Les infections nosocomiales en Belgique, volet II: Impact sur la mortalité et sur les coûts

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Federaal Kenniscentrum voor de Gezondheidszorg
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PRÉFACE

Il y a chaque année en Belgique près de 50.000 accidents de la route qui tuent environ 1.500 personnes. Ces statistiques sont tenues à jour régulièrement ; des efforts et des budgets importants sont consentis pour réduire ces chiffres. Pourquoi les infections nosocomiales, qui sont deux fois plus nombreuses que les accidents de la route, sont elles encore si peu étudiées, et pourquoi leurs conséquences sont-elles encore si mal connues dans notre pays ?

La situation est en train de changer. La commissaire européenne en charge de la santé a récemment proposé aux états membres des actions spécifiquement liées à « la sécurité du patient et à la qualité des soins des services de santé, y compris la prévention et le contrôle des infections associées aux soins de santé ».

C'est dans cet esprit que le KCE a voulu ajouter une pierre à l'édifice de tous ceux qui veillent à l'hygiène hospitalière à l'intérieur des hôpitaux, en essayant de combler certaines lacunes en matière d'information sur la taille et l'ampleur du problème.

Un premier rapport, publié en novembre 2008, a donné une estimation du nombre total d'infections, des types d'infections les plus courantes et des services où elles se produisent. Pour les combattre le plus efficacement, il fallait aussi savoir lesquelles étaient les plus mortelles et les plus coûteuses. Ce sont les questions auxquelles nous essayons de répondre dans ce deuxième volet de notre étude.

Gert Peeters
Directeur général adjoint a.i.

Jean-Pierre Closon
Directeur général a.i.

Résumé

INTRODUCTION

Une infection nosocomiale (IN) ou infection d'origine hospitalière est une infection qui se déclare chez un patient hospitalisé après son admission. Les infections nosocomiales représentent la complication la plus fréquente affectant les patients hospitalisés. Elles sont localisées essentiellement au niveau du tractus urinaire, des plaies opératoires, des voies respiratoires inférieures, du sang (septicémies) et du système digestif. Les infections nosocomiales augmentent la morbidité et la mortalité des patients, prolongent le séjour hospitalier et génèrent des dépenses importantes. Tous les hôpitaux belges sont dotés d'une unité de contrôle d'hygiène hospitalière, dirigée par un médecin hygiéniste. Ces équipes encouragent les bonnes pratiques qui réduisent les infections nosocomiales. Le budget annuel consacré au financement de ces équipes est de 16 millions d'euros en Belgique.

Dans un premier volet de ce rapport publié précédemment (KCE Rapport n° 92, 2008), nous avons présenté les résultats d'une étude de prévalence ponctuelle menée par les unités de contrôle d'hygiène hospitalière dans plus de la moitié des hôpitaux aigus belges. Les deux rapports doivent être lus ensemble. Une prévalence globale de 6,2% d'IN a été observée parmi les patients hospitalisés, un chiffre similaire aux taux de prévalence publiés récemment dans les pays voisins. Comme on s'y attendait, ce sont les unités de soins intensifs (USI) qui présentent le taux de prévalence le plus élevé. Toutefois, en chiffres absolus, ce sont les services médicaux, chirurgicaux, gériatriques et de réadaptation fonctionnelle qui comptent le plus de patients atteints d'une IN.

Avant de pouvoir évaluer le rapport coût-efficacité des mesures de maîtrise des infections, une quantification précise des infections nosocomiales et des dépenses de santé qui en découlent était indispensable. Ces mesures sont réputées pouvoir réduire l'incidence des IN de 30% environ.

Dans ce second volet du rapport, nous procédons à une estimation des dépenses de santé pour chaque sous-groupe d'infections nosocomiales et nous déterminons le coût annuel global pour la collectivité des soins de santé entraînés par les infections nosocomiales en Belgique (sans tenir compte donc des dépenses à charge des patients). Nous estimons aussi quel est l'impact des IN sur la mortalité.

SOURCES ET METHODES

Nous avons procédé à une revue de la littérature consacrée au coût attribuable aux infections nosocomiales, y compris une recherche sur les méthodes statistiques pour estimer ces coûts. Après avoir sélectionné une méthode statistique qui pouvait s'appliquer à des données administratives (« matched cohort study » ou étude de cohortes appariées), nous avons effectué deux analyses distinctes. D'abord, nous avons étudié les cas de septicémies rapportées en 2003 au Programme de Surveillance nationale des Infections hospitalières (NSIH) de l'Institut belge de Santé publique (ISP). Ensuite, et c'est l'aspect le plus important, nous avons analysé les cas d'IN identifiés durant l'étude de prévalence ponctuelle réalisée en 2007 dans tout le pays. En nous basant en partie sur la littérature, mais essentiellement sur les résultats des deux études de cohortes appariées, nous avons calculé les estimations globales pour la Belgique pour la surmortalité et l'allongement de la durée du séjour hospitalier.

Revue des méthodes statistiques pour évaluer le surcoût lié aux infections nosocomiales

Un premier groupe de méthodes se base sur l'avis d'un expert examinateur qui estime le nombre de journées supplémentaires d'hospitalisation de manière plus ou moins normalisée. De telles méthodes d'attribution directe restent subjectives et ne sont dès lors pas bien acceptées.

Le second groupe de méthodes utilise des techniques d'attribution comparatives qui tiennent compte des données relatives au séjour hospitalier des patients indemnes d'IN et atteints d'IN en utilisant des études de cohortes appariées ou des modèles statistiques de régression multivariée. Le défi réside dans l'isolement de l'effet indépendant de l'IN sur les résultats en termes de coûts, en procédant à un ajustement pour tous les facteurs confondants pertinents et observables. Bien entendu, il ne faut apparier ou ajuster que pour les variables qui ne sont pas influencées par la présence d'une IN.

Les IN étant plus fréquentes chez les patients qui sont également susceptibles de séjourner plus longuement à l'hôpital, les méthodes comparatives ont en commun une caractéristique : plus le nombre de variables pertinentes sont appariées ou ajustées, plus la différence de durées de séjour s'amenuise entre les patients indemnes et atteints d'IN. En réalité, il s'avère rapidement difficile de trouver des patients témoins appariables puisque le nombre de variables a augmenté. Il convient de faire un compromis entre la validité externe (apparier tous les patients sur un faible nombre de critères) et la validité interne (apparier moins de patients sur un nombre plus élevé de critères). Les études antérieures qui n'appariaient que pour quelques variables risquent dès lors d'avoir surestimé l'allongement de la durée d'hospitalisation. Des méthodes similaires sont utilisées pour évaluer la surmortalité associée aux IN.

Justification et design des deux études de cohortes appariées

Ayant eu la possibilité de sélectionner des patients témoins dans les bases de données administratives nationales, nous avons choisi la formule de cohortes appariées aux fins de l'analyse statistique, à la fois pour les cas de septicémies en 2003 et les données de prévalence ponctuelle de 2007.

En utilisant les données couplées RCM-RFM (Résumé Clinique Minimal, Résumé Financier Minimal) pour 2003, nous avons pu sélectionner des patients témoins de la même année sans IN dans le même hôpital et avec le même APR-DRG que les cas infectés. Les cas infectés et les patients témoins ont été appariés 1 :1 pour l'hôpital, l'APR-DRG, l'âge (écart maximum de 10 ans), le diagnostic principal, le score de Charlson (une échelle pronostique basée sur la comorbidité) et la durée du séjour jusqu'à l'infection subclinique (définie en tant que date de l'infection clinique moins deux jours de période d'incubation). Outre les facteurs « hôpital » et APR-DRG, les facteurs d'appariement possibles ont été examinés afin d'étudier la faisabilité de l'appariement et l'influence des critères d'appariement sur l'estimation du coût différentiel.

Pour les cas de l'étude de prévalence ponctuelle de 2007, nous avons apparié 1 :1 à 1 :4 avec les patients témoins de 2005 pour l'hôpital, l'APR-DRG, l'âge (écart maximum de 15 ans), le service (gériatrique, revalidation ou autre), le score de Charlson, la durée estimée du séjour jusqu'à l'infection et la destination après la sortie (uniquement pour l'estimation de la durée du séjour). Nous avons utilisé la destination après la sortie plutôt que la résidence du patient avant son hospitalisation car nous ne disposions pas directement de cette dernière information pour notre analyse. Il s'est également révélé impossible d'identifier et d'exclure les patients atteints d'une IN dans le groupe témoin. Nous avons sélectionné uniquement les patients témoins qui avaient séjourné à l'hôpital pour au moins la même période que celle jusqu'à laquelle l'infection nosocomiale était présumée débuter dans le cas apparié. Au moment de l'étude de prévalence ponctuelle, on a présumé que l'IN était présente depuis 5 jours dans tous les cas, à l'exception de certaines IN spécifiques pour lesquelles on a présumé que l'infection était en cours depuis 3 jours (par exemple, une infection du tractus urinaire) ou 10 jours (par exemple, des infections osseuses). Des analyses de sensibilité ont été réalisées pour différentes hypothèses concernant la « durée de l'infection en cours » et pour l'appariement en utilisant plus ou moins de variables, y compris le sexe.

RESULTATS

RÉSULTATS DE LA REVUE DE LA LITTÉRATURE SUR LES SURCOÛTS

En se fondant sur la littérature, il apparaît clairement que la majeure partie du surcoût des IN résulte d'un séjour hospitalier de plus longue durée. Pour cette raison, on parle souvent d'allongement de la durée de séjour en lieu et place de surcoût. Cela facilite également la comparaison internationale et peut être utile aussi dans un même pays en cas de modification du système de financement des hôpitaux.

Une revue de la littérature publiée en 2005 a été identifiée et a été mise à jour avec des études originales récemment publiées. On observe une importante hétérogénéité parmi les études au niveau de leur conception, de leur perspective économique et de leurs résultats. Il n'a pas été possible de dériver de ces études des estimations fiables pour la Belgique. Les seules estimations ayant trait à notre pays, trouvées dans la littérature grise, étaient fondées sur une publication américaine de 1993 qui rapportait un allongement de la durée du séjour moyen de 4 jours après une IN. En l'absence de données quant à l'incidence locale et les coûts pour la Belgique en 2006, l'estimation de 107.500 infections nosocomiales a été calculée sur la base d'une extrapolation des septicémies, ce qui conduit à un total de 110 millions d'euros (en se basant sur 4 jours supplémentaires et sur une base de 250 euros par journée d'hospitalisation). Une autre présentation (ISP, 2005), qui se fonde essentiellement sur la littérature internationale, évoque un coût annuel de 110 à 300 millions d'euros pour la Belgique. Ladite présentation contenait également des estimations d'allongement de la durée de séjour et de surmortalité pour les septicémies et des voies respiratoires inférieures, fondées sur les données de surveillances des unités de soins intensifs (USI) durant la période 1997-2003 (voir tableau A).

RÉSULTATS DES DEUX ÉTUDES DE COHORTES APPARIÉES

Résultats basés sur les septicémies rapportées en 2003

Au total, 1839 séjours de patients souffrant d'une septicémie rapportée en 2003 par 19 hôpitaux étaient disponibles aux fins de l'appariement. Parmi ces cas, la mortalité était de 32% tout séjours confondus, et de 46% dans les séjours en USI. Au total, 665 paires cas-contrôle (y compris 72 cas USI) ont été appariées. La durée de séjour des contrôles ne pouvait jamais être inférieure à la durée de séjour des cas avant l'apparition de l'infection subclinique. Ceci a eu un impact majeur en réduisant l'estimation de l'allongement du séjour de moitié. L'appariement des cas USI s'est révélé difficile et a été considéré comme insatisfaisant. L'allongement du séjour après une septicémie en dehors d'une USI chez les patients survivants était en moyenne de 9,3 jours. L'écart médian était de 7 jours (voir tableau A).

Résultats basés sur l'étude de prévalence ponctuelle de 2007

Notre analyse a porté sur les 978 cas d'IN identifiés durant l'étude de prévalence. Cette étude a eu lieu après un séjour moyen de 31 jours. La mortalité à l'hôpital était de 32,1% chez 156 patients USI et de 11,7% chez 822 autres patients. Pour 818 cas (128 en USI), il a été possible d'analyser le coût total dans la perspective du payeur des soins de santé. Ce montant est en moyenne de 39 196 euros pour les séjours incluant une admission en USI (durée moyenne du séjour : 56 jours, soit 700 euros par jour) et 22 339 euros pour les séjours hors USI (durée moyenne du séjour : 45 jours ou 496 euros par jour).

Aux fins de la sélection des contrôles, nous disposions au total de 74 204 séjours hospitaliers de 2005. Nous les avons appariés avec 910 cas (pour la mortalité) ou 765 cas de survie (pour la durée de séjour). Dans l'ensemble, pour les contrôles, la durée moyenne de séjour était de 14 jours. La majorité des contrôles n'a pas donc pas pu être appariée, cette durée étant trop courte. Le ratio contrôle-cas était de 3.3 en moyenne pour l'analyse de mortalité et de 2.8 pour l'allongement de la durée du séjour.

En raison du faible nombre de cas et de la complexité du séjour hospitalier pour les cas et les patients témoins qui séjournent au moins quelques jours en USI, l'appariement s'est révélé un véritable défi pour le groupe et il n'a pas été possible de fournir des estimations fiables.

L'allongement moyen de la durée du séjour pour les IN hors unités de soins intensifs était compris entre 4,1 jours pour les infections urinaires et 10,6 jours pour les infections des voies respiratoires inférieures (voir tableau A). Les analyses de sensibilité ont par la suite révélé que nos estimations étaient sensibles à la variable 'durée de l'infection' à l'époque de l'étude de prévalence : l'allongement de la durée du séjour varie en moyenne de 0,8 jour lorsque la période au cours de laquelle on suppose que l'IN est en cours présente un écart d'un jour en plus ou en moins par rapport à l'hypothèse actuelle de 5 jours pour la majorité des IN (2,5 jours pour les infections du tractus urinaire).

Les mécanismes de financement des médicaments et des implants ayant été modifiés entre 2005 (année de sélection des contrôles) et 2007 (année de l'étude de prévalence ponctuelle), ces éléments n'ont pas été pris en compte dans la comparaison appariée. Nous partons du principe qu'il n'y a pas de différences au niveau des implants entre les cas et les patients témoins. Pour les médicaments, nous avons utilisé le coût journalier moyen de 47 euros pour les cas (en nous fondant sur une moyenne de 2203 euros pour un séjour moyen de 47 jours) et nous avons multiplié ce montant par l'allongement de la durée de séjour par type d'IN. Ce montant a été additionné à la différence du coût de contrôle de cas par séjour. Le coût de séjour hospitalier fixé par jour (de 371 euros en moyenne par séjour pour 2008) représente plus des deux tiers du surcoût, comme l'illustre le tableau A.

Tableau A. Estimations de la durée de séjour et des coûts de soins de santé **additionnels (à charge de la collectivité), par cas d'infection nosocomiale**

Ward	NI type	Excess LOS / case median days	Excess LOS / case mean days	Excess cost / case°° median €	Excess cost / case°° mean €
ICU	BSI	7,0*	10,2**	4900	7140
	LRI	7,0	11,4**	4900	7980
	Other	4,0	7,2	2800	5040
Non ICU	BSI	7,0*	9,3*	4030*	5515*
	LRI	7,0	10,6	3787	5357
	SSI	5,1	5,6	1660	2491
	GI	3,5	7,3	2143	3846
	UTI°	0,5	4,1	210	1942
	Other	4,0	7,2	1887	3446
Overall		3,6	6,7	1890	3557

°°for non-ICU, based on matched cohort of point-prevalence study, for drugs: €47 / day used for ICU, a cost per excess day of €700 was used

*matched cohort, based on BSIs reported in 2003, per diem 2008 cost used (€371)

**based in ICU surveillance data (IPH)

°results obtained for a duration of UTI of 5 days and when also those patients were matched for whom no cost data were available; excess costs adjusted proportionally

ESTIMATIONS GLOBALES POUR LA BELGIQUE

Incidence des infections nosocomiales

L'incidence annuelle des infections nosocomiales (IN) de 103 000 patients a été estimée pour la Belgique en se basant sur les résultats de l'étude de prévalence ponctuelle présentée en détail dans le KCE Report n° 92, 2008. Pour le calcul de l'incidence à partir de la prévalence, un seul facteur de conversion a été utilisé, indépendant du type d'infection (sous l'hypothèse une durée moyenne d'infection de 10 jours). Si l'on ajuste pour la durée plus courte de 5 jours pour les infections urinaires, l'incidence cumulée de ces infections est encore plus élevée, et le nombre total de patients infectés sur une année avec une IN est de 125 500.

Estimation globale de l'impact sur la mortalité

Pour la Belgique, nous estimons qu'il y se produit chaque année environ 17 500 décès à l'hôpital après une infection nosocomiale, dont 2625 (soit 15%) peuvent être attribués à l'IN. La surmortalité globale chez les 125 500 patients atteints d'une IN est donc de 2.1%, comme l'illustre en détail le tableau B.

Dans notre étude de cohorte appariée, la surmortalité en hôpital dans les services hors USI a été estimée à 1.6%, soit 1731 décès par an. Dans les services hors USI, pratiquement la moitié des cas de surmortalité ont été observés après une infection des voies respiratoires inférieures. Les septicémies arrivent en deuxième place des IN les plus létales. Aucune surmortalité n'a été observée pour les infections urinaires. Toutefois, en raison de la taille restreinte de l'échantillon, il est malaisé de fournir des estimations précises par type d'IN. Nous avons utilisé les pourcentages de surmortalité pour les septicémies et les infections des voies respiratoires inférieures en unités de soins intensifs tels qu'estimés par l'Institut de Santé Publique (ISP) et fondés sur un vaste ensemble de données.

Nous n'avons pas estimé le nombre d'années de vie perdues attribuables aux IN. Cependant, en se basant sur la moyenne d'âge relativement basse des patients atteints d'une septicémie en USI ou d'une infection de plaie opératoire (65 ans), ces IN pourraient contribuer de manière importante à cette variable.

Tableau B. Estimation de la mortalité totale et de la surmortalité hospitalières annuelles en Belgique chez les patients ayant contracté une infection nosocomiale

		Patients with NI*	Median age	Total in-hospital mortality		Excess in-hospital mortality	
Ward		N	years	N	%**	N	%**
ICU	BSI	3791	62,5	1369	36,1%	372	9,8%°
	LRI	9163	73,0	3051	33,3%	522	5,7%°
	Other	3475	69,0	841	24,2%	NA	NA
Non ICU	overall	109109	73,7	12233	11,2%	1731	1,6%
Overall		125538	73,2	17494	13,9%	2625	2,1%

*incidence derived from prevalence assuming a duration of NI of 10 days; except for UTI (5 days)
**percentage of the patients with a NI
°based in ICU surveillance data (IPH)
NA = not available

Estimation globale de l'allongement du séjour hospitalier et des coûts pour l'assurance maladie

Les tables A et C ci-dessous présentent les estimations globales pour l'allongement du séjour hospitalier et le surcoût. L'analyse de cohorte appariée fondée sur l'étude de prévalence ponctuelle de 2007 constitue la principale source pour nos estimations relatives à la plupart des infections nosocomiales hors unités de soins intensifs (USI). Pour les septicémies hors USI, nous avons utilisé l'étude de cohorte appariée fondée sur les septicémies rapportées en 2003. Les séjours en USI étant difficiles à apparier dans les deux études de cohorte, nous avons utilisé les estimations de l'ISP pour l'allongement de la durée de séjour dans les cas USI de septicémies ou des voies respiratoires inférieures. Celles-ci se fondent sur l'allongement de la durée du séjour en USI uniquement. Pour les valeurs médianes et les « autres » IN en USI, nous avons utilisé les estimations dérivées pour les cas hors USI. Pour les cas de septicémies hors USI, nous avons été rassurés de constater que les estimations d'allongement de séjour fondées sur nos deux études de cohortes appariées étaient pratiquement identiques (estimation médiane : 6 et 7 jours ; moyenne : 9.2 et 9.3 jours). Nous avons observé que ce sont les septicémies, les infections des voies respiratoires inférieures et les infections urinaires qui sont les infections nosocomiales associées à l'allongement du séjour et au surcoût les plus importants. On observe une valeur moyenne globale d'une semaine d'allongement de séjour pour tous les types d'IN confondus, correspondant à un total d'environ 700 000 journées d'hospitalisation supplémentaires.

S'agissant des dépenses en soins de santé à charge de la collectivité, nous avons procédé à un ajustement pour tenir compte du changement survenu entre 2005 et 2007 au niveau du financement des médicaments et nous avons utilisé un coût moyen pondéré (valeur de 2008) de 371 euros pour une journée d'hospitalisation, tant pour les cas que pour les patients témoins.

Pour les septicémies, nous avons utilisé l'étude de cohorte appariée basée sur les cas de septicémies rapportés en 2003 à l'ISP, après ajustement du coût journalier à 371 euros. Pour le surcoût des séjours hospitaliers incluant un séjour en USI, nous avons utilisé un coût moyen journalier de 700 euros, selon le calcul ci-dessus.

Table C. Estimations du nombre et du coût des journées d'hospitalisation causées par les infections nosocomiales, sur une année en Belgique

Ward	NI type	Patients with NI* N	Patients survivors N	Overall excess LOS median days	Overall excess LOS mean days	Overall excess cost median Mio €	Overall excess cost mean Mio €
ICU	BSI	3791	2423	16959	24712	11,9	17,3
	LRI	9163	6111	42780	69670	29,9	48,8
	Other	3475	2634	10538	18968	7,4	13,3
Non ICU	BSI	12427	10737	75161	99857	43,3	59,2
	LRI	12533	9588	67113	101628	36,3	51,4
	SSI	13165	12217	62306	68414	20,3	30,4
	GI	10321	9062	31717	66152	19,4	34,9
	UTI	45076	40838	20419	167436	8,6	79,3
	Other	15587	14433	57734	103921	27,2	49,7
Overall		125538	108043	384726	720757	204,3	384,3

*incidence derived from prevalence assuming a duration of NI of 10 days; except for UTI (5 days)

FORCES ET FAIBLESSES DE L'ÉTUDE

Les résultats obtenus contribuent de manière importante à l'évaluation de la charge que représentent les infections nosocomiales en Belgique.

D'abord, nous avons étudié tous les types d'infections nosocomiales et dérivé l'incidence d'une étude nationale de prévalence ponctuelle. Plus de la moitié des hôpitaux aigus ont participé à cette étude. Les IN étaient identifiées automatiquement après l'encodage des signes et symptômes des patients dans un logiciel développé spécifiquement pour cette étude. Dans ce logiciel, les critères CDC étaient programmés. Ces règles strictes nous ont peut-être conduit à écarter certains patients dont l'infection était insuffisamment documentée. En conséquence, le taux de prévalence pourrait être une sous-estimation de la réalité. En outre, pratiquement la moitié des hôpitaux belges n'a pas participé à l'étude de prévalence ponctuelle, pour des raisons qui ne sont pas documentées. On pourrait conjecturer qu'au moins quelques établissements n'ont pas participé parce qu'ils accordaient peu d'attention à la maîtrise des infections.

Ensuite, nous avons utilisé des bases de données administratives (RCM-RFM-IMA), ce qui a permis de réaliser deux études de cohortes appariées, en sélectionnant plusieurs patients contrôle par patient infecté, sur base de plusieurs facteurs d'appariement pertinents. Nous avons pu reproduire les estimations d'allongement de la durée du séjour en hôpital après une septicémie hors USI dans les deux analyses de cohortes appariées indépendantes.

Il est à noter que d'autres méthodes statistiques récentes existent pour estimer l'effet des IN. Ces méthodes plus sophistiquées nécessitent l'accès à des données cliniques et temporelles détaillées. Les résultats obtenus en utilisant des telles méthodes montrent les études de cohorte appariées tendent à surestimer l'effet des NI. En raison de la surestimation inhérente au design des cohortes appariées, l'estimation basée sur la moyenne pourrait être considérée comme le cas le plus défavorable aux fins de la prise de décision. D'autre part, en raison d'autres aspects conceptuels de l'étude, nous avons peut-être sous-estimé l'allongement global du séjour hospitalier de même que les dépenses induites par les infections nosocomiales. Ces aspects conceptuels qui ont mené à une possible sous estimation de l'effet sont : une possible sous-estimation de l'incidence, une possible sous-estimation de l'allongement global du séjour hospitalier pour les cas en unités de soins intensifs, l'exclusion des coûts liées aux patients décédés, l'inclusion de la destination après hospitalisation comme critère d'appariement, ainsi que la non exclusion des séjours avec IN des contrôles dans une des deux études de cohortes appariées.

Nous avons montré que le degré d'appariement, y compris sur la durée d'hospitalisation avant infection, est déterminant lorsqu'on souhaite obtenir des estimations plausibles de l'allongement de la durée du séjour. L'importance de cet ajustement est cruciale. Malheureusement, une correction pour la durée du séjour avant l'IN fait défaut dans de nombreuses études publiées récemment. La durée présumée d'une IN au moment de l'étude de prévalence est aussi essentielle pour définir la durée de séjour minimale des contrôles appariés. À elle seule, cette variable a un impact déterminant sur l'estimation de l'allongement de la durée du séjour par cas d'infection nosocomiale. Pour l'estimation du surcoût total, les effets de cette durée présumée de l'IN sont contrebalancés par son effet sur le calcul de l'incidence cumulée à partir de la prévalence, et a donc très peu d'impact sur le nombre total de journées d'hospitalisation supplémentaires causées par les infections (environ 700 000 journées d'hospitalisation).

Enfin, nous avons introduit un coût actualisé pour une journée d'hospitalisation. Ce coût a été pondéré pour tous les hôpitaux belges.

DISCUSSION ET CONCLUSIONS

Nous avons utilisé les données disponibles pour estimer la surmortalité à l'hôpital de même que les dépenses en soins de santé à charge de la collectivité qui sont attribuables aux infections nosocomiales en Belgique. En moyenne, les patients atteints d'une infection nosocomiale séjournent une semaine de plus à l'hôpital par rapport aux patients témoins appariés. Nous avons estimé la surmortalité à 2625 décès par an et le surcoût à presque 400 millions d'euros par an. Ce montant est supérieur à toutes les estimations publiées précédemment pour la Belgique, essentiellement parce que notre estimation de l'allongement de la durée du séjour hospitalier est le double des estimations précédentes et parce que le coût journalier a fortement augmenté de 288 euros par jour en 2005 à 371 euros actuellement.

Une estimation inférieure d'une demi semaine pour l'allongement de la durée du séjour et 200 millions d'euros de surcoût se fonde sur la différence médiane observée entre les patients infectés et les patients témoins. Ces estimations sont probablement plus correctes pour les cas « typiques », tandis que les valeurs moyennes prennent également en compte les complications découlant de cas « atypiques » pour lesquels l'appariement avec un patient témoin est moins évident par définition. Les valeurs aberrantes élevées représentent très probablement les cas complexes atteints de multiples complications mais qui finissent par survivre.

S'agissant des infections du tractus urinaire, la valeur médiane de 0,5 jours est effectivement plus « typique », conformément à la littérature et à la pratique clinique, par rapport à une valeur moyenne relativement élevée de 4,1. Ces valeurs pour la médiane et la moyenne proviennent d'une analyse où la durée de l'infection urinaire est de 5 jours, et inclut aussi tous les cas dans l'analyse, même ceux pour lesquels les données de coût n'étaient pas disponibles (mais bien la durée de séjour). Sous la même hypothèse d'une durée d'infection de 5 jours pour les infections urinaires, l'incidence est plus élevée, et concerne 45 000 patients par an. Dès lors, il y a une assez grande marge d'incertitude autour de notre estimation de presque 80 millions d'euros pour les infections du tractus urinaire. Dans le cas des infections des plaies opératoires, les valeurs médianes et moyennes présentent des écarts moindres et l'estimation du surcoût en hôpital associé à ce type d'infection pourrait sembler relativement basse. Ceci pourrait s'expliquer par des séjours hospitaliers de plus courte durée après une chirurgie et un plus grand nombre d'infections des plaies qui surviennent ou sont traitées au sein de la collectivité après le séjour en hôpital. Ces coûts ne sont pas inclus dans nos estimations.

Les résultats montrent que si la charge des IN en termes de mortalité et de coût pour les patients en USI est lourde, en termes absolus, elle est aussi importante pour les services hors USI, notamment les services médicaux, chirurgicaux, gériatriques et de revalidation fonctionnelle. Les infections nosocomiales qui sont responsables de la majeure partie de la mortalité et des coûts sont les infections des voies respiratoires inférieures (environ 1000 cas de surmortalité et 100 millions d'euros de dépenses) et les septicémies (pratiquement 1000 cas de surmortalité et 80 millions d'euros de dépenses). Au niveau des dépenses globales, les infections du tractus urinaires restent importantes, probablement en raison du nombre important de cas plus complexes chez les patients âgés des deux sexes (âge médian 78 ans) qui survivent.

Dans ce rapport, nous avons estimé la charge des infections nosocomiales pour la collectivité en termes de journées d'hospitalisation supplémentaires et de coûts associés. Il est à noter que la réduction de la durée d'hospitalisation amènera à une utilisation plus efficiente des ressources dans le court terme, sans nécessairement avoir d'impact sur les dépenses totales en soins de santé. L'estimation de l'effet net de la libération de lits pour permettre le traitement de patients supplémentaires requiert un calcul minutieux des bénéfices et des coûts.

Dans le chef du gestionnaire hospitalier, les choses sont différentes. Il est clair que du point de vue de l'hôpital, des ressources vont être épargnées (les coûts variables vont être réduits) en prévenant les infections. Cependant, la majorité des dépenses associées aux ressources de l'hôpital sont fixes et difficiles à éviter dans le court terme (l'infrastructure par exemple).

Distinguer les conséquences économiques de la prévention des infections nosocomiales du point de vue de l'hôpital ou du point de vue des dépenses publiques est complexe, ne rentrait pas dans l'objet de notre étude, et nécessite des études additionnelles. De telles études rentrent dans le cadre d'une évaluation coût-efficacité globale des mesures de prévention. Le message pour les preneurs de décision est que les coûts supplémentaires causés par les infections ne doivent pas être interprétés comme des montants qui seraient rapidement disponibles en cash si des infections nosocomiales étaient évitées. Néanmoins, il est clair que ces considérations économiques ne doivent en rien limiter l'importance à accorder à la prévention des infections nosocomiales.

RECOMMENDATIONS

- Si la charge relative que représentent les infections nosocomiales chez les patients séjournant en unité des soins intensifs est lourde au niveau de la mortalité et des coûts, elle est importante aussi en termes absolus dans les services médicaux, chirurgicaux, gériatriques et de revalidation fonctionnelle. Le KCE recommande dès lors que l'on s'intéresse également à ces services, au moyen d'études d'incidence ou de prévalence.
- Les infections des voies respiratoires inférieures et les septicémies sont associées à une surmortalité et à un surcoût élevé. Les infections du tractus urinaire vont de pair avec un surcoût élevé. Le KCE recommande que ces trois types d'infections soient inscrits dans la liste des priorités pour les mesures préventives et que la surveillance soit élargie aux infections en question.
- Des études de prévalence menées à intervalles réguliers peuvent être utilisées pour surveiller l'effet global des campagnes de prévention nationales. En conséquence, la participation aux études de prévalence devrait devenir obligatoire pour tous les hôpitaux aigus.

Agenda de recherche

- Des recherches complémentaires s'imposent dans le but d'identifier les interventions les plus efficaces et les plus coût-efficaces pour réduire la charge que représentent les infections nosocomiales.
- Par rapport aux autres infections nosocomiales, les infections des plaies chirurgicales sont associés à un surcoût relativement faible. Ce constat est peut-être dû au fait que seules les infections survenant durant l'hospitalisation ont été prises en compte mais aussi parce que seuls les coûts en hôpital ont été inclus. Des recherches spécifiques sur les infections des plaies chirurgicales sont nécessaires pour estimer de manière précise et globale leur incidence et la charge qu'elles représentent.
- Des études supplémentaires sont nécessaires sur les conséquences du portage de germes résistants, ainsi que sur les possibles conséquences des interactions entre les hôpitaux et les maisons de repos/maisons de repos et de soins.
- La charge des infections acquises dans d'autres institutions (maisons de repos, maisons de repos et de soins) mériteraient aussi des études complémentaires.

Scientific summary

Table of contents

LIST OF ABBREVIATIONS **3**
1 BACKGROUND AND INTRODUCTION **4**
1.1 INTRODUCTION 4
1.2 MAIN RESULTS FROM THE PREVALENCE SURVEY 4
1.3 AIMS, SCOPE AND METHODS 6
2 COSTS OF NOSOCOMIAL INFECTIONS, RESULTS FROM A LITERATURE REVIEW **8**
2.1 INTRODUCTION 8
2.2 METHODS 8
2.3 RESULTS 8
2.3.1 Costs estimations from literature 8
2.3.2 Discussion of the different designs used to estimate attributable costs of NI 12
2.4 DISCUSSION 15
3 A SUBSTUDY ON THE IMPACT OF NOSOCOMIAL BLOODSTREAM INFECTIONS **17**
3.1 INTRODUCTION 17
3.2 METHODS 17
3.2.1 Databases 17
3.2.2 Coupling the databases 18
3.2.3 Study Design 18
3.2.4 Definition of Cases and Controls 18
3.2.5 The choice of matching factors 19
3.2.6 Analyses 20
3.3 RESULTS 21
3.3.1 Data received 21
3.3.2 Description of patients infected by a NBSI 22
3.3.3 Influence of matching factors on estimates of LOS attributable to NBSI 28
3.3.4 Los and Costs attributable to NBSI 29
3.4 DISCUSSION 31
4 A MATCHED COHORT STUDY TO ESTIMATE THE ADDITIONAL LENGTH OF STAY AND COSTS ATTRIBUTABLE TO NOSOCOMIAL INFECTIONS **33**
4.1 INTRODUCTION 33
4.2 METHODS 33
4.2.1 Databases 33
4.2.2 Coupling the databases, authorization from privacy commission. 34
4.2.3 Definitions of Cases, Controls and matching factors 34
4.2.4 Statistical Analyses: 37
4.3 RESULTS 37
4.3.1 MCD Data of infected patients (CASES) 37
4.3.2 Cost data of infected patients (CASES) 38
4.3.3 MCD of control patients 41
4.3.4 Data included in Matched Analyses 42
4.3.5 Estimation of Mortality associated with NIs 42
4.3.6 Availability of Cost data for Controls 44
4.3.7 Estimation of additional LOS and costs associated with NIs 44
4.4 CONCLUSIONS 47
5 SUMMARY AND OVERALL ESTIMATES **48**
5.1 RESULTS OF THE LITERATURE REVIEW ON EXCESS COSTS 48
5.2 RESULTS OF THE TWO MATCHED COHORT STUDIES 48
5.2.1 Results based on Bloodstream Infections reported in 2003 48

5.2.2 Results based on the Point Prevalence Data of 2007 48
5.3 OVERALL ESTIMATES 48
5.3.1 Incidence of NIs 49
5.3.2 Overall Estimate of Excess Mortality 49
5.3.3 Overall Estimate of Excess Length of Stay and Healthcare Payer Costs 50
6 STRENGTHS AND WEAKNESSES OF THE STUDY 50
7 DISCUSSION AND CONCLUSIONS 53
8 APPENDICES 54
9 REFERENCES 85

LIST OF ABBREVIATIONS

APR-DRG	all patients refined diagnosis related group
CDC	Center for disease and prevention
CI	confidence interval
GI	gastrointestinal infection
HAI	hospital acquired infection
ICU	intensive care unit
IMA	
INAMI/RIZIV	National Institute for Illness and Invalidity Insurance
IPH	Institute of Public Health
LOS	length of stay
LRI	lower respiratory tract infection
MCD	minimal clinical data
MDC	major diagnostic group
MFD	minimal financial data
NBSI	nosocomial bloodstream infection
NI	nosocomial infection
NSIH	national surveillance of infections in hospital (Belgium)
SD	standard deviation
SSI	surgical site infection
TCT	Technical Cell
TTP	Third Trusted Party
UTI	urinary tract infection
VAP	ventilator associated pneumonia

1 BACKGROUND AND INTRODUCTION

1.1 INTRODUCTION

A nosocomial infection (NI), or hospital-acquired infection (HAI), or cross-infection (MESH term) occurs during a hospital stay and is not present at hospital admission. Nosocomial infections are the most common type of complication affecting hospitalized patients and affect primarily the urinary tract, the gastrointestinal tract, the surgical site, the lower respiratory tract, and the bloodstream. These infections increase patient morbidity and mortality, prolong hospital stay and generate substantial costs. All hospitals in Belgium have a hospital control unit headed by a medical doctor hygienist. These teams promote good practices that reduce nosocomial infections.

In a first part of this report, published as KCE report no 92[1], we reviewed the literature on the prevalence of nosocomial infections in Europe and estimated the incidence and prevalence of nosocomial infections in Belgian acute care hospitals. This was based on a point prevalence study, by the hospital infection control teams of more than half of the Belgian acute hospitals. An overall prevalence of 6.2% was found, which is similar to the most recently published prevalence for the neighbouring countries.

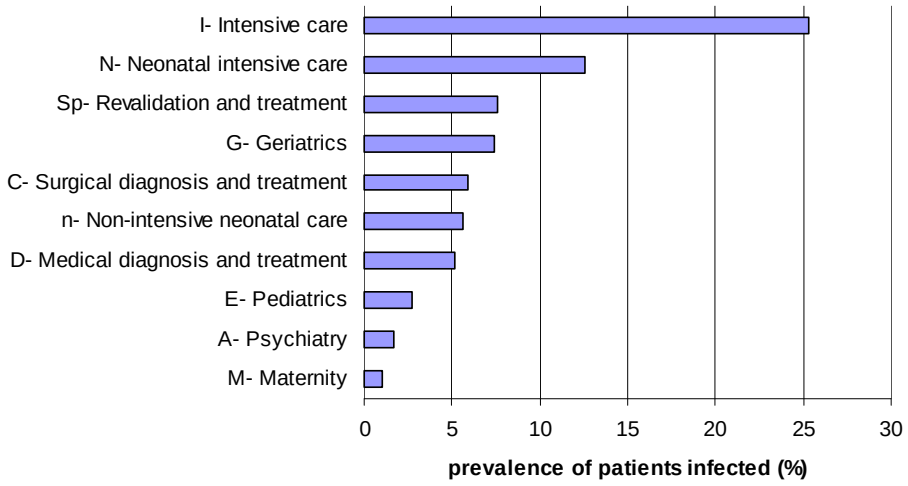
In this second part of the report we estimate for each nosocomial infection subgroup, the healthcare costs and its main drivers, as well as the overall annual cost of nosocomial infections in Belgium from a healthcare payer perspective. Also the excess mortality caused by the nosocomial infections will be estimated.

1.2 MAIN RESULTS FROM THE PREVALENCE SURVEY

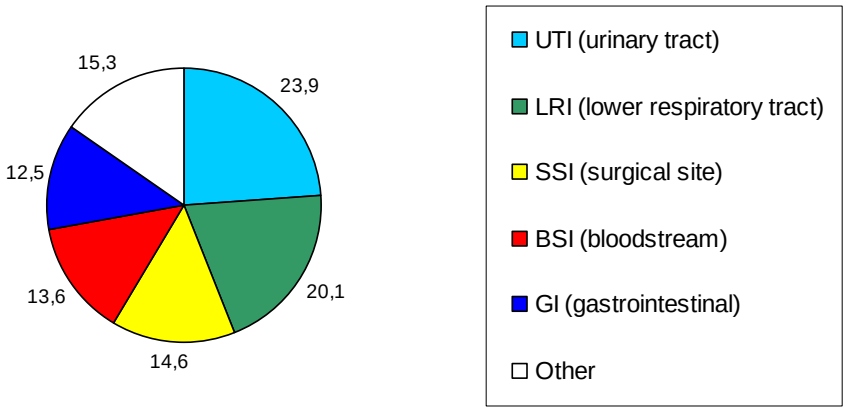
In total, 63 out of the 113 acute hospitals participated (53%), constituting a representative sample, both in terms of country region, distribution of wards, hospital size and status (general or university). Most hospitals included all patients hospitalized. Some mainly larger hospitals participated with all wards but selected to study 50% of all patients per ward (selected at random). In total 17 343 hospitalized patients were surveyed.

The prevalence of patients infected in Belgian hospitals was 6.2% (95%CI 5.9-6.5). These rates are very similar to recent data published in 2007 for the Netherlands (6.9%) and France (5.03-6.77% depending on the type of acute hospital). Also the prevalence for bloodstream infections in Belgium (0.96%) is similar when compared with the Netherlands (0.9%) and somewhat higher compared with the prevalence published for France (0.33-0.67%).

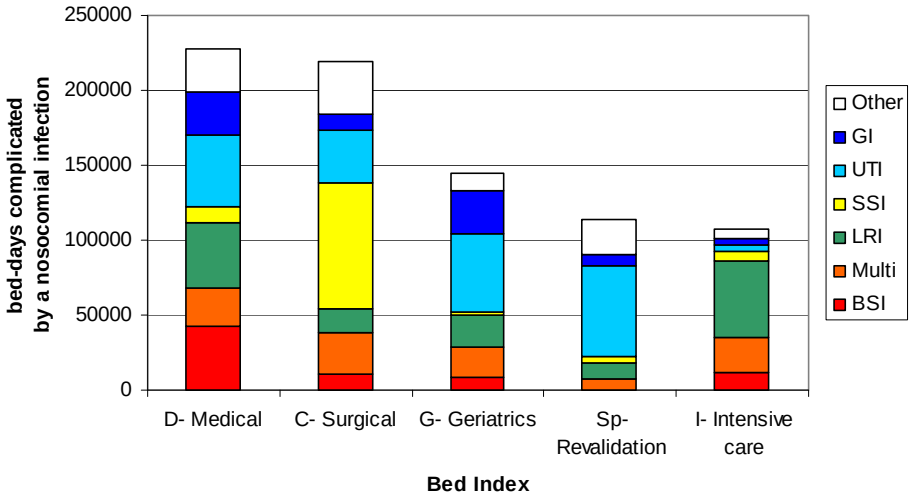
Intensive care units (both for adults and for neonates) have a high prevalence of patients infected (25.3% for adults and 12.6% for neonates). Surgical and medical units have a lower prevalence of nosocomial infections (5.9% and 5.2%) but comprise approximately half of the observed infections. SP services have a prevalence of 7.6%.



The most prevalent nosocomial infection types are urinary tract infections (UTI) (23.9%), lower respiratory tract infections (LRI) (20.1%), SSI (14.6%), bloodstream infections (BSI) (13.6%) and gastrointestinal infections (GI) (12.5%). These proportions are very dependent on the type of ward. On surgical wards, the most prevalent nosocomial infection type is SSI (38.7%), while on medical wards the types of infections are more heterogeneous (UTI 23.6%, BSI 22.8%, LRI 20.4%, SSI 6.2%). On geriatrics wards the nosocomial infection types are mainly UTI (37%) and GI (24.4%). In intensive care units half of infections are LRI (50.8%), and 20% are BSI. On SP wards more than half of the infections are UTI (54.5%).



The prevalence results obtained at a single day were extrapolated to a full year and for all Belgian acute hospitals. Of the roughly 15 million hospitalisation days in acute hospitals in Belgium every year, 900 000 hospitalisation bed days are complicated by the presence of at least one nosocomial infection present that day. The bed days linked to a patient suffering from a nosocomial infection are seen mainly on five types of ward: medical and surgical (+- 200 000 days each), geriatrics (+- 150 000 days), SPs and Intensive Care (+- 100 000 days each).



The number of patients infected per year by a nosocomial infection can be approximated based on the results of the prevalence survey. The absolute maximum estimate, assuming cumulative incidence equals prevalence, is around 116 000 patients per year for Belgium. Under more realistic assumptions (cumulative incidence lower than prevalence), the number of patients can be estimated at 103 000 per year.

1.3 AIMS, SCOPE AND METHODS

Nosocomial infections affect patient morbidity and mortality, prolong hospital stay and generate substantial economic costs. Quantification of the impact of nosocomial infections on patient health and on their induced costs is needed to help justify the cost of infection control measures.

The aims of the second part of this KCE healthcare services research project were:

1. To calculate for each nosocomial infection type, the attributable costs and the main drivers of these costs.
2. To calculate from a healthcare payer perspective the overall annual cost attributable to nosocomial infections in Belgium.

We consider in this project only nosocomial infections occurring in the acute hospital setting, thus excluding e.g. long stay psychiatric care hospitals, and day care activities (one day clinic). Infections appearing after discharge (such as some surgical sites infections) were not included either.

We started this project with a review of the economic literature related to nosocomial infections. Results of this literature search, presented in chapter 2, were very heterogeneous, and as only a few studies were performed in Belgium, those results could not be used to estimate the global burden of infections in Belgium. We choose therefore to conduct more broad cost studies to answer that question.

Because nosocomial septicemia are believed to be the most costly and life-threatening infections, a specific substudy was first performed to study these infections in details. Data from the surveillance of septicemia network (from the national surveillance of infections in hospital, NSIH) were linked to administrative clinical and financial hospital databases. The results of this substudy are presented in chapter 3.

Data on the other types of infections were missing, as no recent prevalence or incidence data were available for Belgium. A nation-wide large point prevalence study was organised and conducted in collaboration with Belgian hospital infection control specialists (KCE report 92 [1]). The minimal administrative clinical data of those patients surveyed and infected during the prevalence survey were collected. Control patients were identified in the administrative database from 2005.

Health economic data were obtained from linking these databases to the detailed health care use databases from the sickness funds. The results of this study are presented in chapter 4.

In chapter 5, an estimation of the overall burden of nosocomial infections in Belgium is presented. Mortality, prolonged hospitalisation and its associated costs are the three outcomes of interest. Data from the different sources studied (national prevalence study BNNIS, national surveillance of infections in hospital NSIH, literature) are compiled in order to provide the most accurate overall estimate.

Chapter 6 presents the strengths and limitations of the study.

Chapter 7 discusses the results and presents the conclusion.

Recommendations for decision makers are presented in the executive summary.

2 COSTS OF NOSOCOMIAL INFECTIONS, RESULTS FROM A LITERATURE REVIEW

2.1 INTRODUCTION

Nosocomial infections are thought to constitute a substantial economic burden: hospital stay is prolonged, and additional costs arise from diagnosing and treating the infections.[2] To quantify those costs, numerous studies have been undertaken, starting with the pioneering work of Haley in the late 70's.[3, 4]

Estimating costs due to NIs requires one is able to distinguish incremental costs associated with diagnosing and treating the infection (and its complications) from costs arising from the diagnosis and management of the problems for which the patient was originally admitted.

The main direct expenses attributable to the diagnosis and management of NIs can be categorized into

1. additional hospital days
2. use of laboratory services
3. drugs
4. medical and surgical procedures
5. special nursing care

Due to the high variability in costs and charges between hospitals and between countries, investigators tend to report principally the additional number of days of stay to estimate the incremental costs of treating NIs.

The aim of this chapter is to review estimates of additional length of hospital stay (LOS) and costs attributable to NI, based on the scientific literature, to review the different designs, their strengths and pitfalls, and finally to assess to which extent these results can be useful in the estimation of the burden at a national level in Belgium.

2.2 METHODS

A literature review was performed to identify studies dealing with the economics of nosocomial infections. The search was conducted in different parts:

1. recent reviews of high quality
2. individual studies for specific NIs (BSI, LRI, SSI, UTI)
3. references from selected publications were also screened

For that purpose, Medline and the CRD databases were searched, using MESH terms and key words. A PUBMED query specific to HSR studies[a] query was used to identify studies specific to the economics of NIs. All search algorithms are presented in appendix.

2.3 RESULTS

2.3.1 Costs estimations from literature

The first step of the search identified 6 reviews published since 2000[5 6 7 8 9 10] (table in appendix 1). The most recent review is from Stone et al, published in 2005 [5] and described below.

This review includes 70 studies published between 2001 and 2004, from the US (39 studies), from Europe (17 studies), from Australia/New Zeeland (4 studies) or from other countries (10 studies).

a http://www.nlm.nih.gov/nichsr/hedges/search.html

All results were extracted using methods recommended to audit systematically the economic evaluations. Table 2.1 present the characteristics of those studies, and shows that differences across them are striking. Less than half of the studies for example used the criteria of the CDC (Centers for Disease Control and Prevention) [11]) to identify the NIs. The perspective of the analysis, which is also fundamental in an economic evaluation, also varies: it was based on the hospital perspective in 63 studies, the healthcare sector perspective in 6 studies or on the societal perspective in 1 study. Hence the preference to compare results based on outcomes which are not affected by the perspective of the evaluation, such as the length of hospital stay. This can facilitate the comparison of the results across studies.

Table 2.1: Characteristics of 70 economic studies of costs of NI (Stone 2005 [5])

Paper characteristic	n	%	Economic methods	n	%
Country of study			Type of analysis		
United States	39	56	Cost analysis of infection	40	57
Europe	17	24	Cost analysis of intervention†	30	43
Australia/New Zealand	4	6			
Other	10	14	Perspective of analysis		
			Hospital	63	90
Source of funding*			Health care sector	6	9
Government	14	20	Societal	1	1
Industry	13	19			
Foundation	2	3	Costs included*		
In-kind	1	1	Intervention	25	36
Not stated	43	61	Hospitalization	60	86
			Outpatient	3	4
HAI analyzed			Antibiotics	9	13
Surgical	18	23.7	Nonhealth care	0	0
Bloodstream	14	18.4			
Pneumonia	6	7.9	Source of cost estimate*		
Urinary tract	2	2.6	Published data	14	20
Organism specific	25	32.9	Microcosting	50	71
Other	11	14.5	Estimated by authors	29	41
			Claims	25	36
Antibiotic resistance considered			Other	3	4
Yes	21	30			
			Time horizon		
Definition of HAI			1 year or less	69	99
CDC	29	41	Greater than 1 year	1	1
Other	31	44			
Not stated	10	14	Quality score		
			4 or less	35	50
			Greater than 4	35	50

N = 70.
*Categories are not mutually exclusive.
†Twenty of these studies had no comparator and therefore were not formal economic evaluations. Five of the studies were cost-effectiveness analyses, 3 were cost-consequence analyses, and 2 were cost-minimization analyses.

From the 70 studies analyzed, results from 21 costs analyses could be used to provide a cost per infection specific by body site: bloodstream infections, surgical site infections, ventilator-associated-infections and urinary tract infections. Mean costs (in 2002 US dollars) are presented for those 21 studies in Table 2.2.

Bloodstream infections were found to be the most expensive; however SD of costs of all infections types were quite large, indicating wide variations in estimated costs per patient.

Table 2.2: Attributable costs of NI (in 2002 US dollars), Stone 2005 [5]

	Attributable costs of NI (US Dollars 2002)					Refs
Infection type	Mean	SD	Min	Max	N studies	
SSI	25546	39875	1783	134602	8	12 13 14 15 16 17 18 19
BSI	36441	37078	1822	107156	9	20 21 22 23 24 25 26 27 28
VAP	9969	2920	7904	12034	2	29 30
UTI	1006	503	650	1361	2	31 32

Another review was performed by Graves in 2003 [9]. In this review, studies before 1980 were excluded to reduce bias arising from changes in LOS, treatment regimens and clinical practice that would have occurred over time. The purpose of this research was not per se to perform a review, but to include estimates of attributable LOS in a Monte-Carlo simulation model, used to give a estimate of the impact of NI at a national level in New Zeeland. Graves identified 55 studies for 6 major sites of infection. We did not report all those results, as only one study dates from later than 2000 [33].

As mentioned before, simply averaging attributable costs from different international studies, with different designs, is not very appropriate to estimate the impact on the Belgian healthcare budget. On the other hand, the estimation of additional LOS can be converted to costs using Belgian values for one hospitalisation day.

Table 2.3 presents the results of individual studies, for 4 body sites of infection: bloodstream infection (catheter related or not), lower tract infections (VAP or not), surgical sites infections and urinary tract infections. We do not claim this table represents the results of an exhaustive systematic search, but it shows the diversity of results from different studies, even when a robust outcome such as LOS is used (as opposed to costs). Only studies from Europe, US, Australia and New Zeeland are presented.

Eight original studies describe the additional LOS and costs of NBSI, of which 3 were performed in Belgium: one published by Blot et al.[34] on catheter related bloodstream infection in ICU and two by Pirson et al.[35 36] on bloodstream infections on any type of ward. All studies used a matched cohort design. The estimations of additional LOS reported in the literature vary greatly, from 4.5 days to 30 days. The 30 days estimate in the Pirson study is probably an overestimation of the attributable LOS, as only a single variable was used in the matching procedure (APR-DRG).

Eight original studies on lower respiratory tract infections were identified (ventilator associated or not), none from Belgium. The estimates of additional LOS are very constant around 10 days. One study reports 25 days, but this results from an unadjusted comparison[30]. Another study reports estimated only 2.6 additional days in hospital.[2] However, this study is based on few patients (n=27) and the regression model also (over)adjusted for events during hospitalization (eg falls) which might have been the results of a NI.

Nine studies specific to surgical site infections were identified, one performed in Belgium[37]. There is more variation in the estimates of attributable LOS, from 3 to 21, depending on the type of surgery.

Six studies specific to UTI were identified, none from Belgium. The estimates were of attributable LOS were much lower, around 3 to 7 days. One study adjusted too many variables (including complications which might have been the result of a NI) and even found no attributable LOS[2].

Another study not specific to a type of infection but on neonates hospitalized in intensive care was performed in a Belgian hospital.[38] The additional LOS of infected neonates was 24 days.

Table 2.3: Results of the literature review on the additional LOS due to NBSI

Body site	Author	Year	Country	Wards	Design	Factors	N Infected	Add LOS
CR-BSI	**Blot [34]**	**2005**	**Belgium**	**ICU**	**M.C.**	**APACHE II, principal diagnosis, LOS before CR-BSI**	**176**	**12(m)**
BSI	Digiovine [39]	1999	US	ICU	M.C.	Score of predicted mortality, sex, age, race, LOS prior BSI, admission, principal diagnosis, chronic health	68	4.5
BSI	Morano Amado [40]	2002	Spain	All	M.C.	RDG, age, main diagnosis and n secx diagnoses	100	19.5(m)
BSI	Orsi [25]	2002	Italy	ICU	M.C.	Score for ward, gender, age, diagnosis, CVC, LOS prior BSI	65	15.7
				surgical	M.C.	Score for ward, gender, age, diagnosis, CVC, LOS prior BSI	40	24.6
BSI	**Pirson [35]**	**2005**	**Belgium**	**All**	**M.C.**	**APR-DRG**	**46**	**21.1**
BSI	**Pirson [36]**	**2008**	**Belgium**	**All**	**M.C.**	**APR-DRG**	**?**	**30**
BSI	Pittet [41]	1994	US	SICU	M.C.	Primary diagnosis, age, sex, LOS before BSI, total N of discharge diagnoses	86	14 (m)
CR-BSI	Warren [42]	2005	US	ICU	R.M.	severity of illness	41	7.5
VAP	Hugonnet [43]	2004	Switzerland	ICU	M.C.	Number of discharge diagnoses, duration of ventilation before VAP, age, admission diagnosis, gender and study period	97	10
VAP	Kappstein [44]	1992	Germany	ICU	M.C.	Not mentioned in abstract	34	10
Chest	Pena [45]	1996	Spain	all	M.C.	Not mentioned in abstract	30	10
LRT	Plowman [33]	2001	UK	all	R.M.	Age, sex, admission specialty, diagnosis, n co-morbidities and admission type	48	8.4
VAP	Rello [46]	2002	US	ICU	M.C.	duration of mechanical ventilation, severity of illness on admission (predicted mortality), type of admission (medical, surgical, trauma), and age	842	11
LRTI	Graves [2]	2007	Australia	All	R.M.	Detailed patients characteristics	27	2.6
VAP	Warren [30]	2003	US	ICU	M.C.	Other ventilated patients	127	25**
SSI	Coello [47]	1993	UK	Surgery, gynecology and orthopedics	M.C.	first operative procedure and primary diagnosis, and on the secondary features of sex, age and surgical service	12	10.2
SSI	Coello [48]	2005	UK	surgery	R.M	age, sex, pre-operative length of hospital, stay, ASA score, wound class, duration of operation, elective/emergency surgery, multiple procedures through the same incision, implants and operation due to trauma	2832	3 to 21
SSI	Kappstein [49]	1992	Germany	Cardiac s	M.C.	Not mentioned in abstract	22	12
SSI	Kirkland [50]	1999	US	general	M.C.	procedure, National Nosocomial Infection Surveillance System risk index, date of surgery, and surgeon	255	6.5 ??
SSI	Pena [45]	1996	Spain	All	M.C.	Not mentioned in abstract	63	11
SSI	Plowman [33]	2001	UK	All	R.M	Age, sex, admission specialty, diagnosis, n co-morbidities and admission type	38	7.1
SSI	**Ronveaux [37]**	**1996**	**Belgium**	**all**	**R.M**	**Risk factors**	**269**	**9**
UTI	Coello [47]	1993	UK	Surgery, gynecology and orthopedics	M.C.	first operative procedure and primary diagnosis, and on the secondary features of sex, age and surgical service	36	3.6
UTI	Medina [51]	1997	Spain	Surgery	R.M.	surgical procedure, ASA score, age (+/- 10 years), emergency surgery, pre-operative stay, and urinary catheter	33	5
UTI	Moris de la Tassa [52]	2003	Spain	all	M.C.	DRG, gender, age, admission date, department, comparison of length of stays, main diagnosis, co-morbidities, number of secondary diagnoses and procedures	64	3
UTI	Pena [45]	1996	Spain	all	M.C.	Not mentioned in abstract	55	7
UTI	Graves [2]	2007	Australia	All	R.M/	Detailed patients characteristics	59	0
UTI	Plowman [33]	2001	UK	all	R. M..	Age, sex, admission specialty, diagnosis, n co-morbidities and admission type	107	5.1
ALL	**Mahieu [38]**	**2001**	**Belgium**	**Neonatal ICU**	**MC**	gestational age, surgery, artificial ventilation and patent ductus arteriosus	**45**	**24**

CR-BSI catheter related bloodstream infection
M.C. matched cohort study
R. M. regression model
SIU surgical ICU
** unadjusted comparison
m=median
Belgian costs studies are indicated in bold

2.3.2 Discussion of the different designs used to estimate attributable costs of NI

Different methods exist for the estimation of the additional days of hospitalization: non-comparative methods (which evaluate the additional days based only on patients infected) and comparative methods (which compare infected patients to non infected patients). Recently some new advanced statistical methods have also been proposed.

Non Comparative Methods:

Implicit Physician Assessment. With this method, each medical record is reviewed by a physician to estimate the additional number of days attributed to the NI. The obvious disadvantage of this method is the subjectivity of the assessment.

Appropriateness Evaluation Protocol (AEP) Based Methodology: Wakefield [53, 54] developed a method based on appropriateness evaluation protocol (AEP), which is a standardized method to evaluate the appropriateness of both hospital admission and days of hospitalization. This approach categorizes all days of hospitalization between those related to the original cause of hospitalization and the other related to the NIs. This method has been applied successfully to different types of infections [55 56 57] However, despite the standardization also this method remains a somewhat subjective judgment by the assessor.

Comparative Methods:

Unmatched Group Comparison. The LOS is calculated for 2 groups of patients: those with the infection and those without. The difference between the 2 groups is attributed to the NI. This method usually leads to an overestimation of the attributable difference, as it is confounded by patient's severity (comorbidity, disease severity). A refinement of this method is thus to adjust for the underlying patient's severity in a *regression model*, taking into account confounding variables such as age, sex, diagnosis, number of comorbidities, admission speciality and admission type [33].

Matched Cohort Studies. In this method, patients with NI are matched with uninfected but otherwise similar patients (controls). The key difficulty is to determine enough matching factors, so that the resulting difference between the 2 groups can be entirely attributed to the NI. Such studies are sometimes mistakenly referred as case-control studies, where cases and controls are matched to evaluate risk factors (predictors) of the infection (outcome), whereas in the economic studies, the infection is the predictor, and the cost is the outcome. Thus these studies are really cohort studies, where the cohorts are selected based on a causal factor (the infection), and followed over time to measure the outcome (extra LOS and costs). The group of control patients is usually chosen so that they have the same expected LOS and hospital costs as the infected patients if the nosocomial infection had not occurred.

In the past, studies were using simple matching characteristics such as age, sex, service, first diagnosis and first operation. However, matching factors should be chosen as predicting both the expected LOS and the infection risk (ie, true confounding variables). Thus, it was advocated to use the Diagnosis-Related-Groups (DRG) system as a matching factor, as it was specifically designed to predict the costs, and as studies have shown that they might as well predict the differences in nosocomial infections risk [58]. This matching factor has already been partially used in two Belgian studies studying the cost of nosocomial infections [35 36].

In order to properly account for the severity of illness, several authors use common risk scales (such as APACHE II). Alternatively, the number of secondary diagnoses has been proposed as a good proxy. It has also been shown to be significantly associated with LOS and the risk of nosocomial infection [58]. Other studies have used measures of comorbidities identified with ICD-9 Cm codes in administrative databases, such as the Charlson index score.[21, 59].

In addition to the matching criteria mentioned above, recent studies have selected their control group of patients on the duration of hospitalisation prior to the infection [60 25 34].

Matched cohort studies have the disadvantage that infected patient can only be matched to uninfected controls for a limited number of variables. Finding matching controls soon becomes impossible as the number of variables increases. Consequently, costs attributed to NI are often overstated, as indicated by prior research [58]. A trade off must then be found between external validity (matching all patients on a few number of criteria) and internal validity (matching fewer patients on a higher number of criteria).

A summary of advantages and disadvantages of all methods can be found in Table 2.4.

Table 2.4: Characteristics of Methods used to estimate extra LOS due to NIs[7]

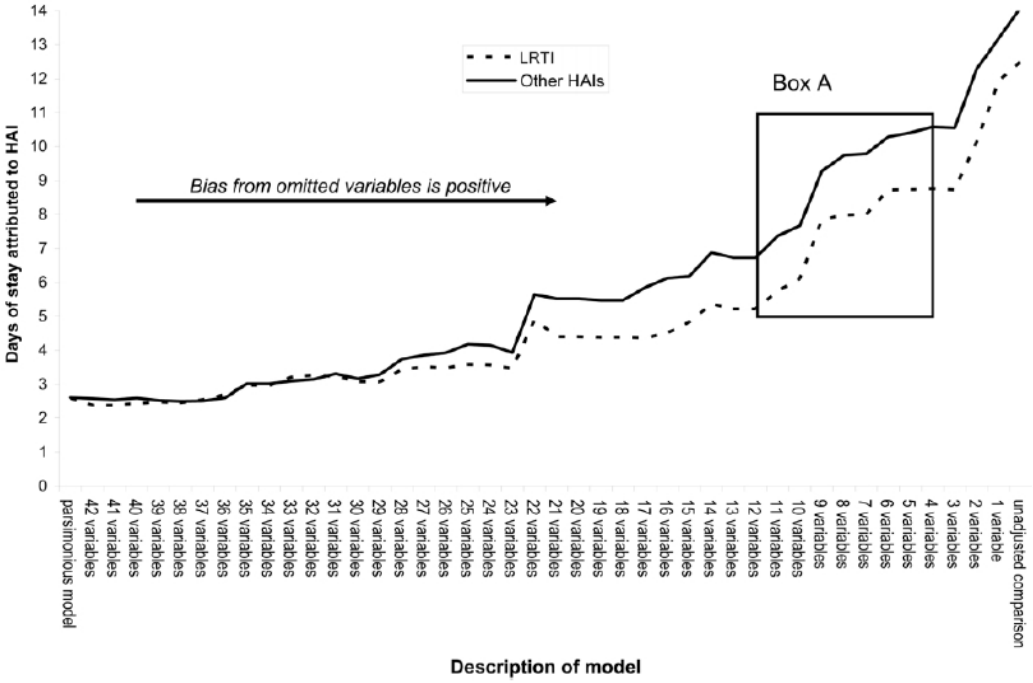
Table 2
Characteristics of methods used for estimating extra length of stay due to NIs.

	Physician assessment	Unmatched group comparison	Matched control	AEP-based methodology
ADVANTAGE	• Review of clinical data • Ease in using	• Inexpensive, readily available data for large numbers of patients	• Two groups matched for variables that could also influence the length of stay	• Inclusion of all patients with NIs in the appraisal, • Evaluation of the care provided rather than the simple length of stay • Data available in the medical records • Based on explicit criteria • Available additional information.
DISADVANTAGE	• Subjectivity • Low reliability	• Not evaluated, other inherent differences between the two groups	• Difficulty of selecting and measuring all appropriate variables	• Degree of difficultly when the partial AEP is conducted
OUTCOME	• Low estimate of an additional day	• Overestimate the incremental days due to NI	• Overestimate the incremental days due to NI	• Provided individual and group appraisal of NI attributed days

Some authors have compared different methods using the same set of data. For instance, Asensio et al.[61] compared the matched cohort approach with the regression approach. While their conclusion goes in favour of the last one, it is unclear how this conclusion can be made in absence of a gold standard to which results from both approaches could be confronted.

A recent prospective study [2] aimed to estimate the effect of NI on LOS and costs in a regression model, with specific attention at the bias introduced in the analysis by taking or not taking certain variables into account. For that purpose, the study prospectively recorded an extensive list of symptoms and diagnoses which occurred during hospital stay. The estimates, when corrected for all variables, are lower than those usually cited in literature. This is explained by the amount of bias that can be introduced in the estimation by not taking into account some variables, as shown in Figure 2.1. Unfortunately, the list of variables also contained events which may have been caused by the NI, eg falls during hospital stay. Therefore the excess LOS may have been underestimated in this report. The study found that UTI are not associated with an increase of LOS and costs, and that LTRI are associated with a modest increase of 2.6 days in hospital stay and a moderate cost increase. The other types of infections were not studied.

Figure 2.1: An illustration of bias from omitted variables in models that describe the relationship between lower respiratory tract infections (LRTI) or other NI and additional LOS, from Graves [2]



Recently, more advanced statistical methods have been introduced, due to the problems of matched cohort studies: exclusion from patients from analysis and potential for bias from omitted variables. These new methods are described below, but require access to detailed records of daily clinical or therapeutic activity on infected and non infected patients. These daily data are usually only in part available in administrative databases.

More advanced Statistical Models[b]

The increased availability of large databases that contain detailed records of daily clinical or therapeutic activity on infected and non infected has led to the development of new statistical techniques, briefly described below.

Some of the papers discuss the need to adjust appropriately for the time-dependent nature of the infection event, either by applying a time-dependent Cox Proportional Hazards model for time to mortality or time to hospital discharge [62] that will consider a patient to belong to the group of infected ones only from the day at which the infection starts (belonging to the control group otherwise), either by introducing "multi-state" models [63] that formally take into account the various states patients go through when proceeding from being admitted over getting infected towards achieving the studied outcome events mortality or discharge. Also aiming to provide appropriate adjustment for the time-dependency of the NI effect on hospital-LOS, Graves [64] proposed a method based on instrumental variables, which is a well known method in econometrics to disentangle endogeneous effects from exogeneous effects.

Other research [65, 66] focuses on the outcome events hospital mortality, and argues that for patients for whom the outcome is not observed or missing due to discharge of the patient from the hospital (or unit), the classical assumption of "non-informative" censoring or missingness or the outcome event is likely violated. Here, one assumes that the reason for the missing outcome (discharged) is unrelated to the outcome event (mortality), which is unlikely in the hospital setting because patients will only leave the hospital alive when their health status allows them to do so.

b this specific section has been written by Karl Mertens (statistician, IPH).

As a solution for the violation of this assumption, some studies consider the event "discharge alive from the hospital" as a competing risk event for the outcome mortality. As opposed to a regular analysis of survival time, a competing risk approach keeps censored individuals in the risk set from the time they experience the competing risk, more specifically a proportional hazards model for the subdistribution hazard for mortality [67] adjusted for competing risk event "discharge alive" can be used.

Yet other research [68 69] uses methods developed by Robins and colleagues [70] to adjust the effect of NI on mortality for the informative censoring described above. By weighting patient days for the inverse cumulative and conditional probability of remaining in the hospital until a particular day (using so-called daily Inverse-Probability-of-Censoring (IPC) weights), these methods will try to construct an artificial population in which informative censoring is absent and thus the assumption of non-informative censoring is not violated.

These weighting methods fall within the framework of "causal" inference because they formally acknowledge the confounding and selection bias that occurs in this type of observational data and they aim to estimate attributable effect of NI on mortality and LOS that is unconfounded or unbiased and therefore has causal interpretation under the usual assumptions of no model misspecification and no unmeasured confounders. Next to the above described selection bias due to non-informative censoring, time-dependent confounding bias is likely to happen when the time-dependent infection is stratified (for example by adjustment in a regression model) for time-dependent confounders that act as both cause and effect of infection (for example daily measured antibiotic treatment or mechanical ventilation). In the same way as with informative censoring, this time-dependent confounding is resolved by weighting patient days for their Inverse-Probability-of-Exposure (IPE, exposure equivalent to NI) history, once again creating an artificial population in which the infection-outcome association is unconfounded by time-dependent prognostic factors. Once achieved, the effect of NI on outcome can be estimated by fitting a time-dependent Proportional Hazards model adjusted for baseline confounders. This IPE- and IPC-weighted Cox model is also named Marginal Structural Cox model in the literature [71].

2.4 DISCUSSION

It is difficult to accurately estimate the additional length of stay or costs induced by a NI, as shown by the number of studies on that subject since the 70s. Different methodologies have been used for that purpose, each having advantages and disadvantages. Non comparative methods include the direct assessment of the physician (based on its judgment) and the appropriateness evaluation protocol (AEP) methodology, a refinement of the previous methods to standardize the physician evaluation. Comparative methods include the unmatched group comparison (comparing costs of NIs to costs of other hospitalized patients), the matched cohort study (comparing costs of NIs to costs of uninfected but otherwise similar patients), and the use of regression models (to avoid the problems of not finding controls when the number of matching factors increases). The methods used in most of the health-economic studies published so far have probably overestimated the burden caused by a NI. The better one corrects for co-morbidity present before the NI, the smaller the differences between cases and controls become, as shown by Haley in the 80s [4] and again elegantly demonstrated (but perhaps over adjusted) recently by Graves et al [2]. Most recent statistical models using competing risks and multistate models are still being developed to account for the exact timing of events.[65, 66] Discussion will however remain on the relationship eg between a fall occurring during the subclinical phase of a nosocomial infection, and the NI, and whether one should adjust for it (eg match with a control who also had a fall but no NI).

A systematic review of those economic studies was performed in 2005 by Stone [5] who identified 70 studies. The differences in methodologies are striking: from the definition of the infection (CDC criteria or not), the type of analysis (economic evaluation with or without comparator, the perspective of the evaluation (hospital, health care sector, societal), and the costs included (hospitalisation, outpatient, etc..). Given those differences in methodologies, heterogeneous results are observed, rendering meaningless any attempt to summarize those results. When the exercise is nevertheless done (averaging on all studies from all countries), BSI are the most costly infections, followed by SSI and VAP. UTI have the lowest costs.

Key messages

- **It is difficult to accurately estimate the additional length of stay or costs induced by a NI, due to the confounding by patient's frailty, comorbidity, procedures, and other potentially confounding factors (frail patients have a higher risk to be infected, and also incur greater costs, independently of the NI). Time spent in the hospital is also an important confounding factor, as the probability of infection increases with time spent in hospital.**
- **As these confounding factors induce bias in the same direction, the methods used in most of the health-economic studies published so far have probably overestimated the burden caused by a NI.**
- **Studies have also shown that the more matching factors are used, the lower the difference becomes in costs and length of stay attributed to the nosocomial infection.**
- **A systematic review of those economic studies was performed in 2005. Results are extremely different due to different methodologies used in those studies. Overall, bloodstream infections appear to be the most costly, followed by surgical site infections and ventilator associated pneumonia. Urinary tract infections have the lowest costs.**

3 A SUBSTUDY ON THE IMPACT OF NOSOCOMIAL BLOODSTREAM INFECTIONS

3.1 INTRODUCTION

The results of the review of costs attributable to NI in the literature (see previous chapter) revealed that the bloodstream infections were the most costly infections, followed by the surgical site infections. BSIs are a severe type of infection, and represent 14% of all prevalent nosocomial infections in Belgium (and 16% of all patients who suffer from one or more NIs) [1]. It is estimated that approximately 16000 patients are infected each year in Belgium. The BSIs are the subject of a specific surveillance in the National Surveillance of Infections in Hospitals program [72]. This surveillance is not specific to the ICU, as data are gathered from all wards. Giving the importance of these infections, a specific substudy was set up. Its objective was to estimate the additional cost (from a healthcare payer perspective) and length of stay attributable to nosocomial bloodstream infections (NBSI), in the acute hospital setting. Because the literature review showed the importance of the choice of the matching factors, the impact of this selection was also explored.

3.2 METHODS

3.2.1 Databases

3.2.1.1 The National program for Surveillance of Hospital Infections

The NSIH program [73] organizes, among others, the surveillance of nosocomial bloodstream infections, in all the wards of the hospital (thus not specifically related to the ICU).

This substudy used data from the surveillance of bloodstream infections for the limited number of hospitals who participated the entire year (2003) to the surveillance program. For each infection, data regarding the origin of infection, the time from admission to infection, the reporting service and the list of pathogens identified are recorded in the database. The complete description of this database can be found in the NSIH protocol.[72]

3.2.1.2 Minimal Clinical Data (MCD), coupled with Minimal Financial Data (MFD)

The Minimal Clinical database is an administrative clinical database ("Résumé Clinique Minimum/ Minimale Klinische Gegevens" or RCM/MKG) which is transmitted by each hospital to the Ministry of Public Health. All non-psychiatric hospitals must participate to this data collection. The available information concerns outpatient or inpatient stays discharged during 2003 and contains year of birth, sex, place of residence zip code, length of stay, year and month of admission and discharge, in addition to all diagnoses and procedures coded in ICD-9-CM (International Classification of Disease, 9th revision, Clinical modification). The Ministry runs the APR-DRG version 15th grouper program to assign an APR-DRG (All-Patient Refined Diagnosis Related Group).

The purpose of MCD registration is to:

- determine the need for hospital facilities
- define the qualitative and quantitative recognition standards of hospitals and their services
- organize the financing of hospitals
- determine the policy concerning the practicing of medicine
- outline an epidemiological policy
- help the hospitals in their internal management (feed-backs on their data)

Because of the frequency of registration, data from MCD registration are available with a one year delay, after a limited validation process. The database contains information from every Belgian hospital.

The second database, the Financial Administrative database, gathers the inpatient claims data provided by the hospitals to the health insurers. This database gives information on the resources used during the stay (reimbursed medical acts, medical supplies, implants and reimbursed drugs). After using a patient encryption algorithm, insurers send these financial data ("Résumé Financier Minimum/ Minimale Financiële Gegevens" or RFM/MFG) to the INAMI/RIZIV (National Institute for Illness and Invalidity Insurance). After a second encryption, validation and quality check by the Ministry and by the INAMI/RIZIV, the two records are transmitted to an interface body called the Technical Cell (or "Cellule Technique/Technische Cel") in order to be linked using the encrypted patient key. The data are linked at the level of each stay so that tracing the patient medical history becomes possible. In 2003, the linkage was possible for 95 % of the inpatient stays[c].

3.2.2 Coupling the databases

These two databases were coupled (based on the MCD number as a unique identifier), and anonymized by the Technical Cell (see appendix). A specific request was made to the Sectorial Committee Social Security of the Privacy Commission, which authorized the Technical Cell to transfer this coupled database to the KCE and to the NSIH (authorization number SCSZ/06/054[d]). The coupling scheme is in appendix.

Specifically, the NSIH did send to each of the hygienists the list of NBSI identified in 2003 in their respective hospitals. The hygienist then provided a table with the link with the MCD unique identifier of the hospitalisation, and transferred these data directly to the Technical Cell. The TC then identified these stays in the administrative database, and transferred the data to the KCE after recoding hospitals and patient's identifiers. No MCD identifier was transferred to the KCE or to the NSIH. Only hospitals who participated to the surveillance during the full year 2003 were contacted to participate to this study.

3.2.3 Study Design

Studies using administrative data are usually good candidates for matched procedures, as the large number of control patients available (theoretically) permits to achieve a high percentage of matched cases. In the study, the first two matching factors were the hospital and the APR-DRG, meaning that for each patient with a NBSI reported to the NSIH, data from all patients from the same hospital and from the same APR-DRG were made available to the KCE, and could be used to find the best control patients. No other matching factors were defined at the moment of the study planning, to allow for the investigation of the impact of more specific matching factors on the estimation of the additional cost.

3.2.4 Definition of Cases and Controls

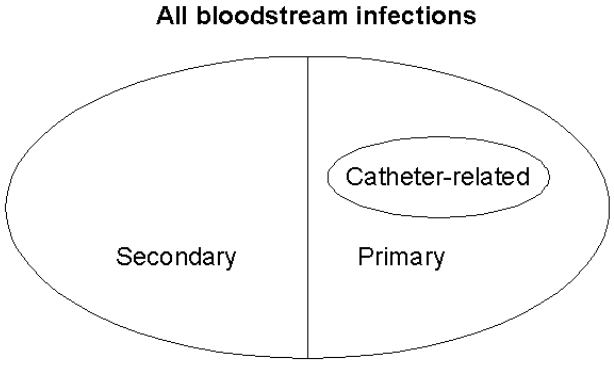
3.2.4.1 Source and Definition of Cases

The surveillance of NBSI, a component of the NSIH program, provided a list of cases for the year 2003.

The extensive definition of a nosocomial bloodstream infection used by the NSIH program can be found in the NSIH protocol.[72] All infections need to be confirmed by laboratory tests. The protocol distinguishes between primary infections (no other site of infection, includes catheter-related NBSIs) and secondary infections (another site of infection is present, with the same pathogen).

c https://tct.fgov.be/etct/html/fr/index.jsp

d NL : http://www.privacycommission.be/nl/docs/SZ-SS/2006/beraadslaging_SZ_18_2006.pdf, FR: http://www.privacycommission.be/fr/docs/SZ-SS/2006/deliberation_SS_18_2006.pdf



3.2.4.2 Source and Definition of Control Patients

A large group of control patients (ie patients without a NBSI) was selected with the following algorithm: for each stay with a NBSI, all stays discharged in 2003 from the same hospital, and included in the same APR-DRG, were included in the control group. This large selection was afterwards refined in the cost analyses.

3.2.4.3 Source and Definition of costs data

All costs data are derived from the Minimal Financial Data (MFD). These costs include

1. The cost of each day hospitalized (based on the 2003 100% per diem price, for participating hospitals)
2. The cost of clinical biology (partially) and nuclear medicine
3. The cost of implants
4. The costs of all pharmaceutical products
5. The costs of all medical acts
6. The costs of blood, plasma, milk and isotopes for therapeutic use

3.2.5 The choice of matching factors

All variables tested in the matching procedure are described below. The majority of these variables were considered as categorical variables, but for some the effect of using a range instead was also investigated. The variables can be divided into those present at admission, and which can be thus used in the matching procedure, and those that can be influenced by the complications occurring during the stay, such as a nosocomial infection. As the effect of those latter variables can lead to biased results, they were investigated in the exploratory phase but not retained in final analyses.

Admission characteristics

- Hospital (Hosp)
- APR-DRG (DRG)
- Age group: divided in 4 classes (<1 , 1-17, 18-70, +70) (Age) or with a range (controls within 10 years of case). Age is used as a surrogate variable of many unobserved variables.
- Gender: male, female (Sex)
- Principal Diagnosis; ICD-9 with 3 main digits (Diag.)
- Charlson Index (0, 1-2, 3-4, >4) (Comorb.). The Charlson score is a validated score predicting 1-year mortality, based on comorbidities [59, 74, 75]. The Charlson score is the sum of some predefined weights attributed to some specific conditions (see Table 3.2). The higher the score, the higher the probability of 1-year mortality. The controls selected in the same class (0, 1-2, 3-4, >4) than cases.

Table 3.1: Charlson score: Scoring the co-morbidity index from secondary diagnoses

Weights	Conditions	ICD-9 codes
1	Myocardial infarct	410, 411
	Congestive heart failure	398, 402, 428
	Peripheral vascular disease	440–447
	Dementia	290, 291, 294
	Cerebrovascular disease	430–433, 435
	Chronic pulmonary disease	491–493
	Connective tissue disease	710, 714, 725
	Ulcer disease	531–534
	Mild liver disease	571, 573
2	Hemiplegia	342, 434, 436, 437
	Moderate or severe renal disease	403, 404, 580–586
	Diabetes	250
	Any tumor	140–195
	Leukemia	204–208
	Lymphoma	200, 202, 203
3	Moderate or severe liver disease	070, 570, 572
6	Metastatic solid tumor	196–199

table from D'Hoore [59]

- The time to infection: the LOS of controls must be at least equal to the time to diagnosis of the infection (the number of days between admission and start of NBSI) (time). To allow for a certain incubation period, a gap of 2 days has also been allowed (time2)

Characteristics that can be influenced by complications (admission + discharge)

- Severity of APR-DRG: as assessed by the grouper: 1, 2, 3, 4 (DRG-sev). The severity of the APR-DRG takes into account all secondary diagnoses and complications which occurred during the hospitalisation.
- Stay with a passage in a ICU unit: yes or no (ICU)

3.2.6 Analyses

Additional LOS and costs attributable to NBSI were estimated in a matched cohort study (1 case: 1 control). Per design, the 2 first matching factors are the hospital and the APR-DRG. Next, a series of different possible matching factors were examined in order to study the feasibility of the matching and the influence of the matching criteria on the estimate of attributable LOS.

The difference in outcome (LOS and Cost) for each case-control pair was then computed. The additional LOS and cost attributable to NBSI, and corresponding 95% CI, was computed based on these differences. A paired t-test was used to test the hypothesis that the attributable LOS and cost are not null.

To test whether the additional LOS and costs were consistent across different baseline characteristics, subgroup analyses were performed, and the interaction between the additional LOS and costs and the subgroup were tested in an ANOVA model.

The results of the 1:1 matching procedure were also compared to the results of the 1:4 matching procedure (allowing from a variable number of controls per case, from 1 to a maximum of 4 controls, data not shown).

3.3 RESULTS

3.3.1 Data received

3.3.1.1 Participating Hospitals in Study

Of the 22 hospitals which participated during the full year 2003 to the surveillance of nosocomial bloodstream infections, 20 hospitals accepted to participate to the study and did send their data within the planned timeframe to the Technical Cell (closing date 15 July 2006). For a technical reason (a problem of software version), the data from 1 hospital could not be used. Thus the present report is based on data from 19 hospitals. The list of participating hospitals is in appendix.

3.3.1.2 Number of Nosocomial Bloodstream Infections

A total of 3302 bloodstream infections were reported to the NSIH during the year 2003 by the 19 participating hospitals. Some of these infections started within 2 days of hospital admission, and are therefore considered as non nosocomial. A total of 2762 corresponding stays (83.6%) only could be retrieved from the Minimal Clinical Data (MCD) database. One possible explanation for the incompleteness of the linkage is that the MCD 2003 database is based on patients discharged in 2003, while the NBSI database contains also patients infected in 2003 but discharged in 2004. From the 2762 linked infections, 787 were declared within 2 days of hospital admission, and were excluded from analysis. The link was made with the Minimal Financial Data (MFD), and other checks were performed to verify the consistency of the data. Finally, 1839 stays were available for the cost analysis.

Table 3.2: Participation to the Study

	N
Hospitals participating to the NSIH full year 2003 surveillance	22
Hospitals participating to this study	19
All Bloodstream infections reported to NSIH in 2003	3302
Corresponding stays retrieved in Minimal Clinical Database (MCD)	2762
Non nosocomial bloodstream infections	787
Nosocomial Bloodstream infections	1975
Nosocomial Bloodstream Infection with Cost data (Minimal Financial Data) Available	1839

The 1839 stays with a NBSI are distributed across 254 different APR-DRG. The 10 most common APR-DRGs are given in Table 3.3 (all data are in appendix). The three most common APR-DRGs are surgical (tracheotomy, bowel procedures and procedures not related to the diagnosis of admission).

While it was confirmed that these infections were not the reason for admission, the fact that 51 stays (2.7%) are classified in the APR-DRG Septicemia brings some doubts to the coding of these hospitalisations. This coding problem was not restricted to a few hospitals.

Table 3.3: APR-DRG of cases (sorted by number of cases in APR-DRG, 10 first APR-DRG only – all data in appendices)

APR_DRG	N
004-TRACHEOSTOMY EXCEPT FOR FACE, MOUTH & NECK DIAGNOSES / p3 - P	119
221-MAJOR SMALL & LARGE BOWEL PROCEDURES / 6 – P	99
950-EXTENSIVE PROCEDURE UNRELATED TO PRINCIPAL DIAGNOSIS / 0 - P	53
720-SEPTICEMIA / 18 – M	51
690-ACUTE LEUKEMIA / 17 – M	37
194-HEART FAILURE / 5 – M	35
045-CVA W INFARCT / 1 – M	32
130-RESPIRATORY SYSTEM DIAGNOSIS W VENTILATOR SUPPORT 96+ HOURS / 4 – M	31
691-LYMPHOMA & NON-ACUTE LEUKEMIA / 17 – M	30
220-MAJOR STOMACH, ESOPHAGEAL & DUODENAL PROCEDURES / 6 – P	28

3.3.2 Description of patients infected by a NBSI

3.3.2.1 Baseline Characteristics

Some demographic characteristics (age and sex) are presented below. Mean age of patients was 67 years. More than 50% of the patients were above 70 years old. 58% were male.

Table 3.4: Age and Gender Distribution for Stays with NBSI

	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Age				
< 1	33	1.79	33	1.79
1-4	6	0.33	39	2.12
5-9	4	0.22	43	2.34
10-17	8	0.44	51	2.77
18-29	41	2.23	92	5.00
30-39	54	2.94	146	7.94
40-49	99	5.38	245	13.32
50-59	224	12.18	469	25.50
60-69	358	19.47	827	44.97
70-79	589	32.03	1416	77.00
80-89	361	19.63	1777	96.63
>= 90	62	3.37	1839	100.00
Sex				
Male	1070	58.18	1070	58.18
Female	769	41.82	1839	100.00

Age (years)					
N	**Mean**	**Std Dev**	**Median**	**Minimum**	**Maximum**
1839	66.9	18.2	72.0	0.0	101.0

3.3.2.2 *Principal Diagnosis (ICD-9 – 3 digits)*

Table 3.5 presents the principal diagnosis at admission, for patients infected by a NBSI for the 10 most common principal diagnoses. As explained above, the fact that septicemia is coded as diagnosis of admission for 54 cases is probably related to coding problems.

Table 3.5: Ten most common principal diagnoses

diag_main	N_sep
038 -SEPTICEMIA*	54
428 -HEART FAILURE*	51
414 -OTH CHR ISCHEMIC HRT DIS*	42
205 -MYELOID LEUKEMIA*	39
820 -FRACTURE NECK OF FEMUR*	37
996 -REPLACE & GRAFT COMPLIC*	35
V58 -ENCOUNTR PROC-AFTRCR NEC*	35
434 -CEREBRAL ARTERY OCCLUS*	33
153 -MALIGNANT NEOPLASM COLON*	32
197 -SECONDRY MAL NEO GI-RESP*	29
427 -CARDIAC DYSRHYTHMIAS*	29
560 -INTESTINAL OBSTRUCTION*	29

3.3.2.3 *Comorbidity Measures*

The following measures of comorbidity and severity of disease are presented below: the APR-DRG severity, the APR-DRG mortality risk, and the Charlson Score (with its different components). It should be noted that these measures do not represent the comorbidity at entry, but are based on discharge data and thus include all complications during the stay, such as the NBSI. This explains part of the very high scores for the APR-DRG severity and risk of mortality. The Charlson index score is probably less affected by this problem, as the septicemia is not included in the calculation of the score (the definition of Charlson score is given in appendix and presented in Table 3.6).

Table 3.6: APR-DRG Severity and APR_DRG Mortality Risk

	Frequency	Percent	Cumulative Frequency	Cumulative Percent
APR-DRG Severity				
1	29	1.58	29	1.58
2	126	6.86	155	8.44
3	458	24.93	613	33.37
4	1224	66.63	1837	100.00
APR-DRG Mortality Risk				
1	122	6.64	122	6.64
2	191	10.40	313	17.04
3	564	30.70	877	47.74
4	960	52.26	1837	100.00

Table 3.7: Comorbidity Measure: the Charlson Index Score

Weight	Comorbidities Included in Charlson Score	n	%
1	Myocardial Infarct	59	3.2
	Congestive Heart Failure	260	14.1
	Peripheral vascular disease	198	10.8
	Dementia	166	9.0
	Cerebrovascular disease	90	4.9
	Chronic pulmonary disease	335	18.2
	Connective tissue disease	31	1.7
	Ulcer disease	122	6.6
	Mild liver disease	153	8.3
2	Hemiplegia	171	9.3
	Moderate or severe renal disease	495	26.9
	Diabetes	328	17.8
	Any tumour	276	15.0
	Leukemia	52	2.8
	Lymphoma	49	2.7
3	Moderate or severe liver disease	101	5.5
6	Metastatic solid tumor	218	11.9

It should also be noted that for only 64% of the reported NBSI stays, septicemia was recorded as a secondary diagnosis.

Table 3.8: Coding of Septicemia or Bacteremia as Secondary Diagnosis

Secondary Diagnoses	Frequency	Percent
	(N = 1839)	
Septicemia or bacteriema	1180	64.17
Septicemia	1150	62.53
Bacteriema	51	2.77

3.3.2.4 Details of infections

Table 3.8 to to Table 3.12 present details of the infections.

More than half of the BSI are primary infections (23% from catheter, 33% from unknown source). For secondary infections, primary sites include mainly UTI, pneumonia and GI infections. 22% of the BSI were reported by the intensive care units. The majority (72%) of the patients developed the infection in the first 3 weeks of admission; the overall mean hospital stay to the diagnosis of the nosocomial septicemia was 19 days.

Table 3.9: Origin of Infection

	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Origin of NBSI				
Cathether	415	22.57	415	22.57
Unknown	598	32.52	1013	55.08
Secondary/invasive procedure	826	44.92	1839	100.00
Detailed Origin				
central cathether	335	20.40	335	20.40
peripheral catheter	27	1.64	362	22.05
arterial cathether	4	0.24	366	22.29
invasive procedure	48	2.92	414	25.21
foreign body	19	1.16	433	26.37
other infection	719	43.79	1152	70.16
unknown	490	29.84	1642	100.00
Primary Infection if Other				
Urinary tract	263	31.84	263	31.84
Surgical Site	31	3.75	294	35.59
Pneumonia	142	17.19	436	52.78
Bone/Joint	8	0.97	444	53.75
Central Nervous System	10	1.21	454	54.96
Central Venous System	11	1.33	465	56.30
Ear/Nose	13	1.57	478	57.87
Gastrointestinal	141	17.07	619	74.94
Lower respiratory	57	6.90	676	81.84
Reproductive tract	5	0.61	681	82.45
Skin and soft tissue	55	6.66	736	89.10
Systematic	3	0.36	739	89.47
Other/Unknown	87	10.53	826	100.00

Table 3.10: Reporting Service

	Frequency	Percent
Service		
Burn	7	0.38
Cardiology	105	5.71
Cardiovasc.surg	48	2.61
Endocrinology	3	0.16
General/abdom surg.	214	11.64
Geriatrics	233	12.67
Gynecology	6	0.33
Intensive care	403	21.91
Internal Medicine	278	15.12
Medicine, other	32	1.74
Mixed surgical/medic	29	1.58
Neonatal Intensive Care	24	1.31
Nephrology	26	1.41
Neurosurgery	29	1.58
Obstetrics	7	0.38
Oncology/Hematology	189	10.28
Orthopedics	48	2.61
Other types	26	1.41
Otorhinolaryngology	1	0.05
Pediatrics	16	0.87
Pneumology	59	3.21
Psychiatry	1	0.05
Revalidation	12	0.65
Trauma/Emergency	3	0.16
Urology	40	2.18

Table 3.11: Time from Admission to Infection

Time from admission to Infection (days)					
N	Mean	Median	Std Dev	Minimum	Maximum
1839	18.9	13.0	20.4	2.0	207.0

Table 3.12: Time from Admission to Infection

Period to start of infection	Frequency	Percent	Cumulative Frequency	Cumulative Percent
week 1	536	29.15	536	29.15
week 2	493	26.81	1029	55.95
week 3	303	16.48	1332	72.43
week 4	164	8.92	1496	81.35
month 2	266	14.46	1762	95.81
month 3	50	2.72	1812	98.53
>= month 4	27	1.47	1839	100.00

3.3.2.5 Pathogens

The list of pathogens identified is presented in Table 3.13. Most frequent pathogens are E. coli, Staph epidermidis and Staph. Aureus.

Table 3.13: List of Pathogens Identified (with occurrence at least 1%) – per decreasing occurrence

Pathogen	Frequency	Percent
ESCHERICHIA COLI	334	15.46
STAPHYLOCOCCUS EPIDERMIDIS	216	10.00
STAPHYLOCOCCUS AUREUS	207	9.58
STAPHYLOCOCCUS, COAGULASE NEGATIVE	184	8.51
PSEUDOMONAS AERUGINOSA	97	4.49
CANDIDA ALBICANS	93	4.30
ENTEROCOCCUS FAECALIS	85	3.93
KLEBSIELLA PNEUMONIAE	78	3.61
ENTEROBACTER CLOACAE	73	3.38
ENTEROBACTER AEROGENES	58	2.68
KLEBSIELLA OXYTOCA	56	2.59
STAPHYLOCOCCUS AUREUS,METHICILLIN RESIS	53	2.45
ACINETOBACTER BAUMANNII	45	2.08
CANDIDA GLABRATA	43	1.99
STREPTOCOCCUS PNEUMONIAE	42	1.94
PROTEUS MIRABILIS	33	1.53
SERRATIA MARCESCENS	32	1.48
ENTEROCOCCUS SPECIES	29	1.34
ENTEROCOCCUS FAECIUM	29	1.34

3.3.2.6 In hospital mortality

Overall in hospital mortality was 32% for patients infected with a nosocomial bloodstream infection. Mortality in geriatric ward was 47%, and 46% in intensive care. Mortality per pathogen is presented in appendix.

Table 3.14: In hospital mortality of patients infected by a NBSI, per ward

	N	N death	% death
All	**1839**	**585**	**31.8**
Burn	7	2	28.6
Cardiology	105	25	23.8
Cardiovasc.surg	48	9	18.8
Endocrinology	3	0	0
General/abdom surg.	214	35	16.4
Geriatrics	233	109	46.8
Gynecology	6	1	16.7
Intensive care	**403**	**184**	**45.7**
Internal Medicine	278	70	25.2
Medicine, other	32	17	53.1
Mixed surgical/medic	29	9	31.0
Neonatal Intensive Care	24	4	16.7
Nephrology	26	10	38.5
Neurosurgery	29	9	31.0
Obstetrics	7	0	0
Oncology/Hematology	189	58	30.7
Orthopedics	48	13	27.1
Other types	26	6	23.1
Otorhinolaryngology	1	1	100.0
Pediatrics	16	0	0
Pneumology	59	19	32.2
Psychiatry	1	0	0
Revalidation	12	1	8.3
Trauma/Emergency	3	1	33.3
Urology	40	2	5.0

3.3.2.7 LOS and Detailed Costs Data of NBSI

Table 3.15 presents cost data for all patients with a NBSI. On average, these patients did spend 42.6 days (median 33) in the hospital, and their stay did cost 22 330 euros (median 16 990).

Table 3.15: LOS and Costs of Stays with a NBSI

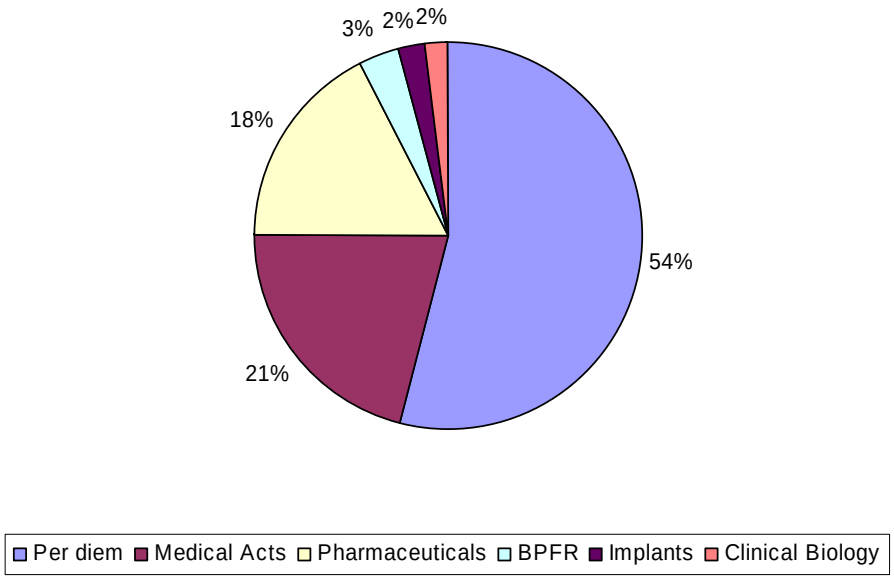
Label	N	Mean	Std Dev	Median	Minimum	Maximum
LOS	1839	42.6	35.4	33	1	290
Cost Per Diem	1839	12050.3	10974.5	8975.9	341.9	128477
Cost Clinical Biology	1839	460.3	562.2	257.4	1.6	5923.4
Cost Implants	861	1017.8	1979.1	371.8	3.2	25489.2
Cost Pharmaceuticals	1837	3954.8	5402.6	2202.2	2	55270.2
Cost Antibiotics	1803	1397.3	2214.5	711.5	0.4	25737
Cost Medical Acts + Imaging	1839	4675.2	4583.5	3091.8	140.2	42779.4
Cost Blood-Plasma-Formula-Radio Isotope	1264	1044.6	2317.8	334.6	18.2	31888.1
Total Cost without Per Diem	1839	10280.4	10944.5	6658	159.3	104360
Total Cost Stay	**1839**	**22330.8**	**19258.5**	**16990.1**	**501.2**	**193437**

The set of 36 patients who did not have any antibiotics (including antifungal) billed, has been investigated further. Thirteen of these patients died during their hospitalisation, and might have been DNR (do not resuscitate) patients. For another 7 patients the bloodstream infection was catheter-related, and antibiotics were probably not clinically indicated in their situation.

For the other 16 patients, the fact that antibiotics were given but not billed cannot be excluded. It was nevertheless decided to keep this set of patients in the analysis, to avoid the introduction of bias.

Figure 3.1 presents the main drivers of the hospitalisation cost. More than half of the cost (54%) comes from the per diem expenses. Medical acts represent 21% of the total cost, and pharmaceutical products 18% (of which 35% is due to antibiotic products). Clinical Biology represents 2%..

Figure 3.1 Distribution of the Total Costs of Stays with NBSI



3.3.3 Influence of matching factors on estimates of LOS attributable to NBSI

Table 3.16 presents the percentage of cases that would be excluded from the analysis because no corresponding control was found, for the different matching schema. It is obvious that the more matching factors are used, the bigger the part of the data that needs to be excluded. A trade off must then be found between internal validity (no bias) and external validity (generality of the results), as increasing the number of factors will lead to estimates that are less confounded by the underlying severity, but might introduce another bias due to the exclusion of a selected population of patients, those for which no control could be found.

For the final analysis, the following matching factors were use: hospital, APR-DRG, age (range of 10 years), principal diagnosis, comorbidity (Charlson index class) and time to infection (minus 2 days to allow for incubation time).

Table 3.16: Results of the Matching Procedure

Matching Criteria		N of	Cases (N=1839)			Controls
N	Description	cells	N in	N out	% out	N
On Admission criteria Only						
2	Hosp. DRG	1051	1828	11	0.6	109924
3	Hosp. DRG Age	1258	1810	29	1.6	69981
4	Hosp. DRG Age Sex	1433	1780	59	3.2	46373
4	Hosp. DRG Age Diag.	1579	1444	395	21.5	37751
5	Hosp. DRG Age Diag. Comorb.	1724	1169	670	36.4	17756
5	Hosp. DRG Age (Range) Diag. Comorb.	--	1148	691	37.6	16479
6	Hosp. DRG Age (Range) Diag. Comorb. Time	--	894	945	51.4	7240
6	**Hosp. DRG Age (Range) Diag. Comorb. Time2**	**--**	**926**	**913**	**49.6**	**8484**
On Admission + Discharge Criteria						
4	Hosp. DRG Age DRG-sev	1417	1556	283	15.4	18115
6	Hosp. DRG Age Diag. Comorb. ICU	1747	1019	820	44.6	14717

Table 3.17 presents the impact of the matching criteria on the estimation of the additional LOS. As expected, the impact is huge. If cases and controls are matched only for hospital and APR-DRG, the estimated additional number of days is 26. If comorbidity measures and primary diagnosis are also taken into account this difference decreases to 21 days. But the variable that most dramatically impacts on this difference is the time to infection. If each control patient is chosen so that he/she has a LOS at least as long as the time to the start of the infection (minus 2 days to allow for incubation time) of the patient with a NBSI, the difference decreases to 6.7 days. This estimate even decreases to 5.2 days if the minimum hospital stay of control patients equals the time to diagnosis of the NBSI. It is important to note that the more matching criteria are used, the less severe is the population of cases (this is detailed in the appendix). When only surviving patients (cases and controls) are matched, the difference in LOS is 9.9 days.

Table 3.17: Impact of Matching Criteria on Additional LOS

	NBSI				No NBSI				**Diff in**
Matching criteria	N	mean	std	Med	N	Mean	std	Med	**means**
On Admission criteria Only									
Hosp. DRG	1828	42.5	35.4	33	1828	16.8	22.6	10.0	25.8
Hosp. DRG Age	1810	42.5	35.5	33	1810	17.0	21.6	11.0	25.5
Hosp. DRG Age patsex	1780	42.4	35.2	32	1780	17.5	22.4	10.0	24.9
Hosp. DRG Age Diag.	1444	39.4	33.0	30	1444	15.7	19.0	10.5	23.7
Hosp. DRG Age Diag. Comorb.	1169	38.4	33.0	29	1169	17.2	19.4	11.0	21.2
Hosp. DRG Age (Range) Diag. Comorb.	1148	37.9	33.0	29	1148	16.9	21.5	11	21.0
On Admission criteria and Time to Infection									
Hosp DRG Age (range) Time2	1640	39.6	32.5	30.0	1640	30.5	29.1	21.0	9.1
Hosp DRG Age (range) Diag Time2	1198	34.8	28.7	27.0	1198	27.1	27.1	19.0	7.8
Hosp. DRG Age (Range) Diag. Comorb. Time (without incubation time)	894	32.2	26.6	25	894	27.0	27.5	19	5.2
Hosp. DRG Age (Range) Diag. Comorb. Time (+ 2 days incubation time)	926	32.2	26.4	25	926	25.5	27.1	18	6.7
On Admission + Discharge Criteria									
Hosp. DRG Age DRG-sev	1556	41.3	33.6	31	1556	27.1	29.2	18.0	14.1
Hosp. DRG Age Diag. Comorb. ICU	1019	36.9	31.6	29	1019	17.8	22.1	12.0	19.1
Only on Survivors									
Hosp. DRG Age (Range) Diag. Comorb. Time **(+ 2 days incubation time)**	**665**	**32.6**	**27.9**	**25**	**665**	**22.8**	**22.8**	**17**	**9.9**

3.3.4 Los and Costs attributable to NBSI

Table 3.18 presents the estimation of additional costs due to NSBI (for patients not included in ICU). The estimation is based on the 593 patients who were not infected in ICU. A NBSI results in an additional 4420 euros on average (median 3139 euros): 61% of this additional cost is due to the per diem expenses (LOS), 20% is due to pharmaceuticals products (11% antibiotics, 9% other than antibiotics), 12% is due to medical acts, and 2% is due to clinical biology (taking into account the lump sums only).

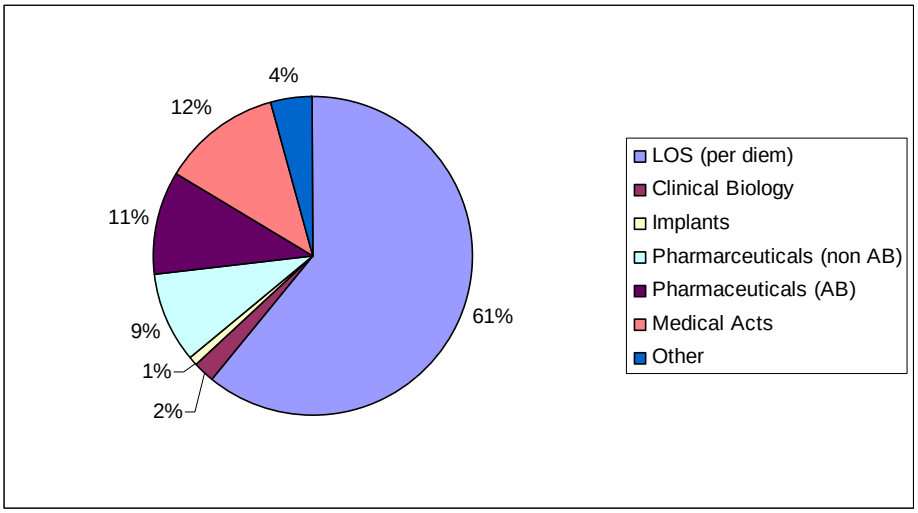
Table 3.18: Additional LOS and Costs Attributable to NBSI (all patients)

	NBSI				No NBSI			
	N	mean	Std	Median	N	Mean	std	Median
LOS	665	32.6	27.9	25.0	665	22.8	22.8	17.0
Total Cost Stay	665	15952.6	12639.5	12252.2	665	11059.8	10233.4	8084.4
Cost per diem	665	9224.8	7896.6	7088.2	665	6397.3	6087.3	4604.9
Cost C. Biology	665	268.7	283.6	165.5	648	155.3	192.2	88.9
Cost Implant	232	1120.2	2129.0	444.1	217	1056.6	1695.5	444.1
Cost Pharma.	664	2446.2	3444.5	1228.0	665	1457.7	3442.2	454.4
Cost Antibiotics	650	925.1	1512.2	406.2	488	577.7	1719.7	86.7
Cost Med. Acts	665	3132.1	3036.7	2209.3	665	2389.8	2363.9	1605.9
Cost BPFR	394	833.0	1564.7	220.1	291	728.9	1371.2	200.8

Differences:	N	Mean	Lower 95% CL for Mean	Upper 95% CL for Mean	Std Dev	Median	Mean cost PER ADD DAY
LOS (days)	665	9.9	7.8	11.9	26.5	7.0	--
Total Cost Stay	665	4892.8	4035.0	5750.5	11264.9	3301.9	494.2
Cost per diem	665	2827.6	2263.5	3391.6	7407.6	1861.6	285.6
Cost C. Biology	665	117.4	100.2	134.6	225.8	70.3	11.9
Cost Implant	665	46.0	-51.0	143.1	1274.5	0.0	4.6
Cost Pharmaceuticals	665	984.8	742.4	1227.3	3184.3	502.7	99.5
Cost Antibiotics	665	480.2	371.2	589.3	1432.3	248.3	48.5
Cost Med. Acts	665	742.3	573.3	911.4	2220.1	468.9	75.0
Cost BPFR	665	174.6	100.5	248.6	972.6	0.0	17.6

	Variable	N	Mean	Lower 95% CL for Mean	Upper 95% CL for Mean	Std Dev	Median
IC	LOS (days)	72	14.5	7.7	21.3	28.9	10.0
	Total Cost Stay	72	8784.8	5614.6	11955.0	13490.9	5269.8
	Cost per diem	72	3966.1	2135.8	5796.3	7788.6	2919.5
	Cost C. Biology	72	305.3	209.7	401.0	407.1	200.3
	Cost Implant	72	119.5	-169.6	408.7	1230.5	0.0
	Cost Pharmaceuticals	72	1871.8	1101.1	2642.5	3279.7	1005.4
	Cost Antibiotics	72	538.3	169.5	907.1	1569.5	307.1
	Cost Med. Acts	72	2426.3	1634.3	3218.3	3370.4	1816.4
	Cost BPFR	72	95.7	-38.1	229.6	569.5	0.0
NOT IC	**LOS (days)**	**593**	**9.3**	**7.2**	**11.4**	**26.1**	**7.0**
	Total Cost Stay	**593**	**4420.2**	**3542.5**	**5297.9**	**10882.9**	**3139.1**
	Cost per diem	**593**	**2689.3**	**2096.2**	**3282.5**	**7354.9**	**1841.2**
	Cost C. Biology	**593**	**94.6**	**80.1**	**109.2**	**180.2**	**63.7**
	Cost Implant	**593**	**37.1**	**-66.2**	**140.4**	**1280.4**	**0.0**
	Cost Pharmaceuticals	**593**	**877.1**	**622.4**	**1131.9**	**3158.5**	**472.1**
	Cost Antibiotics	**593**	**473.2**	**359.0**	**587.4**	**1416.0**	**236.4**
	Cost Med. Acts	**593**	**537.9**	**381.1**	**694.7**	**1944.0**	**382.1**
	Cost BPFR	**593**	**184.1**	**102.6**	**265.7**	**1416.0**	**236.4**

Figure 3.2: Distribution of Additional Costs due to NBSI (only for patients not from ICU)



3.4 DISCUSSION

As discussed in the previous chapter, the effect of NIs on length of hospital stay and cost is significantly reduced after correction for the many variables which also impact those outcomes. This is confirmed in our analysis, based on a large sample of patients with a well-documented NBSIs and an even larger pool of control patients, selected using the existing Belgian administrative databases. The more matching variables that were included, the smaller the increase in length of stay and associated health insurance costs. Especially the inclusion of length of hospital stay preceding the NBSI was important. After this correction, our final estimate of 9.9 extra days in hospital after a NBSI (median 7 days), is lower compared with the 21 days and the 12 days published before by Belgian researchers: the first study, by Pirson et al. [35], used a matched cohort design to compare the LOS and the costs of patients in a specific hospital with a NBSI (36 patients) to a set of controls patients (1308), selected from the same APR-DRG. No other matching factor to account for the severity of disease was used. The estimation of 21 additional days due to nosocomial bloodstream infection is comparable to our initial estimate of 25 days using the same matching factors. The second study, by Blot et al [34], focuses on catheter-associated nosocomial bloodstream infections (CR-BSI) in the ICU setting. This study also used a matched cohort design (ratio of case patients to control subjects 1:2 or 1:1), with matching factors including disease severity, diagnostic category and length in ICU before onset of BSI. The study showed that patients with a CR-BSI had a longer period both in the ICU department (median 28 days versus 20 days) and for the total hospitalization stay (median 53 days vs 41 days, difference of 12 days). Our final estimate of 10 days is lower than this study, but the patient population is also different (BSI from all over the hospital, not only ICU). We also have taken care that the better matching effort did not result in the exclusion of too many cases, and thus remain confident in the external validity of the study. The extra cost induced by a NBSI was estimated at 4420 euros (consisting for about 61% of a per diem cost associated with the prolonged hospitalisation, 20% due to extra pharmaceutical products and 12% due to additional medical acts).

As a side remark we note that the Belgian MCD data are not a sensitive source for the selection of NBSI. The NBSIs reported to the IPH are well-documented but were not always coded in the MCD dataset. In fact, the infection was coded only in 64% as a secondary diagnosis (and in some cases even as primary diagnosis at admission).

The main limitation of the study is that it is partially based on administrative databases, and hence it inherits their usual pitfalls: consistency and completeness of coding, lack of clinical parameters, inconsistencies in data that cannot be reconciled (because it are retrospective data). Another limitation of this study is that not all nosocomial infections could be linked to a stay in the administrative database (84% linkage). This is partially explained by the different time frames of the two databases (MCD all stays discharged in 2003, NSIH all infection in 2003), other factors are unknown and hence a selection of cases cannot be ruled out. Another usual limitation of matched cohort study applies here: the necessary trade off between internal validity (a lot of matching factors on a small subset of patient) and external validity (a few matching factors on a large subset of patients). A last limitation is that no costs data were available after hospitalisation, eg wound care at home in case of surgical wound infections causing the septicemia.

The use of administrative database is also part of the strengths of this study, as it allows selecting good matches from a wide pool of control patients. Detailed costs data are also directly available for all controls (no additional data collection). Another strength of this study is that infected patients are identified directly from the surveillance program, and not using the administrative databases. All infections are thus laboratory confirmed, and no selection bias is introduced by applying some detection algorithm on the administrative database. Important characteristics, such as time to infection and pathogens were also available.

Key messages:

- **A study was set up to specifically estimate the additional LOS and costs attributable to nosocomial bloodstream infections. Confirmed nosocomial infections from the national surveillance system (NSIH) were linked to administrative hospital data (MCD and MFD). Control patients were selected from these administrative databases.**
- **The median age of the patients infected with a NBSI was 72 years. Infections started after 13 days of hospitalisation (median), and 20% of all NBSI were acquired in intensive care. Mortality is extremely high, as 1 out of 3 patient died during the hospitalisation (up to almost 1 out of 2 patients in intensive are and in geriatric unit. More than half of the BSI are primary infections (23% from catheter, 33% from unknown source). For secondary infections, primary sites include mainly UTI, pneumonia and GI infections). Most frequent pathogens are E. coli, Staph. Epidermidis and Staph. Aureus.**
- **This study confirmed the importance of good matching factors, as our estimate dramatically decreased with an increasing number of matching variables.**
- **For patients in ICU, administrative databases lack important daily information, and good matching of those patients could not be achieved. All results are thus presented on the patients outside ICU.**
- **Probably the most accurate estimate was obtained by selecting controls that stayed hospitalized at least the time to diagnosis of infection of cases minus two days (correcting for the incubation period). This led to an estimate of 9.3 extra hospital days, and an extra cost of 4420 euros attributable to NBSI (for 61% composed of a per diem cost due to prolonged hospitalisation, 20% due to extra pharmaceutical products and 12% due to additional medical acts).**
- **This study also revealed the lack of sensitivity of using administrative databases to select cases of NBSI based on secondary diagnoses.**

4 A MATCHED COHORT STUDY TO ESTIMATE THE ADDITIONAL LENGTH OF STAY AND COSTS ATTRIBUTABLE TO NOSOCOMIAL INFECTIONS

4.1 INTRODUCTION

A matched cohort study was set up to estimate the additional LOS and costs attributable to nosocomial infections. Infected patients are those identified during the national prevalence study of end 2007, for which detailed clinical data were asked directly at the hospital (to avoid the usual 2 years delay to have access to national MCD data). Those infected patients were then matched on a series of confounding factors on historical controls from 2005, identified on administrative databases. To collect costs of all those patients, those data were linked to health insurers databases, containing detailed information on all reimbursed healthcare costs.

4.2 METHODS

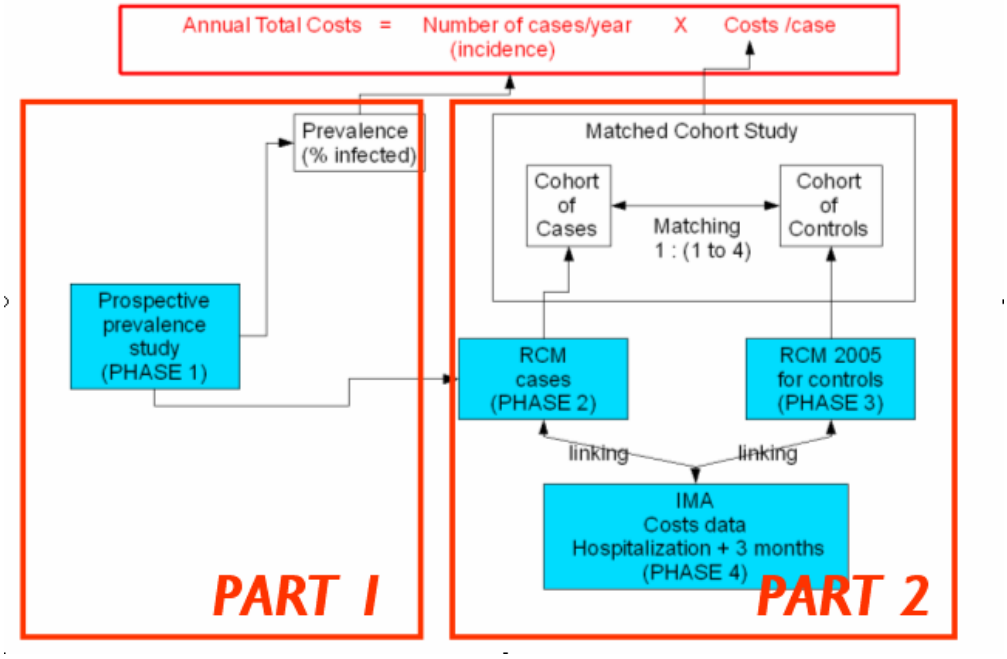
4.2.1 Databases

Different databases have been used and coupled for this study.

- The prevalence study database (described in KCE report 92 [1])
- The MCD data (discharge hospital data), described in section 3.2.1.2.
- The AMI/IMA cost data, containing all reimbursed healthcare costs by the health insurers. This database is described in section 4.2.3.5.

The study design is presented below.

Figure 4.1: Study Design



* RCM = MCD

4.2.2 Coupling the databases, authorization from privacy commission.

The authorization to couple these databases has been granted in February 2008 by the sectoral committee social security and healthcare data of the Belgian privacy commission[e]. A Third Trusted party (TTP) gathered the prevalence and the MCD database from all infected patients in one file, recoded the patient and hospital identifiers, and transferred the final recoded database to the KCE for analysis. The databases of MCD/MFD of control patients were received from the TCT. The database containing all costs data were received from the AMI/IMA.

4.2.3 Definitions of Cases, Controls and matching factors

4.2.3.1 Definition of cases:

Cases are those patients surveyed and infected at the time of the prevalence study of nosocomial infections, which occurred in October and November 2007. For those patients, a subset of variables of the MCD (minimal clinical data) was received directly from the hospitals (via a specific data entry software developed by KCE). Date of admission, date of discharge, destination after discharge, principal and secondary diagnoses, procedures, and APR-DRG were available for those infected patients.

All infections were diagnosed based on CDC criteria, as detailed in KCE report 92[1].

4.2.3.2 Definition of the Set of Potential Controls

Control patients were selected from the large number of patients who were hospitalized in 2005 for the same reason (same APR-DRG) and in the same hospital as the infected patients.

4.2.3.3 Definition of the matching criteria

The matching criteria are set up to ensure that control patients are similar to cases in respect to factors influencing length of stay and costs. The criteria are:

1. The hospital (controls from the same hospital than cases)
2. The APR-DRG (controls in the same APR-DRG than cases)
3. The age (controls selected the closest to cases, within the range of +- 15 years of the case)
4. The ward (only for those cases in geriatric or SP revalidation ward, controls are also selected from the same ward). A different matching criterion applies to patients in intensive unit care (see further).
5. The Charlson score is a validated score predicting 1-year mortality, based on comorbidities [59, 74, 75]. The Charlson score is the sum of some predefined weights attributed to some specific conditions (see Table 3.1). The higher the score, the higher the probability of 1-year mortality. The controls selected are the ones closest to the cases, without use of a range limit.
6. The exposure duration: the exposure to the risk of contracting a nosocomial infection while in hospital. This criterion is used to select control patients who have a similar exposure duration as the cases. Because the exposure duration was not recorded during this survey, it was derived as follows. (see Figure 4.2). The dates of admission and survey were compared for each case. On the survey day, it was assumed that each patient with a NI was halfway through the infection. The exposure duration of cases was the number of days from admission to the onset of infection. Control patients were thus selected if their LOS was at least equal to the exposure duration of the corresponding case.
   Others have proposed treatment duration as a proxy for infection duration (as proposed by Graves et al [76]).

   Duration of infection used per type of NI:

e http://www.privacycommission.be/nl/docs/SZ-SS/2008/beraadslaging_SZ_007_2008.pdf and http://www.privacycommission.be/fr/docs/SZ-SS/2008/deliberation_SS_007_2008.pdf

All infections: 10 days

Except:

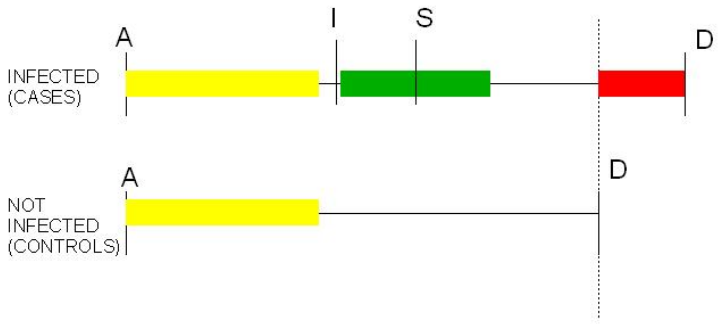
Urinary Tract Infections and Eye, Ear, Mouth infections: 6 days

Bone and Joint infections: 20 days

Example:

A patient surveyed the 30th day of his stay has a nosocomial bloodstream infection. This 30th day is then assumed to be the fifth day of the infection (total duration of 10 days), implying that the exposure time of this patient is 25 days. Controls will be selected among those staying at least 25 days in the hospital.

Figure 4.2: Selection of control patients based on their exposure duration compared to the exposure duration of cases



A = admission date
I = infection start date (estimated)
S = prevalence study date (patient is infected)
D = discharge date

Los attributable to infection

Exposure duration

Infection duration

7. Destination after discharge (home or other). This criterion is not used in the analysis of in hospital mortality, but in the analysis of the LOS.

The matching ratio

Each case is matched to the available number of controls, with a maximum of 4 controls. The weight of each case-control pair was proportionally lowered in function of the number of controls used.

The matching algorithm

The matching algorithm is based on the greedy algorithm: the distance between a case and all controls is computed, and the controls closest to the case are selected randomly. Once a control is matched to a case, the link cannot be broken to match to another case. The SAS macro used was developed by the Mayo Clinic [77] For the purpose of this analysis, the weight given to the Charlson score was half the weight given to other variables (so that one unit of distance was equivalent to a one year difference or half a point difference on the Charlson scale).

Matching on wards

Wards of infected patients were recorded during the prevalence survey. For control patients, the ward was evident when there was no transfer. In case of transfer, the ward attributed was the one where the patient stayed the longest time. This algorithm obviously does not select correctly control patients for the intensive care unit, as patients are transferred to and from the ICU, where a patient would not spend the majority of his stay. Therefore, to be eligible controls for cases in ICU, patients had to spend at least 2 days in ICU.

4.2.3.4 Patients with multiple infections, and categories of infections

The infection ratio in the prevalence survey was 1.15 (KCE report 92[1]), with 12% of the patients having multiple infections. Because BSI and LRI were the most commonly infections in these multi infections (see data in appendix) infections categories were redefined as followed:

- Patient with BSI + other infection = BSI
- Patient with LRI + other infection, other than BSI = LRI
- Patients with multiple infections other than BSI and LRI = Other

The following categories of infections are used consistently in this report:

- Patients in ICU:
  - BSI: BSI only or BSI + other infection
  - LRI: LRI only or LRI + other infection (but not BSI)
  - Other: all other infections

Patients in other wards than ICU

- UTI: UTI only
- SSI: SSI only
- BSI: BSI only or BSI + other infection
- LRI: LRI only or LRI + other infection (but not BSI)
- GI: GI only
- Other: all other infections

4.2.3.5 Cost Data from IMA database

The Data

Since in principle all persons living in Belgium are insured by one of the sickness funds, the joint IMA-data cover the whole population. For all individuals in the study, we have detailed information on health care expenditures. Health care expenditures consist of reimbursements of the RIZIV/INAMI, co-payments and supplements. For the scope of this project, only reimbursements are of interest. This information is available at the most detailed level possible, i.e. at the level of the specific services included in the nomenclature. Therefore, some aggregation of nomenclature codes was necessary, and is detailed below.

Aggregation of cost data

The aggregation of nomenclature codes were based on the N groups in a first step (99 categories). Cost data were calculated for these categories, and were grouped into 7 cost groups: 1-medical fees, 2-pharmaceutical products, 3-lab tests, 4-medical imaging, 5-implants & other, 6-revalidation & physical therapy, 7-IC and reanimation. The list of aggregated N groups is presented in appendix.

Due to huge changes in hospital financing in Belgium between 2005 and 2007, pharmaceuticals products and implants are not taken into account in the comparison, but were included in the descriptive analysis of cases.

PER DIEM prices (costs of one hospital day)

In Belgium, hospital per diem costs are covered by 2 distinct systems of public health funding. A major part is covered through fixed monthly hospital payments. Additional remuneration consists of a lump sum billed per admission and a lump sum billed per day of hospital stay. We recalculated the average 100% cost per day of stay in a Belgian hospital based on the 100% per diem costs per hospital and per type of stay, published by INAMI[f], and weighted for hospital stay volume. The resulting average cost is 371 euros per hospital day in acute wards (valid last semester 2008), and has been used in all cost calculations. This amount clearly increased over the last years as the amount for 2004 and 2005 was 289 euro. For chronic wards (Sp) the per diem calculated costs is 227 euros for the second half of 2008 (source: KCE calculations). For this reason, cost data from groups N85 and N87 were not taken into account in the analysis.

4.2.4 Statistical Analyses:

The statistical analyses of this matched cohort study are very similar to the analysis of the matched cohort study of nosocomial bloodstream infections, presented in the previous chapter (see analysis section 3.2.6), with the only difference that in this study the number of control patients per case is variable (from 1 to 4). .

We performed two analyses, one for each outcome: mortality and LOS:

1. to compare the mortality of infected patients to the mortality in the group of matched control patients. Conditional logistic regression models are used to account for the different numbers of controls per case.
2. to compare the LOS between cases and controls, for surviving patients. The mean LOS is computed for each group of control patients associated with one case, and the difference between each case-group of controls is then computed.

LOS is analysed in survivors only, as NIs can cause premature death and a reduced LOS. Newer methods include both endpoints in a single analysis (competing risk analysis), but these have not been applied here.

4.3 RESULTS

4.3.1 MCD Data of infected patients (CASES)

At the time of analysis, MCD data were available for 1000 out of the 1037 infected patients. A total of 978 records were valid for analysis (94%). (Table with records excluded in appendix)

Table 4.2 presents descriptive results of those 978 infected patients. Median age was 72 years old. Older patients are those with UTI (78 years old), younger patients are those with SSI (65 years old). The median length of stay of infected patients was 43 days (mean 58.5 due to skewed distribution), and was highly dependent on the bed index and type of infection. Longer stays were observed in SP-revalidation wards (median 94 days, data in appendix), and for patients surveyed in the intensive care median 52 days versus 43 days for all other wards). This correlates with longer LOS (median 43 days) for patients infected with UTI. This LOS should be contrasted to the number of days from admission to the time of prevalence survey (time to study): mean was 30.9 days (median 21 days).

A total of 14.9% of the patients infected died during their hospitalisation (32% of patients in intensive care, 12% in other wards). For patients not in ICU, mortality was the highest for patients with LRI (23.5%), BSI (13.6%) and GI (12.%). This is not an estimation of the excess mortality due to the infection, which requires the comparison to a control group. The results of this analysis are presented in the next chapter.

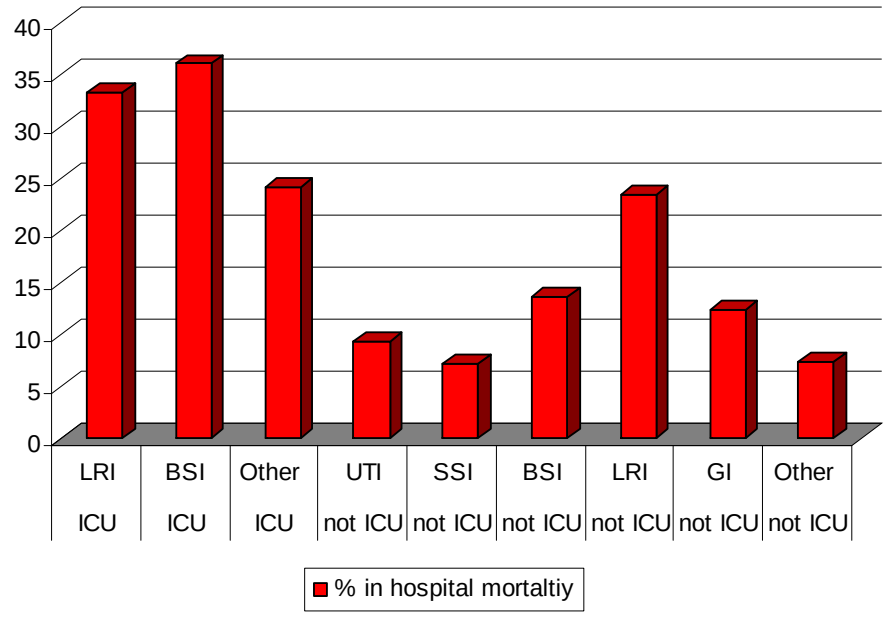
[f] http://www.inami.fgov.be/care/fr/hospitals/specific-information/prices-day/index.htm

Table 4.1: Descriptive data for infections patients (CASES)

Ward	Infection	N	%	Md Age	In hospital Mortality %	LOS (days) ALL Mn	LOS (days) ALL Md	LOS (days) Survivors Mn	LOS (days) Survivors Md	Time to Survey (days) Mn	Time to Survey (days) Md
ICU	LRI	87	8.9	73.0	33.3	68.0	50.0	77.2	58.0	24.2	17.0
ICU	BSI	36	3.7	62.5	36.1	71.1	57.5	81.7	67.0	26.9	22.0
ICU	Other	33	3.4	69.0	24.2	75.5	73.0	79.1	73.0	21.4	21.0
total ICU	**all**	**156**	**16.0**	**70.0**	**32.1**	**70.3**	**52.0**	**78.6**	**66.5**	**24.2**	**19.5**
not ICU	UTI	214	21.9	78.0	9.4	63.4	43.0	63.5	43.0	36.4	21.5
not ICU	SSI	125	12.8	65.0	7.2	48.4	33.0	44.6	32.0	29.0	20.0
not ICU	BSI	118	12.1	70.0	13.6	51.9	41.5	49.6	40.0	27.0	22.5
not ICU	LRI	119	12.2	75.0	23.5	52.3	39.0	49.4	38.0	27.6	19.0
not ICU	GI	98	10.0	74.5	12.2	52.7	41.5	53.6	42.5	30.7	22.5
not ICU	Other	148	15.1	70.0	7.4	61.9	43.0	61.6	43.0	37.6	26.0
total not IC	**All**	**822**	**84.0**	**73.0**	**11.7**	**56.3**	**41.0**	**55.9**	**40.0**	**32.2**	**21.0**
All	**Total**	**978**	**100.0**	**72.0**	**14.9**	**58.5**	**43.0**	**58.2**	**42.0**	**30.9**	**21,0**

Mn mean, Md median
N = N patients
Other contains multiple infections (except with BSI or LRI)

Figure 4.3: In hospital mortality of patients infected, by major site of infection



4.3.2 Cost data of infected patients (CASES)

From the 978 patients available with valid MCD data (see above), a total of 932 were retrieved from the IMA database. From these, 68 patients (7%) had to be excluded because some problems were encountered during the data cleaning phase (problems in date of birth, admission date could not be identified because more than 1 admission during the same month, regularisations leading to negative total costs).

An additional set of 48 patients were also excluded from descriptive analysis because they corresponded to huge outliers: either LOS above 142 (95 percentile of LOS) either costs of hospitalisation other than per diem above 50 000 euros (99% percentile of costs). A total of 868 patients are thus included in the descriptive analysis of cost data.

The hospitalisation costs of infected patients were approximately 25 000 euros on average: 66% are due to per diem costs, 9.5% to medical fees, 9% to pharmaceutical products and 5.8% to lab tests (Table 4.2).

Table 4.2: Hospitalisation costs (euros) for infected patients

Label	N	Mean	Std Dev	Median
total costs	816	24963	17112	20380
LOS (days)	816	47	31	40
Hospital stay fees	816	16562	10774	14149
total costs without per diem	816	8401	8691	5052
Medical fees	814	2353	2980	1318
Pharmaceutical products	812	2203	3776	752
Lab tests	809	1458	1208	1068
Medical imaging (RX, US & scinti)	808	687	622	496
Implants, disposables, ortheses & other	525	911	1605	269
Revalidation & physical therapy	694	679	914	424
IC & reanimation	418	1116	1166	575

Figure 4.4: Hospitalisation costs (euros) for infected patients

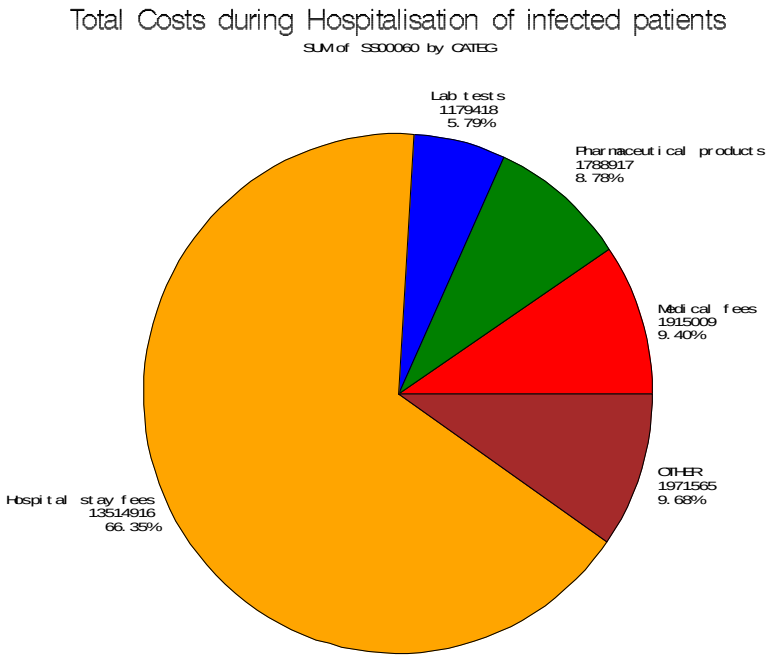
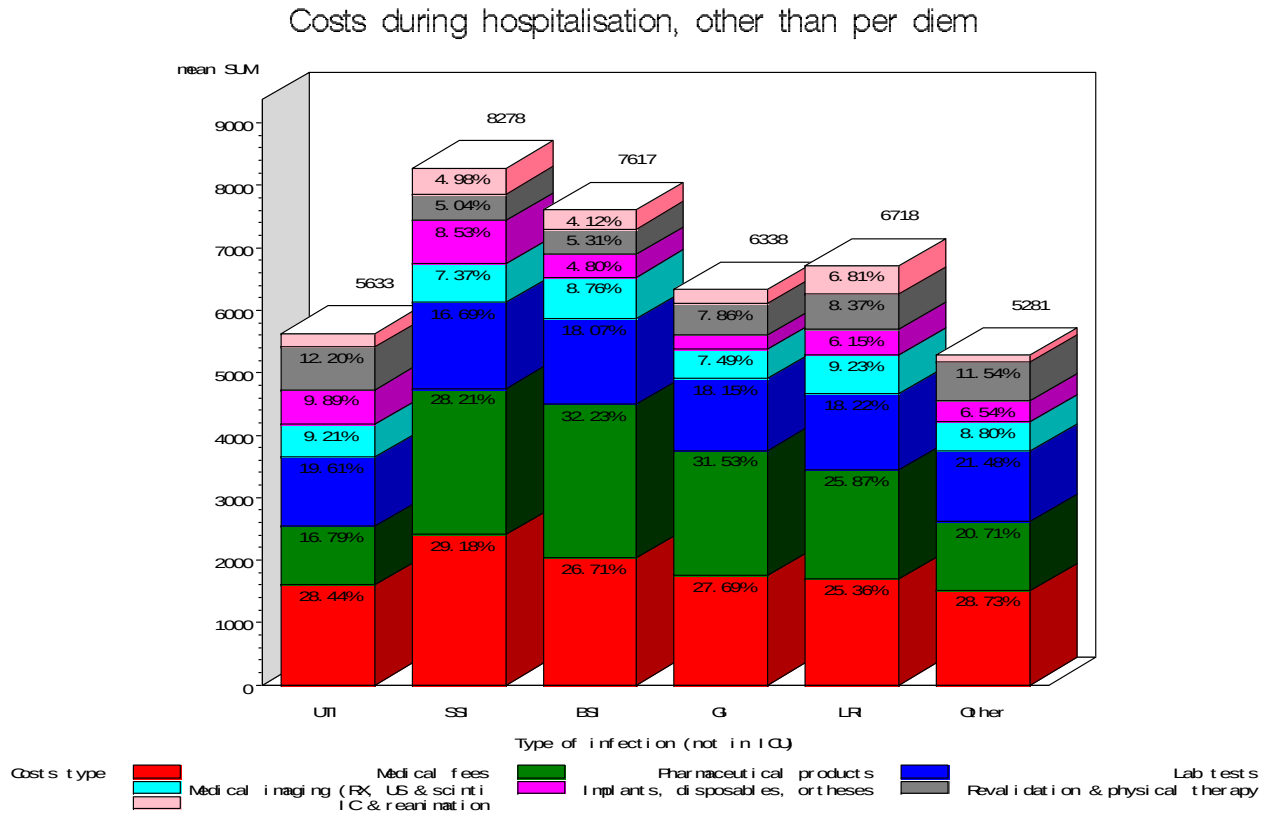


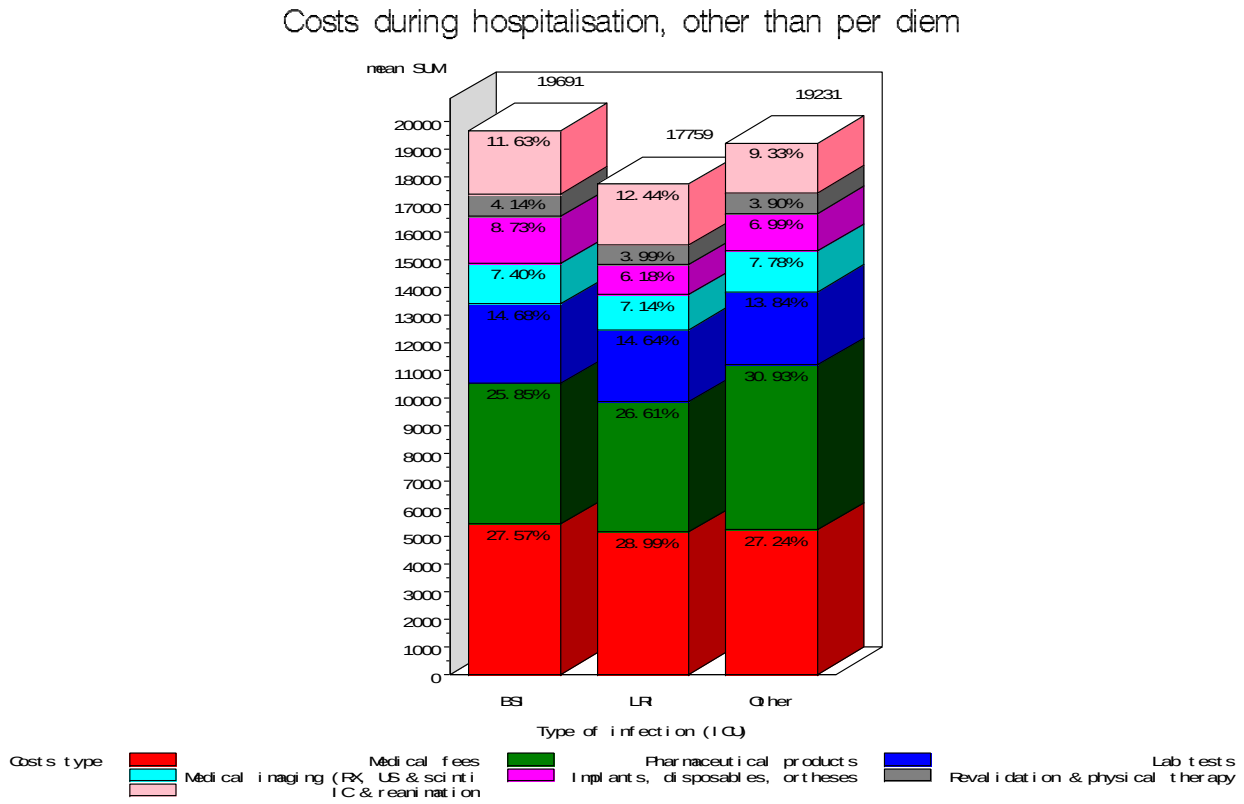
Table 4.4 and Figure 45 present the hospitalisation cost per ward (ICU/not ICU) and per type of infection. The costs of patients infected while surveyed in ICU are almost twice the costs of patients hospitalised in other wards. In terms of non per diem costs outside the ICU, SSI and BSI are the most costly. Approximately 30% of the non per diem expenses are due to medical fees, and from 18 to 36% are due to pharmaceutical products.

Table 4.3: Hospitalisation costs (euros) per type of infection

			Total Costs		Per diem				Other costs	
Ward	Infection	N	Mean	Median	Mean LOS	Median LOS	Mean Costs	% of total	Mean	Median
ICU	BSI	31	41019	38316	58	51	21329	52.0	19691	18232
ICU	LRI	69	37492	33214	53	46	19733	52.6	17759	14459
ICU	Other	27	41458	37093	60	50	22227	53.6	19231	15362
ICU	ALL	127	39196	37643	56	49	20653	52.7	18543	17020
NOT ICU	UTI	169	21270	17993	46	40	15637	73.5	5633	3774
NOT ICU	SSI	111	23501	17388	42	33	15223	64.8	8278	4809
NOT ICU	BSI	99	24252	20333	45	40	16635	68.6	7617	5308
NOT ICU	GI	85	21855	16649	44	39	15517	71.0	6338	3751
NOT ICU	LRI	103	21804	18837	42	37	15086	69.2	6718	4267
NOT ICU	Other	122	22001	19357	48	42	16720	76.0	5281	4331
NOT ICU	ALL	689	22339	18826	45	38	15808	70.8	6531	4404
ALL	ALL	816	24963	20380	47	40	16562	66.3	8401	5052

Figure 4.5: Hospitalisation costs (euros) per type of infection





As a validation exercise, the costs of the BSI in the substudy (1839 patients) were compared to costs of the 131 patients with BSI in the prevalence study. The two tables are presented on other sections of this report: Table 3.15 for the NBSI study, Table 8.16 for the BSI in the prevalence survey. LOS and non per diem costs are compared, as per diem costs increased between 2003 and 2008. There is a remarkable consistency between the two estimates, which are both around 10 000 euros

4.3.3 MCD of control patients

The set of controls was selected from the 2005 MCD database among the stays at the same hospital with the same APR-DRG as for the infected patients (cases).

A total of 94 444 stays were received and 74 204 stays were valid as potential control patients (see Table 8.15 in appendix). Exclusions are stays with no validated flag (from TCT), admission for psychiatry (AAA APR-DRG) and LOS less than 2 days (by definition those are not at risk of nosocomial infections).

All APR-DRG of cases and potential controls are presented in appendix. A few APR-DRGs have no control patients (because there was no stay in that APR-DRG in that hospital in 2005) and therefore cannot be included in the analysis. As this is also the case for 7 neonates on 19 (MDC 15), it was decided to exclude all neonates from the matched analysis.

The median age of potential control patients was 66 years, and the median LOS was 8 days (mean 14 days). (Table 4.5). This contrasts to age of cases (median age 73 years) and LOS (median 43 days, mean 58.5 days). Overall mortality of potential control patients was 5.7%. (14.9% mortality of cases).

80% of the control patients had no transfer during their stay. For the other 20%, we used the ward where the patient stayed for the longest period. (table 4.5).

Table 4.4 Wards of potential CONTROL patients (RCM-RFM 2005), Age and total LOS, and mortality

		Age			LOS			Mortality	
	N	Mean	Median	Std	Mean	Median	Std	N	%
new_bed									
A- Psychiatry	193	50.7	49.0	15.0	36.9	34.0	24.2	3	1.6
C- Surgical	27438	60.6	63.0	17.5	11.4	8.0	14.3	482	1.8
D- Medical	25497	65.6	69.0	16.3	11.4	7.0	13.5	1642	6.4
E- Pediatrics	4472	4.6	3.0	4.7	5.9	4.0	7.0	5	0.1
G- Geriatrics	7151	82.4	83.0	7.4	24.5	19.0	20.2	895	12.5
H- Usual admission	1404	61.2	62.0	15.8	8.5	5.0	9.4	77	5.5
I- Intensive care (most of the stay)	1649	66.5	70.0	15.6	25.0	15.0	29.1	795	48.2
L- Contagious diseases	66	44.9	41.0	19.3	21.6	12.0	24.7	4	6.1
M- Maternity	3425	29.7	29.0	5.0	6.6	6.0	5.5	0	0.0
N/n- NIC/non NIC	49	0.0	0.0	0.0	24.7	20.0	19.3	1	2.0
Sp- Revalidation	2860	73.0	76.0	13.4	53.9	43.0	42.9	325	11.4
All	74204	60.2	66.0	23.0	14.1	8.0	19.1	4229	5.7

4.3.4 Data included in Matched Analyses

Some of the cases are excluded of these analyses for the following reasons (Table 4.5):

- Neonates : they represent a small sample (19 cases) and a very heterogeneous group
- Psychiatric patients: patients hospitalized in Psychiatric beds (12 patients) or hospitalized for Mental Disorder (MDC 19) or for Alcohol/Drug Use and Alcohol Drug Use organic Mental disorder (MDC 20): also a small group of patients very heterogeneous
- Maternity: too small sample (9 patients infected)
- Pediatric patients: also small group (13 patients)

The total number of cases available for mortality and costs analyses are thus 910 and 765, respectively.

Table 4.5: Cases available for matched analysis

Valid cases	978
Cases excluded from analysis	68
Neonates (MDC 15)	19
Patients hospitalized in psychiatric beds	12
Patients hospitalized for mental disorder or alcohol abuse (MDC 20, 21)	15
Patients hospitalized in maternity	9
Patients hospitalized in pediatry	13
Cases available for matched analysis of mortality	910
Cases available for matched analysis of LOS (discharged alive only)	765

4.3.5 Estimation of Mortality associated with NIs

These analyses include all 910 patients. Because different matching factors have been used for patients in ICU, results are presented separately for those patients. On the 910 cases, 707 could be matched to at least 1 control patient (78%). The ratio of controls patients to cases was 3.3. (Table 4.7)

Table 4.6: Cases included/excluded in/from analysis of mortality

WARD of case	All cases	N cases out of matching (no control found)	N cases in matching procedure	% cases included	N controls	Ratio Controls to Cases
Not ICU	754	169	585	78%	1926	3.3
ICU	156	34	122	79%	397	3.3
TOTAL	910	201	707	78%	2323	3.3

Table 4.7 compares the mortality of patients matched (with at least one control) to the one of patients not matched, and therefore excluded from analysis. For the patients in all wards except ICU, mortality is very similar between matched cases (12.8%) and non matched cases (11.8%). For patients in ICU, mortality of non matched cases (47.1%) is much higher than the mortality of matched cases (27.9%) indicating that the matching procedure selected a specific group of patients (less severe conditions). For this reason, no further analyses are presented on the group of patients from ICU.

Table 4.7: Mortality of cases matched and NOT matched (because no similar control was available)

Ward of cases		N	N death	% death
All wards ICU	All cases	754	95	12.6
	Matched	585	75	12.8
	NOT matched	169	20	11.8
ICU	All cases	156	50	32.1
	Matched	122	34	27.9
	NOT matched	34	16	47.1

Table 4.9 presents the results of the mortality analyses. For patients not in ICU, mortality was 12.8% in the infected patient group, and 10.8% in the control group (after adjustment for the different numbers of controls per case). The excess mortality (absolute difference) is thus 2.0%. This difference did not reach statistical significance, as the odds ratio and 95% CI was 1.31 (0.96, 1.80), but the study was also not powered to detect such effects (but to detect a 4 days difference in LOS). The estimates of attributable mortality vary according to type of infection, with LRI showing the strongest and statistically significant effect (absolute difference of 9.6%, OR and 95% CI 2.19 (1.16, 4.13). The second effect in terms of absolute differences, although not statistically significant, is seen in the group of patients infected with a BSI (6.2% absolute difference, OR 1.73 (0.82, 3.62)). It should also be noted that the mortality in our BSI group is remarkably lower than the mortality of the BSI study (chapter 3), which was 27% (excluding patients from ICU).

Negative effects (ie mortality of cases *lower* than mortality of control group), although again not statistically significant, are seen in the group of patients with UTI, and in the "Other" group. For UTI, the OR estimate is close to 1 and the 95% is large, thus sampling variability is probably the reason of the negative estimate. On the other hand in the group of "other" infections, the result is surprising, because the mortality is almost doubled in the group of controls than in the group of cases. We do not have an explanation for this surprising result, which is also difficult to interpret due to the heterogeneity of this group of patients.

Table 4.8: Estimation of attributable mortality, by bed index and major site of infection

	In hospital mortality								
	CASES			CONTROLS					
	N	n	%	N	%*	Odds ratio	95% CI		Absolute Difference
ALL	585	75	12.8	1926	10.8	1.31	0.96	1.80	2.0%
UTI	145	15	10.3	492	11.7	0.92	0.46	1.86	-1.4%
SSI	91	6	6.6	299	3.9	2.61	0.73	9.37	2.7%
BSI	88	14	15.9	201	9.8	1.73	0.82	3.62	6.2%
GI	61	10	16.4	199	13.3	1.47	0.61	3.52	3.1%
LRI	98	22	22.4	294	12.8	2.19	1.16	4.13	9.6%
Other	102	8	7.8	124	13.2	0.53	0.23	1.23	-5.4%
* % adjusted for different matching ratios % in hospital mortality									

4.3.6 Availability of Cost data for Controls

1381 stays retrieved from IMA cost databases, corresponding to 1295 patients. Some records were excluded because of data problems: 2 patients with invalid cost data, 62 records because of problems in dates (versus MCD), 53 records corresponding to 19 cases that were not retrieved from database. Some hospitalisation stays were also extreme outliers, they are excluded from the descriptive analyses below (same exclusion criteria as for the cases): 8 patients with either LOS above 142 (95% percentile of LOS of cases) or hospitalization costs excluding per diem are above 50 000 euros (percentile 99 of cases). 74 controls patients were finally excluded because cost data were not available for the corresponding matched case.

Table 4.9 present the number of cases and controls available for cost analysis. A total of 1096 control patients were included in the analysis. The ratio of the number of matched control to 1 case was 2.8.

Table 4.9: Number of Cases included/excluded in/from analysis of LOS, for patients discharged alive (other than ICU)

Type of infection	N cases included in matching procedure	N controls in matching procedure	Ratio controls to cases	N cases excluded	% cases included
UTI	95	275	2.9	35	73.1
SSI	70	220	3.1	15	87.5
BSI	54	142	2.6	20	73.0
GI	39	107	2.7	12	76.5
LRI	60	172	2.9	16	78.9
Other	69	180	2.6	25	73.4
ALL	**387**	**1096**	**2.8**	**123**	**75.9**

4.3.7 Estimation of additional LOS and costs associated with NIs

Table 4.10 and Figure 4.6 present the estimations of the LOS attributable to NI, for patients not in ICU. Infected patients stayed on average 7.6 days (95% CI 5.3 days, 9.8 days) longer than non-infected patients. The median of the excess LOS was lower, 4 days, indicating that there were some outliers in the infected patients, probably due to complications. The two infections leading to the longest prolongations of LOS are the LRI: 10.6 days (95%CI 4.7, 16.4 days, median 7 days) and the BSI: 9.2 days (95% CI 2.9, 15.5 days, median 6 days). Next are the GI infections (mean 7.3 days, median 3.5 days), for which the prolongation is not statistically significant, but this is due to the small sample size (39 patients), and the heterogeneous group of "other infections".

SSIs prolong the LOS with 5.6 days on average (median 5.1 days). UTI prolong LOS of 6.5 days, with a median of 2.5 days.

Several sensitivity analyses on the matching factors and on the time of exposures have been performed and are presented in appendix (Table 4.11).

Table 4.10: LOS attributable to NI, per type of infections (and for patients NOT in ICU)

		Cases		Controls		Attributable Difference in LOS				
	N	Mean	Median	Mean	Median	mean	95% CI		Std	Median
UTI*	95	37.2	29.0	30.7	25.0	6.5	1.8	11.2	23.2	2.5
SSI	70	33.4	30.0	27.8	20.0	5.6	0.8	10.4	20.4	5.1
BSI	54	37.8	31.5	28.6	22.3	9.2	2.9	15.5	23.7	6.0
GI	39	45.8	36.0	38.5	28.0	7.3	-0.9	15.5	26.1	3.5
LRI	60	37.5	30.0	26.9	24.0	10.6	4.7	16.4	23.2	7.0
Other	69	40.4	34.0	33.2	26.0	7.2	2.6	11.8	19.5	4.0
ALL	**387**	**38.1**	**31.0**	**30.5**	**23.5**	**7.6**	**5.3**	**9.8**	**22.4**	**4.0**

* these values are based on a assumed duration of UTI of 6 days. If cases were included for whom no cost data were available (25 additional patients), the mean value is 4.5 days (3.7 days for UTI assumed duration of 4 days). As an estimate for a disease duration of 5 days, the average of 4.1 days (median value is 0.5 days) was used in the overall estimation presented in the next chapter.

Figure 4.6: LOS attributable to NI, per type of infections (and for patients NOT in ICU)

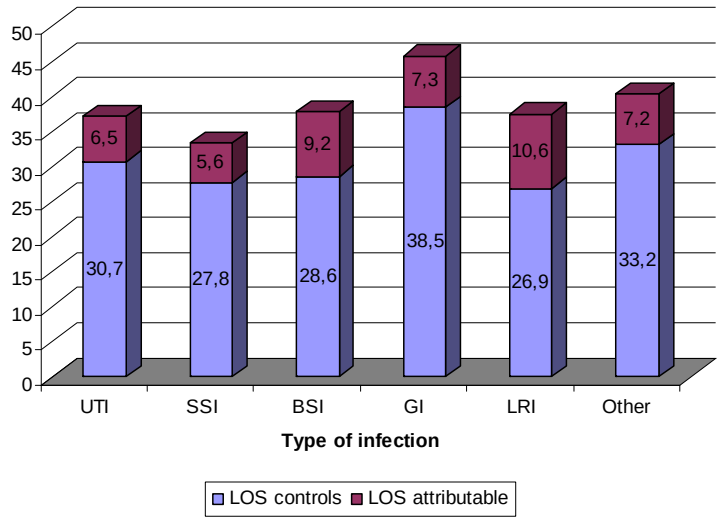


Table 4.11 presents the estimation of the excess costs due to NI, in the non-ICU setting. Due to huge changes in hospital financing in Belgium between 2005 and 2007, pharmaceuticals products and implants are not taken into account in the comparison. Each NI increases the cost of the patient stay on average by 3398 euros (median 1813 euros) plus the cost of drugs. Again LRI and BSI are the most costly.

Table 4.11: Total costs attributable to NI (patients NOT in ICU, after exclusion of pharmaceuticals and implants)

		Cases		Controls		Attributable Difference in Total Costs				
	N	Mean	Median	Mean	Median	**Mean**	95% CI		Std	Median
UTI	95	16366	13361	13480	11546	2886	861	4912	10072	930
SSI	70	16268	14117	14040	10899	2228	101	4355	9081	1420
BSI	54	18054	15379	13571	11076	4484	1796	7171	10075	3024
GI	39	20110	15502	16607	15067	3503	249	6756	10367	1978
LRI	60	17490	14676	12631	10564	4859	2451	7268	9519	3458
Other	69	18094	14851	14986	11388	3108	1256	4960	7850	1699
ALL	387	17444	14585	14046	11235	**3398**	**2455**	**4340**	9460	1813

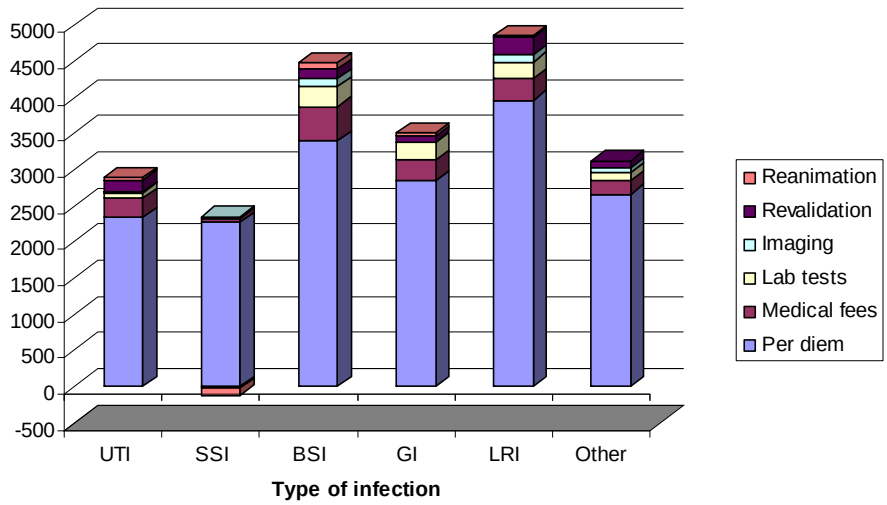
Table 4.12 and Figure 4.7 present the source of these incurred costs. The proportion of the per diem costs in the total costs cannot be calculated, as the pharmaceuticals and implants costs could not be taken into account. Asides the per diem cost, a NI increases on average the cost by 500 euros (including medical fees, lab, imaging, revalidation and reanimation).

The most costly infections are again the BSI (1083 extra) and the LRI (897 extra). For the UTI, GI and other infections, the extra cost is around 500 euros per case. For SSI infections the data suggest that there is no extra cost incurred (but again pharmaceuticals were not included).

Table 4.12: Source of Differences in costs:

		Means Differences between Cases and Controls							
	N	Total	Per diem	**Not Per diem**	Medical fee	Lab	Imaging	Reval	Rea
UTI	95	2886	2334	**553**	264	80	16	160	33
SSI	70	2228	2277	**-49**	52	-1	22	-16	-107
BSI	54	4484	3401	**1083**	474	269	120	122	98
GI	39	3503	2842	**660**	294	237	13	71	45
LRI	60	4859	3962	**897**	298	233	93	240	33
Other	69	3108	2657	**451**	196	109	54	108	-15
ALL	**387**	**3398**	**2834**	**564**	**251**	**137**	**50**	**117**	**9**
				100%	44%	24%	10%	21%	1%

Figure 4.7: Extra costs attributable to NI, per type of infections (and for patients NOT in ICU)



4.4 CONCLUSIONS

This study, based on a sample of approximately a thousand infected patients identified during the national prevalence study end of 2007, confirms that there is a huge burden of excess mortality and excess LOS after nosocomial infections.

Our design, a matched cohort study, is very common in this research field. We were able to match almost 600 patients that were infected outside the ICU to almost 2000 control patients. Because administrative databases do not have detailed information of the ICU department, we were not able to match correctly those patients, and restricted our analysis to the group of patients surveyed outside the ICU.

The analysis of mortality revealed that there is a 2 percentage point difference (in absolute values) in mortality between the group of infected patients and their control group. The fact that this difference did not reach statistical significance (but was very close too), is due to the fact that this study was powered to detect a 4 days difference in terms of LOS, and not for differences in mortality.

Lower respiratory infections showed a statistically significant doubling of the mortality, corresponding to a difference of 10 percentage points.

Our analysis of the excess LOS and cost was based on surviving patients only, and we could match almost 400 cases to approximately 1000 cases.

Our final estimate was approximately 8 days, which is twice the estimate of 4 days, based on old US data, but totally in line with the review of the literature described in Table 2.1.

Our estimate of 10 days for BSI studies is lower than those previously estimated in Belgian studies, and we have explained the reasons in the previous chapter. Our estimate of 10 days for LRI is also very consistent with 5 of the 7 studies described in the literature, and we have previously discussed why one of those other studies might have underestimated the effect of the infection.

For surgical site infections, the estimates of additional LOS in the literature were a lot more heterogeneous than for BSI and LRI. Our estimate of 5.6 is at the lower end of the published estimates, but more and more cases may be treated in the community.

Finally, the estimate of 6.5 additional days for a UTI might seem high, but is not that much higher than the estimate of 5.1 days from a high standard UK study from Plowman in 2001 [33], also based on more than 100 patients. This high estimate might be the result of complications in elderly patients (median age 78 years) hospitalised mainly in geriatric or revalidation ward, and who survive their hospitalisation.

The limitations of the study are discussed in chapters 6 and 7.

Key Messages:

- **A matched cohort study was set up to estimate excess mortality, LOS and costs attributable to NIS. Cases were those patients identified during the Belgium prevalence survey organized end 2007. Control patients were identified from 2005 hospital administrative databases, and were selected from the same hospital, APR-DRG, ward, age range, comorbidity measure, and exposure duration than cases. A maximum of 4 controls were selected for each case. Because of the lack of detailed information in ICU ward, our analysis is restricted to patients outside ICU ward.**
- **The population of infected patients is at high risk of mortality: 15% of the patients infected died during their hospitalisation: 32% of patients in ICU, 12% of patients in other wards.**
- **The excess mortality that can be attributed to the NI (outside the ICU) is 2%. LRI (excess 10%) and BSI (excess 6%) are the most important killer infections.**
- **The excess LOS attributed to the NI for surviving patients is on average 8 days (11 days for LRI, 9 days for BSI, 7 days for GI, and 6 days for UTI and SSI).**

5 SUMMARY AND OVERALL ESTIMATES

5.1 RESULTS OF THE LITERATURE REVIEW ON EXCESS COSTS

Based on the literature it is clear that most of the excess costs of NIs result from a longer hospital stay. Excess length of stay (excess LOS) is therefore often used as a surrogate for excess costs. It also facilitates international comparison, and can prove to be of use even within the same country in case of changing systems of hospital financing.

A review published in 2005 was identified, which was updated with recently published original studies. There is large heterogeneity among the studies in terms of designs, economic perspective and results, and no reliable estimates for Belgium could be derived from these studies. The only estimates for Belgium found in the grey literature were based on a 1993 US publication, which reported an average excess LOS of 4 days after a NI. In the absence of local incidence and cost data for Belgium in 2006, an estimated total number of nosocomial infections of 107 500 was based on an extrapolation of the number of BSIs. This resulted in a total of €110 million (assuming an excess LOS of 4 days and a cost per hospital day of €250). Another presentation (IPH, 2005) mentioned a yearly cost of €110 to €300 million for Belgium, mainly based on the international literature. Also estimates for excess LOS and mortality for BSI and LRI in ICU were given in this presentation, based on the Belgian ICU surveillance data of the 1997-2003 period. (see also table 5.1)

5.2 RESULTS OF THE TWO MATCHED COHORT STUDIES

5.2.1 Results based on Bloodstream Infections reported in 2003

A total of 1839 stays with a BSI reported in 2003 by 19 hospitals were available for matching. Among the cases, the mortality was 32%, and 46% among the 404 ICU stays. In total 665 case-control pairs (including 72 ICU cases) were matched. Imposing a minimum period of stay for controls (in-hospital stay until subclinical infection in matching case) had a major impact and about halved the excess LOS estimate. Matching of ICU cases proved difficult and was considered not satisfactory. The excess LOS after non-ICU BSI in surviving patients was on average 9.3 days. The median difference was 7 days (see table 5.1).

5.2.2 Results based on the Point Prevalence Data of 2007

A total of 978 cases of NIs identified during the point-prevalence study were available for analysis, and the point prevalence study took place after a median hospital stay of about 21 days in this group. In-hospital mortality was 32.1% in 156 ICU patients and 11.7% among the 822 other patients. For 818 cases (128 on ICU) the total healthcare payer costs could be analysed: on average € 39 196 for stays which included ICU (mean LOS: 56 days, or €700 per day) and € 22 339 for non-ICU stays (mean LOS: 45 days or €496 per day).

A total of 74 204 hospitals stays of 2005 were available for selection of controls. They were matched with 910 cases (for mortality) or 765 surviving cases (for LOS). The mean LOS in controls overall was 14 days, thus the majority of controls could not be matched because the LOS was too short. The controls-to-case ratio was 3.3 on average for the analysis of mortality and 2.8 for the analysis of excess LOS. Because of the low number of cases and the complexity of the hospital stay of cases and control patients who pass at least some days on the ICU, matching remained a challenge for this group, and no reliable estimates could be produced.

The mean excess LOS for non-ICU NIs varied from 4.1 days for UTIs to 10.6 days for LRIs (see table A). Sensitivity analyses further showed our estimates are sensitive to the variable 'duration of the infection' at the time of the prevalence study: excess LOS varies on average with 0.8 days when the period the NI is assumed to be ongoing is varied with 1 day around the current assumption of 5 days for most NIs (2.5 days for UTIs).

As the financing mechanisms of pharmaceuticals and implants changed between 2005 (year of selection of controls) and 2007 (year of point prevalence study) these cost items were left out of the matched comparison. We assume no differences in use of implants between cases and controls. For pharmaceuticals we used the average cost per day of €47 in cases (based on an average of €2203 for an average stay of 47 days) and multiplied with the excess LOS per type of NI. This amount was added to the case-control cost difference per stay. The per diem fixed hospital stay cost (on average €371 per day for 2008) accounts for more than two thirds of the excess costs, as presented in table A.

Table 5.1. Estimates of excess in-hospital stay (LOS) and healthcare payer costs, per case of nosocomial infection.

Ward	NI type	Excess LOS / case median days	Excess LOS / case mean days	Excess cost / case°° median €	Excess cost / case°° mean €
ICU	BSI	7,0*	10,2**	4900	7140
	LRI	7,0	11,4**	4900	7980
	Other	4,0	7,2	2800	5040
Non ICU	BSI	7,0*	9,3*	4030*	5515*
	LRI	7,0	10,6	3787	5357
	SSI	5,1	5,6	1660	2491
	GI	3,5	7,3	2143	3846
	UTI°	0,5	4,1	210	1942
	Other	4,0	7,2	1887	3446
Overall		3,6	6,7	1890	3557

°°for non-ICU, based on matched cohort of point-prevalence study, for drugs: €47 / day used for ICU, a cost per excess day of €700 was used

*matched cohort, based on BSIs reported in 2003, per diem 2008 cost used (€371)

**based in ICU surveillance data (IPH)

°results obtained for a duration of UTI of 5 days and when also those patients were matched for whom no cost data were available; excess costs adjusted proportionally

5.3 OVERALL ESTIMATES

5.3.1 Incidence of NIs

A yearly incidence of NIs in 103 000 patients was estimated for Belgium. This was derived from a prevalence of 116 000 patients based on the point-prevalence study as detailed in the KCE report no 92, 2008. For the calculation of the incidence from the prevalence a single conversion factor was applied independent of the NI type (assumed mean duration of a NI of 10 days). If one adjusts for the shorter assumed duration of 5 days for UTIs, the incidence of UTIs doubles, and the overall yearly incidence is 125 500 patients with a NI.

5.3.2 Overall Estimate of Excess Mortality

We estimate for Belgium about 17 500 in-hospital deaths per year after a nosocomial infection, of which 2625 deaths (or 15%) can be attributed to the NI. Overall excess mortality among the 125 500 patients with a NI is thus 2.1%, as detailed below in table 5.2.

Excess in-hospital mortality in non-ICU wards was estimated at 1.6% in our matched cohort study, or 1731 deaths per year. On non-ICU wards nearly half of the excess deaths were seen after LRI. BSI was the second most important killer NI. For UTIs no excess mortality was observed. Because of the small sample size it is however difficult to provide accurate estimates per NI type. We used the excess mortality percentages for BSI and LRI at the ICU as estimated by the IPH and based on a large dataset. We did not estimate the life years lost attributable to NIs. Based on the relatively low median age of patients with a BSI in ICU or with a SSI (65 years), these NIs could potentially contribute significantly with respect to this endpoint.

Table 5.2 Estimates of yearly total and excess in-hospital mortality in patients with a nosocomial infection in Belgium.

Ward		Patients with NI* N	Median age years	Total in-hospital mortality N	Total in-hospital mortality %**	Excess in-hospital mortality N	Excess in-hospital mortality %**
ICU	BSI	3791	62,5	1369	36,1%	372	9,8%°
	LRI	9163	73,0	3051	33,3%	522	5,7%°
	Other	3475	69,0	841	24,2%	NA	NA
Non ICU	overall	109109	73,7	12233	11,2%	1731	1,6%
Overall		125538	73,2	17494	13,9%	2625	2,1%

*incidence derived from prevalence assuming a duration of NI of 10 days; except for UTI (5 days)
**percentage of the patients with a NI
°based in ICU surveillance data (IPH)
NA = not available

5.3.3 Overall Estimate of Excess Length of Stay and Healthcare Payer Costs

Table 5.1 and table 5.3 below present the overall estimates for excess LOS and cost. The matched cohort analysis based on the 2007 point-prevalence study is the main source for our estimates for most non-ICU NIs. For non-ICU BSI we used the matched cohort study based on the BSIs reported in 2003. Because the stays at ICU were difficult to match in both cohort studies, we used the IPH estimates for mean excess LOS of ICU cases of LRI and BSI. These are based on excess LOS in ICU only. For median values and for "other" NIs in ICU we used the estimates derived for non-ICU cases. For the non-ICU BSI cases, it was reassuring to find that excess LOS estimates based on our two matched cohort studies were nearly identical (median: 6 and 7 days, mean: 9.2 and 9.3 days). LRI, BSI and UTI were found to be the NIs with the largest excess LOS and cost. An overall mean excess LOS of one week is found across all types of NI, corresponding to a total of about 700 000 extra days.

For healthcare payer costs, we adjusted for the change in hospital financing of pharmaceuticals between 2005 and 2007 and used a weighted average per diem cost (2008 value) of €371 both for cases and controls. For BSI we used the matched cohort study based on BSI cases reported in 2003 to the IPH after adjusting the per diem cost to €371. For the excess cost of hospital stays which included ICU we used an average cost per day of €700 as calculated above.

Table 5.3. Estimates of yearly excess in-hospital stay (LOS) and healthcare payer costs of patients with a nosocomial infection in Belgium.

Ward	NI type	Patients with NI* N	Patients survivors N	Overall excess LOS median days	Overall excess LOS mean days	Overall excess cost median Mio €	Overall excess cost mean Mio €
ICU	BSI	3791	2423	16959	24712	11,9	17,3
	LRI	9163	6111	42780	69670	29,9	48,8
	Other	3475	2634	10538	18968	7,4	13,3
Non ICU	BSI	12427	10737	75161	99857	43,3	59,2
	LRI	12533	9588	67113	101628	36,3	51,4
	SSI	13165	12217	62306	68414	20,3	30,4
	GI	10321	9062	31717	66152	19,4	34,9
	UTI	45076	40838	20419	167436	8,6	79,3
	Other	15587	14433	57734	103921	27,2	49,7
Overall		125538	108043	384726	720757	204,3	384,3

*incidence derived from prevalence assuming a duration of NI of 10 days; except for UTI (5 days)

6 STRENGTHS AND WEAKNESSES OF THE STUDY

Our results contribute significantly to the assessment of the burden caused by NIs in Belgium.

First, we studied all types of NIs in a national point-prevalence study. More than half of the acute hospitals participated in this study and the NIs were well-documented applying strict CDC criteria embedded in a novel rule-based data-entry software. However, cases where there was a suspicion of a NI but without sufficient documentation according to the CDC criteria, were not included. The prevalence rate may therefore be an underestimation of the reality. In addition, nearly half of the Belgian hospitals did not participate to the point-prevalence study, and the reasons are not documented. One could speculate that at least some hospitals did not participate because infection control was given little attention.

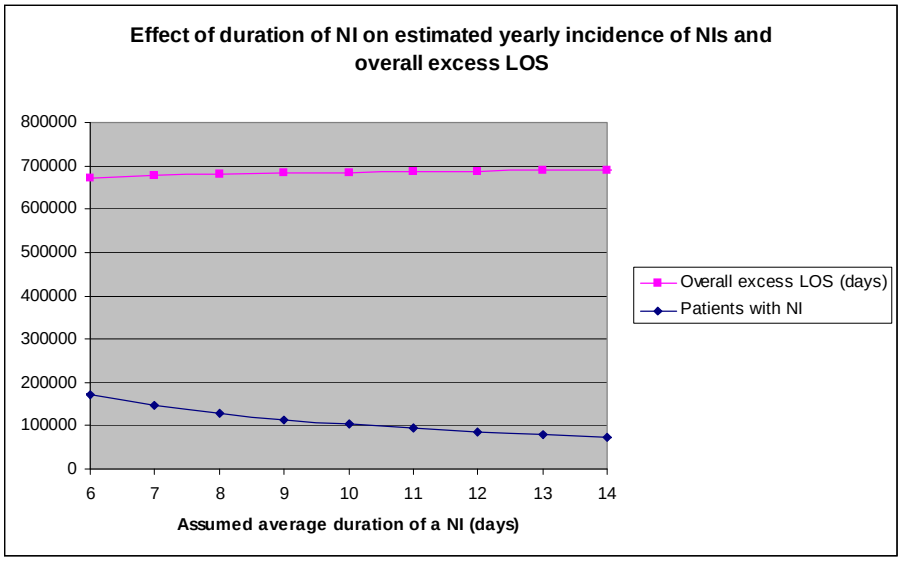
We used national clinical-cost administrative databases allowing for an appropriate selection of multiple controls per case and for performing two matched cohort analyses using broad sets of relevant variables. We were able to reproduce the excess LOS estimates after non-ICU BSI in the two independent matched cohort analyses.

Of note, new sophisticated statistical methods exist to derive such estimates. They require access to detailed clinical data. The results obtained using such methods indicate that matched cohort studies tend to overestimate the effect of NIs. Because of the overestimation inherent to the matched cohort design, the mean-based estimate, could be considered a worst-case estimate for decision making. On the other hand, as explained before, because of other study design aspects we may have underestimated the overall excess LOS and cost after NIs. These design aspects include an underestimation of the incidence, also because of the way prevalence was converted to incidence, a possible underestimation of the overall hospital excess LOS for ICU cases, exclusion of excess costs in non-surviving patients, matching for residence after discharge, and the non-exclusion of stays with a NI from the controls in one of the two matched cohort studies.

We demonstrated that matching, also for the length of hospital stay prior to the NI, is crucial for obtaining credible estimates for excess LOS in cases. The importance of this adjustment can thus not be overstated. Unfortunately, a correction for duration of stay prior to the NI is lacking in many previously published studies. As discussed before, the assumed duration of the NI at the time of the point prevalence study is of key importance for defining the minimum LOS of matched controls. This variable alone has a major impact on the estimated excess LOS per individual NI. For the overall estimation of excess costs, the effect of the assumed duration of a NI is however counterbalanced by its effect on the calculation of the cumulative incidence starting from the prevalence, and has little effect on the overall number of excess hospital days (about 700 000 days), as illustrated in Figure 5.1.

Finally, we introduced an up-to-date per diem hospital stay cost, weighed across all Belgian hospitals.

Figure 5.1. Overall excess LOS and yearly number of patients with a NI by assumed duration of NI.



7 DISCUSSION AND CONCLUSIONS

We have used the available data to estimate the excess in-hospital mortality and healthcare payer costs attributable to nosocomial infections in Belgium. On average, patients with a nosocomial infection stay one week longer in hospital compared with matched control patients. We found an excess mortality of 2625 deaths per year and excess costs for the healthcare payer of nearly € 400 million per year. This amount is higher than all previously published estimates for Belgium, mainly because our estimate for excess LOS is about the double of previous estimates and because the per diem cost has strongly increased to € 371 from € 288 per day in 2005.

A lower and more conservative estimate of half a week of excess LOS and about € 200 million excess costs is based on the median differences found between cases and controls. These probably represent accurate and robust estimates for the *'typical'* cases, whereas the mean values also take into account complications arising in *'atypical'* cases for which matching with a control patient is less straightforward by definition. The high outlier values most likely represent complex cases suffering from many complications, but who finally survive.

For UTI cases a median of 0.5 days is indeed a more 'typical' value, in line with the literature and clinical practice, compared with a rather high mean value of 4.1 days. The median and mean values were obtained when a UTI duration of 5 days was assumed and also cases were included for whom no cost data were available. Under the same assumption of a UTI duration of 5 days, the incidence is high, affecting 45 000 patients per year. These cases probably include large numbers of more complex cases in elderly female and male patients (median age 78 years) who survive.

There is thus a relatively large margin of uncertainty around our overall estimate of nearly € 80 million for the excess cost induced by UTIs. For SSI the median and mean values differ less and the estimated in-hospital excess cost linked to SSIs may seem relatively low. This could possibly be explained by shorter hospital stays after surgery and more SSIs occurring or being treated in the community after the hospital stay. These costs are not included in our estimates.

The results show that the burden of NIs in terms of mortality and costs for ICU patients is large but in absolute numbers it is even larger for non-ICU wards such as medical, surgical, geriatric and rehabilitation units. The NIs which cause most excess mortality and healthcare payer costs are LRIs (about 1000 excess deaths, and € 100 million costs) and BSIs (nearly 1000 excess deaths, and € 80 million costs). In terms of overall costs also UTIs are important (€ 80 million).

In this report, we estimated the burden of NIs in terms of extra bed days and the related gross costs from a public healthcare payer perspective. From this perspective the reduction of the length of stay will lead to a more efficient use of resources in the short term, without necessarily impact on the overall healthcare expenditures. The estimation of the net effect of making beds available allowing treatment of additional patients needs a careful calculation of benefits and costs.

The perspective of the hospital is different. It is clear that from a hospital perspective, resources will be saved (variable costs will be reduced) by preventing infections. However, it has been shown that the majority of the expenditures associated with hospital resources are fixed and difficult to avoid in the short term, eg infrastructure.

Evaluating the economics of preventing nosocomial infection from a hospital perspective or from a healthcare payer perspective is complex, was not within the scope of this study, and requires additional study. Such studies should also be part of any cost-effectiveness evaluations of preventive measures. The message for decision makers is that the excess costs estimated for NIs should not be interpreted as cash which would become available in the short term if some NIs would be prevented. These considerations should however not cast any doubt on the desirability to avoid nosocomial infections.

8 APPENDICES

A.1. SEARCH STRATEGY COST STUDIES

Author	France Vrijens
Project number	HSR 20
Project name	Cost of Nosocomial Infections
Keywords	Nosocomial infection Hospital Acquired Infection Costs Length of Stay
MESH terms	Cross infection [MESH] Length of Stay [MESH]

Search 1	**Only reviews on impact of nosocomial infections on costs (published in the last ten years)**
Date	May, 7 2007
	Updated February 21, 2008
	Updated November 19, 2008 (#3)
Database (name + access ; eg Medline OVID)	Medline Pubmed
Search Strategy	

Search	Most Recent Queries	Time	Result
#3	Search **("Cross Infection" [MESH]) AND (costs[tiab] OR cost effective[tiab] OR economic[tiab])** Limits: **published in the last 10 years, Review**		204
#7	Search **("Cross Infection" [MESH]) AND (costs[tiab] OR cost effective[tiab] OR economic[tiab])** Limits: **English, French, Spanish, Dutch, Publication Date from 1990 to 2007, Review**		211
#6	Search **("Cross Infection" [MESH]) AND (costs[tiab] OR cost effective[tiab] OR economic[tiab])** Limits: **English, French, Spanish, Dutch, Publication Date from 1990 to 2007**		711
#5	Search **("Cross Infection" [MESH]) AND (costs[tiab] OR cost effective[tiab] OR economic[tiab])** Limits: **Publication Date from 1990 to 2007**		785
#4	Search **("Cross Infection" [MESH]) AND (costs[tiab] OR cost effective[tiab] OR economic[tiab])** Limits: **Publication Date from 1980 to 2007**		927
#3	Search **("Cross Infection" [MESH]) AND (costs[tiab] OR cost effective[tiab] OR economic[tiab])**		946
#2	Search **Cross infection [MESH]**		32210

Note	Use Pubmed HSR query, category « economics », scope « broad, sensitive search »
Results	204 hits
Pertinent results	Exclusions criteria - specific patient population (ex: end stage renal disease) - specific pathogen (clostridum difficile, MRSA) - not based on European countries, US and New Zealand

Search 2	**Reviews and individual studies, from 1998**
Date	May, 7 2007
	Updated February 21, 2008
Database (name + access ; eg Medline OVID)	CRD (DARE, NHS EED, HTA)
Search Strategy	nosocomial OR "hospital acquired" OR "hospital-acquired" OR"HAI" RESTRICT YR 1998 2008:
Note	
Results	• All results (192) • DARE (59) • NHS EED (121) • HTA (12)
Pertinent results	0 retained (no additional information compared to search 1).

Search 3	**Only Individual Studies (from 2000)**
Date	May, 7 2007
	November 19, 2007
Database (name + access ; eg Medline OVID)	Medline Pubmed
Search Strategy	
#16 Search **#14 and #15** Limits:**Publication Date from 2004 to 2008** 98 #15 Search **length of stay** Limits:**Publication Date from 2004 to 2007** 16101 #14 Search **("Cross Infection" [MESH]) AND (costs[tiab] OR cost effective[tiab] OR economic[tiab])** Limits:**Publication Date from 2004 to 2008** 398	
Note	Use Pubmed HSR query, category « economics », scope « broad, sensitive search »
Results	98 hits
Pertinent results	Same exclusions criteria than search 1

A.2. LIST OF SELECTED COSTS REVIEWS

#	Title	Reference	Author	Year
1	Systematic review of economic analyses of health care-associated infections.	[5]	Stone PW	2005
2	Clinical and economic consequences of ventilator-associated pneumonia: a systematic review.	[6]	Safdar N	2005
3	The impact of nosocomial infections on hospital care costs.	[7]	Lauria FN	2003
4	Socioeconomic burden of nosocomial infections.	[8]	Yalcin AN	2003
5	Modeling the costs of hospital-acquired infections in New Zealand	[9]	Graves	2003
6	A systematic audit of economic evidence linking nosocomial infections and infection control interventions: 1990-2000	[10]	Stone	2002

A.3 APPENDICES FROM CHAPTER 3, THE NBSI STUDY

Figure 8.1: Coupling the databases

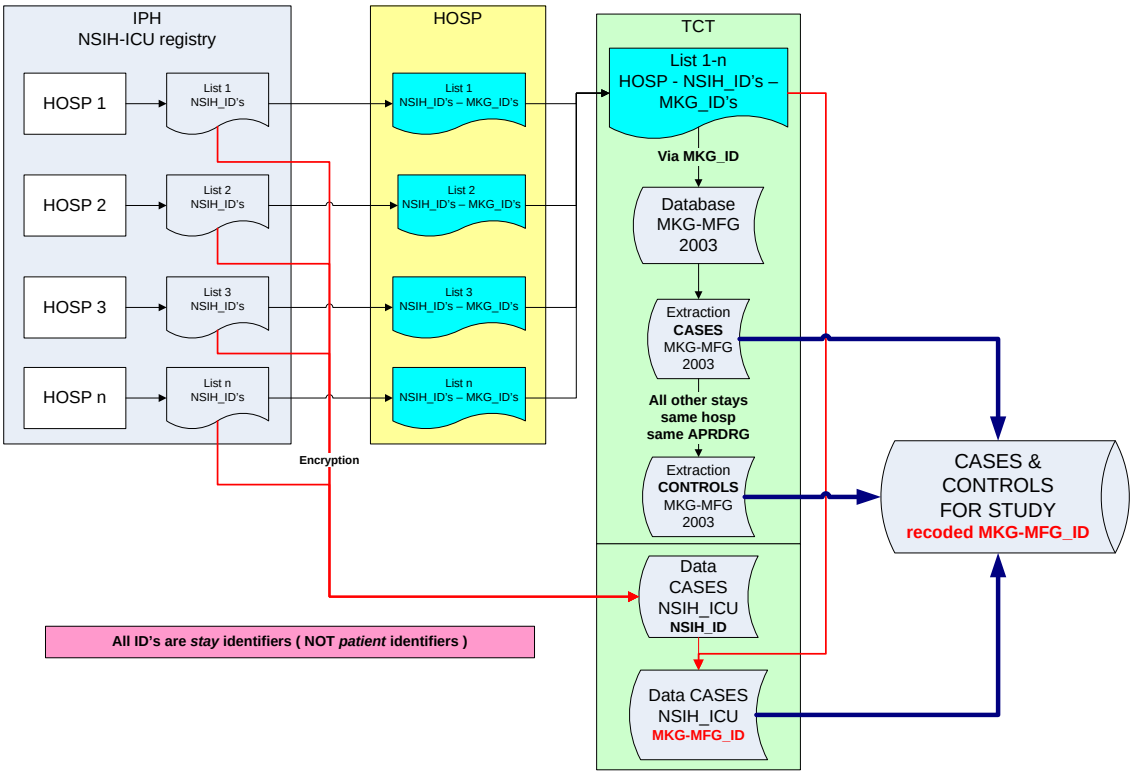


Table 8.1: List of participating hospitals

CIV	nsih_code	Name of Institution	Campus Name	City
015	3404	AZ GROENINGE		KORTRIJK
042	3601	HEILIG HARTZIEKENHUIS		ROESELARE-MENEN
048	3810	K.G.W. ST- AUGUSTINUSKLINIEK	S.A.V.	VEURNE
066	1104	ZNA STER (AZ STUIVENBERG - ST ERASMUS)	Campus Stuivenberg	ANTWERPEN
	1111	ZNA ST/ER	Campus Erasmus	BORGERHOUT
082	1203	IMELDAZIEKENHUIS		BONHEIDEN
093	1201	AZ ST-MAARTEN	Campus Mechelen, St-Jozef	MECHELEN
139	2404	RZ HEILIG HART		LEUVEN
173	2120	HOPITAUX IRIS SUD	C H E I : Site Ixelles	BRUXELLES
194	2501	CHIREC	Site H"p. Br. L'Alleud-Waterloo	BRAINE-L'ALLEUD
198	4102	ONZE-LIEVE-VROUWZIEKENHUIS	Campus Aalst	AALST
218	4410	AZ ST-LUCAS	Sint-Lucas & Volkskliniek	GENT
221	4403	UZ RUG GENT		GENT
254	4402	AZ ST-ELISABETH		ZOTTEGEM
281	5501	CHU DE TIVOLI		LA LOUVIERE
300	5402	CHM DE MOUCRON	Site Le Refuge	MOUSCRON
328	6204	C H C asbl	Site Notre-Dame d'Hermalle	HERMALLE-SOUS-ARGENTEAU
	6210	C H C asbl	Site St-Joseph	LIEGE
	6222	C H C asbl	Site Clinique de l'Esp,rance	SAINT-NICOLAS
364	7202	MARIA ZIEKENHUIS NOORD-LIMBURG	Site M. Middelares	LOMMEL
370	7103	RZ ST-TRUDO		SINT-TRUIDEN
372	7304	AZ VESALIUS	Campus Jacobus	TONGEREN
390	9101	CLINIQUES UCL Mont-Godinne		YVOIR
393	9203	CHR DE NAMUR		NAMUR
451	6206	CHR DE LA CITADELLE	Site La Citadelle	LIEGE

Table 8.2: List of all ICD-9 CM diagnoses codes to identify Bloodstream Infections in MCD

0031 -SALMONELLA SEPTICEMIA

0362 -MENINGOCOCCEMIA

0380 -STREPTOCOCCAL SEPTICEMIA
03810 -STAPHYLCOCC SEPTICEM NOS
03811 -STAPH AUREUS SEPTICEMIA
03819 -STAPHYLCOCC SEPTICEM NEC
0382 -PNEUMOCOCCAL SEPTICEMIA
0383 -ANAEROBIC SEPTICEMIA
03840 -GRAM-NEG SEPTICEMIA NOS
03841 -H. INFLUENZAE SEPTICEMIA
03842 -E COLI SEPTICEMIA
03843 -PSEUDOMONAS SEPTICEMIA
03844 -SERRATIA SEPTICEMIA
03849 -GRAM-NEG SEPTICEMIA NEC
0388 -SEPTICEMIA NEC
0389 -SEPTICEMIA NOS

0545 -HERPETIC SEPTICEMIA

7907 -BACTEREMIA

Table 8.3: All APR-DRG for patients infected (and their control patients)

AP_DRG versie 15	N_sep	N_no_sep
001-LIVER TRANSPLANT / p1 - P	4	45
002-HEART &/OR LUNG TRANSPLANT / p4 - P	2	5
003-BONE MARROW TRANSPLANT / p2 - P	24	112
004-TRACHEOSTOMY EXCEPT FOR FACE, MOUTH & NECK DIAGNOSES / p3 - P	119	435
005-TRACHEOSTOMY FOR FACE, MOUTH & NECK DIAGNOSES / p3 - P	2	58
020-CRANIOTOMY FOR TRAUMA / 1 - P	8	110
021-CRANIOTOMY EXCEPT FOR TRAUMA / 1 - P	21	870
022-VENTRICULAR SHUNT PROCEDURES / 1 - P	7	103
023-SPINAL PROCEDURES / 1 - P	2	43
024-EXTRACRANIAL VASCULAR PROCEDURES / 1 - P	3	113
025-NERVOUS SYSTEM PROC FOR PERIPHERAL NERVE DISORDERS / 1 - P	1	5
026-NERVOUS SYST PROC FOR CRANIAL NERV & OTH NERV SYS DISORD / 1 - P	3	50
041-NERVOUS SYSTEM NEOPLASMS / 1 - M	4	204
042-DEGENERATIVE NERVOUS SYSTEM DISORDERS / 1 - M	8	1587
043-MULTIPLE SCLEROSIS & CEREBELLAR ATAXIA / 1 - M	2	6
044-INTRACRANIAL HEMORRHAGE / 1 - M	11	333
045-CVA W INFARCT / 1 - M	32	1975
046-NONSPECIFIC CVA & PRECEREBRAL OCCLUSION W/O INFARCT / 1 - M	19	1109
047-TRANSIENT ISCHEMIA / 1 - M	3	195
048-CRANIAL & PERIPHERAL NERVE DISORDERS / 1 - M	2	115
049-BACTERIAL & TUBERCULOUS INFECTIONS OF NERVOUS SYSTEM / 1 - M	2	73
050-NON-BACTERIAL INFECTIONS OF NERVOUS SYSTEM EXC VIRAL MENINGITIS / 1 - M	3	39

052-NONTRAUMATIC STUPOR & COMA / 1 - M	4	253
053-SEIZURE / 1 - M	8	1371
055-HEAD TRAUMA W COMA > 1 HR OR HEMORRHAGE / 1 - M	6	198
058-OTHER DISORDERS OF NERVOUS SYSTEM / 1 - M	3	716
072-EXTRAOCULAR PROCEDURES EXCEPT ORBIT / 2 - P	1	41
090-MAJOR LARYNX & TRACHEAL PROCEDURES EXCEPT TRACHEOSTOMY / 3 - P	2	35
093-SINUS & MASTOID PROCEDURES / 3 - P	1	469
094-MOUTH PROCEDURES / 3 - P	2	86
097-TONSILLECTOMY & ADENOIDECTOMY PROCEDURES / 3 - P	1	252
110-EAR, NOSE, MOUTH & THROAT MALIGNANCY / 3 - M	5	174
112-EPISTAXIS / 3 - M	2	49
113-EPIGLOTTITIS, OTITIS MEDIA, URI & LARYNGOTRACHEITIS / 3 - M	2	338
120-MAJOR RESPIRATORY PROCEDURES / 4 - P	4	125
121-NON-MAJOR RESPIRATORY PROCEDURES / 4 - P	4	156
122-OTHER RESPIRATORY SYSTEM PROCEDURES / 4 - P	4	33
130-RESPIRATORY SYSTEM DIAGNOSIS W VENTILATOR SUPPORT 96+ HOURS / 4 - M	31	313
133-PULMONARY EDEMA & RESPIRATORY FAILURE / 4 - M	5	379
134-PULMONARY EMBOLISM / 4 - M	5	396
135-MAJOR CHEST TRAUMA / 4 - M	2	55
136-RESPIRATORY MALIGNANCY / 4 - M	17	1506
137-RESPIRATORY INFECTIONS & INFLAMMATIONS / 4 - M	19	1077
139-SIMPLE PNEUMONIA / 4 - M	19	4269
140-CHRONIC OBSTRUCTIVE PULMONARY DISEASE / 4 - M	18	3775
142-INTERSTITIAL LUNG DISEASE / 4 - M	1	18
143-PNEUMOTHORAX & PLEURAL EFFUSION / 4 - M	2	101
144-RESPIRATORY SYSTEM SIGNS, SYMPTOMS & OTHER DIAGNOSES / 4 - M	7	3385
160-MAJOR CARDIOTHORACIC REPAIR OF HEART ANOMALY / 5 - P	1	34
161-CARDIAC DEFIBRILLATOR IMPLANT / 5 - P	4	154
162-CARDIAC VALVE PROCEDURES W CARDIAC CATHETERIZATION / 5 - P	16	274
163-CARDIAC VALVE PROCEDURES W/O CARDIAC CATHETERIZATION / 5 - P	6	757
165-CORONARY BYPASS W/O MALFUNCTIONING CORONARY BYPASS W CARDIAC CATH / 5 - P	20	801
166-CORONARY BYPASS W/O MALFUNCTIONING CORONARY BYPASS W/O CARDIAC CATH / 5 - P	14	1270
167-OTHER CARDIOTHORACIC PROCEDURES / 5 - P	1	55
168-MAJOR THORACIC VASCULAR PROCEDURES / 5 - P	8	498
169-MAJOR ABDOMINAL VASCULAR PROCEDURES / 5 - P	9	121
170-PERMANENT CARDIAC PACEMAKER IMPLANT W AMI, HEART FAILURE OR SHOCK / 5 - P	3	38
171-PERM CARDIAC PACEMAKER IMPLANT W/O AMI, HEART FAILURE OR SHOCK / 5 - P	4	432
172-AMPUTATION FOR CIRC SYSTEM DISORDER EXCEPT UPPER LIMB & TOE / 5 - P	16	158
173-OTHER VASCULAR PROCEDURES / 5 - P	20	2807
174-PERCUTANEOUS CARDIOVASCULAR PROCEDURES W AMI / 5 - P	3	184

175-PERCUTANEOUS CARDIOVASCULAR PROCEDURES W/O AMI / 5 - P	12	3987
176-CARDIAC PACEMAKER & DEFIBRILLATOR DEVICE REPLACEMENT / 5 - P	1	32
178-UPPER LIMB & TOE AMPUTATION FOR CIRC SYSTEM DISORDERS / 5 - P	1	37
180-OTHER CIRCULATORY SYSTEM PROCEDURES / 5 - P	3	115
190-CIRCULATORY DISORDERS W AMI / 5 - M	13	828
191-CARDIAC CATHETERIZATION W CIRC DISORD EXC ISCHEMIC HEART DISEASE / 5 - M	7	1346
192-CARDIAC CATHETERIZATION FOR ISCHEMIC HEART DISEASE / 5 - M	4	2025
193-ACUTE & SUBACUTE ENDOCARDITIS / 5 - M	4	20
194-HEART FAILURE / 5 - M	35	3142
196-CARDIAC ARREST, UNEXPLAINED / 5 - M	4	104
197-PERIPHERAL & OTHER VASCULAR DISORDERS / 5 - M	8	640
198-ATHEROSCLEROSIS / 5 - M	3	485
199-HYPERTENSION / 5 - M	3	113
200-CARDIAC CONGENITAL & VALVULAR DISORDERS / 5 - M	2	133
201-CARDIAC ARRHYTHMIA & CONDUCTION DISORDERS / 5 - M	13	1692
202-ANGINA PECTORIS / 5 - M	2	364
204-SYNCOPE & COLLAPSE / 5 - M	2	335
206-MALFUNCTION, REACTION & COMP OF CARDIAC OR VASC DEVICE OR PROC / 5 - M	4	128
207-OTHER CIRCULATORY SYSTEM DIAGNOSES / 5 - M	3	298
220-MAJOR STOMACH, ESOPHAGEAL & DUODENAL PROCEDURES / 6 - P	28	748
221-MAJOR SMALL & LARGE BOWEL PROCEDURES / 6 - P	99	2651
223-MINOR SMALL & LARGE BOWEL PROCEDURES / 6 - P	7	126
224-PERITONEAL ADHESIOLYSIS / 6 - P	5	143
226-ANAL & STOMAL PROCEDURES / 6 - P	4	844
227-HERNIA PROCEDURES EXCEPT INGUINAL & FEMORAL / 6 - P	3	386
228-INGUINAL & FEMORAL HERNIA PROCEDURES / 6 - P	1	610
229-OTHER DIGESTIVE SYSTEM PROCEDURES / 6 - P	16	450
240-DIGESTIVE MALIGNANCY / 6 - M	22	1087
241-PEPTIC ULCER & GASTRITIS / 6 - M	7	849
242-MAJOR ESOPHAGEAL DISORDERS / 6 - M	1	10
243-OTHER ESOPHAGEAL DISORDERS / 6 - M	4	321
244-DIVERTICULITIS & DIVERTICULOSIS / 6 - M	3	298
245-INFLAMMATORY BOWEL DISEASE / 6 - M	4	191
246-G.I. VASCULAR INSUFFICIENCY / 6 - M	4	55
247-G.I. OBSTRUCTION / 6 - M	8	823
249-NONBACTERIAL GASTROENTERITIS & ABDOMINAL PAIN / 6 - M	4	2281
250-OTHER DIGESTIVE SYSTEM DIAGNOSES / 6 - M	16	4370
260-PANCREAS, LIVER & SHUNT PROCEDURES / 7 - P	21	282
261-MAJOR BILIARY TRACT PROCEDURES / 7 - P	10	84
262-CHOLECYSTECTOMY EXCEPT LAPAROSCOPIC / 7 - P	6	69
263-LAPAROSCOPIC CHOLECYSTECTOMY / 7 - P	12	1532
264-OTHER HEPATOBILIARY & PANCREAS PROCEDURES / 7 - P	8	138

280-CIRRHOSIS & ALCOHOLIC HEPATITIS / 7 - M	16	681
281-MALIGNANCY OF HEPATOBILIARY SYSTEM & PANCREAS / 7 - M	23	755
282-DISORDERS OF PANCREAS EXCEPT MALIGNANCY / 7 - M	14	777
283-DISORDERS OF LIVER EXCEPT MALIG, CIRRHOSIS OR ALCOHOLIC HEPATITIS / 7 - M	9	423
284-DISORDERS OF THE BILIARY TRACT / 7 - M	20	900
300-BILATERAL & MULTIPLE MAJOR JOINT PROCS OF LOWER EXTREMITY / 8 - P	1	20
301-MAJOR JOINT & LIMB REATTACH PROC OF LOWER EXTREMITY FOR TRAUMA / 8 - P	21	922
302-MAJOR JOINT & LIMB REATTACH PROC OF LOWER EXTREM EXC FOR TRAUMA / 8 - P	12	1927
303-DORSAL & LUMBAR FUSION PROC FOR CURVATURE OF BACK / 8 - P	1	17
304-DORSAL & LUMBAR FUSION PROC EXCEPT FOR CURVATURE OF BACK / 8 - P	3	367
305-AMPUTATION FOR MUSCULOSKELET SYSTEM & CONN TISSUE DISORDERS / 8 - P	2	13
308-HIP & FEMUR PROCEDURES EXCEPT MAJOR JOINT FOR TRAUMA / 8 - P	14	1178
309-HIP & FEMUR PROCEDURES EXCEPT MAJOR JOINT FOR NONTRAUMA / 8 - P	1	31
310-BACK & NECK PROCEDURES EXCEPT DORSAL & LUMBAR FUSION / 8 - P	12	2957
312-SKIN GRFT & WND DEBRID EXC OPN WND, FOR MS & CONN TIS DIS, EXC HAND / 8 - P	3	30
313-KNEE & LOWER LEG PROCEDURES EXCEPT FOOT / 8 - P	1	673
315-SHOULDER, ELBOW & FOREARM PROCEDURES / 8 - P	5	1581
317-SOFT TISSUE PROCEDURES / 8 - P	1	97
318-REMOVAL OF INTERNAL FIXATION DEVICE / 8 - P	1	148
319-LOCAL EXCISION OF MUSCULOSKELETAL SYSTEM / 8 - P	1	24
320-OTHER MUSCULOSKELETEL SYSTEM & CONNECTIVE TISSUE PROCEDURES / 8 - P	5	358
340-FRACTURES OF FEMUR / 8 - M	1	14
341-FRACTURE OF PELVIS OR DISLOCATION OF HIP / 8 - M	2	106
342-FRACTURE OR DISLOCATION EXCEPT FEMUR & PELVIS / 8 - M	1	44
343-MUSCULOSKELETAL & CONN TISS MALIGNANCY & PATHOLOGICAL FRACTURES / 8 - M	18	972
344-OSTEOMYELITIS / 8 - M	2	29
345-SEPTIC ARTHRITIS / 8 - M	2	16
346-CONNECTIVE TISSUE DISORDERS / 8 - M	8	566
347-MEDICAL BACK PROBLEMS / 8 - M	8	1995
348-OTHER BONE DISEASES / 8 - M	6	323
349-MALFUNCTION, REACTION & COMP OF ORTHOPEDIC DEVICE OR PROCEDURE / 8 - M	3	109
350-MUSCULOSKELETAL SIGNS, SYMPTOMS, SPRAINS & MINOR INFLAMMATORY DIS / 8 - M	2	108
351-OTHER MUSCULOSKELETAL SYSTEM & CONNECTIVE TISSUE DIAGNOSES / 8 - M	1	148
360-SKIN GRAFT & WOUND DEBRID FOR SKIN ULCER & CELLULITIS / 9 - P	7	119
361-SKIN GRAFT & WOUND DEBRID EXC FOR SKIN ULCER & CELLULITIS / 9 - P	6	449
362-MASTECTOMY PROCEDURES / 9 - P	1	21
364-OTHER SKIN, SUBCUTANEOUS TISSUE & BREAST PROCEDURES / 9 - P	2	395

380-SKIN ULCERS / 9 - M	1	75
382-MALIGNANT BREAST DISORDERS / 9 - M	4	105
383-CELLULITIS / 9 - M	4	729
384-TRAUMA TO THE SKIN, SUBCUTANEOUS TISSUE & BREAST / 9 - M	1	130
385-OTHER SKIN & BREAST DISORDERS / 9 - M	6	254
401-ADRENAL & PITUITARY PROCEDURES / 10 - P	1	8
403-PROCEDURES FOR OBESITY / 10 - P	3	228
404-THYROID, PARATHYROID & THYROGLOSSAL PROCEDURES / 10 - P	1	96
405-OTHER ENDOCRINE, NUTRITITIONAL & METABOLIC PROCEDURES / 10 - P	2	15
420-DIABETES / 10 - M	4	764
421-NUTRITIONAL & MISC METABOLIC DISORDERS / 10 - M	2	372
422-HYPOVOLEMIA & ELECTROLYTE DISORDERS / 10 - M	10	1299
424-OTHER ENDOCRINE DISORDERS / 10 - M	4	127
440-KIDNEY TRANSPLANT / 11 - P	3	57
441-MAJOR BLADDER PROCEDURES / 11 - P	12	127
442-KIDNEY & URINARY TRACT PROCEDURES FOR MALIGNANCY / 11 - P	6	129
443-KIDNEY & URINARY TRACT PROCEDURES FOR NONMALIGNANCY / 11 - P	10	378
445-MINOR BLADDER PROCEDURES / 11 - P	4	131
446-URETHRAL & TRANSURETHRAL PROCEDURES / 11 - P	13	1895
447-OTHER KIDNEY & URINARY TRACT PROCEDURES / 11 - P	8	291
460-RENAL FAILURE / 11 - M	12	701
461-KIDNEY & URINARY TRACT MALIGNANCY / 11 - M	3	95
462-NEPHRITIS / 11 - M	2	16
463-KIDNEY & URINARY TRACT INFECTIONS / 11 - M	20	1822
465-URINARY STONES W/O ESW LITHOTRIPSY / 11 - M	2	524
466-MALFUNCTIONS, REACTIONS & COMP OF GU DEVICE, GRAFT OR TRANSPLANT / 11 - M	2	55
467-KIDNEY & URINARY TRACT SIGNS & SYMPTOMS / 11 - M	1	61
468-OTHER KIDNEY & URINARY TRACT DIAGNOSES / 11 - M	1	62
480-MAJOR MALE PELVIC PROCEDURES / 12 - P	3	207
482-TRANSURETHRAL PROSTATECTOMY / 12 - P	16	1385
483-TESTES PROCEDURES / 12 - P	1	36
484-OTHER MALE REPRODUCTIVE SYSTEM PROCEDURES / 12 - P	1	56
501-MALE REPRODUCTIVE SYSTEM DIAGNOSES EXCEPT MALIGNANCY / 12 - M	3	143
510-PELVIC EVISCERATION, RADICAL HYSTERECTECTOMY & RADICAL VULVECTOMY / 13 - P	3	82
511-UTERINE & ADNEXA PROCEDURES FOR OVARIAN & ADNEXAL MALIGNANCY / 13 - P	3	33
512-UTERINE & ADNEXA PROCEDURES FOR NON-OVARIAN & NON-ADNEXAL MALIG / 13 - P	1	10
513-UTERINE & ADNEXA PROCEDURES FOR CA IN SITU & NONMALIGNANCY / 13 - P	4	1768
518-OTHER FEMALE REPRODUCTIVE SYSTEM PROCEDURES / 13 - P	5	86
530-FEMALE REPRODUCTIVE SYSTEM MALIGNANCY / 13 - M	1	41
531-FEMALE REPRODUCTIVE SYSTEM INFECTIONS / 13 - M	1	23
532-MENSTRUAL & OTHER FEMALE REPRODUCTIVE SYSTEM DISORDERS / 13 - M	1	16

540-CESAREAN DELIVERY / 14 - P	8	1602
541-VAGINAL DELIVERY W STERILIZATION &/OR D&C / 14 - P	1	4
542-VAGINAL DELIVERY W PROC EXCEPT STERILIZATION &/OR D&C / 14 - P	1	4
560-VAGINAL DELIVERY / 14 - M	3	5009
561-POSTPARTUM & POST ABORTION DIAGNOSES W/O PROCEDURE / 14 - M	1	12
590-NEONATE, BIRTHWT <750G W MAJOR PROCEDURE / 15 - P	1	0
591-NEONATE, BIRTHWT <750G W/O MAJOR PROCEDURE / 15 - M	1	6
593-NEONATE, BIRTHWT 750G-999G W/O MAJOR PROCEDURE / 15 - M	1	0
601-NEONATE, BIRTHWT 1000-1499G W MAJOR ANOM OR HEREDITARY CONDITION / 15 - M	3	18
602-NEONATE, BIRTHWT 1000-1499G W RESPIRATORY DISTRESS SYNDROME / 15 - M	1	21
603-OTHER NEONATE, BIRTHWT 1000-1499G / 15 - M	1	24
611-NEONATE, BIRTHWT 1500-1999G W MAJOR ANOM OR HEREDITARY CONDITION / 15 - M	2	7
612-NEONATE, BIRTHWT 1500-1999G W RESPIRATORY DISTRESS SYNDROME / 15 - M	2	26
613-NEONATE, BIRTHWT 1500-1999G W CONGENITAL OR PERINATAL INFECTIONS / 15 - M	2	1
614-OTHER NEONATE, BIRTHWT 1500-1999G / 15 - M	2	29
625-NEONATE, BIRTHWT 2000-2499G, BORN HERE, W OTHER SIGNIF CONDTN / 15 - M	1	9
631-NEONATE, BIRTHWT > 2499G W OTHER MAJOR PROCEDURE / 15 - P	1	3
632-NEONATE, BIRTHWT > 2499G W OTHER PROCEDURE / 15 - P	1	1
633-NEONATE, BIRTHWT > 2499G W MAJOR ANOMALY OR HEREDITARY CONDITION / 15 - M	3	58
634-NEONATE, BIRTHWT > 2499G W RESPIRATORY DISTRESS SYNDROME / 15 - M	1	29
636-NEONATE, BIRTHWT > 2499G W CONGENITAL/PERINATAL INFECTIONS / 15 - M	1	6
650-SPLENECTOMY / 16 - P	2	12
660-AGRANULOCYTOSIS & OTHER NEUTROPENIA / 16 - M	1	107
661-COAGULATION DISORDERS / 16 - M	1	38
663-RED BLOOD CELL DISORDERS EXCEPT SICKLE CELL ANEMIA CRISIS / 16 - M	9	710
664-OTHER DISORDERS OF BLOOD & BLOOD FORMING ORGANS / 16 - M	1	22
680-LYMPHOMA & LEUKEMIA W MAJOR PROCEDURE / 17 - P	3	32
681-LYMPHOMA & LEUKEMIA W ANY OTHER PROCEDURE / 17 - P	7	88
682-MYELOPROLIF DISORDER & POORLY DIFF NEOPL W MAJOR PROCEDURE / 17 - P	3	34
683-MYELOPROLIF DISORDER & POORLY DIFF NEOPL W ANY OTHER PROCEDURE / 17 - P	2	39
690-ACUTE LEUKEMIA / 17 - M	37	356
691-LYMPHOMA & NON-ACUTE LEUKEMIA / 17 - M	30	669
692-RADIOTHERAPY / 17 - M	1	37
693-CHEMOTHERAPY / 17 - M	25	2909
694-OTHER MYELOPROLIF DISORDERS & POORLY DIFF NEOPLASM DIAGNOSIS / 17 - M	1	120
710-PROCEDURES FOR INFECTIOUS & PARASITIC DISEASES / 18 - P	13	119
711-PROCEDURES FOR POSTOPERATIVE & POST TRAUMATIC INFECTIONS / 18 - P	3	89

720-SEPTICEMIA / 18 - M	51	1123
721-POSTOPERATIVE & POST-TRAUMATIC INFECTIONS / 18 - M	2	114
724-OTHER INFECTIOUS & PARASITIC DISEASES / 18 - M	4	227
740-PROCEDURE W PRINCIPAL DIAGNOSES OF MENTAL ILLNESS / 19 - P	3	54
751-PSYCHOSES / 19 - M	3	170
753-BIPOLAR DISORDERS / 19 - M	2	41
754-DEPRESSION / 19 - M	1	113
756-ACUTE ADJUST REACT & DISTURBANCE OF PSYCHOSOCIAL DYSFUNCTION / 19 - M	1	108
757-ORGANIC DISTURBANCES & MENTAL RETARDATION / 19 - M	17	1371
759-COMPULSIVE NUTRITION DISORDERS / 19 - M	1	4
760-OTHER MENTAL DISORDERS / 19 - M	1	61
775-ALCOHOL ABUSE & DEPENDENCE / 20 - M	2	470
790-SKIN GRAFT & WOUND DEBRIDEMENT FOR INJURIES / 21 - P	2	43
791-PROCEDURES FOR COMPLICATIONS OF TREATMENT / 21 - P	8	310
792-OTHER PROCEDURES FOR INJURIES / 21 - P	1	41
810-INJURIES TO UNSPECIFIED OR MULTIPLE SITES / 21 - M	1	12
812-POISONING & TOXIC EFFECTS OF DRUGS / 21 - M	7	865
813-COMPLICATIONS OF TREATMENT / 21 - M	4	316
830-BURNS, TRANSFERRED TO ANOTHER ACUTE CARE FACILITY / 22 - M	1	1
832-NONEXTENSIVE BURNS W SKIN GRAFT / 22 - P	6	17
840-BURNS W/O PROCEDURE / 22 - M	2	30
850-PROCEDURE W DIAGNOSES OF OTHER CONTACT W HEALTH SERVICES / 23 - P	5	143
860-REHABILITATION / 23 - M	9	1013
861-SIGNS & SYMPTOMS / 23 - M	3	88
862-OTHER FACTORS INFLUENCING HEALTH STATUS / 23 - M	5	817
871-HIV W PROC W MULTIPLE MAJOR HIV RELATED INFECTIONS / 24 - P	1	0
891-HIV W MAJ HIV REL DIAG W MULT MAJ OR SIGNIF HIV REL DIAG / 24 - M	1	0
910-CRANIOTOMY, SPINE, HIP & MAJOR LIMB PROC FOR MULTIPLE SIG TRAUMA / 25 - P	7	68
911-OTHER PROCEDURES FOR MULTIPLE SIGNIFICANT TRAUMA / 25 - P	5	46
930-HEAD, CHEST & LOWER LIMB DIAGNOSES OF MULTIPLE SIGNIFICANT TRAUMA / 25 - M	5	26
931-OTHER DIAGNOSES OF MULTIPLE SIGNIFICANT TRAUMA / 25 - M	2	1
950-EXTENSIVE PROCEDURE UNRELATED TO PRINCIPAL DIAGNOSIS / 0 - P	53	986
951-PROSTATIC PROCEDURE UNRELATED TO PRINCIPAL DIAGNOSIS / 0 - P	2	30
952-NONEXTENSIVE PROCEDURE UNRELATED TO PRINCIPAL DIAGNOSIS / 0 - P	22	586
AAA	2	3004

Table 8.4: All Pathogens identified in patients with NBSI (see next page)

label	Frequency	Percent
ABIOTROPHIA ADIACENS	1	0.05
ACHROMOBACTER SPECIES	1	0.05
ACINETOBACTER SPECIES	4	0.19
ACINETOBACTER BAUMANNII	45	2.08
ACINETOBACTER CALCOACETICUS	1	0.05
ACINETOBACTER JUNII	1	0.05
ACINETOBACTER LWOFFI	2	0.09
AEROMONAS HYDROPHILA	1	0.05
ALCALIGENES FAECALIS	1	0.05
BABESIA SPECIES	1	0.05
BACILLUS SPECIES	3	0.14
BACILLUS CEREUS	2	0.09
BACTEROIDES SPECIES	3	0.14
BACTEROIDES DISTASONIS	1	0.05
BACTEROIDES FRAGILIS	18	0.83
BACTEROIDES OVATUS	2	0.09
BACTEROIDES SPECIES, NOT SPECIFIED	1	0.05
BACTEROIDES THETAIOTAOMICRON	2	0.09
BACTEROIDES UNIFORMIS	1	0.05
BACTEROIDES VULGATUS	1	0.05
CAMPYLOBACTER FETUS FETUS	1	0.05
CAMPYLOBACTER JEJUNI	1	0.05
CANDIDA SPECIES	9	0.42
CANDIDA ALBICANS	93	4.30
CANDIDA GLABRATA	43	1.99
CANDIDA LUSITANIAE	2	0.09
CANDIDA PARAPSILOSIS	19	0.88
CANDIDA SPECIES, NOT SPECIFIED	1	0.05
CANDIDA TROPICALIS	6	0.28
CAPNOCYTOPHAGIA SPECIES	1	0.05
CAPNOCYTOPHAGIA OCHRACEA	1	0.05
CAPNOCYTOPHAGIA SPUTIGENA	1	0.05
CITROBACTER SPECIES	3	0.14
CITROBACTER FREUNDII	9	0.42
CLOSTRIDIUM SPECIES	1	0.05
CLOSTRIDIUM CLOSTRIDIIFORME	1	0.05
CLOSTRIDIUM DIFFICILE	1	0.05
CLOSTRIDIUM PERFRINGENS	4	0.19
COAGULASE-NEGATIVE STAFYLOCOCCI, NOT SPECIFIED	3	0.14
CONIDIOBOLUS	1	0.05
CORYNEBACTERIUM SPECIES	2	0.09
CORYNEBACTERIUM JEIKEIUM	1	0.05
CORYNEBACTERIUM SPECIES, NOT SPECIFIED	2	0.09
CORYNEBACTERIUM ULCERANS	1	0.05
ENTAMOEBA COLI	2	0.09
ENTEROBACTER SPECIES	15	0.69
ENTEROBACTER AEROGENES	58	2.68
ENTEROBACTER AGGLOMERANS	1	0.05
ENTEROBACTER CLOACAE	73	3.38
ENTEROBACTER SAKAZAKII	1	0.05
ENTEROBACTER SPECIES, NOT SPECIFIED	1	0.05
ENTEROCOCCUS SPECIES	29	1.34
ENTEROCOCCUS FAECALIS	85	3.93
ENTEROCOCCUS FAECIUM	29	1.34
ENTEROCOCCUS SPECIES, NOT SPECIFIED	1	0.05
ESCHERICHIA COLI	334	15.46
FUSOBACTERIUM SPECIES	1	0.05
GEMELLA HAEMOLYSANS	2	0.09
GEMELLA MORBILLORUM	1	0.05
GEOTRICHUM SPECIES	2	0.09
HAEMOPHILUS INFLUENZAE	1	0.05
HAFNIA ALVEI	3	0.14
KLEBSIELLA SPECIES	2	0.09

label	Frequency	Percent
KLEBSIELLA ORNITHINOLYTICA	1	0.05
KLEBSIELLA OXYTOCA	56	2.59
KLEBSIELLA OZAENAE	1	0.05
KLEBSIELLA PNEUMONIAE	78	3.61
KLEBSIELLA SPECIES, NOT SPECIFIED	1	0.05
LACTOBACILLUS SPECIES	5	0.23
LEUCONOSTOC SPECIES	1	0.05
LISTERIA MONOCYTOGENES	2	0.09
MICRO-ORGANISM NOT IDENTIFIED OR NOT FOUND	2	0.09
MICROCOCCUS SPECIES	1	0.05
MORAXELLA SPECIES	2	0.09
MORAXELLA CATARRHALIS	1	0.05
MORGANELLA MORGANII	14	0.65
PASTEURELLA AEROGENES	1	0.05
PASTEURELLA MULTOCIDA	1	0.05
PEPTOSTREPTOCOCCUS SPECIES	2	0.09
PEPTOSTREPTOCOCCUS ANAEROBIUS	1	0.05
PREVOTELLA INTERMEDIA	1	0.05
PREVOTELLA LOESCHEII	1	0.05
PREVOTELLA MELANINOGENICA	2	0.09
PROTEUS SPECIES	4	0.19
PROTEUS MIRABILIS	33	1.53
PROTEUS VULGARIS	8	0.37
PROVIDENCIA SPECIES	1	0.05
PROVIDENCIA STUARTII	4	0.19
PSEUDOMONAS SPECIES	4	0.19
PSEUDOMONAS AERUGINOSA	97	4.49
PSEUDOMONAS MALTOPHILIA	4	0.19
PSEUDOMONAS PUTIDA	1	0.05
SACCHAROMYCES SPECIES	1	0.05
SALMONELLA SPECIES	3	0.14
SALMONELLA ENTERITIDIS	2	0.09
SALMONELLA TYPHIMURIUM	1	0.05
SALMONELLA VIRCHOW	1	0.05
SERRATIA SPECIES	2	0.09
SERRATIA LIQUEFACIENS	1	0.05
SERRATIA MARCESCENS	32	1.48
STAPHYLOCOCCUS SPECIES	3	0.14
STAPHYLOCOCCUS AUREUS	207	9.58
STAPHYLOCOCCUS AUREUS,METHICILLIN RESIS	53	2.45
STAPHYLOCOCCUS CAPITIS	3	0.14
STAPHYLOCOCCUS COHNII	12	0.56
STAPHYLOCOCCUS EPIDERMIDIS	216	10.00
STAPHYLOCOCCUS HAEMOLYTICUS	10	0.46
STAPHYLOCOCCUS HOMINIS	7	0.32
STAPHYLOCOCCUS SCHLEIFERI	2	0.09
STAPHYLOCOCCUS SIMULANS	3	0.14
STAPHYLOCOCCUS WARNERI	7	0.32
STAPHYLOCOCCUS, COAGULASE NEGATIVE	184	8.51
STAPHYLOCOCCUS, COAGULASE POSITIVE	2	0.09
STENOTROPHOMONAS MALTOPHILIA	6	0.28
STREPTOCOCCI, ALPHA-HEMOLYTIC	1	0.05
STREPTOCOCCI, BETA-HEMOLYTIC	2	0.09
STREPTOCOCCI, BETA-HEMOLYTIC OF GROUP A	1	0.05
STREPTOCOCCI, BETA-HEMOLYTIC OF GROUP B	3	0.14
STREPTOCOCCI, BETA-HEMOLYTIC OF GROUP C	1	0.05
STREPTOCOCCI, BETA-HEMOLYTIC OF GROUP G	3	0.14
STREPTOCOCCI, GAMMA-HEMOLYTIC	1	0.05
STREPTOCOCCUS SPECIES	7	0.32
STREPTOCOCCUS AGALACTIAE	6	0.28
STREPTOCOCCUS BOVIS	12	0.56
STREPTOCOCCUS MILLERI	5	0.23
STREPTOCOCCUS MITIS	15	0.69

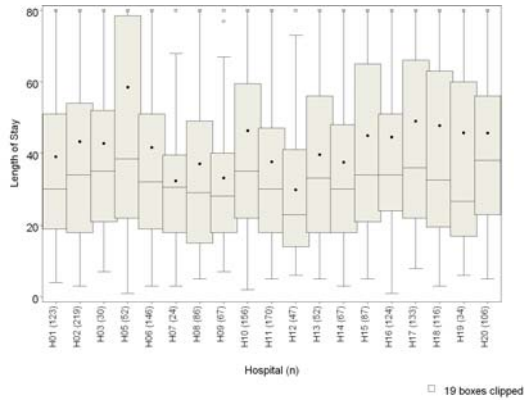
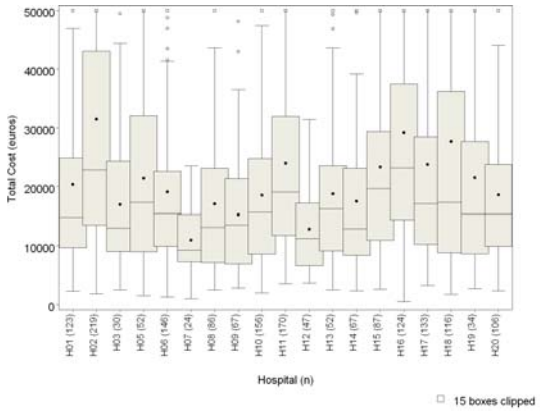
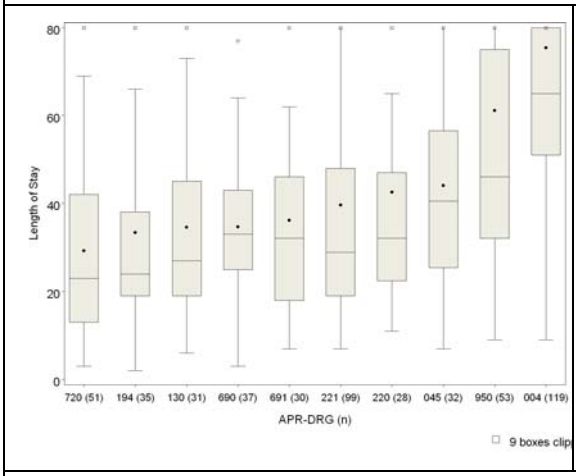
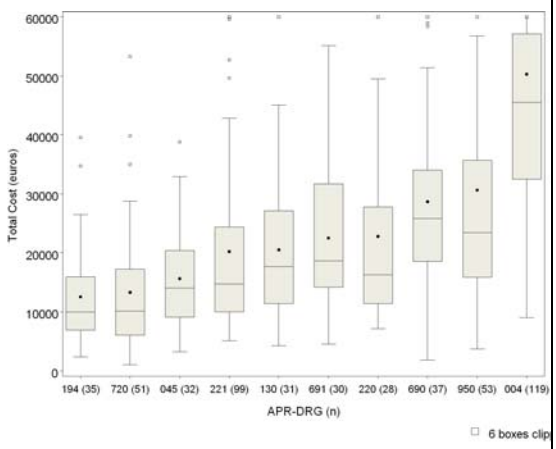
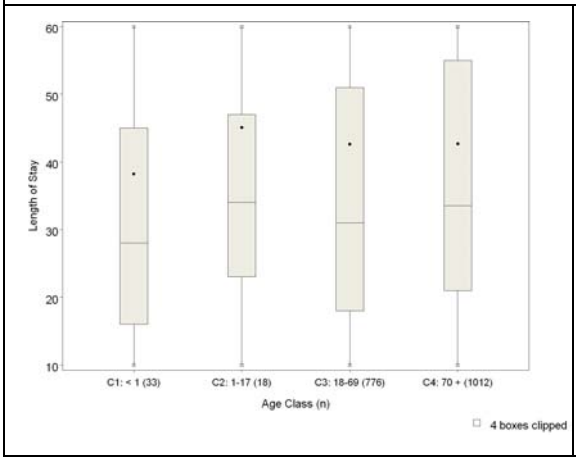
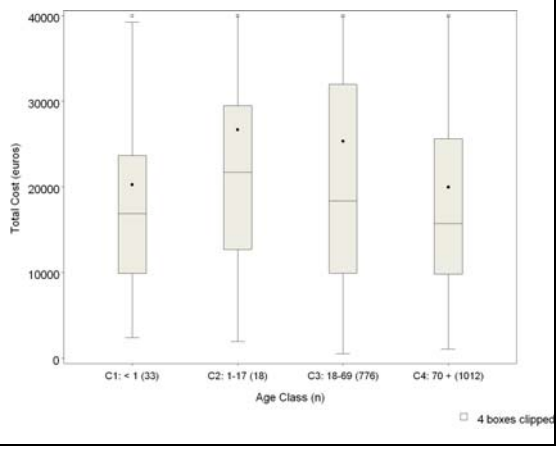
label	Frequency	Percent
STREPTOCOCCUS OF GROUP D	3	0.14
STREPTOCOCCUS PNEUMONIAE	42	1.94
STREPTOCOCCUS PYOGENES	4	0.19
STREPTOCOCCUS SALIVARIUS	3	0.14
STREPTOCOCCUS SANGUIS	2	0.09
STREPTOCOCCUS SPECIES, NOT SPECIFIED	1	0.05
STREPTOCOCCUS VIRIDANS	19	0.88
YEASTS	2	0.09

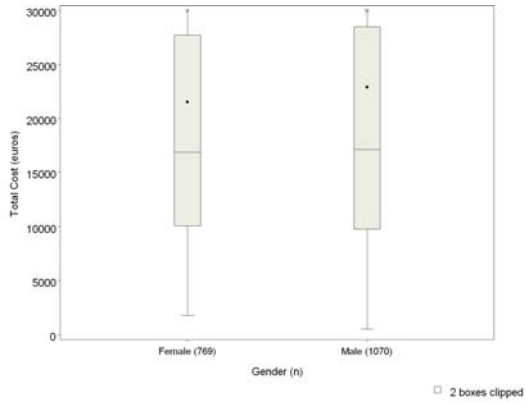
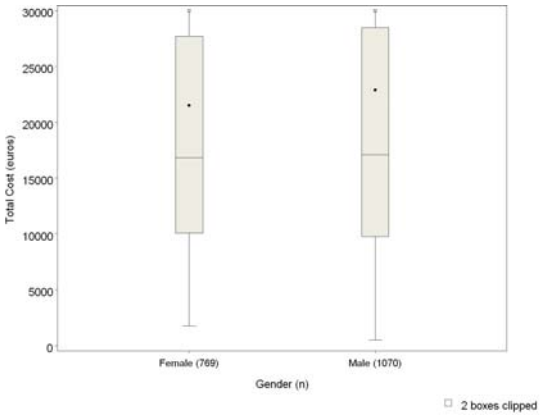
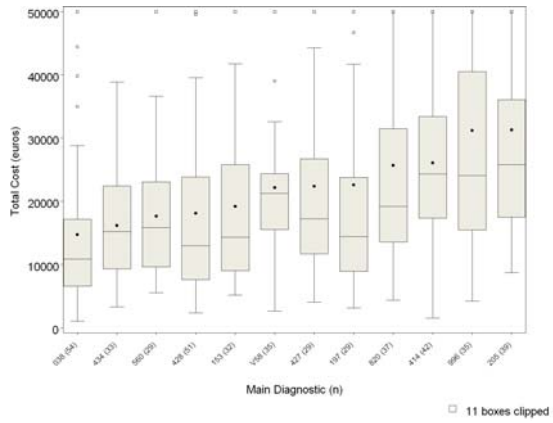
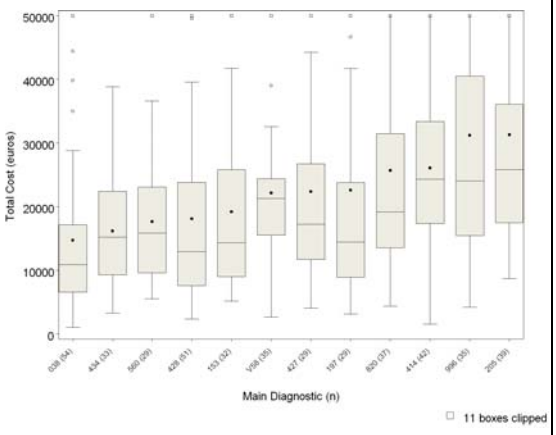
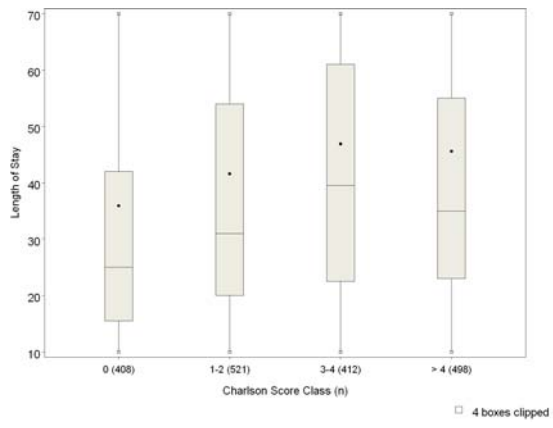
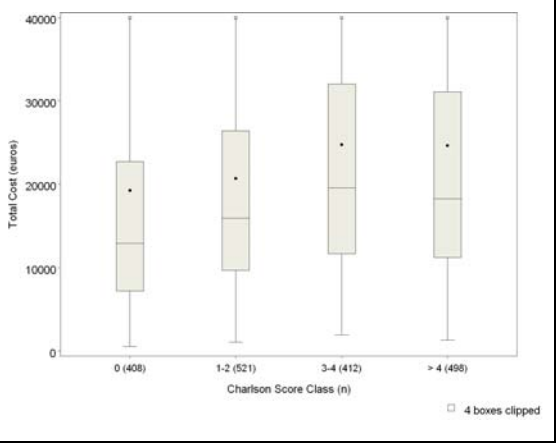
Table 8.4 Mortality in patients with a NBSI, per pathogen identified

Pathogen identified (family)	N_tot	n_death	%
ACINETOBACTER SPECIES	53	11	20.8
BACTEROIDES SPECIES	28	13	46.4
CANDIDA SPECIES	172	88	51.2
CITROBACTER SPECIES	12	2	16.7
COAGULASE-NEGATIVE STAFYLOCOCCI (CNS)	444	126	28.4
ENTEROBACTER SPECIES	148	50	33.8
ENTEROCOCCUS SPECIES	143	41	28.7
ESCHERICHIA COLI	334	85	25.4
GRAM NEGATIVE COCCI	3	1	33.3
GRAM POSITIVE BACILLI	16	6	37.5
HAEMOPHILUS SPECIES	1	.	.
KLEBSIELLA SPECIES	138	37	26.8
MICRO-ORGANISM NOT IDENTIFIED OR NOT FOUND	1	1	100.0
OTH. GRAM- BAC., NON ENTEROBACTERIACIAEA	10	1	10.0
OTHER ANAEROBES	15	8	53.3
OTHER ENTEROBACTERIACEAE	29	14	48.3
OTHER GRAM POSITIVE COCCI	9	3	33.3
OTHER PARASITES	9	5	55.6
PROTEUS SPECIES	45	17	37.8
PSEUDOMONADACEAE FAMILY, OTHER	9	1	11.1
PSEUDOMONAS AERUGINOSA	97	36	37.1
SERRATIA SPECIES	35	9	25.7
STAPHYLOCOCCUS AUREUS	207	70	33.8
STENOTROPHOMONAS MALTOPHILIA	6	2	33.3
STREPTOCOCCUS SPECIES	130	39	30.0

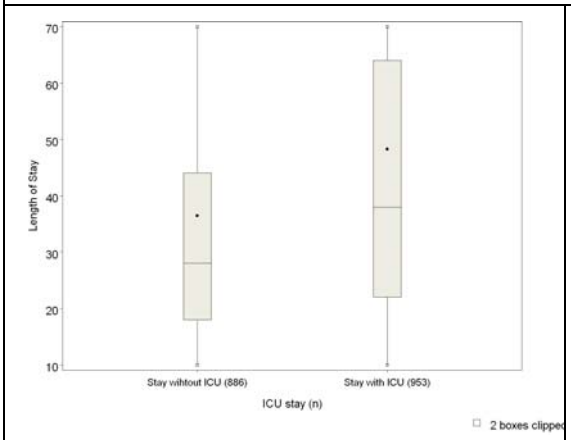
Variability in LOS and Costs for infected patients

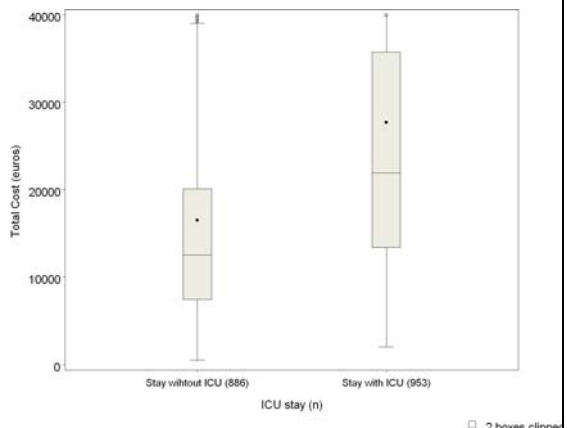
Figures below present subgroup analyses (on the total cost and on the LOS). These figures show the variation that exists (both for total cost and for LOS) between the hospitals, the APR-DRGs, the age classes, the gender, the main diagnostics, the Charlson index class, and the stays with/without ICU. As all these factors (except the gender) are potential confounding factors (they influence both the costs and the risk of nosocomial infection), they are therefore used in the matching procedure described afterwards.

LOS	Total Cost
Hospital	
	
APR-DRG	
	
Age Class	
	

LOS	Total Cost
Gender	
	
Main Diagnostic	
	
Charlson Index	
	

LOS	Total Cost
ICU stay	





Subgroup Analyses

Table 8.5 present subgroup analyses on the LOS, based on the matching including all patients (survivors and deaths). Although there are some observed differences between the subgroup, none was statistically significant, hence it can be concluded that the estimations of attributable LOS are consistent across the different categories.

Table 8.5: Subgroup Analyses on Additional LOS

Subgroup (p-value subgroup effect)	N	NBSI Mean	Control Mean	Diff Mean	95% CI Lower	95% CI Upper
All Data	926	32.2	25.5	6.7	4.8	8.5
Age (p =0.735)						
< 1	17	25.9	28.2	-2.3	-13.9	9.3
1-17	9	23.0	20.7	2.3	-8.8	13.4
18-59	160	27.7	21.8	5.9	0.6	11.2
60-69	179	30.0	22.1	7.9	4.4	11.4
70-79	329	33.0	26.8	6.1	3.1	9.2
>= 80	232	36.6	28.8	7.8	3.9	11.8
Origin of NBSI (p = 0.391)						
Cathether	210	32.9	25.8	7.1	2.8	11.3
Unknown	325	30.2	25.2	5.0	1.8	8.2
Secondary/invasive procedure	391	33.4	25.5	7.9	5.2	10.6
MDC (p = 0.405)						
00-Restgroup	7	52.4	58.4	-6.0	-32.6	20.6
01-Diseases & disorders of the nervous system	84	35.4	34.8	0.5	-8.6	9.7
03-Diseases & disorders of the ear, nose, mouth & throat	3	14.3	18.7	-4.3	-20.3	11.6
04-Diseases & disorders of the respiratory system	80	30.1	23.8	6.4	1.7	11.0
05-Diseases & disorders of the circulatory system	149	30.8	22.0	8.7	4.7	12.7
06-Diseases & disorders of the digestive system	137	32.8	22.5	10.4	5.8	15.0
07-Diseases & disorders of the hepatobiliary system &	74	29.5	20.2	9.3	4.2	14.3
08-Diseases & disorders of the musculoskeletal system	77	41.4	32.4	9.0	0.6	17.3
09-Diseases & disorders of the skin, subcutaneous tis	8	55.0	33.6	21.4	-7.8	50.6
10-Endocrine, nutritional & metabolic diseases & diso	14	21.5	16.1	5.4	-1.0	11.7
11-Diseases & disorders of the kidney & urinary tract	48	23.7	16.1	7.6	3.5	11.8
12-Diseases & disorders of the male reproductive syst	19	20.6	9.4	11.2	-0.0	22.4

Subgroup (p-value subgroup effect)	N	NBSI Mean	Control Mean	Diff Mean	95% CI Lower	95% CI Upper
13-Diseases & disorders of the female reproductive sy	8	22.9	13.1	9.8	3.5	16.0
14-Pregnancy, childbirth & the puerperium	10	11.9	10.0	1.9	-0.1	3.9
15-Newborns & other neonates	13	28.0	32.0	-4.0	-19.1	11.1
16-Diseases & disorders of blood, blood forming organ	7	29.9	13.1	16.7	-2.6	36.0
17-Myeloproliferative diseases & disorders,poorly dif	65	30.0	25.3	4.6	-0.4	9.6
18-Infectious & parasitic diseases, systemic or unspe	43	27.7	20.4	7.3	0.8	13.9
19-Mental diseases & disorders	19	39.6	46.6	-7.0	-36.8	22.8
20-Alcohol/drug use & alcohol/drug induced organic me	2	48.0	37.0	11.0	-357.5	379.5
21-Injuries, poisonings & toxic effects of drugs	7	15.6	14.9	0.7	-6.0	7.4
22-Burns	2	23.0	2.0	21.0	-245.8	287.8
23-Factors influencing hlth stat & othr contacts with	15	58.2	50.6	7.6	-12.8	28.0
p1-Pre MDC : Liver Transplant	3	40.3	21.3	19.0	-4.7	42.7
p2-Pre MDC : Bone Marrow Transplant	17	25.9	25.6	0.2	-5.2	5.7
p3-Pre MDC : Tracheostomy	15	55.7	63.6	-7.9	-42.1	26.2
Time to infection (p = 0.658)						
week 1	352	21.1	15.2	5.8	3.5	8.2
week 2	297	29.5	22.0	7.4	4.6	10.2
week 3	150	41.0	31.9	9.1	3.2	14.9
week 4	67	46.4	40.8	5.6	-1.5	12.6
>= month 2	60	73.1	69.8	3.3	-10.2	16.8
Reporting Service (p = 0.729)						
Cardiology	73	33.9	24.7	9.2	1.9	16.5
Cardiovasc.surg	24	30.4	16.6	13.8	5.9	21.7
General/abdom surg.	107	27.6	21.7	5.9	1.8	10.0
Geriatrics	107	38.0	34.8	3.2	-3.8	10.2
Gynecology	4	11.8	11.5	0.3	-3.3	3.8
Intensive care	140	36.6	31.7	4.9	-1.5	11.3
Internal Medicine	167	28.2	20.9	7.3	3.8	10.9
Medicine, other	20	37.5	32.3	5.2	-6.2	16.6
Mixed surgical/medic	14	30.3	30.3	0.0	-30.9	30.9
Neonatal Intensive Care	13	28.0	32.0	-4.0	-19.1	11.1
Nephrology	13	23.8	23.2	0.5	-6.1	7.2
Neurosurgery	15	31.9	18.8	13.1	4.0	22.2
Obstetrics	5	8.2	6.4	1.8	-1.3	4.9
Oncology/Hematology	94	30.2	24.7	5.5	2.0	9.0
Orthopedics	31	42.8	26.2	16.6	1.3	31.9
Other types	21	43.9	29.3	14.6	0.5	28.6
Pediatrics	7	24.6	18.3	6.3	-6.7	19.3
Pneumology	33	34.7	24.6	10.1	1.7	18.5
Revalidation	5	19.8	18.8	1.0	-4.5	6.5
Urology	33	25.0	15.4	9.6	1.7	17.5
Pathogens *						
FUNGI, YEASTS	59	41.2	36.0	5.1	-6.3	16.6
GRAM-NEGATIVE BACILLI, ANAEROBIC	22	26.4	35.5	-9.1	-19.4	1.2
GRAM-NEGATIVE BACILLI, ENTEROBACTERIACE	381	30.6	23.1	7.4	5.1	9.8
GRAM-NEGATIVE BACILLI, OTHER	83	36.8	28.5	8.3	2.5	14.1
GRAM-NEGATIVE COCCI, AEROBIC	1	63.0	60.0	3.0	.	.
GRAM-POSITIVE BACILLI, AEROBIC	8	24.4	19.9	4.5	-5.5	14.5
GRAM-POSITIVE BACILLI, ANAEROBIC	7	41.1	62.6	-21.4	-89.2	46.3
GRAM-POSITIVE COCCI, AEROBIC	455	32.7	24.8	8.0	5.3	10.6
GRAM-POSITIVE COCCI, ANAEROBIC	2	49.5	33.0	16.5	-104.2	137.2
PROTOZOA	2	18.0	19.5	-1.5	-173.0	170.0

* A patient might have several pathogen identified.

Table 8.6 Definition of the CHARLSON Score

Weight	Conditions	ICD-9 code
1	Myocardial infarct	410, 411
	Congestive heart failure	398, 402, 428
	Peripheral vascular disease	440-447
	Dementia	290, 291, 294
	Cerebrovascular disease	430-433, 435
	Chronic pulmonary disease	491-493
	Connective tissue disease	710, 714, 725
	Ulcer disease	531-534
	Mild liver disease	571, 573
2	Hemiplegia	342, 434, 436, 437
	Moderate or severe renal disease	403, 404, 580-586
	Diabetes	250
	Any tumour	140-195
	Leukemia	204-208
	Lymphoma	200, 202, 203
3	Moderate or severe liver disease	070, 270, 572
6	Metastatic solid tumor	196-199

A.4. APPENDICES FROM THE MATCHED COHORT STUDY

Table 8.7 APR-DRG of all cases (identified in prevalence survey) and potential controls (RCM-RFM 2005)

(see next page)

Frequency (CO. = CONTROS, CA. = CASES)	CO.	**CA.**
001-LIVER TRANSPLANT / p1 - P	36	**2**
003-BONE MARROW TRANSPLANT / p2 - P	137	**6**
004-TRACHEOSTOMY EXCEPT FOR FACE, MOUTH & NECK DIAGNOSES / p3 - P	786	**67**
005-TRACHEOSTOMY FOR FACE, MOUTH & NECK DIAGNOSES / p3 - P	10	**2**
020-CRANIOTOMY FOR TRAUMA / 1 - P	37	**3**
021-CRANIOTOMY EXCEPT FOR TRAUMA / 1 - P	916	**14**
023-SPINAL PROCEDURES / 1 - P	71	**3**
024-EXTRACRANIAL VASCULAR PROCEDURES / 1 - P	14	**1**
040-SPINAL DISORDERS & INJURIES / 1 - M	14	**2**
041-NERVOUS SYSTEM NEOPLASMS / 1 - M	67	**2**
042-DEGENERATIVE NERVOUS SYSTEM DISORDERS / 1 - M	967	**11**
044-INTRACRANIAL HEMORRHAGE / 1 - M	335	**9**
045-CVA W INFARCT / 1 - M	2373	**26**
046-NONSPECIFIC CVA & PRECEREBRAL OCCLUSION W/O INFARCT / 1 - M	81	**2**
047-TRANSIENT ISCHEMIA / 1 - M	281	**4**
049-BACTERIAL & TUBERCULOUS INFECTIONS OF NERVOUS SYSTEM / 1 - M	4	**1**
050-NON-BACTERIAL INFECTIONS OF NERVOUS SYSTEM EXC VIRAL MENINGITIS / 1 - M	5	**1**
052-NONTRAUMATIC STUPOR & COMA / 1 - M	17	**2**
053-SEIZURE / 1 - M	480	**6**
055-HEAD TRAUMA W COMA > 1 HR OR HEMORRHAGE / 1 - M	67	**2**
058-OTHER DISORDERS OF NERVOUS SYSTEM / 1 - M	614	**7**
071-INTRAOCULAR PROCEDURES EXCEPT LENS / 2 - P	1	**1**
073-LENS PROCEDURES W OR W/O VITRECTOMY / 2 - P	10	**1**
090-MAJOR LARYNX & TRACHEAL PROCEDURES EXCEPT TRACHEOSTOMY / 3 - P	32	**1**
094-MOUTH PROCEDURES / 3 - P	15	**1**
111-DYSEQUILIBRIUM / 3 - M	4	**1**
113-EPIGLOTTITIS, OTITIS MEDIA, URI & LARYNGOTRACHEITIS / 3 - M	62	**1**
114-DENTAL & ORAL DISEASE / 3 - M	115	**3**
120-MAJOR RESPIRATORY PROCEDURES / 4 - P	124	**3**
121-NON-MAJOR RESPIRATORY PROCEDURES / 4 - P	85	**2**
122-OTHER RESPIRATORY SYSTEM PROCEDURES / 4 - P	3	**2**
130-RESPIRATORY SYSTEM DIAGNOSIS W VENTILATOR SUPPORT 96+ HOURS / 4 - M	280	**13**
133-PULMONARY EDEMA & RESPIRATORY FAILURE / 4 - M	256	**7**
134-PULMONARY EMBOLISM / 4 - M	26	**1**
135-MAJOR CHEST TRAUMA / 4 - M	21	**1**
136-RESPIRATORY MALIGNANCY / 4 - M	481	**8**
137-RESPIRATORY INFECTIONS & INFLAMMATIONS / 4 - M	759	**10**
139-SIMPLE PNEUMONIA / 4 - M	5119	**21**
140-CHRONIC OBSTRUCTIVE PULMONARY DISEASE / 4 - M	2987	**15**
141-ASTHMA & BRONCHIOLITIS / 4 - M	215	**3**
142-INTERSTITIAL LUNG DISEASE / 4 - M	**0**	**1**
143-PNEUMOTHORAX & PLEURAL EFFUSION / 4 - M	81	**3**
144-RESPIRATORY SYSTEM SIGNS, SYMPTOMS & OTHER DIAGNOSES / 4 - M	1133	**7**
162-CARDIAC VALVE PROCEDURES W CARDIAC CATHETERIZATION / 5 - P	256	**8**
163-CARDIAC VALVE PROCEDURES W/O CARDIAC CATHETERIZATION / 5 - P	1006	**10**
165-CORONARY BYPASS W/O MALFUNCTIONING CORONARY BYPASS W CARDIAC CATH / 5 - P	421	**5**
166-CORONARY BYPASS W/O MALFUNCTIONING CORONARY BYPASS W/O CARDIAC CATH / 5 - P	957	**6**
168-MAJOR THORACIC VASCULAR PROCEDURES / 5 - P	661	**11**
169-MAJOR ABDOMINAL VASCULAR PROCEDURES / 5 - P	153	**5**
171-PERM CARDIAC PACEMAKER IMPLANT W/O AMI, HEART FAILURE OR SHOCK / 5 - P	50	**1**
172-AMPUTATION FOR CIRC SYSTEM DISORDER EXCEPT UPPER LIMB & TOE / 5 - P	84	**7**
173-OTHER VASCULAR PROCEDURES / 5 - P	1653	**12**

Frequency (CO. = CONTROS, CA. = CASES)	CO.	**CA.**
174-PERCUTANEOUS CARDIOVASCULAR PROCEDURES W AMI / 5 - P	495	**2**
175-PERCUTANEOUS CARDIOVASCULAR PROCEDURES W/O AMI / 5 - P	1033	**4**
177-CARDIAC PACEMAKER & DEFIBRILLATOR REVISION EXCEPT DEVICE REPLACEMENT / 5 - P	**0**	**1**
178-UPPER LIMB & TOE AMPUTATION FOR CIRC SYSTEM DISORDERS / 5 - P	20	**2**
180-OTHER CIRCULATORY SYSTEM PROCEDURES / 5 - P	14	**2**
190-CIRCULATORY DISORDERS W AMI / 5 - M	141	**3**
192-CARDIAC CATHETERIZATION FOR ISCHEMIC HEART DISEASE / 5 - M	796	**1**
194-HEART FAILURE / 5 - M	2700	**17**
197-PERIPHERAL & OTHER VASCULAR DISORDERS / 5 - M	341	**5**
198-ATHEROSCLEROSIS / 5 - M	28	**1**
201-CARDIAC ARRHYTHMIA & CONDUCTION DISORDERS / 5 - M	384	**3**
202-ANGINA PECTORIS / 5 - M	33	**1**
204-SYNCOPE & COLLAPSE / 5 - M	152	**3**
206-MALFUNCTION, REACTION & COMP OF CARDIAC OR VASC DEVICE OR PROC / 5 - M	57	**3**
207-OTHER CIRCULATORY SYSTEM DIAGNOSES / 5 - M	80	**2**
220-MAJOR STOMACH, ESOPHAGEAL & DUODENAL PROCEDURES / 6 - P	748	**13**
221-MAJOR SMALL & LARGE BOWEL PROCEDURES / 6 - P	3789	**41**
223-MINOR SMALL & LARGE BOWEL PROCEDURES / 6 - P	79	**2**
224-PERITONEAL ADHESIOLYSIS / 6 - P	25	**3**
225-APPENDECTOMY / 6 - P	243	**2**
226-ANAL & STOMAL PROCEDURES / 6 - P	39	**2**
227-HERNIA PROCEDURES EXCEPT INGUINAL & FEMORAL / 6 - P	70	**3**
229-OTHER DIGESTIVE SYSTEM PROCEDURES / 6 - P	69	**4**
240-DIGESTIVE MALIGNANCY / 6 - M	417	**6**
241-PEPTIC ULCER & GASTRITIS / 6 - M	307	**5**
242-MAJOR ESOPHAGEAL DISORDERS / 6 - M	6	**1**
243-OTHER ESOPHAGEAL DISORDERS / 6 - M	73	**2**
244-DIVERTICULITIS & DIVERTICULOSIS / 6 - M	155	**3**
246-G.I. VASCULAR INSUFFICIENCY / 6 - M	9	**1**
247-G.I. OBSTRUCTION / 6 - M	57	**1**
249-NONBACTERIAL GASTROENTERITIS & ABDOMINAL PAIN / 6 - M	449	**4**
250-OTHER DIGESTIVE SYSTEM DIAGNOSES / 6 - M	1722	**8**
260-PANCREAS, LIVER & SHUNT PROCEDURES / 7 - P	298	**7**
261-MAJOR BILIARY TRACT PROCEDURES / 7 - P	48	**3**
262-CHOLECYSTECTOMY EXCEPT LAPAROSCOPIC / 7 - P	5	**2**
263-LAPAROSCOPIC CHOLECYSTECTOMY / 7 - P	341	**2**
264-OTHER HEPATOBILIARY & PANCREAS PROCEDURES / 7 - P	13	**2**
280-CIRRHOSIS & ALCOHOLIC HEPATITIS / 7 - M	122	**3**
281-MALIGNANCY OF HEPATOBILIARY SYSTEM & PANCREAS / 7 - M	79	**2**
282-DISORDERS OF PANCREAS EXCEPT MALIGNANCY / 7 - M	196	**2**
283-DISORDERS OF LIVER EXCEPT MALIG, CIRRHOSIS OR ALCOHOLIC HEPATITIS / 7 - M	151	**2**
284-DISORDERS OF THE BILIARY TRACT / 7 - M	214	**5**
300-BILATERAL & MULTIPLE MAJOR JOINT PROCS OF LOWER EXTREMITY / 8 - P	1	**1**
301-MAJOR JOINT & LIMB REATTACH PROC OF LOWER EXTREMITY FOR TRAUMA / 8 - P	624	**10**
302-MAJOR JOINT & LIMB REATTACH PROC OF LOWER EXTREM EXC FOR TRAUMA / 8 - P	4818	**21**
303-DORSAL & LUMBAR FUSION PROC FOR CURVATURE OF BACK / 8 - P	34	**1**
304-DORSAL & LUMBAR FUSION PROC EXCEPT FOR CURVATURE OF BACK / 8 - P	467	**4**
308-HIP & FEMUR PROCEDURES EXCEPT MAJOR JOINT FOR TRAUMA / 8 - P	1576	**20**
309-HIP & FEMUR PROCEDURES EXCEPT MAJOR JOINT FOR NONTRAUMA / 8 - P	152	**7**
310-BACK & NECK PROCEDURES EXCEPT DORSAL & LUMBAR FUSION / 8 - P	1408	**8**
312-SKIN GRFT & WND DEBRID EXC OPN WND, FOR MS & CONN TIS DIS, EXC HAND / 8 - P	2	**1**

Frequency (CO. = CONTROS, CA. = CASES)	CO.	**CA.**
313-KNEE & LOWER LEG PROCEDURES EXCEPT FOOT / 8 - P	960	**7**
315-SHOULDER, ELBOW & FOREARM PROCEDURES / 8 - P	130	**1**
316-HAND & WRIST PROCEDURES / 8 - P	12	**1**
317-SOFT TISSUE PROCEDURES / 8 - P	240	**2**
318-REMOVAL OF INTERNAL FIXATION DEVICE / 8 - P	25	**3**
319-LOCAL EXCISION OF MUSCULOSKELETAL SYSTEM / 8 - P	49	**1**
320-OTHER MUSCULOSKELETEL SYSTEM & CONNECTIVE TISSUE PROCEDURES / 8 - P	238	**3**
340-FRACTURES OF FEMUR / 8 - M	25	**2**
341-FRACTURE OF PELVIS OR DISLOCATION OF HIP / 8 - M	147	**5**
342-FRACTURE OR DISLOCATION EXCEPT FEMUR & PELVIS / 8 - M	308	**3**
343-MUSCULOSKELETAL & CONN TISS MALIGNANCY & PATHOLOGICAL FRACTURES / 8 - M	493	**7**
344-OSTEOMYELITIS / 8 - M	3	**2**
346-CONNECTIVE TISSUE DISORDERS / 8 - M	312	**2**
347-MEDICAL BACK PROBLEMS / 8 - M	1001	**7**
348-OTHER BONE DISEASES / 8 - M	22	**1**
349-MALFUNCTION, REACTION & COMP OF ORTHOPEDIC DEVICE OR PROCEDURE / 8 - M	25	**2**
350-MUSCULOSKELETAL SIGNS, SYMPTOMS, SPRAINS & MINOR INFLAMMATORY DIS / 8 - M	33	**1**
351-OTHER MUSCULOSKELETAL SYSTEM & CONNECTIVE TISSUE DIAGNOSES / 8 - M	141	**3**
360-SKIN GRAFT & WOUND DEBRID FOR SKIN ULCER & CELLULITIS / 9 - P	58	**6**
364-OTHER SKIN, SUBCUTANEOUS TISSUE & BREAST PROCEDURES / 9 - P	253	**3**
380-SKIN ULCERS / 9 - M	26	**2**
383-CELLULITIS / 9 - M	524	**5**
384-TRAUMA TO THE SKIN, SUBCUTANEOUS TISSUE & BREAST / 9 - M	206	**5**
385-OTHER SKIN & BREAST DISORDERS / 9 - M	12	**1**
403-PROCEDURES FOR OBESITY / 10 - P	358	**3**
405-OTHER ENDOCRINE, NUTRITITIONAL & METABOLIC PROCEDURES / 10 - P	23	**1**
420-DIABETES / 10 - M	95	**1**
421-NUTRITIONAL & MISC METABOLIC DISORDERS / 10 - M	75	**2**
422-HYPOVOLEMIA & ELECTROLYTE DISORDERS / 10 - M	574	**6**
424-OTHER ENDOCRINE DISORDERS / 10 - M	11	**1**
440-KIDNEY TRANSPLANT / 11 - P	54	**1**
441-MAJOR BLADDER PROCEDURES / 11 - P	53	**3**
443-KIDNEY & URINARY TRACT PROCEDURES FOR NONMALIGNANCY / 11 - P	182	**4**
445-MINOR BLADDER PROCEDURES / 11 - P	50	**1**
446-URETHRAL & TRANSURETHRAL PROCEDURES / 11 - P	147	**1**
447-OTHER KIDNEY & URINARY TRACT PROCEDURES / 11 - P	20	**1**
460-RENAL FAILURE / 11 - M	311	**7**
461-KIDNEY & URINARY TRACT MALIGNANCY / 11 - M	11	**1**
462-NEPHRITIS / 11 - M	9	**1**
463-KIDNEY & URINARY TRACT INFECTIONS / 11 - M	1405	**12**
466-MALFUNCTIONS, REACTIONS & COMP OF GU DEVICE, GRAFT OR TRANSPLANT / 11 - M	27	**1**
467-KIDNEY & URINARY TRACT SIGNS & SYMPTOMS / 11 - M	21	**1**
468-OTHER KIDNEY & URINARY TRACT DIAGNOSES / 11 - M	38	**2**
482-TRANSURETHRAL PROSTATECTOMY / 12 - P	211	**2**
483-TESTES PROCEDURES / 12 - P	7	**1**
484-OTHER MALE REPRODUCTIVE SYSTEM PROCEDURES / 12 - P	15	**1**
510-PELVIC EVISCERATION, RADICAL HYSTERECTECTOMY & RADICAL VULVECTOMY / 13 - P	74	**4**
512-UTERINE & ADNEXA PROCEDURES FOR NON-OVARIAN & NON-ADNEXAL MALIG / 13 - P	5	**1**

Frequency (CO. = CONTROS, CA. = CASES)	CO.	**CA.**
513-UTERINE & ADNEXA PROCEDURES FOR CA IN SITU & NONMALIGNANCY / 13 - P	1729	**5**
514-FEMALE REPRODUCTIVE SYSTEM RECONSTRUCTIVE PROCEDURES / 13 - P	28	**1**
518-OTHER FEMALE REPRODUCTIVE SYSTEM PROCEDURES / 13 - P	5	**1**
530-FEMALE REPRODUCTIVE SYSTEM MALIGNANCY / 13 - M	81	**6**
540-CESAREAN DELIVERY / 14 - P	1931	**4**
541-VAGINAL DELIVERY W STERILIZATION &/OR D&C / 14 - P	3	**1**
543-POSTPARTUM & POST ABORTION DIAGNOSES W PROCEDURE / 14 - P	3	**1**
560-VAGINAL DELIVERY / 14 - M	1325	**2**
561-POSTPARTUM & POST ABORTION DIAGNOSES W/O PROCEDURE / 14 - M	**0**	**1**
562-ECTOPIC PREGNANCY / 14 - M	30	**1**
563-THREATENED ABORTION / 14 - M	151	**1**
590-NEONATE, BIRTHWT <750G W MAJOR PROCEDURE / 15 - P	**0**	**1**
591-NEONATE, BIRTHWT <750G W/O MAJOR PROCEDURE / 15 - M	**0**	**3**
593-NEONATE, BIRTHWT 750G-999G W/O MAJOR PROCEDURE / 15 - M	**1**	**1**
600-NEONATE, BIRTHWT 1000-1499G W MAJOR PROCEDURE / 15 - P	**3**	**1**
602-NEONATE, BIRTHWT 1000-1499G W RESPIRATORY DISTRESS SYNDROME / 15 - M	**8**	**3**
611-NEONATE, BIRTHWT 1500-1999G W MAJOR ANOM OR HEREDITARY CONDITION / 15 - M	**9**	**1**
612-NEONATE, BIRTHWT 1500-1999G W RESPIRATORY DISTRESS SYNDROME / 15 - M	**10**	**2**
623-NEONATE, BIRTHWT 2000-2499G W CONGENITAL OR PERINATAL INFECTIONS / 15 - M	**1**	**1**
625-NEONATE, BIRTHWT 2000-2499G, BORN HERE, W OTHER SIGNIF CONDTN / 15 - M	**0**	**1**
633-NEONATE, BIRTHWT > 2499G W MAJOR ANOMALY OR HEREDITARY CONDITION / 15 - M	**4**	**1**
636-NEONATE, BIRTHWT > 2499G W CONGENITAL/PERINATAL INFECTIONS / 15 - M	**0**	**2**
638-NEONATE, BIRTHWT > 2499G, NOT BORN HERE, PDX OTHER PROBLEM / 15 - M	**12**	**1**
640-NEONATE, BWT > 2499G, BORN HERE, NORMAL NB & NB W OTHER PROB / 15 - M	**4**	**1**
650-SPLENECTOMY / 16 - P	8	**1**
660-AGRANULOCYTOSIS & OTHER NEUTROPENIA / 16 - M	139	**3**
663-RED BLOOD CELL DISORDERS EXCEPT SICKLE CELL ANEMIA CRISIS / 16 - M	243	**3**
680-LYMPHOMA & LEUKEMIA W MAJOR PROCEDURE / 17 - P	5	**2**
681-LYMPHOMA & LEUKEMIA W ANY OTHER PROCEDURE / 17 - P	37	**3**
683-MYELOPROLIF DISORDER & POORLY DIFF NEOPL W ANY OTHER PROCEDURE / 17 - P	9	**1**
690-ACUTE LEUKEMIA / 17 - M	326	**4**
691-LYMPHOMA & NON-ACUTE LEUKEMIA / 17 - M	118	**4**
693-CHEMOTHERAPY / 17 - M	2143	**5**
694-OTHER MYELOPROLIF DISORDERS & POORLY DIFF NEOPLASM DIAGNOSIS / 17 - M	10	**1**
710-PROCEDURES FOR INFECTIOUS & PARASITIC DISEASES / 18 - P	95	**12**
711-PROCEDURES FOR POSTOPERATIVE & POST TRAUMATIC INFECTIONS / 18 - P	58	**6**
720-SEPTICEMIA / 18 - M	667	**17**
721-POSTOPERATIVE & POST-TRAUMATIC INFECTIONS / 18 - M	333	**19**
722-FEVER OF UNKNOWN ORIGIN / 18 - M	76	**1**
724-OTHER INFECTIOUS & PARASITIC DISEASES / 18 - M	17	**2**
740-PROCEDURE W PRINCIPAL DIAGNOSES OF MENTAL ILLNESS / 19 - P	20	**1**
751-PSYCHOSES / 19 - M	440	**3**
752-DISORDERS OF PERSONALITY & IMPULSE CONTROL / 19 - M	3	**1**
754-DEPRESSION / 19 - M	48	**3**
755-NEUROSES EXCEPT DEPRESSIVE / 19 - M	5	**1**

Frequency (CO. = CONTROS, CA. = CASES)	CO.	**CA.**
756-ACUTE ADJUST REACT & DISTURBANCE OF PSYCHOSOCIAL DYSFUNCTION / 19 - M	60	**1**
757-ORGANIC DISTURBANCES & MENTAL RETARDATION / 19 - M	404	**5**
772-ALCOHOL & DRUG DEPENDENCE W REHABILITATION THERAPY / 20 - M	4	**1**
773-OPIOID ABUSE & DEPENDENCE / 20 - M	**0**	**1**
775-ALCOHOL ABUSE & DEPENDENCE / 20 - M	293	**5**
776-OTHER DRUG ABUSE & DEPENDENCE / 20 - M	17	**1**
790-SKIN GRAFT & WOUND DEBRIDEMENT FOR INJURIES / 21 - P	122	**5**
791-PROCEDURES FOR COMPLICATIONS OF TREATMENT / 21 - P	200	**7**
792-OTHER PROCEDURES FOR INJURIES / 21 - P	10	**1**
810-INJURIES TO UNSPECIFIED OR MULTIPLE SITES / 21 - M	3	**1**
813-COMPLICATIONS OF TREATMENT / 21 - M	259	**8**
831-EXTENSIVE BURNS W PROCEDURE / 22 - P	**0**	**1**
832-NONEXTENSIVE BURNS W SKIN GRAFT / 22 - P	32	**1**
850-PROCEDURE W DIAGNOSES OF OTHER CONTACT W HEALTH SERVICES / 23 - P	318	**8**
860-REHABILITATION / 23 - M	2669	**22**
861-SIGNS & SYMPTOMS / 23 - M	48	**2**
862-OTHER FACTORS INFLUENCING HEALTH STATUS / 23 - M	51	**0**
910-CRANIOTOMY, SPINE, HIP & MAJOR LIMB PROC FOR MULTIPLE SIG TRAUMA / 25 - P	38	**6**
911-OTHER PROCEDURES FOR MULTIPLE SIGNIFICANT TRAUMA / 25 - P	19	**2**
930-HEAD, CHEST & LOWER LIMB DIAGNOSES OF MULTIPLE SIGNIFICANT TRAUMA / 25 - M	16	**4**
931-OTHER DIAGNOSES OF MULTIPLE SIGNIFICANT TRAUMA / 25 - M	4	**1**
950-EXTENSIVE PROCEDURE UNRELATED TO PRINCIPAL DIAGNOSIS / 0 - P	818	**20**
951-PROSTATIC PROCEDURE UNRELATED TO PRINCIPAL DIAGNOSIS / 0 - P	16	**3**
952-NONEXTENSIVE PROCEDURE UNRELATED TO PRINCIPAL DIAGNOSIS / 0 - P	204	**4**
Total	74204	**978**

Table 8.8 RCM data received for patients infected (identified in prevalence survey)

Number of patients infected	1037
Number of MCD data received	1000
Number of valid MCD data	978 (94%)
Exclusions:	22
APR-DRG not valid	1
Dates not valid	13
APR-DRG AAA	4
Unknown ward	4

Table 8.9: Age of infected patients during prevalence survey, per bed index

	All			
	N	Mean	Median	Std
Bed type				
A- Psychiatry	12	56.6	59.0	13.6
C- Surgical	244	63.4	66.0	16.5
D- Medical	251	68.8	71.0	13.8
E- Pediatrics	13	2.2	1.0	3.4
G- Geriatrics	154	83.0	83.0	6.4
H- Usual admission	26	70.3	74.0	15.8
I- Intensive care	156	66.9	70.0	15.4
M- Maternity	9	29.0	29.0	5.6
N/n- NIC/non NIC	19	0.0	0.0	0.0
Sp- Revalidation	94	69.6	76.0	17.7
All	978	66.8	72.0	20.1

Table 8.10: Total Length of stay of infected patients, per bed index

	All					
	LOS					
	N	Mean	Median	Std	Q1	Q3
Bed type						
A- Psychiatry	12	51.8	37.0	35.5	32.0	62.0
C- Surgical	244	46.7	33.0	46.4	17.0	59.5
D- Medical	251	50.4	39.0	45.2	21.0	63.0
E- Pediatrics	13	12.7	10.0	9.2	6.0	15.0
G- Geriatrics	154	53.1	42.0	36.3	28.0	66.0
H- Usual admission	26	46.7	35.5	35.7	23.0	59.0
I- Intensive care	156	70.3	52.0	50.6	33.0	95.0
M- Maternity	9	15.9	12.0	16.7	6.0	14.0
N/n- NIC/non NIC	19	48.1	43.0	30.2	19.0	61.0
Sp- Revalidation	94	117.1	94.0	91.7	61.0	147.0
All	978	58.5	43.0	54.7	24.0	74.0

Table 8.11: Time from Admission to Prevalence Survey, per bed index

	All					
	Time to prevalence survey (days)					
	N	Mean	Median	Std	Q1	Q3
Bed type						
A- Psychiatry	12	27.1	20.5	20.3	13.5	31.0
C- Surgical	244	28.3	18.0	35.7	10.0	34.5
D- Medical	251	27.6	19.0	32.1	11.0	32.0
E- Pediatrics	13	8.2	7.0	7.3	3.0	8.0
G- Geriatrics	154	31.3	25.0	23.4	17.0	37.0
H- Usual admission	26	25.2	19.0	24.6	8.0	33.0
I- Intensive care	156	24.2	19.5	21.0	12.0	31.0
M- Maternity	9	8.4	6.0	9.6	5.0	6.0
N/n- NIC/non NIC	19	20.1	19.0	13.4	8.0	26.0
Sp- Revalidation	94	66.8	46.5	66.6	28.0	83.0
All	978	30.9	21.0	36.5	12.0	36.0

Table 8.12: Destination at discharge, per bed index

	Unknown/not yet discharged	Home	other hospital	Home for the elderly/psychiatric after care	**Mortality**	Other	Total
A- Psychiatry	1 8.33	10 83.33	0 0.00	1 8.33	**0** **0.00**	0 0.00	12 (100)
C- Surgical	37 15.16	166 68.03	5 2.05	18 7.38	**13** **5.33**	5 2.05	244 (100)
D- Medical	31 12.35	130 51.79	17 6.77	24 9.56	**42** **16.73**	7 2.79	251 (100)
E- Pediatrics	0 0.00	13 100.00	0 0.00	0 0.00	**0** **0.00**	0 0.00	13 (100)
G- Geriatrics	19 12.34	61 39.61	8 5.19	38 24.68	**28** **18.18**	0 0.00	154 (100)
H- Usual admission	3 11.54	18 69.23	2 7.69	1 3.85	**2** **7.69**	0 0.00	26 (100)
I- Intensive care	31 19.87	57 36.54	12 7.69	3 1.92	**50** **32.05**	3 1.92	156 (100)
M- Maternity	1 11.11	8 88.89	0 0.00	0 0.00	**0** **0.00**	0 0.00	9 (100)
N/n- NIC/non NIC	0 0.00	15 78.95	2 10.53	0 0.00	**0** **0.00**	2 10.53	19 (100)
Sp- Revalidation	21 22.34	43 45.74	2 2.13	17 18.09	**11** **11.70**	0 0.00	94 (100)
Total	144 (14.7)	521 (53.3)	48 (4.9)	102 (10.4)	**146** **(14.9)**	17 (1.7)	978 (100)

Table 8.13: Patients with multiple infections

Total of patients infected	978	
		100%
Patients with unique infection	856	87,5
patients with multiple infections	122	12,5
		100%
patients with BSI+ LRI	25	20,5
patients with BSI + infection other than LRI	34	27,9
patients with LRI + other infection than BSI	24	19,7
patients with other combinations	39	32,0

Table 8.14: Comorbidities of Infected patients

	COUNT	PERCENT
	(N=976)	
No comorbidity	296	30.3
Myocardial Infarct (weight 1)	30	3.1
Congestive Heart Failure (weight 1)	117	12.0
Peripheral vascular disease (weight 1)	101	10.3
Dementia (weight 1)	93	9.5
Cerebrovascular disease (weight 1)	36	3.7
Chronic pulmonary disease (weight 1)	166	17.0
Connective tissue disease (weight 1)	14	1.4
Ulcer disease (weight 1)	37	3.8
Mild liver disease (weight 1)	43	4.4
Hemiplegia (weight 2)	79	8.1
Moderate or severe renal disease (weight 2)	204	20.9
Diabetes (weight 2)	209	21.4
Any tumour (weight 2)	73	7.5

	COUNT	PERCENT
Leukemia (weight 2)	20	2.0
Lymphoma (weight 2)	10	1.0
Moderate or severe liver disease (weight 3)	28	2.9
Metastatic solid tumor (weight 6)	80	8.2

Mean Charlson Score

N	Mean	Std Dev	Median	Minimum	Maximum
976	2.4	2.5	2.0	0.0	14.0

Table 8.15 RCM data received for Controls (identified in RCM-RFM 2005)

Number of stays received	94 444
Number of stays valid for controls	74 204
Stays excluded:	20 240
No valid flag	7 845
No APR-DRG (AAA, psychiatry)	2 656
LOS < 2 days	9 739

Validation exercise between the substudy and the costs from prevalence survey.

Very good correspondence: total costs without per diem around 10 000 in both studies

Table 8.16: Costs of BSI identified in prevalence survey (euros)

Label	N	Mean	Std Dev	Median
total costs	131	28215	17763	21820
LOS (days)	131	48	29	42
Hospital stay fees	131	17887	10899	15540
total costs without per diem	131	10328	9668	6715
Medical fees	130	2875	3269	1674
Pharmaceutical products	129	3404	5289	1631
Lab tests	129	1793	1302	1281
Medical imaging (RX, US & scinti)	129	884	661	716
Implants, disposables, ortheses & other	96	933	1450	285
Revalidation & physical therapy	110	597	520	444
IC & reanimation	84	1215	1240	585

Sensitivity analyses on the matching factors

Table 4.11 presents sensitivity analyses on the estimation of the exposure time to select control patients (first block of results) and on the choice of matching criteria (second block of results). The choices done for the main analysis are represented in bold.

Per design, control patients were always selected from the same hospital and in the same APR-DRG than cases. These two criteria are thus not examined.

The influence of the exposure time variable to select control patients who stayed at least the same time than the cases, is as influential as in the NBSI substudy. Not taking the exposure time into consideration results in comparing control patients who stayed on average 2 weeks to cases with a start of infection which started in many cases after two weeks. The estimated excess LOS is thus around 40 days (median 25 days).

Because Belgian guidelines recommend 10 days of antibiotic treatment for the majority of infections, cases were assumed to be in the middle of the treatment course when they were surveyed in the prevalence study. With this approach, the estimated excess LOS is 8 days (median 4 days). When the duration of treatment varies from 6 days to 14 days, the excess LOS varies accordingly between 6.1 days and 9.6 days (median from 2.4 and 5 days).

The other part of the table examines influences of different matching factors (with duration of treatment fixed at 10 days). Results show that, once control patients are selected with at least the same exposure time than cases, other factors play a limited role (age, sex, Charlson score, bed index). The destination after hospital discharge (elderly home or not) was added because it is a known confounding factors (those patients have higher risk of NI and have longer LOS). It is acknowledged that discharge towards elderly home might also be a consequence of the infection (due to complications), and not a risk factor, and that provenance from elderly home would be a better proxy, but this information was not available in our database.

The final analysis was not matched on sex because at the time of retrieving costs data health insurance companies, this information was not available. In the NBSI study sex had very little influence on the estimate, as shown also in this study. This might be due to the fact that patients are matched per APR-DRG, and some operations are gender specific (thus some data are matched per design).

Table 8.17 Influence of matching factors on Estimate of excess LOS

Exposure time	Matching factor	N cases included	Mean	Median	STD	Lower	Upper
Sensitivity analyses based on exposure time							
no	RGRDRG + hosp_id	655	39.4	25.3	56.4	35.1	43.7
no	RGRDRG + hosp_id + patage (15 y)	645	38.3	22.8	54.4	34.1	42.5
Yes (10 days)	**RGRDRG + hosp_id + patage (15 y) + beds (G and Sp)+ charlson + destination (elderly home or not)**	**444**	**8.0**	**4.0**	**28.5**	**5.4**	**10.7**
Yes (TRT 8 days)	idem	441	7.2	3.0	28.9	4.5	9.9
Yes (TRT 6 days)	idem	432	6.1	2.4	27.9	3.5	8.8
Yes (TRT 12 days)	idem	449	8.8	4.5	28.2	6.2	11.5
Yes (TRT 14 days)	idem	456	9.6	5.0	28.4	7.0	12.2
Sensitivity analyses based on matching factors							
yes	RGRDRG + hosp_id	579	9.8	4.8	31.7	7.2	12.3
yes	RGRDRG + hosp_id + patage (15 y)	545	10.0	4.8	31.1	7.3	12.6
yes	RGRDRG + hosp_id + patage (5 y)	477	10.8	5.3	31.4	8.0	13.6

yes	RGRDRG + hosp_id + patage (15 y) + charlson	545	10.0	4.5	31.0	7.3	12.6
yes	RGRDRG + hosp id + patage (15 y) + beds (G and Sp) + charlson	497	10.0	4.5	29.4	7.4	12.6
yes	**RGRDRG + hosp_id + patage (15 y) + beds (G and Sp)+ charlson + destination (elderly home or not)**	**444**	**8.0**	**4.0**	**28.5**	**5.4**	**10.7**
yes	RGRDRG + hosp id + patage (15 y) + SEX + beds (G and Sp)+ charlson + destination (elderly home or not)	378	8.3	4.2	28.0	5.4	11.1

Aggregation of Costs Data= N groups

N_group	Rubrique	Groupment
N00	SURVEILLANCE DES BÉNÉFICIAIRES HOSPITALISÉS	Médic
N01	CONSULTATIONS, VISITES ET AVIS DE MÉDECINS	Médic
N02	PRESTATIONS TECHNIQUES MÉDICALES - PRESTATIONS COURANTES	Médic
N04	SOINS DENTAIRES	Paramédicaux
N05	KINESITHERAPIE	Reval
N06	SOINS DONNÉS PAR INFIRMIÈRES, SOIGNEUSES ET GARDES-MALADES	Paramédicaux
N08	BIOLOGIE CLINIQUE - ARTICLE 3	Labo
N10	ACCOUCHEMENTS - AIDE OPERATOIRE	Médic
N11	GYNÉCOLOGIE ET OBSTÉTRIQUE	Médic
N12	RÉANIMATION	REANI
N13	PRESTATIONS SPECIALES GÉNÉRALES	Médic
N14	ANESTHÉSIOLOGIE	Médic
N15	ASSISTANCE MÉDECIN TRAITANT PENDANT ANESTHÉSIOLOGIE - AIDE OPER.	Médic
N16	STOMATOLOGIE	Médic
N17	PRESTATIONS TECHNIQUES URGENTES - ARTICLE §1 BIS	Médic
N18	OPHTALMOLOGIE	Médic
N19	PRESTATIONS TECHNIQUES URGENTES - ARTICLE 26, §1 ET 1 TER	Médic
N20	CHIRURGIE GÉNÉRALE	Médic
N21	NEUROCHIRURGIE	Médic
N22	CHIRURGIE PLASTIQUE	Médic
N23	CHIRURGIE ABDOMINALE	Médic
N25	CHIRURGIE THORACIQUE	Médic
N26	CHIRURGIE DES VAISSEAUX	Médic
N28	OTO-RHINO-LARYNGOLOGIE	Médic
N30	UROLOGIE	Médic
N32	ORTHOPÉDIE	Médic
N33	TRANSPLANTATIONS	Médic
N40	MÉDECINE INTERNE	Médic
N41	PNEUMOLOGIE	Médic
N42	GASTRO-ENTEROLOGIE	Médic
N45	RADIOTHÉRAPIE ET RADIUMTHÉRAPIE	Médic
N46	MÉDECINE NUCLÉAIRE IN VIVO	IM
N47	MÉDECINE NUCLÉAIRE IN VITRO	Labo
N48	RADIO-ISOTOPES	IMP
N49	TESTS DE BIOLOGIE MOLÉCULAIRE SUR DU MATÉRIEL GÉNÉTIQUE HUMAIN	Labo
N50	RADIODIAGNOSTIC	IM
N51	PRESTATIONS INTERVENTIONNELLES PERCUTANEES	Médic
N53	PART PERSONNELLE POUR PATIENTS HOSPITALISÉS	CPP
N54	PÉDIATRIE	Médic
N55	CARDIOLOGIE	Médic
N56	NEUROPSYCHIATRIE	Médic
N57	PHYSIOTHÉRAPIE	Reval
N59	DERMATO-VÉNÉRÉOLOGIE	Médic
N60	BIOLOGIE CLINIQUE - ARTICLE 24	Labo
N61	COMPLÉMENT D'HONORAIRES - BIOLOGIE CLINIQUE	Labo
N62	HONORAIRES FORFAITAIRES - BIOLOGIE CLINIQUE	Labo
N63	ANATOMO-PATHOLOGIE	Labo
N64	EXAMENS GÉNÉTIQUES	Labo
N70	APPAREILS	IMP
N73	SOINS PAR OPTICIENS	IMP
N75	SOINS PAR ACOUSTICIENS	IMP
N77	URINAL, ANUS ARTIFICIEL ET CANULE TRACHEALE	IMP
N79	BANDAGES, CEINTURES ET PROTHESES DES SEINS	IMP
N80	MATERIEL DE SYNTHESE ART 35 ET 35BIS	IMP
N81	DIALYSE	Médic

N82	MATERIEL DE SYNTHESEART 28 §1	IMP
N83	MATERIEL DE SYNTHESE ART 28 §8	IMP
N84	LOGOPÉDIE	Paramédicaux
N85	QUOTE-PART PERSONNELLE HOSPITALISATION	CPP
N86	PRESTATIONS PHARMACEUTIQUES	Farma
N87	HOSPITALISATION	Séjour
N88	RÉÉDUCATION FONCTIONNELLE ET PROFESSIONNELLE	Reval
N89	PLACEMENT ET FRAIS DÉPLACEMENT QUOTE-PART PERS. PREVENTORIUMS	Reval
N92	CONVENTIONS INTERNATIONALES	Exclus
N93	CODES DE RÉGULARISATION	Exclus
N94	PROJETS ARTICLE 56	Exclus
N97	REMBOURSEMENTS	Exclus

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Dépôt légal : D/2009/10.273/02

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