These activities should be adopted by the European member states. The recommendations serve more as a guideline for a common objective for an increased patient safety.

Not all of the extracted patient safety programmes out of task 11 are European programmes. Anyway, a comparison on how far the selected programmes correspond to the recommendations of the European Union can be executed and the selected programmes can be analysed concerning the Council Recommendations to prioritise patient safety programmes in a structured manner.

In particular, in its report to the Council the European Commission suggests a list of actions to implement. Not all of these measures can be evaluated based on the reviewed patient safety programmes.

Table 13: Council recommendations and their implications for identified programmes

Recommended action	Comment
Adequate risk management plans, structures and actions	Systematic risk management and established guidelines how to contain risk were crucial aspects in the success of interventions. Particularly, the Pressure Ulcer Bundle features risk assessment and risk control for patients at risk of developing pressure ulcers [62].
Adequate numbers of specialised infection control staff in hospitals and other healthcare institutions;	While infection control is very important; simply raising the number of people who are designated to be responsible for infection control may not be enough. Successful programmes integrate infection control in a comprehensive patient safety strategy, where risk management and awareness of staff regarding the dangers of infections play important roles [62].
Sufficient isolation capacity for patients infected or colonised with clinically relevant microorganisms in acute care hospitals;	No reviewed patient safety programme focussed on that particular method.
Standardised surveillance of alcohol hand rub consumption and/or measurement of compliance with good hand hygiene practices;	No reviewed patient safety programme focussed on that particular method.
Training for patients, families and informal carers using also ICT tools;	No reviewed patient safety programme focussed on that particular method.
Regular updating and dissemination of the guide on patient safety education and training for health professionals;	While there has been substantial effort on improving guidelines, there is often a gap to clinical practice. This is due to the large number of relevant guidelines and barriers in changing the behaviour of health professionals. On-going training and education of staff in patient safety is thus a crucial success factor for patient safety programmes (see chapter 6.3.2). An interventions that aim at improving guideline adherence succeeded in improving adherence to guidelines, which resulted in cost-savings [65]. No reviewed patient safety programme addressed the guide on patient safety education.
Reporting as a tool to enhance a patient safety culture in the EU: regular updating and dissemination of guidelines on the implementation and functioning of reporting and learning systems.	No reviewed patient safety programme focussed on that particular method.

Source: GÖ FP

More generally, following subheadings represent Council Recommendations of the European Union on patient safety. The passage below refers the topic to the identified programmes in literature.

Support the establishment and development of national policies and programmes on patient safety

On the basis of the selected programmes it cannot clearly determined if political ambitions exist in respective countries. One of the picked abstracts describes a patient safety programme rolled out in Michigan, a United States member state where about 108 intensive care units are engaged [41]. The programme was also rolled out in other North-American states, more information can be found on the website of the MHA Keystone Center (www.mha.org). The other programmes and practices have been conducted primary in selected hospitals as pilot studies. Two papers seem to have political support in the background, but it could not be confirmed that it is so.

Recommendation: On an international/European basis efforts to enhance patient safety exist in form of the Recommendations of the Council of the European Union above and the Recommendations of the Council of Europe on patient safety and several endeavours to boost patient safety such as WHO projects (e.g. High 5 Project by WHO in 2007). All these recommendations and activities can constitute the basis for national patient safety strategies. These strategies can have a limited duration of validity and should run subsequently through a review process. The results should then build the basis for a revised version of new patient safety strategies. The publication of the results and discussion on an international level could increase the effect that countries learn from each other.

Empower and inform citizens and patients

It is recommended by the European Council that patient organisations and representatives should be involved in the development of policies and programmes on patient safety. Furthermore information should be disseminated to patients on patient safety standards, risk and safety measures which are in place to reduce or prevent errors and harm, the right being informed to facilitate patient choice and decision-making and complaints procedures and available remedies and redress and the terms and conditions applicable. Consideration of possibilities of development of core competencies in patient safety for patients. All these mentioned points may have played a decisive role in the development of the presented programmes, but information about these points could not be extracted.

Recommendation: There is still need for more transparency on how facilities ensure patient safety in their organisation. Quality outcome measures shown in a public accessible website/database would help to empower and inform citizens and patients. Based on that patients could make more informed decisions for planned surgical interventions.

Support the establishment or strengthen blame-free reporting and learning systems on adverse events

While the selected papers do not disclose explicitly if they take a reporting and learning system into consideration of their programme (but implemented surveillance systems for infection control), only one programme contains a reporting and learning system where it also occupies a central position [58]. Due to the fact that the latter programme is a hospital-wide programme we could not identify if there was a special

political ambition for implementation. The reporting and learning system was the greatest source of harm report and its implementation considerably influenced the outcome for decreasing adverse events in the hospital. The European Council recommends EU member-states to support the establishment or strengthen blame-free reporting and learning systems on adverse events that encourage healthcare workers to actively report through the establishment of a reporting environment which is open, fair and non-punitive.

Recommendation: Our analysis show just as well that an establishment of transparent error (and near-misses) reporting systems contribute significantly to enhance patient safety in health care facilities. As shown by the European Commission, Patient Safety and Quality of Care working group [80] the most important function of a reporting system is to use the results of data analysis and investigations to improve healthcare directly and help healthcare professionals to do safer work.

Promote, at the appropriate level, education and training of healthcare workers on patient safety

There is no doubt, that the aim to reduce adverse events cannot be achieved without involving the human resources component. All selected programmes consider education and training of healthcare workers on patient safety (including training on electronic systems). While there is more need of training in the implementation phase, continuous training and communication on patient safety among all involved medical staff members are absolutely necessary. An apparently helpful method to educate involved employees is to train front line staff members to coach their peers on effective use of error prevention techniques [58]. Planning and organizing team meetings to generate a common point of view on patient safety issues are necessary as well.

Recommendation: There is a need for the reduction of barriers to implement patient safety practices in clinical practice. This may be achieved by the encouragement of independent/scientific/patient safety (review) boards in hospitals. Furthermore education initiatives for decision makers in facilities for patient safety should be established as well as continuous trainings for medical staff on patient safety practices. Patient safety affairs should be comprehensively implemented in the curriculum of medical universities.

Classify and measure patient safety at community level, by working with each other and with the Commission

This European Council recommendation cannot be analysed related to the selected programmes as the studies give no information on classifying and measuring at community level.

Recommendation: The lack of adequate information on these points could be explained by two possible scenarios. Either no classification and measuring at community level exists or the studies suffer from deficits in reporting. For the latter case, as mentioned earlier, more transparency and better reporting is needed. In case that countries, regions or other geographical areas lack of cooperation on a community level, more collaboration is strongly recommended, also according to the next point 'working with each other'.

Share knowledge, experience and best practice by working with each other, with the Commission and relevant European and international bodies and develop and promote research on patient safety

As the previous recommendation by the European Council, there is little information on this point. Although not reported it is assumed that sharing knowledge, experience and best practice is common practise in health care institutions (internaly). Anyhow, one of the selected programmes [22] mentions that transparency is widely considered essential to creating and maintaining a high-reliability-organisation. Hospital internal and external transparency has been increased. All data from the preventable harm index which provides a summation of harm events occurring in eight different domains are posted in the intranet. The hospital also posts the rate of serious safety events on its Website (www.nationwidechildrens.org). Raschka et al. [78] show that they share their data with other hospitals participating in the Canadian Nosocomial Infection Surveillance Program. They could reveal that in other hospitals the MRSA rate did not change significantly while in the facilities where the programme has been implemented it decreased dramatically. The decline in rates appeared to coincide with an increase in hand hygiene compliance.

These examples bear that sharing knowledge, experience and best practice can be modelled on other healthcare providers and how important promoting research on these topics is to enhance work on patient safety.

Recommendation: There is more need on transparency of data and patient safety issues. The collaboration on a national as well as on a European level should be forced in this case. Research and publications on patient safety should additionally be fostered. A common database where European countries and facilities have the possibility to show their findings might be helpful. Incentive mechanisms could be a way to enhance research, e.g. with the aid of annually focal points and research prizes.

The European Council recommends to adopt and implement a strategy at the appropriate level for the prevention and control of healthcare associated infections. In light of the conducted analysis strengthening the implementation of prevention and control measures at national or regional level to support the containment of healthcare associated infections as claimed by the European Council can be strongly recommended. Furthermore infection prevention and control at the level of the healthcare institutions in particular by encouraging healthcare institutions can be enhanced. All that should be realised by foster education and training of healthcare workers and providing the technical requirement for the implementation and operation of surveillance systems.

Recommendations on prioritisation of patient safety strategies

In order to make a prioritisation on patient safety programmes a number of key indicators of programmes must be taken into consideration for defining priorities:

- **The prevalence of the problem addressed by the patient safety initiative.** Literature suggests that healthcare-associated infections and adverse drug events are the most common adverse events, and efforts in reducing adverse events should include initiatives to reduce HAI and ADE.

- **The relevance of (easily preventable) adverse events.** Wrong site surgery and death from sepsis are examples for adverse events that incur very high and prevention is possible with reasonable effort. As a result, high potential benefits suggest prioritisation of appropriate patient safety measures.
- **The (established) cost-effectiveness of patient safety practices.** Many patient safety practices are argued to be effective; however published evidence on effectiveness and cost-effectiveness in a clinical setting is rare. Ideally, patient safety programmes should be evaluated in a setting comparable to where implementation is planned.

Furthermore, **relative cost-utility** would be an ideal indicator for prioritising patient safety programmes. For a given AE (group), relevant patient safety interventions could be sorted by cost-utility ratio, i.e. net benefit in terms of QALYs per Euro spent. Unfortunately, a list of programmes sorted by cost-utility based on the publications identified in the literature search on patient safety would not meet reasonable quality criteria. This is due to four main reasons:

- Firstly, the small number of economic evaluations of patient safety programmes means that for most groups of adverse events that only one or even no economic evaluation of a patient safety programme is available.
- Secondly, high variability in prevalence rates and cost estimates of adverse events as well as varying healthcare price level indicators across or even within EU-countries leads to a high range of cost-effectiveness in cost-effectiveness of patient safety programmes[7].
- Thirdly, publications often evaluate interventions that comprise several patient safety practices, hence effects and costs[8] of the intervention cannot be attributed to a single patient safety practice.
- Fourthly, as no evaluation of patient safety programmes uses QALYs or other health-related quality of life indicators as outcome indicator of the intervention; net monetary benefit, i.e. reduction of healthcare expenditures of the hospital is the only indicator that could be used for a comparison of programmes that target different adverse events. Monetary savings of the hospital is however insufficient criteria, and limiting decisions regarding prioritization of patient safety interventions to that indicator would ignore potential improvements in patient welfare that could be realized in programmes that do not result in a positive net financial benefit[9].

Due to scant evidence on patient safety programmes' cost-utility ratios and high variability in baseline prevalence of adverse events among hospitals, prioritization of programmes must follow a process that includes

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7
If price level indicators are applied to cost of both adverse events and patient safety programmes, price level indicators cancel out and do not affect the cost-effectiveness ratio of an intervention.

8
Most publications do not disentangle costs of the intervention, cf. [40].

9
For example, the patient safety programme evaluated by [58] features negative net monetary benefits, but succeeds in reducing harm and mortality in paediatric ICUs.

- Assessment of patient safety deficits in the specific setting
- Identification of appropriate patient safety practices
- Formulation of a precise implementation strategy, including (where appropriate) new guidelines and training of staff
- Economic evaluation of the intervention and dissemination of the evaluation results in academic journals.

7.3.3 Recommendations on further economic assessment of patient safety programmes (Task 13)

After recommendations on the prioritisation, this study also aims to give recommendations on further economic assessment of patient safety programmes. The study will provide, as far as possible, recommendations on how such analyses should be taken forward and how countries can best undertake economic evaluations of investments in patient safety. The first part of this chapter gives recommendations on cost-effectiveness and efficiency indicators, a framework and guidelines for performing economic burden studies and cost-effectiveness analyses in patient safety as well as an assessment of feasibility analysis on periodical surveillance based on economic burden studies and cost-effectiveness and efficiency analyses in patient safety programmes. The second and final part gives concluding thoughts on the economic evaluation of patient safety programmes.

Recommendations on cost-effectiveness and efficiency indicators

The task of cost-effectiveness and efficiency indicators is to inform decisions regarding implementation of programmes and to aid ranking and prioritization of patient safety programmes. To this end, they relate costs of interventions and outcomes of interventions in a one-dimensional measure.

Both costs and outcomes of interventions may be difficult to establish. Regarding costs, publications are often vague, do not itemise total intervention costs or are not specific about which costs are included.

Likewise, difficulties in measuring intervention outcomes entail conceptual difficulties. Generally, the outcome of a patient-safety intervention is to reduce the prevalence of adverse events. The savings associated with that reduction can be deducted from the cost of the adverse event. Several important aspects need to be kept in mind regarding costs of adverse events:

- Publications should be clear about which costs are included – ideally, all costs would be covered, but often, publications only consider monetary costs accrued to the hospital sector.
- Some publications discuss costs of increased mortality or decreased productivity [81]. In general, these costs are difficult to assess but may have a large impact on the total sum of adverse event costs.
- Neglect of non-monetary costs or costs accrued to other stakeholders leads to a distortion in optimal levels of investment in patient safety (see discussion on above).
- In order to compare different types of adverse event, the cost of adverse events and thus savings realized in patient safety interventions should be expressed in Euros and in changes in mortality. Other cost categories, such as reduction in hospital length of stay, are appropriate for the analysis of specific healthcare policy targets.

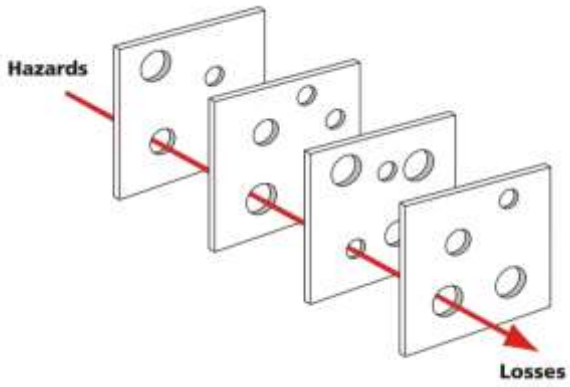
For different adverse events, different units for prevalence and costs may be appropriate. For example, prevalence of wrong site surgery should be measured in terms of per surgical operation and not per hospital day, because only surgical operations involve the risk of wrong site surgery. Healthcare-associated infections, on the other hand, can occur every day of the inpatient stay and should be based on the number of days spent in the hospital.

Transferability of outcomes

Cost-effectiveness indicators report the relationship between costs and outcomes of a specific intervention. In order to evaluate the effects of that intervention in a different setting, costs and outcomes must be transferred. Costs can be transferred by multiplying per patient-day costs, per hospital admission costs

Relative scaling of intervention outcomes seems more plausible than assuming that the same absolute effect, i.e. 10 less cases of postoperative sepsis would occur. This reasoning is in line with the idea of medical errors occurring if a series of balances and checks fail – the Swiss Cheese model [82]. An additional patient safety practice would correspond to an additional layer in Figure 4. Conditional on the distribution of holes in the other Cheese layers being similar in hospitals A and B, the relative effect of the intervention can be expected to be the same.

Figure 4: The Swiss Cheese Model



Source: User Davidmack, Wikimedia Commons

This means that the effect of an intervention decreases with the prevalence of the adverse event that it addresses, and the efficiency of the interventions depends on the current level of prevalence.

Following that logic, the effect of the intervention would be measured in Euro per occurrence of the adverse event in the baseline scenario times the adverse event reduction rate. Costs of the intervention should be measured on the same basis as the baseline rate of adverse events, e.g., per patient-days, hospitalizations or per surgical operations.

Based on costs and occurrence-specific savings, a specific baseline level of occurrence of the adverse event, above which a given intervention is economically efficient, can be calculated.

The best choice for cost-effectiveness or efficiency indicators thus depends on the nature of the adverse event that is to be avoided by the intervention.

Recommendations for a framework and guidelines for performing economic burden studies and cost-effectiveness analyses in patient safety

The main problem in assessing the economic burden of adverse events is poor data availability. Publications that assess the prevalence or the economic burden of adverse events within a country often rely on data from single hospitals, hospital wards or ICUs. Given high variations in prevalence rates of adverse events within and across countries, these figures may not be representative. Furthermore, publications that evaluate the economic burden of adverse events are rare, and for some regions of Europe, no publications were identified.

It is therefore essential to,

- systematically collect data on patient safety related incidents, and
- obtain reliable cost figures for these adverse events in European countries, with a special focus on countries where such studies have not yet been performed.

Several publications discuss which patient safety related indicators should be included in periodic surveillance or how incidence reporting systems should be designed [83-85]. Alternatively, existing diagnosis coding systems could be used to infer some adverse events from routine data [86].

Feasibility analysis on periodical surveillance based on economic burden studies and cost-effectiveness and efficiency analyses in patient safety programmes

Ideally, periodic monitoring of patient safety indicators would assist in setting priorities for patient safety policy. However, data on prevalence of adverse events is not accurate enough to draw conclusions regarding regional differences or trends in patient-safety related indicators.

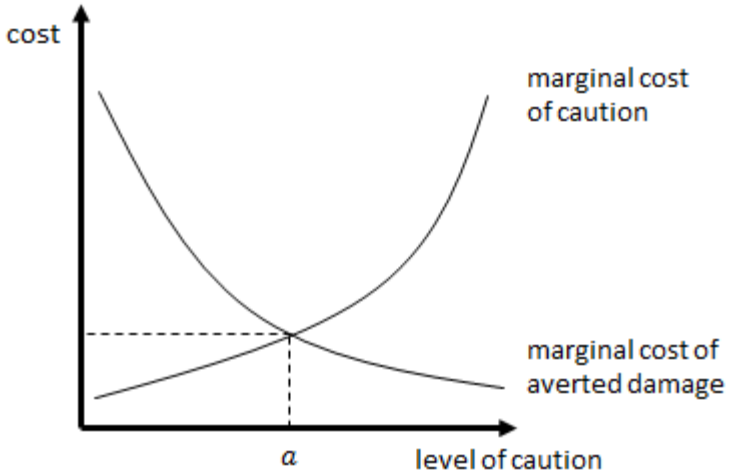
These limitations need to be addressed before systematic assessment of efficiency of patient safety programmes can be performed.

We thus deem any routine/periodical evaluation of economic burden or efficiency of medical care as not feasible.

Final Discussion

According to the well-known formula in risk economics, reduction of risk is efficient if and only if marginal cost of caution is lower than the marginal damage caused by the adverse event. Figure 5 depicts this relation. It is typically assumed that marginal cost of caution increases with the level of caution. The reason for this is straightforward. Consider several possible options to exercise caution. If these are ordered by their efficiency, a rational decision maker would consider implementing the most efficient options first. This results in a decreasing marginal effect per cost unit, as less efficient methods of caution are implemented. For the same reason, marginal damage of the adverse event reduced by exercising caution decreases as the level of caution increases.

Figure 5: Rational level of caution

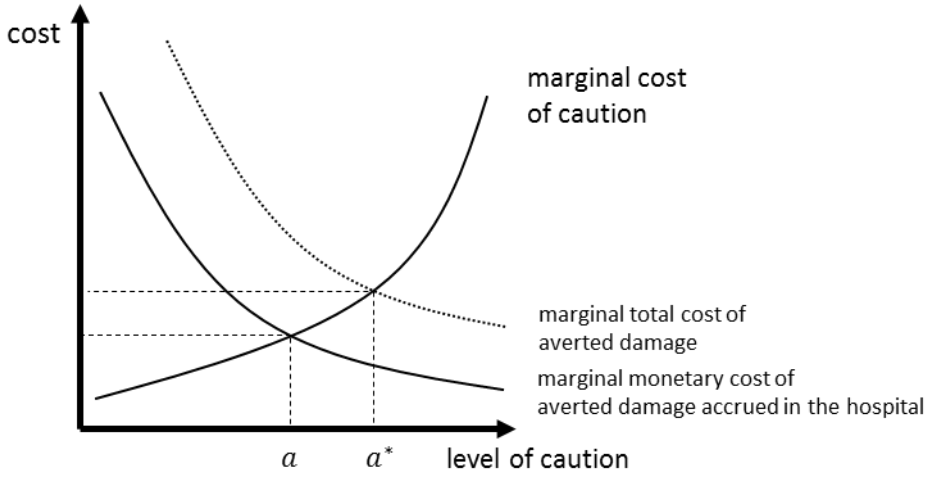


Source: GÖ FP

In Figure 5, the optimal level of caution is given by a. Note that the reasoning behind this illustration puts the distinction between preventable and non-preventable adverse events into perspective. With the necessary amount of caution, every adverse event would be preventable. However, caution exceeding level a is not efficient in that exercising caution incurs more costs than the actual adverse event.

In case of patient safety adverse events, not all costs of damage are covered by the same decision maker, and some costs are non-monetary and therefore difficult to assess. Rational actors only consider costs of caution that accrue to themselves when deciding the optimal level of caution a. If a proportion of costs of adverse events are non-monetary or do not accrue to hospital decision makers, the optimal level of caution a^* is greater than a.

Figure 6: Optimal level of caution (total cost)



Source: GÖ FP

Figure 6 illustrates that exercising caution beyond level a may be efficient if marginal cost of caution is below *total* cost of averted damage, which includes non-monetary

costs and costs accrued to other stakeholders, such as patients or other healthcare providers.

Interventions that aim to bring the level of caution to the optimal level face two types of barriers. Firstly, as many publications have argued consistently, it is difficult to raise awareness for patient safety. Secondly, exercising the socially optimal level of a^* incurs a loss to the hospital operator.

Health policy must thus not only promote patient safety initiatives, but also design and implement ways to reimburse operators for patient safety programmes that are efficient but incur extra costs.

8 Conclusions

With regard to the three main aims of this study we can draw the following conclusions. In general, due to widely spread search terms as "patient safety" and "adverse events" the literature search was a complex task. Identified studies are often based on incomparable study designs and lack of quality. Literature as well as experts give limited information on adverse event groups and more detailed insights in specific adverse events. Therefore an integrated view on adverse events on a macro level is often hindered.

The extraction of figures from literature give prevalence rates for adverse event groups and the degree of preventability, whereat variation in certain groups can't be eliminated entirely. Identified studies deliver no evidence on differences of prevalence of adverse events within Europe. Variation in prevalence rates result from differences within studies and countries or regions, not between them. In general, literature shows that about 4 – 17 percent of patients experience adverse events, whereby 44 – 50 percent of these events are preventable.

The first choice method to calculate the economic burden of adverse events (link prevalence and costs) delivered implausible results due to a lack in adequate cost reporting and incomparable study designs in identified studies. Therefore we executed an alternative approach (share of health expenditure) that delivered feasible results and a range of the economic burden of adverse events for all member states. The bottom-range of estimated direct costs for the public health care sector appear to be a minimum of EUR 2.8 billion, or 0.2 percent of HE, the upper-range costs appear to be a maximum of 84.6 billion or 6 percent of HE following international references. The results from two European references show direct costs of 21.2 billion or 1.5 percent of HE. Anyhow, a mayor finding of this study is that primary studies of epidemiology and costs of adverse events are needed to gain a better grasp of the exact size of economic burden and factors influencing its magnitude. Another question that arises with the economic burden of adverse events is the perspective of costs and who bears the costs in different systems.

Literature search on cost-effective patient safety programmes (or patient safety practices/interventions as referred to in literature) revealed a large number of studies. No studies reported inefficient programmes, only one cost-neutral study was identified. The majority of identified cost-effectiveness studies lack of adequate reporting of effects and/or cost and are therefore not applicable for further analysis in our simulation model. Eleven studies deliver sufficient information, only three out of eleven studies have been conducted in the European Union. These studies focus on labour efforts to prevent pressure ulcers, a theory based approach to implement clinical guidelines and the introduction of electronic medication ordering systems.

A basic simulation model was implemented in Microsoft Excel. It can be used to transfer information from existing cost-effective patient safety programmes to the EU member-states settings. The model calculates costs, effects, cost-effectiveness ratios and savings from selected patient safety programmes on country level for member states. The results of the model are provided in this report, the model itself was provided electronically. Calculation for three selected programmes show EU-wide savings of EUR 300 million for a programme to reduce several HAI, about EUR 2 billion for a programme to reduce pressure ulcers and about EUR 6 billion for implementing an electronic medication ordering system, consisting of a computerized physician order entry system with a Clinical Decision Support System to prevent adverse drug events.

This report aims to give recommendations on the prioritisation of patient safety programmes on the basis of identified studies and calculated cost-efficiency figures. In a first step the Council Recommendations of the European Union are reviewed and matched with the results of the identified literature. In a second step this study gives recommendations on how to choose between two or more patient safety programmes. In order to make a prioritisation on patient safety programmes a number of key indicators of programmes must be taken into consideration for defining priorities. These indicators are the prevalence of the problem, the relevance of (easily preventable) adverse events and the (established) cost-effectiveness of patient safety practices. Furthermore, relative cost-utility would be an ideal indicator for prioritising patient safety programmes, however the application this indicator is problematic to several reasons. Due to scant evidence on patient safety programmes' cost-utility ratios and high variability in baseline prevalence of adverse events among hospitals, this study recommends that prioritization of programmes must follow a process that includes an assessment of patient safety deficits in the specific setting, the identification of appropriate patient safety practices, a formulation of a precise implementation strategy and the incorporation of new guidelines (where appropriate) and training of staff.

Economic assessments of patient safety initiatives face two main challenges. The first one is a conceptual issue that is related to the definition of costs when applied to patient safety. When discussing costs of adverse events, many researchers report expenses of additional medical services that can be attributed to the adverse event, i.e. costs of increased length of stay etc. Costs to the patient are often neglected, because they are typically not included in micro- or macro costing methods. These hidden costs of decreased patient welfare or forgone wages are however also saved if adverse events are prevented. Ignoring them thus distorts economic analyses of patient safety initiatives. The second challenge is the low number and high variability in published figures on prevalence and costs of adverse events. National figures for costs of adverse events are often extrapolated from a very low number of hospitals; and both prevalence rates and costs of adverse events are known to vary substantially across and even within countries. This leads to very broad ranges in estimates of total cost of adverse events. The low number of publications and the high variability of both prevalence rates and costs makes it impossible to assess trends in costs or prevalence of adverse events on national levels. For most European countries we have found no figures on costs of adverse events.

Further improvements in economic appraisal of patient safety thus rely on the precondition of a standardized system for periodic reporting and of adverse events in Europe.

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10 Annexes

Annex 1: Search strategies

Annex 2: Detailed representation of search results

Annex 3: Detailed tables for prevalence and cost results

Annex 4: Cost-effective patient safety programmes

Annex 1: Search strategies

Search strategy Medline, Cochrane, Embase via OVID – Prevalence of adverse events

Search date: 22th April 2015

Databases:

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present,

Embase 1988 to 2015 Week ,

EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 2015,

EBM Reviews - ACP Journal Club 1991 to April 2015,

EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2015,

EBM Reviews - Cochrane Central Register of Controlled Trials April 2015,

EBM Reviews - Cochrane Methodology Register 3rd Quarter 2012,

EBM Reviews - Health Technology Assessment 2nd Quarter 2015,

EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2015

1	(adverse adj5 effect$).ti.	17475
2	(adverse adj5 event$).ti.	18022
3	(adverse adj5 reaction$).ti.	14731
4	side effect$.ti.	26359
5	(drug adj3 toxicit$).ti.	1699
6	(unsafe adj5 care).ti.	59
7	(medica$ adj5 error$).ti.	7560
8	(surgical adj5 error$).ti.	497
9	(medica$ adj5 mistake$).ti.	244
10	(patient$ adj5 safety).ti.	21264
11	(process adj5 error$).ti.	140
12	(administration$ adj5 error$).ti.	555
13	(diagnos$ adj5 error$).ti.	3656
14	(drug$ adj5 error$).ti.	1033
15	(observer adj5 variation$).ti.	628
16	(observer adj5 variabilit$).ti.	702
17	over prescri$.ti.	112
18	(inappropriate adj5 prescri$).ti.	923

19	(healthcare adj5 infection$).ti.	2101
20	(patient$ adj5 harm$).ti.	1388
21	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20	116404
22	exp Medical Errors/td [Trends]	316
23	exp Medical Errors/sn [Statistics & Numerical Data]	5639
24	exp Medical Errors/ut [Utilization]	7
26	exp "Drug-Related Side Effects and Adverse Reactions"/ep [Epidemiology]	6422
28	exp Patient Safety/sn [Statistics & Numerical Data]	282
30	exp Infectious Disease Transmission, Patient-to-Professional/sn [Statistics & Numerical Data]	301
32	exp Infectious Disease Transmission, Professional-to-Patient/sn [Statistics & Numerical Data]	88
34	exp Equipment Contamination/sn [Statistics & Numerical Data]	436
36	exp Drug Contamination/sn [Statistics & Numerical Data]	121
38	exp Epidemiology/	1968511
40	exp Morbidity/	635494
45	22 or 23 or 24 or 26 or 28 or 30 or 32 or 34 or 36	13312
47	38 or 40	2366549
50	45 and 47	3453
58	epidemiolog$.ti.	176844
60	prevalen$.ti.	203476
62	inciden$.ti.	183059
64	58 or 60 or 62	552056
68	21 and 64	2981
79	50 or 68	6275
80	limit 79 to yr="2006 -Current" [Limit not valid in DARE; records were retained]	3987
81	limit 80 to humans [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR, CLCMR; records were retained]	3741
82	limit 81 to (meta analysis or "systematic review") [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CDSR,ACP Journal Club,DARE,CCTR,CLCMR,CLHTA,CLEED; records were retained]	128

83	limit 81 to (meta analysis or "review" or systematic reviews) [Limit not valid in Embase,CDSR, ACP Journal Club,DARE,CCTR,CLCMR,CLHTA,CLEED; records were retained]	634
84	limit 81 to (meta analysis or "review" or "review literature") [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,Embase,CDSR,ACP Journal Club,DARE,CLCMR,CLHTA,CLEED; records were retained]	604
85	82 or 83 or 84	651
86	limit 81 to "reviews (best balance of sensitivity and specificity)" [Limit not valid in CDSR, ACP Journal Club,DARE, CCTR,CLCMR,CLHTA,CLEED; records were retained]	731
87	85 or 86	763
88	remove duplicates from 87	**669**
89	limit 81 to (clinical trial or randomized controlled trial or controlled clinical trial or multicenter study) [Limit not valid in CDSR, ACP Journal Club,DARE, CLCMR,CLHTA,CLEED; records were retained]	459
90	limit 81 to (clinical trial, all or clinical trial or comparative study or controlled clinical trial or evaluation studies or guideline or practice guideline or pragmatic clinical trial or randomized controlled trial or validation studies or clinical trial,all) [Limit not valid in Embase,CDSR,ACP Journal Club,DARE,CCTR,CLCMR,CLHTA,CLEED; records were retained]	667
91	limit 81 to (clinical trial or comparative study or controlled clinical trial or guideline or multicenter study or practice guideline or randomized controlled trial) [Limit not valid in Embase,CDSR, ACP Journal Club,DARE,CLCMR,CLHTA,CLEED; records were retained]	626
92	89 or 90 or 91	698
93	remove duplicates from 92	**616**

Search strategy Cinahl via EBSCOhost Research Databases – Prevalence of adverse events

Search date: 22th April 2015

Databases: Cinahl via EBSCOhost Research Databases

S88	S85 OR S86 OR S87	89
S87	S51 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Clinical Trial, Nursing Interventions, Randomized Controlled Trial, Research, Statistics, Tables/Charts Eingrenzen durch SubjectGeographic0: - continental europe	18

S86	S51 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Clinical Trial, Nursing Interventions, Randomized Controlled Trial, Research, Statistics, Tables/Charts Eingrenzen durch SubjectGeographic0: - uk & ireland	71
S85	S51 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Clinical Trial, Nursing Interventions, Randomized Controlled Trial, Research, Statistics, Tables/Charts Eingrenzen durch SubjectGeographic0: - europe	87
S84	((S51 OR S71) AND (S82 OR S83)) AND (S82 OR S83)	**15**
S83	S51 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Meta Analysis, Meta Synthesis, Practice Guidelines, Review, Systematic Review Eingrenzen durch SubjectGeographic0: - uk & ireland	13
S82	S51 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Meta Analysis, Meta Synthesis, Practice Guidelines, Review, Systematic Review Eingrenzen durch SubjectGeographic0: - europe	13
S81	S51 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Clinical Trial, Nursing Interventions, Randomized Controlled Trial, Research, Statistics, Tables/Charts	305
S80	S51 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Meta Analysis, Meta Synthesis, Practice Guidelines, Review, Systematic Review	38
S79	S51 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231;	775

	MEDLINE-Datensätze ausschließen	
S78	S51 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231	1,899
S77	S51 OR S71	2,589
S71	S35 AND S70	470
S70	S53 OR S54 OR S56 OR S58 OR S59	64,960
S59	TI morbidity	3,237
S58	TI epidemiolog#	5,541
S56	TI inciden#	2,471
S54	TI prevalen#	484
S53	(MH "Morbidity+")	56,275
S51	S36 OR S37 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50	2,161
S50	(MH "Medication Reconciliation/UT/TD/SN/EV")	8
S49	(MH "Observer Bias+/TD/UT/EV")	4
S48	(MH "Drug Contamination/EV/TD/UT")	9
S47	(MH "Drug Contamination/EP")	1
S46	(MH "Equipment Contamination/UT/TD/EV")	78
S45	(MH "Equipment Contamination/EP")	12
S44	(MH "Disease Transmission, Patient-to-Professional/UT/TD/EV")	2
S43	(MH "Disease Transmission, Patient-to-Professional/EP")	5
S42	(MH "Disease Transmission, Professional-to-Patient/UT/TD/EV")	2

S41	(MH "Disease Transmission, Professional-to-Patient/EP")	2
S40	(MH "Patient Safety+/EV/TD/UT")	1,363
S39	(MH "Patient Safety+/EP")	698
S38	(MH "Adverse Health Care Event+")	30,547
S37	(MH "Adverse Health Care Event+/TD/UT/EV")	812
S36	(MH "Adverse Health Care Event+/EP")	698
S35	S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34	15,754
S34	TI treatment N5 error#	41
S33	TI patient N5 harm#	147
S32	TI healthcare N5 infection#	615
S31	TI inappropriate N5 prescription	20
S30	TI inappropriate N5 prescribing	126
S29	TI inappropriate N5 prescri#	0
S28	TI over prescription	65
S27	TI over prescribing	31
S26	TI over prescri#	0
S25	TI observer N5 variabilit#	25
S24	TI observer N5 variation#	17
S23	TI drug# N5 error#	410
S22	TI diagnosis N5 error#	33

S21	TI diagnostic N5 error#	116
S20	TI diagnos# N5 error#	1
S19	TI administration# N5 error#	175
S18	TI process# N5 error#	32
S17	TI patient# N5 safety	6,709
S16	TI medica# N5 mistake#	66
S15	TI surgical N5 error#	62
S14	TI medica# N5 error#	987
S13	TI unsafe N5 care	32
S12	TI drug N5 toxicit#	86
S11	TI side effect#	1,701
S10	TI adverse N5 reaction#	1,010
S9	TI adverse N5 event#	2,479
S8	TI adverse N5 effect#	1,190

Search strategy Scopus – Prevalence of adverse events

Search date: 22th April 2015

Database: Scopus

(((((INDEXTERMS (treatment errors)) OR (INDEXTERMS (diagnostic errors))) OR ((INDEXTERMS (health care errors)) OR (INDEXTERMS (inappropriate prescribing)) OR (INDEXTERMS (adverse drug event)) OR (INDEXTERMS (medical errors)) OR (INDEXTERMS (medication reconciliation))) OR ((INDEXTERMS (observer variation)) OR (INDEXTERMS (observer bias)) OR (INDEXTERMS (drug contamination)) OR (INDEXTERMS (equipment contamination)) OR (INDEXTERMS (patient safety))) OR ((INDEXTERMS (disease transmission, patient-to-professional)) OR (INDEXTERMS (disease transmission, professional-to-patient)) OR (INDEXTERMS (adverse health care event)) OR (INDEXTERMS (adverse effect)) OR (INDEXTERMS (adverse event)))) AND ((INDEXTERMS (cost analysis)) OR ((TITLE (cost*)) OR (TITLE (economic*

w5 impact*)) OR (TITLE (economic* W/5 impact*)) OR (TITLE (economic* W/5 burden*)) OR (TITLE (cost* W/5 burden*)) OR (TITLE (economic* W/5 evaluation*)) OR (TITLE (cost* W/5 analys*))))) OR ((((TITLE (adverse W/5 effect*)) OR (TITLE (adverse W/5 event*)) OR (TITLE (adverse W/5 reaction*)) OR (TITLE (side effect*)) OR (TITLE (drug W/5 toxicit*)) OR (TITLE (unsafe W/5 care)) OR (TITLE (medica* W/5 error*)) OR (TITLE (surgical W/5 error*))) OR ((TITLE (medica* W/5 mistake*)) OR (TITLE (patient* W/5 safety)) OR (TITLE (process* W/5 error*)) OR (TITLE (administration* W/5 error*)) OR (TITLE (diagnos* W/5 error*)) OR (TITLE (drug* W/5 error*)) OR (TITLE (observer W/5 variation*))) OR ((TITLE (observer W/5 variabilit*)) OR (TITLE (over prescri*)) OR (TITLE (inappropriate W/5 prescri*)) OR (TITLE (healthcare W/5 infection*)) OR (TITLE (patient* W/5 harm*)) OR (TITLE (treatment W/5 error*))))) AND ((INDEXTERMS (cost analysis)) OR ((TITLE (cost*)) OR (TITLE (economic* w5 impact*)) OR (TITLE (economic* W/5 impact*)) OR (TITLE (economic* W/5 burden*)) OR (TITLE (cost* W/5 burden*)) OR (TITLE (economic* W/5 evaluation*)) OR (TITLE (cost* W/5 analys*)))))) AND NOT (INDEX (medl)) AND (LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006)) AND (LIMIT-TO (DOCTYPE , "re")) AND (LIMIT-TO (EXACTKEYWORD , "Priority journal")) AND (LIMIT-TO (AFFILCOUNTRY , "United States") OR LIMIT-TO (AFFILCOUNTRY , "Canada"))

74 document results

((TITLE (epidemiolog*)) OR (TITLE (prevalen*)) OR (TITLE (inciden*)) OR (INDEXTERMS (epidemiology)) OR (INDEXTERMS (prevalence)) OR (INDEXTERMS (incidence))) AND ((((TITLE (adverse W/5 effect*)) OR (TITLE (adverse W/5 event*)) OR (TITLE (adverse W/5 reaction*)) OR (TITLE (side effect*)) OR (TITLE (drug W/5 toxicit*)) OR (TITLE (unsafe W/5 care)) OR (TITLE (medica* W/5 error*)) OR (TITLE (surgical W/5 error*))) OR ((TITLE (medica* W/5 mistake*)) OR (TITLE (patient* W/5 safety)) OR (TITLE (process* W/5 error*)) OR (TITLE (administration* W/5 error*)) OR (TITLE (diagnos* W/5 error*)) OR (TITLE (drug* W/5 error*)) OR (TITLE (observer W/5 variation*))) OR ((TITLE (observer W/5 variabilit*)) OR (TITLE (over prescri*)) OR (TITLE (inappropriate W/5 prescri*)) OR (TITLE (healthcare W/5 infection*)) OR (TITLE (patient* W/5 harm*)) OR (TITLE (treatment W/5 error*)))) OR (((INDEXTERMS (treatment errors)) OR (INDEXTERMS (diagnostic errors))) OR ((INDEXTERMS (health care errors)) OR (INDEXTERMS (inappropriate prescribing)) OR (INDEXTERMS (adverse drug event)) OR (INDEXTERMS (medical errors)) OR (INDEXTERMS (medication reconciliation))) OR ((INDEXTERMS (observer variation)) OR (INDEXTERMS (observer bias)) OR (INDEXTERMS (drug contamination)) OR (INDEXTERMS (equipment contamination)) OR (INDEXTERMS (patient safety))) OR ((INDEXTERMS (disease transmission, patient-to-professional)) OR (INDEXTERMS (disease transmission, professional-to-patient)) OR (INDEXTERMS (adverse health care event)) OR (INDEXTERMS (adverse effect)) OR (INDEXTERMS (adverse event)))))) AND NOT (INDEX (medl)) AND (LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006)) AND (LIMIT-TO (

EXACTKEYWORD , "Human") OR LIMIT-TO (EXACTKEYWORD , "Humans")) AND (LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (EXACTKEYWORD , "Priority journal")) AND (LIMIT-TO (AFFILCOUNTRY , "United States") OR LIMIT-TO (AFFILCOUNTRY , "Canada"))

248 documents

History Search Terms (((TITLE (epidemiolog*)) OR (TITLE (prevalen*)) OR (TITLE (inciden*)) OR (INDEXTERMS (epidemiology)) OR (INDEXTERMS (prevalence)) OR (IND EXTERMS (incidence))) AND ((((TITLE (adverse W/5 effect*)) OR (TITLE (fect*)) OR (TITLE (adverse W/5 event*)) OR (TITLE (adverse W/5 reaction*)) OR (TITLE (side effect*)) OR (TITLE (drug W/5 toxicit*)) OR (TIT icit*)) OR (TITLE (unsafe W/5 care)) OR (TITLE (medica* W/5 error*)) OR (TITLE (surgical W/5 error*))) OR ((TITLE (medica* W/5 mistake*)) OR (TITLE (patient* W/5 safety)) OR (TITLE (process* W/5 error*)) OR (TITLE (administration* W/5 error*)) OR (TITLE (diagnos* W/5 error*)) OR (TITLE (drug* W/5 error*)) OR (TITLE (observer W/5 variation*))) OR ((TITLE (observer W/5 v tion*))) OR ((TITLE (observer W/5 variabilit*)) OR (TITLE (over prescri*)) OR (TITLE (inappropriate W/5 prescri*)) OR (TITLE (healthcare W/5 scri*)) OR (TITLE (healthcare W/5 infection*)) OR (TITLE (patient* W/5 ha tion*)) OR (TITLE (patient* W/5 harm*)) OR (TITLE (treatment W/5 error*)))) OR (((INDEXTERMS (treatment errors)) OR (INDEXTERMS (diagnostic rors)) OR (INDEXTERMS (diagnostic errors))) OR ((INDEXTERMS (health ca rors))) OR ((INDEXTERMS (health care errors)) OR (INDEXTERMS (inappro rors)) OR (INDEXTERMS (inappropriate prescribing)) OR (INDEXTERMS (adve ing)) OR (INDEXTERMS (adverse drug event)) OR (INDEXTERMS (medical e rrors)) OR (INDEXTERMS (medication reconciliation))) OR ((INDEXTERMS (o tion))) OR ((INDEXTERMS (observer variation)) OR (INDEXTERMS (observer tion)) OR (INDEXTERMS (observer bias)) OR (INDEXTERMS (drug contamination)) OR (INDEXTERMS (equipment contamination)) OR (INDEXTERMS (pa tion)) OR (INDEXTERMS (patient safety))) OR ((INDEXTERMS (disease tran ty))) OR ((INDEXTERMS (disease transmission, patient-to-professional)) OR (INDEXTERMS (disease transmission, professional-to-patient)) OR (INDEXTERMS (adverse health care event)) OR (INDEXTERMS (tient)) OR (INDEXTERMS (adverse health care event)) OR (INDEXTERMS (a dverse effect)) OR (INDEXTERMS (adverse event)))))) AND NOT (INDEX (medline)) AND (LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006)) AND (LIMIT-man") OR LIMIT-TO (EXACTKEYWORD , "Humans")) AND (LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (AFFILCOUNTRY , "United Kingdom") OR LIMIT-TO (AFFILCOUNTRY , "Germany") OR LIMIT-TO (AFFILCOUNTRY , "Italy") OR LIMIT-TO (AFFILCOUNTRY , "France") OR LIMIT-TO (AFFILCOUNTRY , "Netherlands") OR LIMIT-TO (AFFILCOUNTRY , "Spain") OR LIMIT-TO (AFFILCOUNTRY , "Switzerland") OR LIMIT-TO (AFFILCOUNTRY , "Sweden") OR LIMIT-TO (AFFILCOUNTRY , "Belgium") OR LIMIT-TO (AFFILCOUNTRY , "Denmark") OR LIMIT-TO (AFFILCOUNTRY , "Nor-

way") OR LIMIT-TO (AFFILCOUNTRY , "Austria") OR LIMIT-TO (AFFILCOUNTRY , "Ireland") OR LIMIT-TO (AFFILCOUNTRY , "Greece") OR LIMIT-TO (AFFILCOUNTRY , "Poland") OR LIMIT-TO (AFFILCOUNTRY , "Finland") OR LIMIT-TO (AFFILCOUNTRY , "Czech Republic") OR LIMIT-TO (AFFILCOUNTRY , "Portugal")) AND (LIMIT-TO (EXACTKEYWORD , "Priority journal"))

236 document results

History Search Terms
(((TITLE (epidemiolog*)) OR (TITLE (prevalen*)) OR (TITLE (inciden*)) OR (INDEXTERMS (epidemiology)) OR (INDEXTERMS (prevalence)) OR (IND EXTERMS (incidence))) AND ((((TITLE (adverse W/5 effect*)) OR (TITLE (fect*)) OR (TITLE (adverse W/5 event*)) OR (TITLE (adverse W/5 reaction*)) OR (TITLE (side effect*)) OR (TITLE (drug W/5 toxicit*)) OR (TIT icit*)) OR (TITLE (unsafe W/5 care)) OR (TITLE (medica* W/5 error*)) OR (TITLE (surgical W/5 error*))) OR ((TITLE (medica* W/5 mistake*)) OR (TITLE (patient* W/5 safety)) OR (TITLE (process* W/5 error*)) OR (TITLE (administration* W/5 error*)) OR (TITLE (diagnos* W/5 error*)) OR (TITLE (drug* W/5 error*)) OR (TITLE (observer W/5 variation*))) OR ((TITLE (observer W/5 v tion*))) OR ((TITLE (observer W/5 variabilit*)) OR (TITLE (over prescri*)) OR (TITLE (inappropriate W/5 prescri*)) OR (TITLE (healthcare W/5 scri*)) OR (TITLE (healthcare W/5 infection*)) OR (TITLE (patient* W/5 ha tion*)) OR (TITLE (patient* W/5 harm*)) OR (TITLE (treatment W/5 error*)))) OR (((INDEXTERMS (treatment errors)) OR (INDEXTERMS (diagnostic rors)) OR (INDEXTERMS (diagnostic errors))) OR ((INDEXTERMS (health ca rors))) OR ((INDEXTERMS (health care errors)) OR (INDEXTERMS (inappro rors)) OR (INDEXTERMS (inappropriate prescribing)) OR (INDEXTERMS (adve ing)) OR (INDEXTERMS (adverse drug event)) OR (INDEXTERMS (medical e rrors)) OR (INDEXTERMS (medication reconciliation))) OR ((INDEXTERMS (o tion))) OR ((INDEXTERMS (observer variation)) OR (INDEXTERMS (observer tion)) OR (INDEXTERMS (observer bias)) OR (INDEXTERMS (drug contamination)) OR (INDEXTERMS (equipment contamination)) OR (INDEXTERMS (pa tion)) OR (INDEXTERMS (patient safety))) OR ((INDEXTERMS (disease tran ty))) OR ((INDEXTERMS (disease transmission, patient-to-professional)) OR (INDEXTERMS (disease transmission, professional-to-patient)) OR (INDEXTERMS (adverse health care event)) OR (INDEXTERMS (tient)) OR (INDEXTERMS (adverse health care event)) OR (INDEXTERMS (a dverse effect)) OR (INDEXTERMS (adverse event)))))) AND NOT (INDEX (medline)) AND (LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006)) AND (LIMIT-man") OR LIMIT-TO (EXACTKEYWORD , "Humans")) AND (LIMIT-TO (DOCTYPE , "re")) AND (LIMIT-TO (AFFILCOUNTRY , "United Kingdom") OR LIMIT-TO (AFFILCOUNTRY , "Italy") OR LIMIT-TO (AFFILCOUNTRY , "Germany") OR LIMIT-TO (AFFILCOUNTRY , "France") OR LIMIT-TO (AFFILCOUNTRY , "Spain") OR LIMIT-TO (AFFILCOUNTRY , "Canada") OR LIMIT-TO (AFFILCOUNTRY , "Netherlands") OR LIMIT-

TO (AFFILCOUNTRY , "India") OR LIMIT-TO (AFFILCOUNTRY , "Switzerland") OR LIMIT-TO (AFFILCOUNTRY , "Belgium") OR LIMIT-TO (AFFILCOUNTRY , "Sweden") OR LIMIT-TO (AFFILCOUNTRY , "Austria") OR LIMIT-TO (AFFILCOUNTRY , "Denmark") OR LIMIT-TO (AFFILCOUNTRY , "Greece") OR LIMIT-TO (AFFILCOUNTRY , "Poland") OR LIMIT-TO (AFFILCOUNTRY , "Ireland") OR LIMIT-TO (AFFILCOUNTRY , "Norway") OR LIMIT-TO (AFFILCOUNTRY , "Finland") OR LIMIT-TO (AFFILCOUNTRY , "Portugal") OR LIMIT-TO (AFFILCOUNTRY , "Czech Republic") OR LIMIT-TO (AFFILCOUNTRY , "Slovakia")) AND (LIMIT-TO (EXACTKEYWORD , "Priority journal"))

124 document results

Search strategy Medline, Cochrane, Embase via OVID – Costs

Search date: 20th April 2015

Databases:

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present,

Embase 1988 to 2015 Week ,

EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 2015,

EBM Reviews - ACP Journal Club 1991 to April 2015,

EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2015,

EBM Reviews - Cochrane Central Register of Controlled Trials April 2015,

EBM Reviews - Cochrane Methodology Register 3rd Quarter 2012,

EBM Reviews - Health Technology Assessment 2nd Quarter 2015,

EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2015

1	(adverse adj5 effect$).ti.	17469
2	(adverse adj5 event$).ti.	18011
3	(adverse adj5 reaction$).ti.	14727
4	side effect$.ti.	26356
5	(drug adj3 toxicit$).ti.	1699
6	(unsafe adj5 care).ti.	59
7	(medica$ adj5 error$).ti.	7558
8	(surgical adj5 error$).ti.	497
9	(medica$ adj5 mistake$).ti.	244
10	(patient$ adj5 safety).ti.	21247
11	(process adj5 error$).ti.	140
12	(administration$ adj5 error$).ti.	555
13	(diagnos$ adj5 error$).ti.	3652

14	(drug$ adj5 error$).ti.	1032
15	(observer adj5 variation$).ti.	628
16	(observer adj5 variabilit$).ti.	702
17	over prescri$.ti.	112
18	(inappropriate adj5 prescri$).ti.	923
19	(healthcare adj5 infection$).ti.	2098
20	(patient$ adj5 harm$).ti.	1388
21	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20	116355
22	exp "Costs and Cost Analysis"/	452307
23	cost$.ti.	198173
24	(economic$ adj3 impact).ti.	4431
25	(economic$ adj3 burden).ti.	2504
26	(cost adj3 burden).ti.	370
27	(economic$ adj5 evaluation$).ti.	10397
28	(cost$ adj5 analys$).ti.	23691
29	exp Medical Errors/ec [Economics]	675
30	exp "Drug-Related Side Effects and Adverse Reactions"/ec [Economics]	156
31	exp Patient Harm/ec [Economics]	4
32	exp Patient Safety/ec [Economics]	110
33	exp Infectious Disease Transmission, Patient-to-Professional/ec [Economics]	23
34	exp Infectious Disease Transmission, Professional-to-Patient/ec [Economics]	18
35	exp Equipment Contamination/ec [Economics]	72
36	exp Drug Contamination/ec [Economics]	19
37	29 or 30 or 31 or 32 or 33 or 34 or 35 or 36	1042
38	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20	116355
39	22 or 23 or 24 or 25 or 26 or 27 or 28	544773
40	38 and 39	2500
41	37 or 40	3387
42	limit 41 to yr="2006 -Current" [Limit not valid in DARE; records were retained]	2171

43	limit 42 to humans [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	1936
44	remove duplicates from 43	1629
45	limit 44 to (clinical trial or randomized controlled trial or controlled clinical trial or multicenter study) [Limit not valid in CDSR,ACP Journal Club,DARE,CLCMR,CLHTA,CLEED; records were retained]	108
46	limit 44 to (evidence based medicine or consensus development or meta analysis or outcomes research or "systematic review") [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CDSR,ACP Journal Club,DARE,CCTR,CLCMR,CLHTA,CLEED; records were retained]	140
47	limit 44 to (clinical trial, all or clinical trial or comparative study or controlled clinical trial or evaluation studies or guideline or journal article or meta analysis or multicenter study or observational study or practice guideline or pragmatic clinical trial or randomized controlled trial or "review" or systematic reviews or validation studies or clinical trial,all) [Limit not valid in Embase,CDSR,ACP Journal Club,DARE,CCTR,CLCMR,CLHTA,CLEED; records were retained]	761
48	limit 44 to (clinical trial or comparative study or controlled clinical trial or guideline or journal article or meta analysis or multicenter study or practice guideline or randomized controlled trial or "review" or "review literature") [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,Embase,CDSR,ACP Journal Club,DARE,CLCMR,CLHTA,CLEED; records were retained]	759
49	45 or 46 or 47 or 48	848
50	limit 44 to (meta analysis or "systematic review") [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,CDSR,ACP Journal Club,DARE,CCTR,CLCMR,CLHTA,CLEED; records were retained]	102
51	limit 44 to (meta analysis or "review" or systematic reviews) [Limit not valid in Embase,CDSR,ACP Journal Club,DARE,CCTR,CLCMR,CLHTA,CLEED; records were retained]	271
52	limit 44 to (meta analysis or "review" or "review literature") [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,Embase,CDSR,ACP Journal Club,DARE,CLCMR,CLHTA,CLEED; records were retained]	248
53	50 or 51 or 52	328

Search strategy Cinahl via EBSCOhost Research Databases – Costs

Search date: 20th April 2015

Databases: Cinahl via EBSCOhost Research Databases

S81	S34 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Meta Analysis, Meta Synthesis, Systematic Review	**3**
S80	S34 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; Publikationstyp: Meta Analysis, Meta Synthesis, Systematic Review	30
S79	S76 OR S77 OR S78	**35**
S78	S34 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Academic Journal, Clinical Trial, Journal Article, Meta Analysis, Meta Synthesis, Nursing Diagnoses, Nursing Interventions, Practice Guidelines, Randomized Controlled Trial, Research, Review, Statistics, Systematic Review, Tables/Charts Eingrenzen durch SubjectGeographic0: - uk & ireland	32
S77	S34 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Academic Journal, Clinical Trial, Journal Article, Meta Analysis, Meta Synthesis, Nursing Diagnoses, Nursing Interventions, Practice Guidelines, Randomized Controlled Trial, Research, Review, Statistics, Systematic Review, Tables/Charts Eingrenzen durch SubjectGeographic0: - continental europe	3
S76	S34 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Academic Journal, Clinical Trial, Journal Article, Meta Analysis, Meta Synthesis, Nursing Diagnoses, Nursing Interventions, Practice Guidelines, Randomized Controlled Trial, Research, Review, Statistics, Systematic Review, Tables/Charts Eingrenzen durch SubjectGeographic0: - europe	35

S75	S34 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; MEDLINE-Datensätze ausschließen; Publikationstyp: Academic Journal, Clinical Trial, Journal Article, Meta Analysis, Meta Synthesis, Nursing Diagnoses, Nursing Interventions, Practice Guidelines, Randomized Controlled Trial, Research, Review, Statistics, Systematic Review, Tables/Charts	**214**
S74	S34 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231; Publikationstyp: Academic Journal, Clinical Trial, Journal Article, Meta Analysis, Meta Synthesis, Nursing Diagnoses, Nursing Interventions, Practice Guidelines, Randomized Controlled Trial, Research, Review, Statistics, Systematic Review, Tables/Charts	547
S73	S34 OR S71 Eingrenzungen - Erscheinungsdatum: 20060101-20151231	547
S72	S34 OR S71	720
S71	S62 AND S70	407
S70	S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69	66,211
S69	TI cost# N5 analys#	2
S68	TI economic# N5 evaluation#	824
S67	TI cost# N5 burden#	113
S66	TI economic# N5 burden#	237
S65	TI economic# N5 impact#	487
S64	TI cost#	22,654
S63	(MH "Costs and Cost Analysis+")	57,477
S62	S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61	15,754

S61	TI treatment N5 error#	41
S60	TI patient N5 harm#	147
S59	TI healthcare N5 infection#	615
S58	TI inappropriate N5 prescription	20
S57	TI inappropriate N5 prescribing	126
S56	TI inappropriate N5 prescri#	0
S55	TI over prescription	65
S54	TI over prescribing	31
S53	TI over prescri#	0
S52	TI observer N5 variabilit#	25
S51	TI observer N5 variation#	17
S50	TI drug# N5 error#	410
S49	TI diagnosis N5 error#	33
S48	TI diagnostic N5 error#	116
S47	TI diagnos# N5 error#	1
S46	TI administration# N5 error#	175
S45	TI process# N5 error#	32
S44	TI patient# N5 safety	6,709
S43	TI medica# N5 mistake#	66
S42	TI surgical N5 error#	62
S41	TI medica# N5 error#	987

S40	TI unsafe N5 care	32
S39	TI drug N5 toxicit#	86
S38	TI side effect#	1,701
S37	TI adverse N5 reaction#	1,010
S36	TI adverse N5 event#	2,479
S35	TI adverse N5 effect#	1,190
S34	S18 OR S19 OR S21 OR S24 OR S26 OR S27 OR S29 OR S32	374
S32	(MH "Medication Reconciliation/EC")	3
S29	(MH "Observer Bias+/EC")	0
S27	(MH "Drug Contamination/EC")	3
S26	(MH "Equipment Contamination/EC")	7
S24	(MH "Disease Transmission, Patient-to-Professional/EC")	2
S21	(MH "Disease Transmission, Professional-to-Patient/EC")	1
S19	(MH "Patient Safety+/EC")	359
S18	(MH "Adverse Health Care Event+/EC")	313

Search strategy Scopus – Costs

Search date: 20th April 2015

Database: Scopus

(((((INDEXTERMS(Treatment Errors)) OR (INDEXTERMS(Diagnostic Errors))) OR ((INDEXTERMS(Health Care Errors)) OR (INDEXTERMS(Inappropriate Prescribing)) OR (INDEXTERMS(adverse drug event)) OR (INDEXTERMS(Medical Errors)) OR (INDEXTERMS(Medication Reconciliation))) OR ((INDEXTERMS(Observer Variation)) OR (INDEXTERMS(Observer Bias)) OR (INDEXTERMS(Drug Contamination)) OR (INDEXTERMS(Equipment Contamination)) OR (INDEXTERMS(patient safety))) OR ((INDEXTERMS(Disease Transmission, Patient-to-Professional)) OR (INDEXTERMS(Disease Transmission, Professional-to-Patient)) OR (INDEXTERMS(Adverse Health Care Event)) OR (INDEXTERMS(adverse effect)) OR

(INDEXTERMS(adverse event)))) AND ((INDEXTERMS(cost analysis)) OR ((TITLE(cost*)) OR (TITLE(economic* W5 impact*)) OR (TITLE(economic* W/5 impact*)) OR (TITLE(economic* W/5 burden*)) OR (TITLE(cost* W/5 burden*)) OR (TITLE(economic* W/5 evaluation*)) OR (TITLE(cost* W/5 analys*))))) OR ((((TITLE(adverse W/5 effect*)) OR (TITLE(adverse W/5 event*)) OR (TITLE(adverse W/5 reaction*)) OR (TITLE(side effect*)) OR (TITLE(drug W/5 toxicit*)) OR (TITLE(unsafe W/5 care)) OR (TITLE(medica* W/5 error*)) OR (TITLE(surgical W/5 error*))) OR ((TITLE(medica* W/5 mistake*)) OR (TITLE(patient* W/5 safety)) OR (TITLE(process* W/5 error*)) OR (TITLE(administration* W/5 error*)) OR (TITLE(diagnos* W/5 error*)) OR (TITLE(drug* W/5 error*)) OR (TITLE(observer W/5 variation*))) OR ((TITLE(observer W/5 variabilit*)) OR (TITLE(over prescri*)) OR (TITLE(inappropriate W/5 prescri*)) OR (TITLE(healthcare W/5 infection*)) OR (TITLE(patient* W/5 harm*)) OR (TITLE(treatment W/5 error*)))) AND ((INDEXTERMS(cost analysis)) OR ((TITLE(cost*)) OR (TITLE(economic* W5 impact*)) OR (TITLE(economic* W/5 impact*)) OR (TITLE(economic* W/5 burden*)) OR (TITLE(cost* W/5 burden*)) OR (TITLE(economic* W/5 evaluation*)) OR (TITLE(cost* W/5 analys*)))))) AND NOT (INDEX(medline)) AND (LIMIT-TO(PUBYEAR,2015) OR LIMIT-TO(PUBYEAR,2014) OR LIMIT-TO(PUBYEAR,2013) OR LIMIT-TO(PUBYEAR,2012) OR LIMIT-TO(PUBYEAR,2011) OR LIMIT-TO(PUBYEAR,2010) OR LIMIT-TO(PUBYEAR,2009) OR LIMIT-TO(PUBYEAR,2008) OR LIMIT-TO(PUBYEAR,2007) OR LIMIT-TO(PUBYEAR,2006)) AND (LIMIT-TO(DOCTYPE,"re")) AND (LIMIT-TO(AFFILCOUNTRY,"United Kingdom") OR LIMIT-TO(AFFILCOUNTRY,"Italy") OR LIMIT-TO(AFFILCOUNTRY,"Germany") OR LIMIT-TO(AFFILCOUNTRY,"Spain") OR LIMIT-TO(AFFILCOUNTRY,"Netherlands") OR LIMIT-TO(AFFILCOUNTRY,"France") OR LIMIT-TO(AFFILCOUNTRY,"Switzerland") OR LIMIT-TO(AFFILCOUNTRY,"Belgium") OR LIMIT-TO(AFFILCOUNTRY,"Sweden") OR LIMIT-TO(AFFILCOUNTRY,"Greece") OR LIMIT-TO(AFFILCOUNTRY,"Denmark") OR LIMIT-TO(AFFILCOUNTRY,"Austria") OR LIMIT-TO(AFFILCOUNTRY,"Ireland") OR LIMIT-TO(AFFILCOUNTRY,"Poland") OR LIMIT-TO(AFFILCOUNTRY,"Finland") OR LIMIT-TO(AFFILCOUNTRY,"Norway") OR LIMIT-TO(AFFILCOUNTRY,"Czech Republic") OR LIMIT-TO(AFFILCOUNTRY,"Portugal") OR LIMIT-TO(AFFILCOUNTRY,"Slovenia"))

297 document results

(((((INDEXTERMS(Treatment Errors)) OR (INDEXTERMS(Diagnostic Errors))) OR ((INDEXTERMS(Health Care Errors)) OR (INDEXTERMS(Inappropriate Prescribing)) OR (INDEXTERMS(adverse drug event)) OR (INDEXTERMS(Medical Errors)) OR (INDEXTERMS(Medication Reconciliation))) OR ((INDEXTERMS(Observer Variation)) OR (INDEXTERMS(Observer Bias)) OR (INDEXTERMS(Drug Contamination)) OR (INDEXTERMS(Equipment Contamination)) OR (INDEXTERMS(patient safety))) OR ((INDEXTERMS(Disease Transmission, Patient-to-Professional)) OR (INDEXTERMS(Disease Transmission, Professional-to-Patient)) OR (INDEXTERMS(Adverse Health Care Event)) OR (INDEXTERMS(adverse effect)) OR (INDEXTERMS(adverse event)))) AND ((INDEXTERMS(cost analysis)) OR ((TITLE(cost*)) OR (TITLE(economic* W5 impact*)) OR (TITLE(economic* W/5 impact*)) OR (TITLE(economic* W/5 burden*)) OR (TITLE(cost* W/5 burden*)) OR (TITLE(economic* W/5 evaluation*)) OR (TITLE(cost* W/5 analys*))))) OR ((((TITLE(adverse W/5 effect*)) OR (TITLE(adverse W/5 event*)) OR (TITLE(adverse W/5 reaction*)) OR (TITLE(side effect*)) OR (TITLE(drug W/5 toxicit*)) OR (TITLE(unsafe W/5 care)) OR (TITLE(medica* W/5 error*)) OR (TITLE(surgical W/5 error*))) OR ((TITLE(medica* W/5 mistake*)) OR (TITLE(patient* W/5 safety)) OR (TITLE(process* W/5 error*)) OR (TITLE(administration* W/5 error*)) OR (TITLE(diagnos* W/5 error*)) OR (TITLE(drug* W/5 error*)) OR (TITLE(observer W/5 variation*))) OR ((TITLE(observer W/5 variabilit*)) OR (TITLE(over prescri*)) OR (TITLE(inappropriate W/5 prescri*)) OR (TITLE(healthcare W/5 infection*)) OR

(TITLE(patient* W/5 harm*)) OR (TITLE(treatment W/5 error*)))) AND ((INDEXTERMS(cost analysis)) OR ((TITLE(cost*)) OR (TITLE(economic* W5 impact*)) OR (TITLE(economic* W/5 impact*)) OR (TITLE(economic* W/5 burden*)) OR (TITLE(cost* W/5 burden*)) OR (TITLE(economic* W/5 evaluation*)) OR (TITLE(cost* W/5 analys*)))))) AND NOT (INDEX(medline)) AND (LIMIT-TO(PUBYEAR,2015) OR LIMIT-TO(PUBYEAR,2014) OR LIMIT-TO(PUBYEAR,2013) OR LIMIT-TO(PUBYEAR,2012) OR LIMIT-TO(PUBYEAR,2011) OR LIMIT-TO(PUBYEAR,2010) OR LIMIT-TO(PUBYEAR,2009) OR LIMIT-TO(PUBYEAR,2008) OR LIMIT-TO(PUBYEAR,2007) OR LIMIT-TO(PUBYEAR,2006)) AND (LIMIT-TO(DOCTYPE,"ar")) AND (LIMIT-TO(AFFILCOUNTRY,"United Kingdom") OR LIMIT-TO(AFFILCOUNTRY,"Germany") OR LIMIT-TO(AFFILCOUNTRY,"Netherlands") OR LIMIT-TO(AFFILCOUNTRY,"Italy") OR LIMIT-TO(AFFILCOUNTRY,"France") OR LIMIT-TO(AFFILCOUNTRY,"Spain") OR LIMIT-TO(AFFILCOUNTRY,"Switzerland") OR LIMIT-TO(AFFILCOUNTRY,"Belgium") OR LIMIT-TO(AFFILCOUNTRY,"Sweden") OR LIMIT-TO(AFFILCOUNTRY,"Denmark") OR LIMIT-TO(AFFILCOUNTRY,"Austria") OR LIMIT-TO(AFFILCOUNTRY,"Greece") OR LIMIT-TO(AFFILCOUNTRY,"Ireland") OR LIMIT-TO(AFFILCOUNTRY,"Norway") OR LIMIT-TO(AFFILCOUNTRY,"Poland") OR LIMIT-TO(AFFILCOUNTRY,"Finland") OR LIMIT-TO(AFFILCOUNTRY,"Portugal"))

383 document results

Search strategy Medline, Cochrane, Embase via OVID – Patient Safety Programmes

Search date: 23rd June 2015

Databases:

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present,

Embase 1988 to 2015 Week ,

EBM Reviews - Cochrane Database of Systematic Reviews 2005 to June 2015,

EBM Reviews - ACP Journal Club 1991 to June 2015,

EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2015,

EBM Reviews - Cochrane Central Register of Controlled Trials June 2015,

EBM Reviews - Cochrane Methodology Register 3rd Quarter 2012,

EBM Reviews - Health Technology Assessment 2nd Quarter 2015,

EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2015

1	(patient$ adj5 safety adj5 program$).ab.	1123
2	(patient$ adj5 safety adj5 program$).ti.	288
3	(patient$ adj5 safety adj5 project$).ti.	60
4	(patient$ adj5 safety adj5 project$).ab.	330
5	(safety adj5 management adj5 program$).ab.	206
6	(safety adj5 management adj5 program$).ti.	57
7	(safety adj5 management adj5 project$).ab.	31
8	(safety adj5 management adj5 project$).ti.	4
9	(risk$ adj5 management adj5 program$).ab.	1308
10	(risk$ adj5 management adj5 program$).ti.	326
11	(risk$ adj5 management adj5 project$).ab.	161
12	(risk$ adj5 management adj5 project$).ti.	46

13	exp Cost-Benefit Analysis/	142789
14	exp "Costs and Cost Analysis"/	458912
15	exp Program Evaluation/	69343
16	exp evaluation studies/	228044
17	cost$.ti.	202394
18	cost$.ab.	831475
19	(cost$ adj5 effective$).ti.	57215
20	(cost$ adj5 effective$).ab.	204418
21	(cost$ adj5 efficien$).ab.	25317
22	(cost$ adj5 efficien$).ti.	1973
23	(cost$ adj5 benefit$).ab.	41805
24	(cost$ adj5 benefit$).ti.	8721
25	efficien$.ab.	1264635
26	efficien$.ti.	149652
27	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12	3590
28	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26	2636252
29	27 and 28	759
30	remove duplicates from 29	523
31	limit 30 to yr="2006 -Current" [Limit not valid in DARE; records were retained]	376
32	limit 31 to humans [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	**313**

Search strategy Cinahl via EBSCOhost Research Databases – Patient Safety Programmes

Search date: 23rd June 2015

Databases: Cinahl via EBSCOhost Research Databases

S31	S13 AND S28 Limiters - Published Date: 20060101-20151231; Exclude MEDLINE records	**23**
S30	S13 AND S28 Limiters - Published Date: 20060101-20151231	107
S29	S13 AND S28	151
S28	S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27	155,753
S27	TI efficien*	3,868
S26	AB efficien*	21,403
S25	AB (cost* N5 benefit*)	3,066

S24	TI (cost* N5 benefit*)	863
S23	TI (cost* N5 efficien*)	232
S22	AB (cost* N5 efficien*)	1,548
S21	AB (cost* N5 effective*)	13,857
S20	TI (cost* N5 effective*)	5,288
S19	TI cost*	23,926
S18	AB cost*	54,203
S17	(MH "Evaluation Research+")	18,774
S16	(MH "Program Evaluation")	19,678
S15	(MH "Costs and Cost Analysis+")	58,149
S14	(MH "Cost Benefit Analysis")	14,548
S13	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12	692
S12	TI (risk* N5 management N5 project*)	10
S11	AB (risk* N5 management N5 project*)	19
S10	AB (risk* N5 management N5 program*)	165
S9	TI (risk* N5 management N5 program*)	76
S8	TI (safety N5 management N5 project*)	1
S7	AB (safety N5 management N5 project*)	3
S6	AB (safety N5 management N5 program*)	26
S5	TI (safety N5 management N5 program*)	24
S4	TI (patient* N5 safety N5 project*)	27
S3	AB (patient* N5 safety N5 project*).	59
S2	AB (patient* N5 safety N5 program*).	213
S1	TI (patient* N5 safety N5 program*).	134

Search strategy Scopus – Patient Safety Programmes

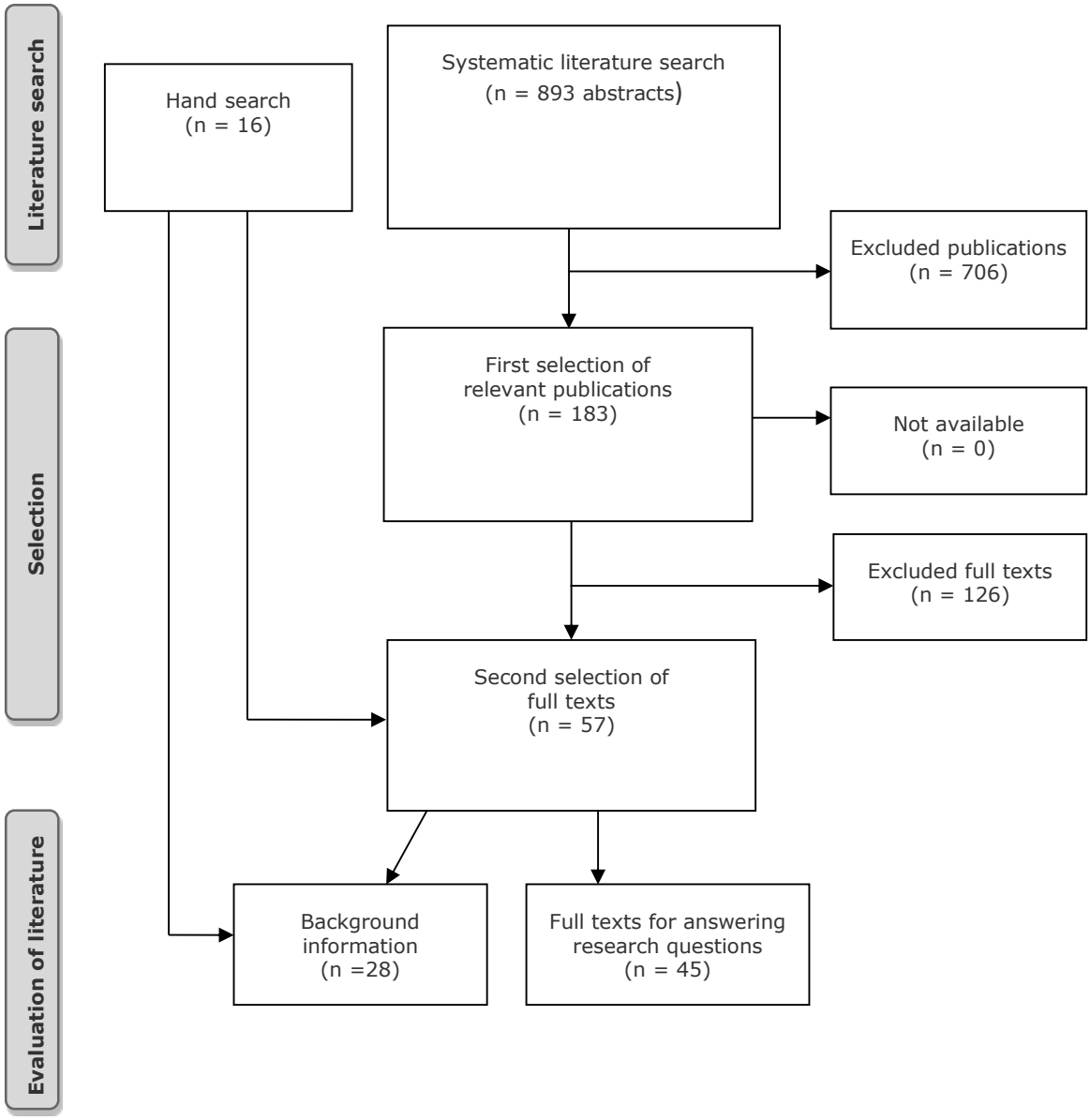
Search date: 23rd June 2015

Database: Scopus

History Search Terms
gram*) OR TITLE (patient* W/5 safety W/5 project*) OR TITLE (safety W/5 ject*) OR TITLE (safety W/5 management W/5 program*) OR TITLE (safety gram*) OR TITLE (safety W/5 management W/5 project*) OR TITLE (risk* W ject*) OR TITLE (risk* W/5 management W/5 program*) OR TITLE (risk* W/ gram*) OR TITLE (risk* W/5 management W/5 project*)) AND ((TITLE (cos ject*)) AND ((TITLE (cost*) OR TITLE (cost* W/5 effective*) OR TITLE (co tive*) OR TITLE (cost* W/5 efficien*) OR TITLE (cost* W/5 bene-fit*)) OR (INDEXTERMS ("Evaluation studies") OR INDEXTERMS ("Program Evaluation") OR INDEXTERMS ("Cost-Benefit Analysis") OR INDEXTERMS ("Costs and Cost Analysis")))) AND NOT (INDEX (medline)) AND (LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006)) **31 document results**

Annex 2: Detailed representation of search results

Figure 7: Graphical illustration of the selection process for prevalence of adverse events



Source: GÖ FP

Included studies from systematic search for answering research questions (prevalence)

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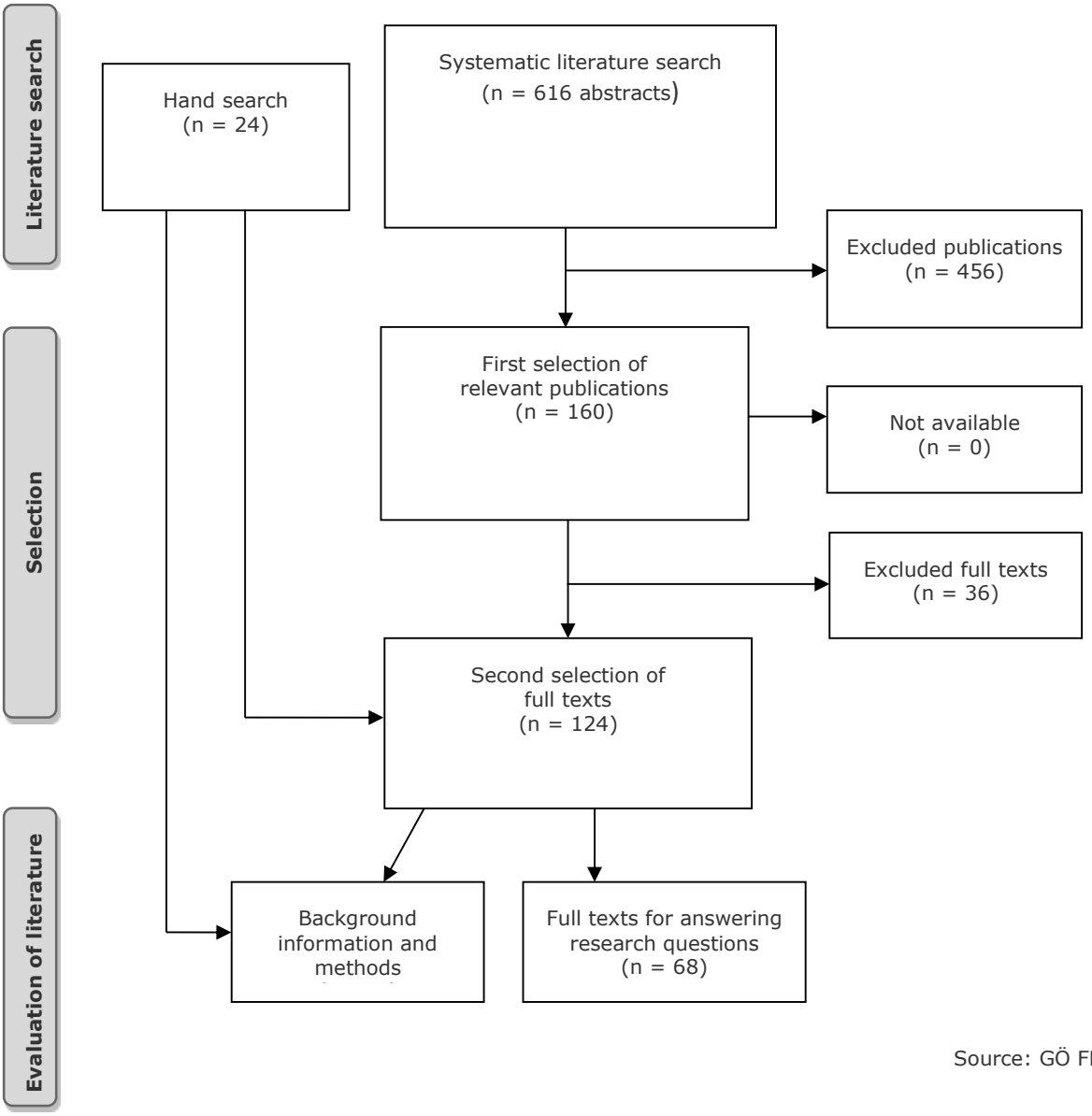
Figure 8: Graphical illustration of the selection process for cost of adverse events



Source: GÖ FP

Included studies of systematic search for answering research questions (costs)

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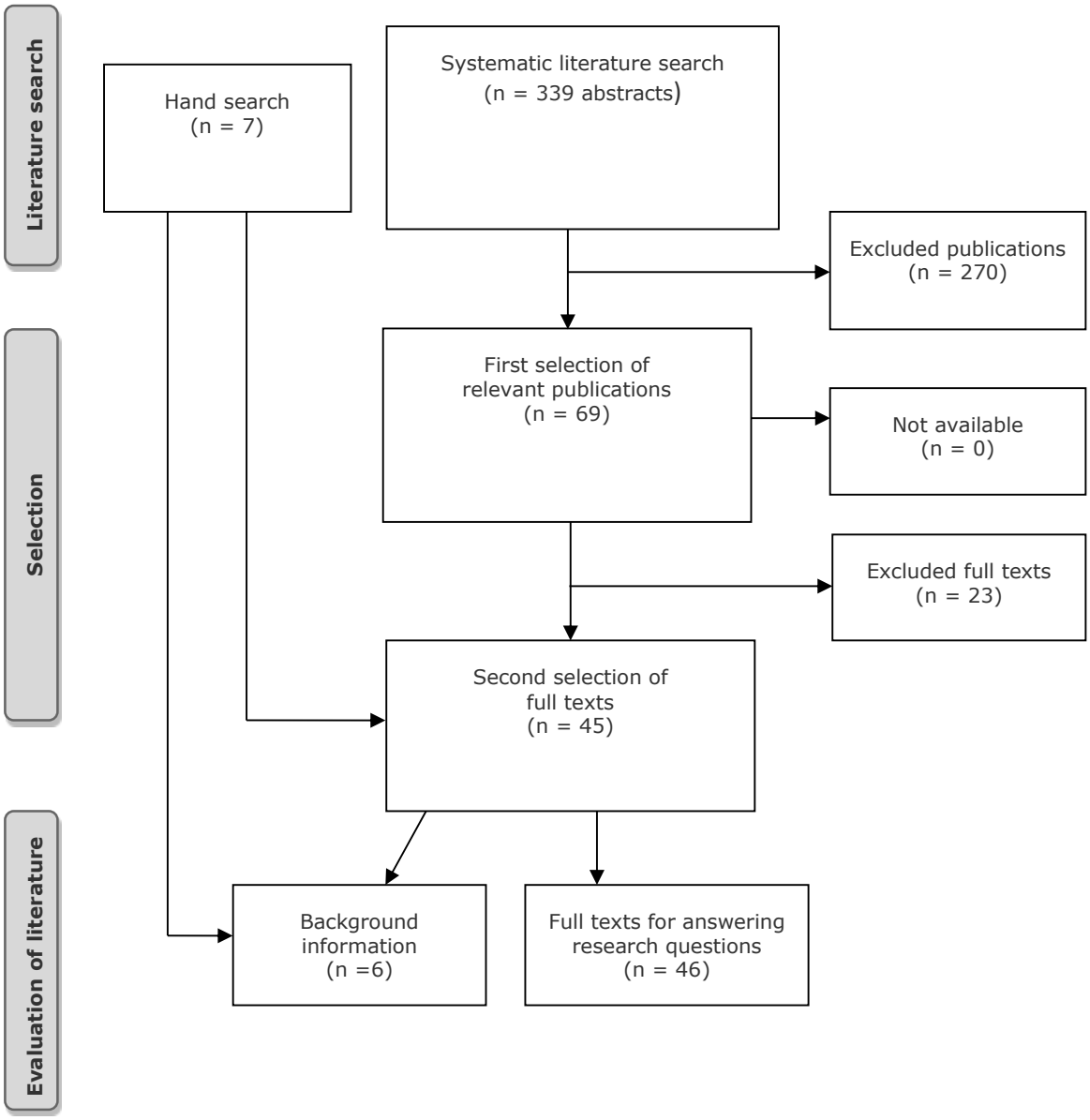
Figure 9: Graphical illustration of the selection process for patient safety programmes



Source: GÖ FP

Included studies of systematic search for answering research questions (patient safety programmes)

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Annex 3: Detailed tables for prevalence and cost results

Epidemiology of adverse Events

Table 14: Prevalence rates for adverse event groups and degree of preventability, if reported

General adverse events					
Region	**Range**	**Figure**		**Preventable**	**Reference**
Int.*	4–16.6%		of patients experience adverse events	50%	Johnstone [87]
Int.		9.2%	of inhospital patients experience adverse events	44%	De Vries [51]
HIC*		14.2%	of patients experience adverse events	-	Jha [32]
LMIC*		12.7%	of patients experience adverse events	-	Jha [32]
Spain		6.84%	of patients experience adverse events	-	Allue [50]
UK		10.8%	of patients experience adverse events	47%	Vincent [53]
Overall	4%–16.6%		of patients experience adverse events		
Acute care / surgical					
Region	**Range**	**Figure**		**Preventable**	**Reference**
UK		14.1%	of patients in surgery had adverse event	41%	Vincent [53]
Adverse drug events					
Region	**Range**	**Figure**		**Preventable**	**Reference**
Int.	8.6-28.3%	19.6%	of opportunities for error	-	Keers [88]
Int.	0.4–13%		of patients experience ADE	11-38%	Thomsen [89]
HIC	2.7–7.2%		of patients experience ADE	-	Jha [32]
LMIC	0.6–5.2%		of patients experience ADE	-	Jha [32]
Australia	5–10%		of patients experience ADE	-	WHO Sum of Evidence [26]
Canada		7.5%	of patients experience ADE	37%	WHO Sum of Evidence [26]
Overall	0.4–28.3%		of patients experience ADE		
Healthcare-associated infections					
Region	**Range**	**Figure**		**Preventable**	**Reference**
EU		10.65	per 1000 patient days	-	Wagenlehner [90]
Belgium		5.9%	of patients in hosp. have infections		Trybou [91]
Europe	3.5–14.8%		of patients in hosp. have infections	-	Who Sum of E. & ECDC [26, 92, 93]

Scotland	8.8-10.2%	9.5%	of patients in hosp. have infections	-	Reilly [94]
USA	4.5–7.7%		of patients in hosp. have infections	-	Magill [95]
Overall	3.5–14.8%		of patients in hosp. have infections		
			Falls		
Region	**Range**	**Figure**		**Preventable**	**Reference**
HIC	0.3–2%		of patients in hospitals suffer from falls	-	Jha [32]
LMIC	1.3%–2%		of patients in hospitals suffer from falls	-	Jha [32]
USA		6.6	per 1000 admissions	-	WHO Sum of Evidence [26]
Ireland		1.32	per 1000 bed days	-	WHO Sum of Evidence [26]
Overall	0.3-2%		of patients in hospitals suffer from falls		
			adverse events due to unsafe blood products		
Region	**Range**	**Figure**		**Preventable**	**Reference**
USA		0.37%	of apheresis collections lead to AE	-	Yuan [96]
			Errors in diagnosis		
Region	**Range**	**Figure**		**Preventable**	**Reference**
USA	2–5%		rate of misdiagnoses, radiology	-	WHO Sum of Evidence [26]
USA	1,4%–5,8%		rate of errors in reading pathology slides	-	WHO Sum of Evidence [26]
USA		5.3%	rate of errors in reading radiology slides that had impact	-	WHO Sum of Evidence [26]
Overall	1.4%–5.8%		rate of misdiagnosis		
			Decubitus ulcers		
Region	**Range**	**Figure**		**Preventable**	**Reference**
HIC	0.8–4.7%		of hospital inpatiensts have decubitus ulcers	-	Jha [32]
LMIC	0,8–4,7%		of hospital inpatiensts have decubitus ulcers	-	Jha [32]
Spain		0,3%	of hospital inpatiensts have decubitus ulcers	-	Allue [50]
USA		10%	of hospital inpatiensts have decubitus ulcers	-	WHO Sum of Evidence [26]
USA		15%	of hospital inpatiensts have decubitus ulcers	-	WHO Sum of Evidence [26]
Germany		11%	of hospital inpatiensts have decubitus ulcers	-	WHO Sum of Evidence [26]
Sweden		12%	of hospital inpatiensts have decubitus ulcers	-	WHO Sum of Evidence [26]
Overall	**0.3–15%**		**of hospital inpatiensts have decubitus ulcers**		

Source: GÖ FP

Costs of adverse events

Table 15: Costs of generic adverse events

References	type of AE	type of cost	area	figure
Baker 2004	generic	death toll	Canada	9,250–23,750k /y
Etchells 2012	generic	cost per case	n/a	CAD 6,124–12,648 /n
Frontier Economics Ltd 2014	generic	monetary nationwide (avoidable excess costs)	UK	GBP 1–2.5m /y
Jha 2012	generic	DALYs per year	HIC	42.7m /y
Kohn 2000	generic	death toll	USA	44–98k /y
Kohn 2000	generic	monetary nationwide (avoidable excess costs), preventable only	USA	17–29b /y
Kohn 2000	generic	% of HE	USA	4–6%
Kohn 2000	generic	monetary nationwide	USA	USD 37.6-50b /y
Milna 2007	generic	monetary nationwide	UK	GBP 2b /y
Milna 2007	generic	death toll	Canada	15–20k /y
Milna 2007	generic	monetary nationwide	Canada	CAD 300m–1.5b /y
Mittmann 2012	generic	cost per case	n/a	USD 4,571; 10,074 /n
Sousa 2014	generic	monetary nationwide (avoidable excess costs due to excess LOS)	UK	1b /y
Sousa 2014	generic	% of HE (preventable AE)	Netherlands	1%
Sousa 2014	generic	excess LOS	n/a	10d /n
Sousa 2014	generic	excess LOS	USA	10.7d /n
Vlayen 2011	generic	total excess LOS	USA	2.4m d
Vlayen 2011	generic	monetary nationwide	USA	USD 9.3b /y
Vlayen 2011	generic	death toll	USA	35,291 /y

Source: GÖ FP

Table 16: Costs of adverse events in acute care

References	type of AE	type of cost	area	figure
Butt 2012	injuries related to med. errors	monetary nationwide	USA	USD 19.5b /y
Butt 2012	injuries related to med. errors	cost per case	USA	USD 13k /n
Butt 2012	transplant pats.	cost per case	USA	USD 55,654 /n
Butt 2012	transplant pats.	monetary nationwide	USA	USD 286m /y
Ehsani 2007	cardiac surgery AE	cost per case	Australia	AUD 5,751 /n
Ehsani 2007	cardiac surgery AE	monetary nationwide	Australia	AUD 45,855m /y
Nichter 2008	failed extubation in PICU	excess LOS	n/a	9.9 d
Jha 2008	Venous thromboembolism	DALYs lost	HIC	2,282,000
Rivard 2008	postop. hemorrhage or hematoma	cost per case	USA	USD 7,863 /n
Rivard 2008	postop. hemorrhage or hematoma	excess LOS	USA	3.9 d
Rivard 2008	postop. hemorrhage or hematoma	excess mortality	USA	4.3
Rivard 2008	postop. respiratory failure	cost per case	USA	USD 39,745 /n
Rivard 2008	postop. respiratory failure	excess LOS	USA	9.1 d
Rivard 2008	postop. respiratory failure	excess mortality	USA	21.8
Rivard 2008	postop. pulmonary embolism or deep-vein thrombosis	cost per case	USA	USD 7,205 /n
Rivard 2008	postop. pulmonary embolism or deep-vein thrombosis	excess LOS	USA	5.4 d
Rivard 2008	postop. pulmonary embolism or deep-vein thrombosis	excess mortality	USA	6.6
Rivard 2008	postop. sepsis	cost per case	USA	USD 31,264 /n
Rivard 2008	postop. sepsis	excess LOS	USA	10.1 d
Rivard 2008	postop. sepsis	excess mortality	USA	21.9
Rivard 2008	postop. wound dehiscence	cost per case	USA	USD 18,905 /n
Rivard 2008	postop. wound dehiscence	excess LOS	USA	9.4 d
Rivard 2008	postop. wound dehiscence	excess mortality	USA	9.6
Rivard 2008	Accidental puncture or laceration	cost per case	USA	USD 3,359 /n
Rivard 2008	Accidental puncture or laceration	excess LOS	USA	1.3 d
Rivard 2008	Accidental puncture or laceration	excess mortality	USA	2.2

Source: GÖ FP

Table 17: Costs of adverse drug events

References	type of AE	type of cost	area	figure
Buck 2009	potentially inappropriate medication	nationwide total excess costs	USA	USD 7.2b /y
Chang 2011	ADE	injuries or deaths	USA	770k /y
Chang 2011	ADE	nationwide total excess costs	USA	USD 1.5–5.5b /y
Chiatti 2012	inappr. medication	excess hospitalisation costs	USA	USD 2b /y
Chiatti 2012	preventable drug events	nationwide total	USA	USD 100b /y
Chiatti 2012	ADE	cost per case	USA	USD 1,310 /n
Chiatti 2012	preventable ADE	cost per case	USA	USD 1,983 /n
Chiatti 2012	ADE and inappr. Prescr. In patients older than 65	nationwide total costs	Canada	USD 35.7m /y
Chiatti 2012	ADE hospitalization	cost per case	Spain	EUR 4,844 /n
Chiatti 2012	ADE hospitalization	cost per case	Netherlandsx	EUR 2,507 /n
Chiatti 2012	inappr. prescription	cost per case	Ireland	EUR 824; 321 /m
Chiatti 2012	inappr. PPI use	nationwide total	USA	USD 233,944 (over-the-counter); 1,655,252 (presrc)
Compagni 2008	ADE	cost per case	various	EUR 793–2,380; 5,505; 1,329; 2,116; 1,887; 3,725; 1,000 /n
Gurwitz	ADE	cost per case	elderly	USD 2,000 /n
Jha	ADE	DALYs lost	HIC	779k
Etchells 2012	ADE	cost per case	n/a	CAD 4,028 /n
Etchells 2012	ADE in medical and surgical cases	cost per case	n/a	CAD 402; 632 /n

Source: GÖ FP

Table 18: Costs of falls

References	type of AE	type of cost	area	figure
de Jong 2013	falls	nationwide monetary	USA	USD 2.82b /y
de Jong 2013	hip fracture	cost per case	USA	USD 20k /y
de Jong 2013	falls	death toll	USA	19.7k
de Jong 2013	falls	death toll	USA	12.9k
de Jong 2013	falls	in percent of total HE	USA	0.85–1.5%
de Jong 2013	falls	nationwide monetary	USA	USD 19.2b /y
de Jong 2013	falls	nationwide monetary	USA	USD 28.2b /y
Jha 2008	falls	incremental costs	n/a	+71%
Jha 2008	falls	incremental LOS	n/a	+61%
Jha 2013	falls	DALYs lost	HIC	27k
Jackson 2011	falls w. fractured neck of femur	cost per case	Australia	AUD 11,991 /n

Source: GÖ FP

Table 19: Costs of adverse events related to unsafe blood products

References	type of AE	type of cost	area	figure
Khamassi 2008	unsafe injections	life years lost	worldwide	26m /y
Khamassi 2008	unsafe injections	direct medical costs	worldwide	USD 535m /y
Tingle 2011	unsafe injections	direct medical costs	worldwide	USD 535m /y

Source: GÖ FP

Table 20: Costs of adverse events related to diagnostic errors

References	type of AE	type of cost	area	figure
Lee 2013	diagnostic errors	death toll	USA	40–80k /y
Lee 2013	radiology errors	monetary nationwide	USA	USD 38b /y

Source: GÖ FP

Table 21: Costs of healthcare-associated infections

Reference	type of infection	type of cost	area	figure
Raschka 2013	Bacteremia	costs per case	Canada	CAD 10,547 /n
Mittmann 2012	BSI	costs per case	Europe	USD 2,604–22,414 /n
Mittmann 2012	BSI	costs per case	USA	USD 21,013 /n
Mittmann 2012	BSI	costs per case	paediatric ICU	USD 49,663 /n
Mittmann 2012	BSI	costs per case	paediatric ICU	USD 71,384 /n
Calfee 2012	CABSI	costs per case	USA	USD 6,461–29,156 /n
Raschka 2013	CABSI	costs per case	Canada	CAD 18,098 /n
Reserach Committee of the Society of Healthcare Epidemiology of America 2010	CABSI	costs per case	USA	USD 10–20k /n
Stone 2009	CABSI	costs per case	USA	USD 36,441 /n
Umscheid 2011	CABSI	costs per case	USA	USD 21,400–110,800 /n
Jha 2012	CABSI	DALYs lost	HIC	1,126k /y
Rodriguez-Paz 2008	CABSI	death toll	USA	28k /y
O'Horo 2012	CABSI	monetary nationwide (payer)	USA	USD 16,550 /n
O'Horo 2012	CABSI	mortality rate	USA	15%–20%
Calfee 2012	CAUTI	costs per case	USA	USD 749–1,007 /n
Stone 2009	CAUTI	costs per case	USA	USD 1,006 /n
Umscheid 2011	CAUTI	costs per case	USA	USD 1,200–4,700 /n
Jha 2012	CAUTI	DALYs lost	HIC	402k /y
Bouza 2012	CDI	costs per case	N/A	EUR 4,067–9,276 /n
Raschka 2013	CDI	costs per case	Canada	CAD 2,552 /n
Reserach Committee of the Society of Healthcare Epidemiology of America 2010	CDI	costs per case	USA	USD 5k /n
Barbut 2011	CDI	death toll	USA	15–20k /y
Bouza 2012	CDI	incremental LOS / case	N/A	1–3 w
Barbut 2011	CDI	monetary nationwide	USA	3.2b /y
Bouza 2012	CDI	monetary nationwide (payer)	USA	USD 433m /y
Bouza 2012	CDI	monetary nationwide (societal)	USA	USD 797m /y
Stone 2009	CDI associated diarrhea	costs per case	USA	USD 4,5k /n
Ghantoji 2009	CDI in special populations	costs per case	USA	USD 6,242–90,664 /n

Reference	type of infection	type of cost	area	figure
Mittmann 2012	generic HAI	costs per case	N/A	USD 2,132–15,018 /n
Allegranzi 2008	generic HAI	death toll	UK and France	5,000 /y
Calfee 2012	generic HAI	death toll	USA	98k /n
Hooven 2014	generic HAI	death toll	USA	90k /y
Reserach Committee of the Society of Healthcare Epidemiology of America 2010	generic HAI	death toll	USA	100k /y
Stone 2009	generic HAI	death toll	USA	100k /y
Allegranzi 2008	generic HAI	incremental LOS / case	USA	10–15 d
Allegranzi 2008	generic HAI	monetary nationwide	USA	7–8b /y
Allegranzi 2008	generic HAI	monetary nationwide	Europe	EUR 800m /y
Allegranzi 2008	generic HAI	monetary nationwide	Turkey	USD 48m /y
Reserach Committee of the Society of Healthcare Epidemiology of America 2010	generic HAI	monetary nationwide	USA	USD 20b /d
Calfee 2012	generic HAI	monetary nationwide (payer)	USA	USD 28–45b /y
Stone 2009	generic HAI	monetary nationwide (payer)	USA	USD 28–45b /y
Mittmann 2012	inf. of nosoc. resp. tract syncytical virus	costs per case	n/a	USD 13,083 /n
Mittmann 2012	MRSA	costs per case	implants patients	USD 81,843 /n
Raschka 2013	MRSA col.	costs per case	Canada	CAD 1,584 /n
Raschka 2013	MRSA inf.	costs per case	Canada	CAD 16,692 /n
Vandijck 2008	MRSA inf.	costs per case	n/a	USD 27,083 /n
Vandijck 2008	MRSA inf.	costs per case	n/a	USD 16,575 /n
Vandijck 2008	MRSA inf.	costs per case	n/a	USD 5,878 /n
Vandijck 2008	MRSA inf.	incremental LOS / case	n/a	12 d; 16 d
Stone 2009	MRSA inf. vs. nMRSA inf.	incremental cost per case	USA	USD 4k /n
Vandijck 2008	nMRSA inf.	costs per case	n/a	USD 9,661 /n
Vandijck 2008	nMRSA inf.	costs per case	n/a	USD 2,073 /n
Vandijck 2008	nMRSA inf.	incremental LOS / case	n/a	4 d, 11 d
Vandijck 2008	nMRSA inf.	incremental LOS / case	n/a	11 d
Vandijck 2008	nMRSA inf.	total costs (not only AE) per case	n/a	USD 12,862 /n
Mittmann 2012	nosoc. Pneumo-nia	costs per case	n/a	USD 856–23,624 /n

Reference	type of infection	type of cost	area	figure
Mittmann 2012	nosoc. respiratory tract inf.	costs per case	n/a	USD 3,476; 4,509 /n
Mittmann 2012	nosoc. Rotavirus inf.	costs per case	paediatric ICU	USD 3,591 /n; 2,210 /n
Mittmann 2012	nosoc. Rotavirus inf.	monetary nationwide	paediatric ICU	USD 11,952,319 /y
Mittmann 2012	nosoc. sepsis	costs per case	n/a	USD 33,872 /n
Mittmann 2012	nosoc. sepsis	costs per case	ICU	USD 44,187 /n
Mittmann 2012	nosoc. UTI	costs per case	n/a	USD 788–18,717 /n
Umscheid 2011	preventable CABSI	monetary nationwide	USA	USD 960m–18.2b /y
Umscheid 2011	preventable CAUTI	monetary nationwide	USA	USD 115m–1.82b /y
Umscheid 2011	preventable SSI	monetary nationwide	USA	USD 116m–345m /y
Umscheid 2011	preventable VAP	monetary nationwide	USA	USD 2.19–3.17b /y
Ghantoji 2009	primary CDI	costs per case	USA	USD 2,871–4,846 /n
Ghantoji 2009	primary CDI	costs per case	non-USA	USD 5,243–8,570 /n
Ghantoji 2009	recurrent CDI	costs per case	USA	USD 13,655–18,067 /n
Ghantoji 2009	recurrent CDI	costs per case	non-USA	USD 13,655 /n
Calfee 2012	SSI	costs per case	USA	USD 11,087–34,670 /n
Cruickshank 2009	SSI	costs per case	USA	USD 3,089 /n
Raschka 2013	SSI	costs per case	Canada	CAD 14,035 /n
Stone 2009	SSI	costs per case	USA	USD 25,546 /n
Umscheid 2011	SSI	costs per case	USA	USD 5,600–12,900 /n
Young 2014	SSI	costs per case	USA	USD 3,937–20k /n
Young 2014	SSI	costs per case	USA	USD 22.1k /n
Mittmann 2012	SSI	costs per case	n/a	USD 1,105; 2,604; 14,422 /n
Cruickshank 2009	SSI	incremental LOS / case	USA	6.5 d
Young 2014	SSI	incremental LOS nationwide	USA	8,000 /y
Raschka 2013	UTI	costs per case	Canada	CAD 862 /n
Calfee 2012	VAP	costs per case	USA	USD 14,806–28,508 /n
Dickson 2009	VAP	costs per case	UK	GBP 7k /n
Stone 2009	VAP	costs per case	USA	USD 9,966 /n
Umscheid 2011	VAP	costs per case	USA	USD 23k /n
Mittmann 2012	VAP	costs per case	paediatric ICU	USD 55,333 /n
Raschka 2013	VRE col.	costs per case	Canada	CAD 7,747 /n

Reference	type of infection	type of cost	area	figure
Raschka 2013	VRE inf.	costs per case	Canada	CAD 16,191 /n
Jackson 2011	Sepsis	costs per case	Australia	AUD 9,400 /n
Jackson 2011	Lower respiratory inf.	costs per case	Australia	AUD 5,496 /n
Jackson 2011	UTI	costs per case	Australia	AUD 3,669 /n
Jackson 2011	MRSA	costs per case	Australia	AUD 19,881 /n
Jackson 2011	Enterocolitis / CDI	costs per case	Australia	AUD 19,743 /n
Jackson 2011	Other drug resistant inf.	costs per case	Australia	AUD 12,292 /n
Rivard 2008	generic HAI	costs per case	USA	USD 13,916 /n
Rivard 2008	generic HAI	excess LOS	USA	9.6 d
Rivard 2008	generic HAI	excess mortality	USA	4.3

Source: GÖ FP

Table 22: Cost of decubitus ulcers

References	type of AE	type of cost	area	figure
Jha 2008	decubitus ulcres	nationwide monetary	UK	GBP 1.4–2.1b /y
Jha 2008	decubitus ulcres	% of HE	UK	4%
Sullivan 2013	decubitus ulcres	death toll	USA	60k /y
Jha 2013	decubitus ulcres	DALY loss	HIC	134k /y
Rivard 2007	decubitus ulcres	excess mortality	USA	7.2
Rivard 2007	decubitus ulcres	excess costs	USA	USD 10,845 /n
Rivard 2007	decubitus ulcres	excess LOS	USA	4 d
Jackson 2011	decubitus ulcres	cost per case	Australia	AUD 8,435 /n

Source: GÖ FP

Table 23: Cost of adverse events related to medical devices

References	type of AE	type of cost	area	figure
Jackson 2011	complications of cardiac and vascular implants excluding septicaemia	cost per case	Australia	AUD 7,749 /n

Source: GÖ FP

Annex 4: Cost-effective patient safety programmes

Efficient programme – cost data available

1. Barrett DL, Secic M, Borowske D. The Gatekeeper Program: proactive identification and case management of at-risk older adults prevents nursing home placement, saving healthcare dollars program evaluation. Home Healthc Nurse. 2010;28(3):191-7.
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Efficient programme – no cost data

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3. Jacobs L, Burns K, Cox-Chapman J, Kelly K. Creating a culture of patient safety in a primary-care Physician group. Connecticut Medicine. 2012;76(5):291-7.

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Annex 5 – List of Contributing Authors

Johannes Zsifkovits – Coordinator

- **Expert in** project management
- **Master's degree in health-economics, Doctor's degree in business in progress**
- **Expert in** health-economic modelling and efficiency analysis
- **Various projects including** economic forecasting **such as**
- **Cost-effectiveness of the Austrian disease management program for**
- **Diabetes mellitus type 2 (Markov Model)**
- **Efficiency of hospitals**
- **Unsafe care and high cost investments**
- Modelling hepatitis B/C **incl. economic burden**
- **Expert in HTA and systematic** literature reviews
- **Expert in** costing methods, budget impact **analysis and calculation of** economic burden
- **Experience in analyzing and extracting** epidemiological studies

Martin Zuba

- **Academic background in economics** (Master's degree), doctor's degree in economics progress
- **Research associate** in the Health Economics Department at the Austrian Health Institute (**GÖG**) since April 2015
- Previously **research and teaching** assistant at Vienna University for Economics and Business, research institute for economics of ageing
- Expertise in **econometrics and statistical modelling and simulation**, including Bayesian statistics, demographic APC-modelling, hierarchical and dynamic regression analysis, etc.
- Previous research projects include **economics of elder's long-term care**, including **systematic literature reviews, quality of care, informal care and employment**, etc.

Wolfgang Geißler

- has studied sociology including training in **empirical social research and statistics**
- has a certificate as **clinical riskmanager**
- **Research associate** in the Federal Institute for Quality in Austrian Health Care (BIQG) at Austrian Health Institute (GÖG) since March 2009
- co-leadership of the **nationwide mandatory quality reporting system for hospitals and stationary rehab-hospitals**
- research and analysis on issues related to **quality of health care**
- specialist contact person for **evaluation and evaluation projects**
- design and realisation of **surveys, evaluations (e.g. the national critical incident reporting system)**
- operates different **data reporting methods**
- **management of patient safety projects,** including the prevention and control of healthcare-associated infections
- development of national **health care guidelines**
- development of quality and **patient safety indicators**
- **consultancy** of hospitals and authorities

Lena Lepuschütz

- Academic background in economics and public policy, including advanced training in econometrics and econometric modelling
- **Research associate** in the Health Economics Department at the Austrian Health Institute (GÖG) since October 2014, previously a consultant to the World Bank
- Professional experience in **survey design** and implementation of **large-scale data collection**
- Experience in **survey analysis, econometric analysis using large-scale microeconomic datasets and conducting impact evaluations as well as modelling the impact of different policy options;**
- Experience in conducting **expert interviews and providing policy recommendations**;
- Experience with **consulting** health ministries in low-income countries
- Experience in **project management** and coordination of international research projects
- Has been working on various **econometric studies and reports**, covering a wide range of social policy issues

Daniela Pertl

- Scientific researcher
- Has been working at Gesundheit Österreich GmbH since 2007, mainly in health economics
- Researcher and expert in **international and national projects on quality and efficiency in health care** (e.g. Health Technology Assessments, National HTA-Strategy, methodology manuals, health systems research, health reports, public health issues)
- Profound methodological knowledge in **health technology assessment** and **systematic reviews**
- Specialised in Health Technology Assessment and **systematic reviews**
- Excellent skills in **managing, organising and coordinating projects** (project management)
- (Co-)Author of a wide range of **reports and publications in the field of effectiveness evaluations in health care**
- (e.g. Methods manual for Health Technology Assessment; Long-term effectiveness of inpatient rehabilitation; Interactions of drugs against dementia; finding and prioritisation of HTA-topics; Computerized Physician Order Entry – effectiveness and efficiency; Abdominal Aorta Aneurysm Screening - Description and technical characteristics of the technology; Screening of and therapy interventions for children with primary speech and language delay or disorder
- Expertise in **economics**, **pharmaceuticals** and **public health**, including health care reporting

Eva Kernstock

- **Head of the Austrian Federal Institute for Quality in Health Care (BIQG),** a business unit of GÖG
- Head of department on **Development of Health Care Quality into Practice**
- Head of the scientific board of the ÖQMed (**Quality Institute of the Austrian Medical Chamber**)
- **Lecturer** at the University of Vienna **"Quality Management and Patient Safety"**

- Extensive experience in **risk-management and management of patient safety programmes** including prevention and control of **healthcare-associated infections**
- Researcher and expert in international and national **projects on quality in health care**, e.g.
    - Development, implementation and evaluation of the Austrian quality strategy in cooperation with all relevant stakeholders,
    - Development, implementation and evaluation of the Austrian Patient safety strategy in cooperation with all stakeholders
    - Development of guidelines, disease management programmes and prevention programmes
    - health care reform,
    - health promotion strategy,
    - National HTA-Strategy,
    - methodology manuals,
    - health systems research,
    - health and quality reports,
    - public health issues,
    - health literacy.
- Methodological expert in **guideline development, patient surveys, integrated care models** for chronic diseases (COPD, Diabetes)
- Experiences in setting up and **coordination of projects**

Herwig Ostermann

- Senior health economist
- **Head of the Health Economics Department** at the Gesundheit Österreich GmbH
- **Advisor of the Austrian Ministry of Health,** being responsible for structural and economic affairs of the health reform
- Various projects including **economic forecasting** such as
    - "Regional services planning and forecasting of long term care services in the Austrian Land Tyrol for 2005 and 2025"
    - "Cost control in nursing homes by the means of economics of scale and care profile optimization"
    - "Analysis of the change in the patterns of outpatient health services demand after annual check-ups"
    - Analysis of the efficiency of the Austrian disease management program for diabetes mellitus type 2
- **Publicly funded research projects** at the Gesundheit Österreich GmbH:
    - "Cost containment path for Austrian health care expenditure"
    - "Forecast of costs for long term care services in Austria from 2010 to 2025"
    - "Regional economic impact of Austrian hospitals" (Joint project with WIFO and Joanneum Research)
    - "Analysis of the economic effect of the shift of cataract surgeries from inpatient care to day care"
    - "Efficiency analysis of Austrian hospitals"
- Attendant and presenter of various **conferences at European level** (including DIA Euro Meeting, EHMA Conference, iHAE/ECHE Conference)
- Country Focal Point for Austria for the Coordinated/Integrated Health Services Delivery (CIHSD) of the World Health Organisation – Regional Office for Europe
- Austrian representative for the peer review on Health System Performance Assessment within the EU

- Founding member of the Austrian network of health economists within the Austrian Health Economics Association (ATHEA)
- **Lector at the summer school "Health Care and Social Systems**" of the European Forum Alpbach"
- **Lector at the MBA-programme "Health Care Management"** of the Medical University Vienna, Austria (Course: Health Economics)
- **Lector at the bachelor programme "Health Sciences"** of the Karl Landsteiner University of Health Sciences, Krems, Austria (Course: Health Economics)
- **Professor for Health Policy and Administration (part-time)** at the Department of Public Health and Health Technology Assessment at the University for Healh Sciences, Medical Informatics and Technology, Hall/Tyrol, Austria
- Contributes to the **Health Systems and Policy Monitor** (HSPM) of the European Observatory for Austria
- **Working in health care for more than ten years**