Strategie NOSO Ambulant

Systematic review on the burden and prevention of healthcare-associated infections in outpatient care

Final report

Walter Zingg, MD, PD; Qiao Fu, MD; Diana Neves, MD

Hôpitaux Universitaires de Genève
Service de Prévention et Contrôle de l'Infection
Hôpitaux Universitaires de Genève
Rue Gabrielle Perret-Gentil 4
1211 Genève

PD Dr. Walter Zingg
Email: walter.zingg@hcuge.ch
Phone: +41 22 372 33 64
Fax: +41 22 372 39 87

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2 ABBREVIATIONS

ARBSI	Access-related bloodstream infection
BSI	Bloodstream infection
CAPD	Continuous ambulatory peritoneal dialysis
CDC	US Centers for Disease Control and Prevention
CHG	Chlorhexidine gluconate
CI95%	95% confidence interval
CLABSI	Central line-associated bloodstream infection
CRBSI	Catheter-related bloodstream infection
CRE	Carbapenem-resistant enterobacterium
CS	Cohort study
FOPH	(Swiss) Federal Office of Public Health
HAI	Healthcare-associated infection
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HUG	Hôpitaux Universitaires de Genève
IHD	In-center haemodialysis
IPC	Infection Prevention and Control
MDRO	Multidrug-resistant Organism
MEAD	Macro-ergonomic Analysis and Design
MRSA	Meticillin resistant *Staphylococcus aureus*
NCBA	Non-controlled before-and-after study
NCITS	Non-controlled interruptive time-series
NHHD	Nightly home haemodialysis
NS	Not specified
OPAT	Outpatient Antibiotic Therapy
OR	Odds ratio
PD	Positive deviance
PICC	Peripherally inserted central catheter
PN	Parenteral nutrition
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
RCT	Randomized controlled trial
RSV	Respiratory syncytial virus
SAFER	Agency for Health Care Research and Quality Systematic Approach for Eliminating Risks
SIGHT	Systematic review and evidence-based guidance on organisation of hospital infection control programmes
SSI	Surgical site infection
SSI-BRST	Breast infection
SSI-S	Superficial surgical site infection
UTI	Urinary tract infection
VRE	Vancomycin-resistant Enterococcus

3 SUMMARY

Context: There is little evidence about healthcare-associated infections (HAIs) in outpatient settings and no systematic review has been performed on the subject. The Swiss Federal Office for Public Health commissioned two systematic reviews about the burden and prevention of HAIs in outpatient care, with the aim to inform strategic planning and decision making of the “Strategie NOSO Ambulant”.

Objective: The objectives were 1) to estimate the epidemiologic burden of HAI in outpatient care (outpatient settings) based on the currently available evidence in the literature; and 2) to summarize and, if possible, assess the scope and impact of reported HAI-prevention strategies in outpatient care.

Data sources: Medline, the Cochrane Controlled Trials Register, Embase, and the Outbreak Database.

Study selection: Reports had to refer directly or indirectly to any HAI or transmission of viruses or multidrug-resistant organisms (MDRO) in any patient undergoing at least one medical visit or care in an outpatient setting or at home, irrespective of the applied medical procedure.

Data extraction: All identified titles and abstracts were assessed by two reviewers. Disagreements were resolved by consensus and a third reviewer was consulted if agreement could not be reached. Extraction of full text reports was done by using extraction tables.

Data synthesis: Reports and studies were grouped into the following topics: Surgical site infection (SSI), endoscopy, haemodialysis, homecare, outpatient parenteral nutrition (PN), dental care, outbreaks, bloodstream infection (BSI) without PN, urinary tract infection (UTI), and other topics.

Results: Our search yielded 7830 titles and abstracts; 564 were eligible for fulltext sift, of which 413 were accessible. One-hundred-fifty-six reports fulfilled the inclusion criteria, 127 for burden and 53 for prevention, with a number of reports serving both outcomes. A total of 35 intervention studies were quality-assessed. The other 17 prevention studies were either outbreak reports (6) or laboratory studies (11).

Discussion: The identified reports and studies were overall quite heterogeneous and generally of low quality. Most information comes from haemodialysis, home parenteral nutrition, and home intravenous therapy for the outcome (catheter-related [-associated]) bloodstream infection. The incidence of bloodstream infections among patients undergoing haemodialysis is high, but also important in parenteral nutrition and home care. The frequency of surgical site infections seems relatively low, but comparison to inpatients is not possible due to different surgical procedures (or the same procedures are performed as outpatient procedures also in acute care hospitals). The one report looking at SSI in general practice, found astonishingly high numbers.

4 BACKGROUND

The Federal Office of Public Health (FOPH) has framed a national strategy to monitor and prevent healthcare-associated infections (HAIs) together with stakeholders in the field of public health and infection prevention and control (IPC): the “Strategie NOSO”. A draft of the strategy addressing the prevention of HAIs addresses four areas of action: governance, monitoring, prevention, and education and research. The “Strategie NOSO” will also address outpatient care with the “Strategie NOSO ambulant”. For targeted planning, information about the evidence-base of the public health burden and IPC measures in outpatient care is needed. Therefore, the FOPH has commissioned two systematic reviews about the burden and prevention of HAIs in such settings. The results of the systematic review will inform strategic planning and decision making of the “Strategie NOSO ambulant”.

Compared to inpatient care, and in particular *acute* inpatient care, the focus of IPC in outpatient settings is different. HAI such as vascular catheter-associated bloodstream infections may occur in longterm intravenous drug therapy such as “outpatient antibiotic therapy” (OPAT), or surgical site infections occur after day care surgery. Specific challenges may occur in haemodialysis,[1-3] dental care,[4-6] endoscopic procedures,[7-9] and homecare.[10]

The objectives of this systematic review were 1) to estimate the epidemiologic and health-economic burden of HAI in outpatient care (outpatient settings) based on the currently available evidence in the literature; and 2) to summarize and, if possible, assess the scope and impact of reported HAI-prevention strategies in outpatient care.

5 METHODS

Setting

The systematic review was performed by the Infection Control Programme of the University of Geneva Hospitals (HUG), Geneva, Switzerland. HUG hosts a state-of-the-art infection control programme with several experts who have generated landmark articles in the field of IPC.[11-17] HUG is also a WHO collaborating centre for patient safety and the coordinator of the Swiss point prevalence survey in 2017 for Swissnoso. The team as a whole has experience in performing systematic reviews.[13, 18]

Systematic review

The systematic review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines.[19, 20]

Search strategy

We searched Medline, the Cochrane Controlled Trials Register, Embase, and the Outbreak Database for reports published between 1 July 1996 and 1 July 2016.

Studies in English, French, German, Italian, Portuguese, and Spanish were eligible when an English title or abstract was available. No age restriction applied. Google search was applied if scientific articles could not be retrieved otherwise.

Search-terms

The search terms were designed to capture all potential outpatient settings such as homecare, private practice, day surgery, by using general MeSH-terms. In order to avoid missing outcomes or settings of interest, the search terms were enlarged with specific MeSH-terms or keywords allowing the identification of studies on endocarditis (after dental procedures), hepatitis (in haemodialysis), surgical site infections, urinary tract infection (in home care patients having a urinary catheter), and bloodstream infections (e.g. by applying home parenteral nutrition or chemotherapy). Furthermore, settings such as dental care, endoscopy, interventional radiology, homecare, ambulatory care, and general practice were addressed by specific keywords or MeSH-terms. The transmission of multidrug-resistant organisms (MDROs) was included in the search term both generically and for the most important pathogens such as methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus (VRE), extended spectrum β-lactamase containing Gram-negative rods, and carbapenem-resistant enterobacteria (CRE).

Pubmed: ((((((((Endocarditis[MeSH Terms] OR Urinary Tract Infections[MeSH Terms] OR Cross Infection[MeSH Terms] OR Wound Infection[MeSH Terms] OR Surgical Wound Infection[MeSH Terms] OR Infectious Disease Transmission, Professional-to-Patient[MeSH Terms] OR Disease Transmission, Infectious[MeSH Terms] OR Bacteremia[MeSH Terms] OR Sepsis[MeSH Terms] OR Hepatitis[MeSH Terms] OR Drug Resistance, Multiple[MeSH Terms] OR Methicillin-Resistant Staphylococcus aureus[MeSH Terms] OR Vancomycin-Resistant Enterococci[MeSH Terms] OR Catheter-Related Infections[MeSH Terms] OR Bloodstream infection[MeSH Terms] OR Blood stream infection[MeSH Terms] OR Esbl [MeSH Terms] OR Extended-spectrum β-lactamase[MeSH Terms] OR carbapenem resistant [MeSH Terms]) AND ("1996/07/01"[PDat] : "2016/07/01"[PDat]))) OR Bloodstream infection) OR Blood stream infection) OR Esbl) OR Extended-spectrum β-lactamase) OR carbapenem resistant) AND ("1996/07/01"[PDat] : "2016/07/01"[PDat]))) AND (Ambulatory care[MeSH Terms] OR Ambulatory Care Facilities[MeSH Terms] OR Outpatient Clinics, Hospital [MeSH Terms] OR Ambulatory Surgical Procedures[MeSH Terms] OR Outpatients[MeSH Terms] OR Dental Clinics[MeSH Terms] OR Home Care Services[MeSH Terms] OR Hemodialysis Units, Hospital[MeSH Terms] OR Endoscopes[MeSH Terms] OR Pediatrics[MeSH Terms] OR Parenteral Nutrition[MeSH Terms] OR Catheterization, Peripheral [MeSH Terms] OR Radiology, Interventional [MeSH Terms] OR General Practice [MeSH Terms] OR Chemotherapy, Adjuvant[MeSH Terms] OR General Practice, Dental [MeSH Terms]) Filters: Publication date from 1996/07/01 to 2016/07/01

Embase: (('endocarditis'/exp OR endocarditis OR (urinary AND tract AND infections) OR (cross AND ('infection'/exp OR infection)) OR ('wound'/exp OR wound AND ('infection'/exp OR infection)) OR (surgical AND ('wound'/exp OR wound) AND ('infection'/exp OR infection)) OR (infectious AND ('disease'/exp OR disease) AND transmission, AND 'professional to patient') OR ('disease'/exp OR disease AND

transmission, AND infectious) OR 'bacteremia'/exp OR bacteremia OR 'sepsis'/exp OR sepsis OR 'hepatitis'/exp OR hepatitis OR ('drug'/exp OR drug AND resistance, AND multiple) OR ('methicillin resistant' AND ('staphylococcus'/exp OR staphylococcus) AND aureus) OR ('vancomycin resistant' AND enterococci) OR ('catheter related' AND infections) OR (bloodstream AND ('infection'/exp OR infection)) OR ('blood'/exp OR blood AND stream AND ('infection'/exp OR infection)) OR 'esbl'/exp OR esbl OR ('extended spectrum' AND 'β lactamase') OR ('carbapenem'/exp OR carbapenem AND resistant)) AND (('ambulatory care'/exp OR 'ambulatory care' OR (ambulatory AND care AND facilities) OR ('outpatient'/exp OR outpatient AND clinics, AND ('hospital'/exp OR hospital)) OR (ambulatory AND surgical AND ('procedures'/exp OR procedures)) OR 'outpatients'/exp OR outpatients OR (dental AND clinics) OR ('home'/exp OR home AND care AND services)) OR ('hemodialysis'/exp OR hemodialysis AND units, AND ('hospital'/exp OR hospital) OR 'endoscopes'/exp OR endoscopes OR 'pediatrics'/exp OR pediatrics OR (parenteral AND ('nutrition'/exp OR nutrition)) OR (catheterization, AND peripheral) OR (radiology, AND interventional) OR (general AND practice) OR (chemotherapy, AND ('adjuvant'/exp OR adjuvant)) OR (general AND practice, AND dental)))) AND ('observational study'/de OR 'randomized controlled trial'/de) AND ([english]/lim OR [french]/lim OR [german]/lim OR [italian]/lim OR [portuguese]/lim OR [spanish]/lim) AND [humans]/lim AND [embase]/lim AND [1996-2016]/py
2946

Eligibility, inclusion and exclusion criteria
Reports had to refer directly or indirectly (e.g. hand hygiene improvement) to any HAI or transmission of viruses or MDRO in any patient undergoing at least one medical visit or care in an outpatient setting or at home, irrespective of the applied medical procedure: HAI as a measured outcome; process indicator such as hand hygiene as a measured outcome; transmission or identification of MDRO as a measured outcome; transmission or identification of viruses as a measured outcome. Focus was done on countries with healthcare systems and standards similar to the Swiss healthcare setting.

> *Burden:* Outcomes on HAI or transmission of viruses or MDRO. Baseline or control data were included from intervention studies.
>
> *Intervention:* Any study with the aim to prevent or reduce HAI, transmission of viruses or MDRO, or to improve process indicators such as hand hygiene.
>
> *Outbreak:* Any outbreak report on HAI, transmission of viruses or MDRO in outpatient care.

Case reports, case series, opinions (editorials and comments), narrative reviews, and studies using a qualitative method (inclusive questionnaires) were excluded. Reports from low- and lower-middle-income countries were excluded.

Data extraction
All identified titles and abstracts were assessed by two reviewers (QF, DN). Disagreements about inclusion/exclusion were resolved by consensus. A third

reviewer (WZ) was consulted if agreement could not be reached. Extraction of full text reports was done by using extraction tables.

Quality assessment

The quality of intervention studies reporting incidence (densities) was assessed using the “Integrated quality Criteria for the Review Of Multiple Study designs” (ICROMS) tool.[21] The tool consists of two parts: 1) a list of quality criteria specific for each study design, as well as criteria applicable across all study designs by using a scoring system; 2) a ‘decision matrix’, which specifies the robustness of the study by identifying minimum requirements according to the study type and the relevance of the study to the review question. The decision matrix directly determines inclusion or exclusion of a study in the review.[21]

Data synthesis

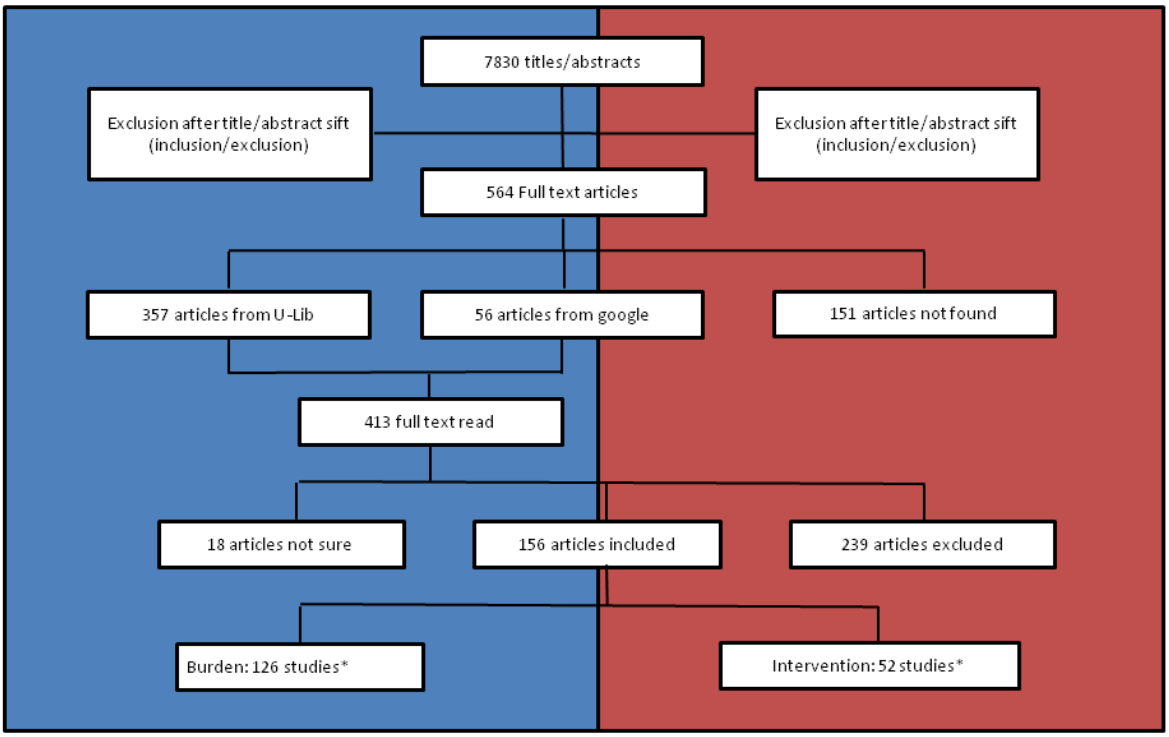
Reports and studies were grouped a priori into the following topics: Surgical site infection (SSI), bloodstream infection (BSI), urinary tract infection (UTI), parenteral nutrition (PN), endoscopy, haemodialysis, homecare, dental care, other topics, and outbreaks. Studies and reports could feed different topics. Based on the findings, new topics could have been created and pre-defined topics may have been removed. The selection of the topics was based on a first sift of the results of overall search term in PubMed and on expert opinion. This selection did not interfere with the inclusion or exclusion criteria or grouping into new topics if supported by the results. Where possible, meta-analyses for incidences were performed by using the STATA metaprop command in a random-effects model to calculate weighted HAI incidence or incidence densities along with the corresponding 95% confidence intervals, and to produce forest plots. All analyses were done using STATA version 14.0 (Stata Corporation, College Station, Texas, USA).

6 RESULTS

6.1 SUMMARY

Our search yielded 7830 titles and abstracts; 564 were eligible for fulltext sift, of which 413 were accessible. One-hundred-fifty-six reports met the inclusion criteria, 126 for HAI burden and 52 for HAI prevention. Seventeen prevention studies were either outbreak reports (6) or laboratory studies (11). A total of 35 intervention studies could be quality-assessed.

Figure 1. Inclusion and exclusion of reports and studies for the burden (blue) and prevention (red) of healthcare-associated infections in the outpatient setting – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care



*Studies may report on both burden and interventions

Topics

Based on the results, the reports and intervention studies were allocated to a number of topics, either stratified by outcome or settings. Single reports could be allocated to two or more topics if applicable (e.g. BSI as an outcome in the setting home parenteral nutrition or haemodialysis). Endoscopy and haemodialysis were considered settings because care is delivered in specific outpatient facilities. Peritoneal dialysis was a topic that emerged during

the process of the systematic review. Outbreaks were grouped separately. Table 1 summarizes the allocation of the publications to outcome, setting, outbreaks, and others.

Table 1. Identified topics – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

	Outcomes			**Settings**						
	SSI	BSI[2]	UTI	Home PN	Endoscopy	Haemodialysis	Peritoneal dialysis	Homecare	Dental care	Other
Burden	20	42	3	15	3	37	6	20	1	3
Intervention	3	16	2	9	7	10	3	10	1	6
Total[1]	23	51	4	20	10	42	7	26	2	8

[1]Studies may report on both burden and prevention
[2]Without home parenteral nutrition
BSI: Bloodstream infection; PN: Parenteral nutrition; SSI: Surgical site infection; UTI: urinary tract infection.

Countries of origin

Table 2 summarizes the countries of origin of the identified reports and studies. Most reports came from the USA (71 [45.5%], followed by the United Kingdom (15 [9.6%]), France (10 [6.4%]), Italy (8 [5.1%]), Japan (8 [5.1%]), and Canada (6 [3.9%]). Together, these countries accounted for three-fourths of the reports. Switzerland contributed only with two studies to the evidence-base. No studies from low-income and lower-middle-income countries were identified.

Table 2. Countries of origin of the reports and studies – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

Country	Reports (N)	Reports (%)
USA	71	45.51
UK	15	9.62
France	10	6.41
Italy	8	5.13
Japan	8	5.13
Canada	6	3.85
Australia	5	3.2
Germany	5	3.2
Brazil	3	1.92
Turkey	3	1.92
Denmark	2	1.28
Greece	2	1.28
Hong Kong	2	1.28
Israel	2	1.28
Netherlands	2	1.28
Poland	2	1.28
Saudi Arabia	2	1.28
Singapore	2	1.28
Switzerland	**2**	**1.28**
Argentina	1	0.64
Mexico	1	0.64
New Zealand	1	0.64
Portugal	1	0.64

6.2 OUTCOMES

6.2.1 SURGICAL SITE INFECTIONS

A total of 23 publications were identified, 20 reports contributing to the burden of SSI (Table 3),[22-41] and 3 studies reporting on SSI prevention.[24, 42, 43]

Burden

Table 3 summarizes the reports on SSI frequency. Most reports (13) were performed in adults. All-SSI was the major but not the only outcome. Although most reports claimed to have used US Centers for Disease Control and Prevention (CDC) definitions, some retrospective analyses applied ICD-9 codes.[38, 41] Data collection was mostly prospective, but a number of reports analysed retrospective data (Table 3). The overall weighted SSI frequency (CI 95%) of the identified publications was 0.69% (0.55%-0.84%). However, given the heterogeneity of the reports in terms of procedures, methodology, and outcome, this number can only be an approximation. The individual reports as summarized in table 3 provide a more accurate picture about the distribution of SSI frequency for the various surgical procedures.

Table 3. Burden of surgical site infections in outpatient topics – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

Study	Year	Country	Population, design	Procedures (type)	Population (N)	Outcome, definition	%
Manian [22]	1997	USA	NS, prosp	Non-specified	88830	SSI, CDC	0.13%
Kleinert [23]	1997	USA	All, prosp	Carpal tunnel release, ganglionectomy, tendon procedures, synovectomy, trigger-finger release	2458	SSI, CDC	1.51%
Gabrielli [24]	2001	Italy	NS, prosp	Plastic surgery	1000	SSI-S other[44]	1.70%
Vilar-Compte [25]	2001	Mexico	Adult, prosp	Skin or soft tissue excision, lymph node biopsy	1350	SSI, CDC	2.74%
Miner [26]	2004	USA	Adult, retro[1]	Breast surgery	1943	SSI-BRST, CDC	1.96%
Hashemi [27]	2004	UK	All, prosp	Hand surgery	1035	SSI, own	1.06%
Amici [28]	2005	France	NS, prosp	Dermatologic surgery	3788	SSI, own	2.09%
Mlangeni [29]	2005	Germany	NS, prosp	Arthroscopic knee surgery and inguinal hernia, vein-stripping	16045	SSI, CDC	0.29%
Hirsemann [30]	2005	Germany	All, prosp	Hernia repair, vein-stripping	1095	SSI, CDC	1.19%
Heal [31]	2006	Australia	All, prosp	General practice: skin and soft tissue excisions	857	SSI-S, own	8.63%
Brebbia [32]	2006	Italy	NS	Hernia repair, excision of cysts and lipomas	226	SSI, NS	1.33%
Price [33]	2008	USA	Adult, non-specified sample	Arthroplasty, arthroscopy, fracture fixation, hand surgery, hardware removal	282	SSI, CDC	3.19%
Bykowski [34]	2011	USA	NS, retro	Hand surgery	8850	SSI, CDC	0.35%
Ahmad [35]	2011	UK	NS, prosp	Not specified	281	MRSA , NA	2.14%
Majholm [36]	2012	Denmark	All, retro	Mixed[2]	57709	HAI, NS	0.43%
Anigian [37]	2014	USA	Adult, retro	Plastic surgery	468	SSI, NS	3.85%
Owens [38]	2014	USA	Adult, retro	Mixed[2]	284098	SSI, ICD-9	0.31%
Dholakia [39]	2015	UK	Male adults, prosp	Hernia repair	64	SSI-S, CDC	7.81%
Rhee [40]	2015	USA	Adult, retro[1]	Hernia repair, cholecystectomy, laminectomy, appendectomy	4045	SSI, CDC	0.87%
Menendez [41]	2015	USA	Adult, retro	Hand surgery	44305	Post surgery visits for SSI, ICD-9 [38]	0.17%

[1]Case finding by claims data
[2]Mixed: procedures specified in the text but include a broad range of interventions

CDC: definition or surgical site infections using the definitions of the US Centers for Disease Control and Prevention; MRSA: colonisation with methicillin resistant *Staphylococcus aureus*; NA: not applicable; NS: not specified; own: own definition, specified in the report; prosp: prospective data collection; retro: retrospective data analysis; SSI: surgical site infection; SSI-BRST: post surgical breast infection; SSI-S: superficial surgical site infection.

Prevention

The three intervention studies were quality-assessed.[24, 34, 42] Only one randomized controlled trial (RCT) fulfilled the minimal criteria and was of high quality.[42] The study investigated the effectiveness of petrolatum ointment in patients undergoing dermatologic surgery. Bacitracin was the comparator. A total of 440 and 444 patients were randomized to the petrolatum and bacitracin group, respectively. Thirteen patients developed SSI (1.5%), 9 (2.0%) in the petrolatum group, and 4 (0.9%) in the bacitracin group (P = 0.37). Eight infections (1.8%) in the petrolatum group but none in the bacitracin group were due to *Staphylococcus aureus* (P = 0.004). No patient using petrolatum but 4 patients using bacitracin developed contact dermatitis (P = 0.12). One of the two other studies was a retrospective cohort study, analysing the effect of antibiotic prophylaxis (vs. none) in elective hand surgery in the outpatient setting over 8 years.[34] The overall SSI incidence was 0.35%; adding antibiotics (substances were not specified) did not significantly change the outcome. The minimal quality criteria were not met. The third intervention study looked at the role of sutures in 1000 plastic surgery outpatients, operated over 18 months.[24] The SSI incidence was 1.7% (17/1000 consecutive patients). Two-layer sutures did not reduce SSI compared to one-layer sutures. Only male sex (OR [CI95%]: 5.9 [1.7-15.9]) and age > 50 years (5.6 [1.9-16]) were independent risk factors for SSI. The minimal quality criteria were not met.

6.2.2 BLOODSTREAM INFECTIONS

A total of 51 publications were identified,[45-95] 42 reports contributing to the burden of BSI (Table 4),[45-55, 58-61, 63-72, 74, 75, 77-82, 84-86, 88, 90, 91, 93, 94, 96] and 16 studies on BSI-prevention strategies.[54, 56, 62, 66, 68, 72, 73, 76, 78, 79, 83, 87-89, 92, 95] Twenty-one and 20 reports addressed haemodialysis and home parenteral nutrition, respectively.

Burden

Table 4 summarizes different BSI outcomes, stratified by haemodialysis, home parenteral nutrition and other settings. Methodological heterogeneity made meta-analysis across settings impossible.

Table 4. Burden of bloodstream infections in outpatient settings – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

	Study	Year	Country	Population (type)	Population (N, type)	Outcome (type)	(%/ID)
Haemodialysis	Tokars [51]	2001	USA	Adults	4134, PM	ARBSI	[1]3.51
	Klevens [58]	2008	USA	NS	NS	ARBSI	[1]1.25
	Patel [78]	2013	USA	NS	28047, PM	ARBSI	[1]7.30
	Stevenson [50]	2000	USA	NS	39096, DS	BSI	[2]0.90
	Dopirak [52]	2002	USA	NS	142525, DS	BSI	[2]1.11
	Colville [55]	2006	Australia	NS	14528, PD	BSI	[3]1.72
	Thomson [57]	2007	UK	Adults	263, PT	BSI	[4]17.11
	Lafrance [65]	2010	Canada	Adults	621, PT	BSI	[4]11.76
	Chan [69]	2012	USA	Adults	293094, PT	BSI	[4]77.00

	Hayes [82]	2014	Canada	Adults	187, PT	BSI	[4]63.10
	Marr [45]	1997	USA	NS	16081, CD	CRBSI	[5]3.90
	Kairaitis [48]	1999	Australia	All	2613, CD	CRBSI	[5]6.51
	Filiopoulos [66]	2011	Greece	Adults	58, PT	CRBSI	[4]34.48
	Li [60]	2009	USA	Adults	3359, PT	MRSAB	[4]2.64
	Fluck [63]	2010	UK	Adults	17359, PT	MRSAB	[4]0.83
	Patel [67]	2011	USA	Adults	93, PT	MRSAB	[4]4.30
	Crowley [70]	2012	UK	Adults	36858, PT	MRSAB	[4]0.37
Home parenteral nutrition	Santarpia [54]	2002	Italy	Adults	110, PT	CRS	[4]20.91
	Wales [68]	2011	Canada	Children	9060, CD	CRBSI	[5]10.04
	Gillanders [71]	2012	Australia	All	13410, CD	Sepsis	[5]2.68
	John [72]	2012	USA	NS	7201, CD	CRBSI	[5]6.53
	Olthof [77]	2013	Netherlands	NS	158, PT	CRBSI	[4]10.76
	Cotogni [74]	2013	Italy	Adults	51308, CD	CRBSI	[5]0.35
	Zhao [80]	2013	USA	Adults	12877, CD	BSI	[5]7.92
	Buchman [81]	2014	USA	All	331, CT	CRBSI	[6]44.41
	Touré [91]	2015	France	Adults	49134, CD	CLABSI	[5]1.63
	Lawinski [88]	2015	Poland	All	404808, CD	CRBSI	[5]0.87
	Elfassy [86]	2015	Canada	Adults	45876, CD	BSI	[5]2.03
	Szeinbach [90]	2015	USA	Adults	19104, CD	CLABSI	[5]0.58
	Cotogni [85]	2015	Italy	Adults	55293, CD	CRBSI	[5]0.05
	Durkin [94]	2016	USA	All	21934, CD	CRBSI	[5]3.10
	Bech [93]	2016	Denmark	Adults	295, CT	CRBSI	[6]26.10
Other settings	Rosenheimer [46]	1998	USA	NS	NS	BSI	[5]1.10
	Do [47]	1999	USA	NS	98483, CD	BSI	[5]0.66
	Tokars [49]	1999	USA	NS	69532, CD	CRBSI	[5]0.99
	Moureau [53]	2002	USA	All	2827917, CD	BSI	[5]0.19
	Leone [59]	2008	NS	NS	2409307, CD	CI	[5]0.24
	Weber [61]	2009	USA	Adults	40763, CD	CLABSI	[5]0.22
	Girard [64]	2010	France	All	68670, CD	CRBSI	[5]0.48
	Keusch	2013	Switzerland	NS	8608, CD	CRBSI	[5]1.28
	Rinke [79]	2013	USA	Children	92385, CD	CLABSI	[5]0.63
	Matveychuk [84]	2014	Israel	Adults	44, BR	BSI	[7]2.27

[1]N/100 patient-months
[2]N/1000 dialysis sessions
[3]N/1000 patient-days
[4]N/100 patients
[5]N/1000 catheter-days
[6]N/100 catheters
[7]N/100 bronchoscopies

ARBSI: Access-related bloodstream infection; BR: bronchoscopy; BSI: bloodstream infection; CD: catheter-day; CI: Catheter infection (local and BSI); CLABSI: Central line-associated bloodstream infection; CRBSI: Catheter-related bloodstream infection; CRS: Catheter-related sepsis; CS: dialysis session; CT: catheter; DS: dialysis session; ID: incidence density; MRSAB: Bloodstream infection with

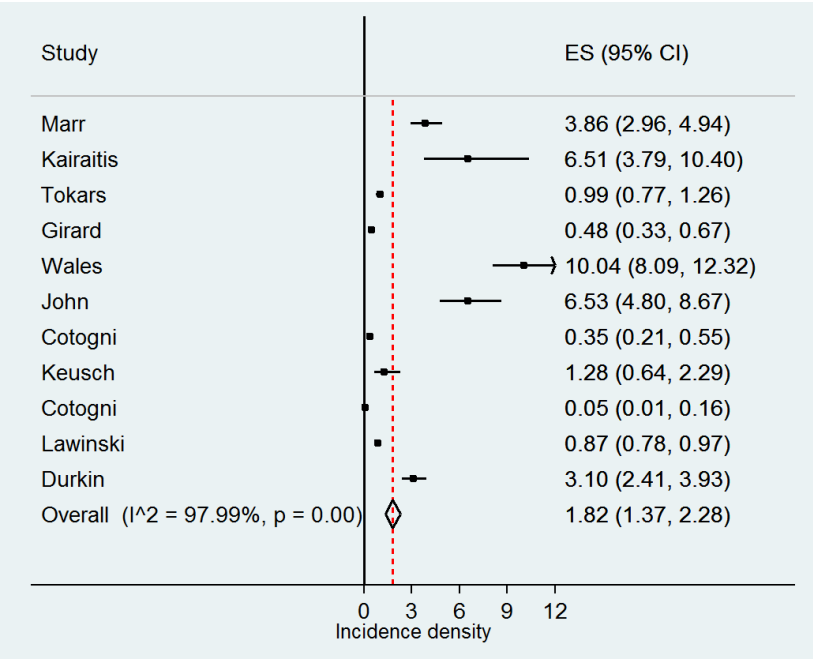
meticillin-resistant *Staphylococcus aureus*; NS: not stated; PD: patient-day; PM: patient month; PT: patient

Incidence density

BSI incidence in haemodialysis was found at 15.4 to 19.5 per 100 patient-years,[69, 82] and 0.21 to 0.31 per 1000 patient-days.[57, 65] All four studies were retrospective. Most patients started haemodialysis on a non-tunnelled CVC but may have received tunnelled catheters or fistulas later on.

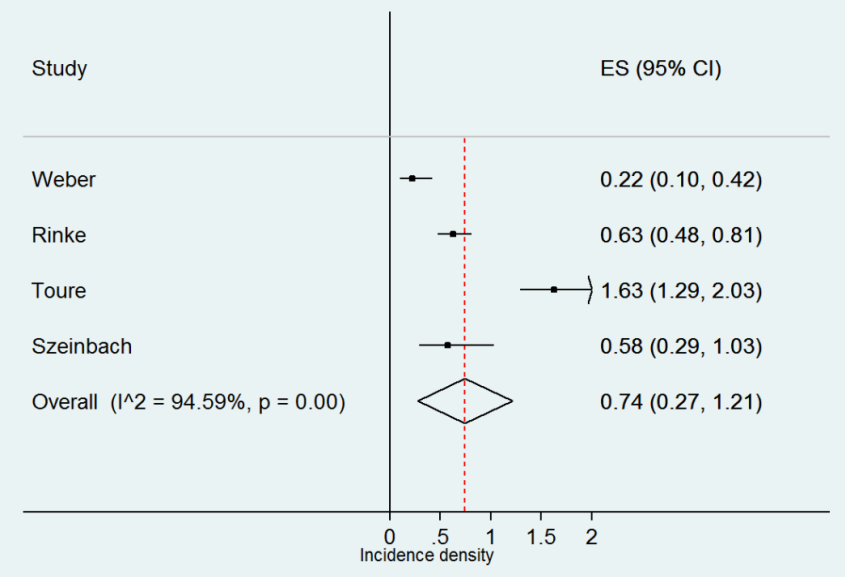
The weighted incidence density (CI 95%) of catheter-related bloodstream infections (CRBSIs) was 1.82 (1.37-2.28) per 1000 catheter-days in haemodialysis or home parenteral nutrition (Figure 2).

Figure 2. Incidence density of catheter-related bloodstream infections in patients undergoing longterm intravascular treatment (haemodialysis or home parenteral nutrition)



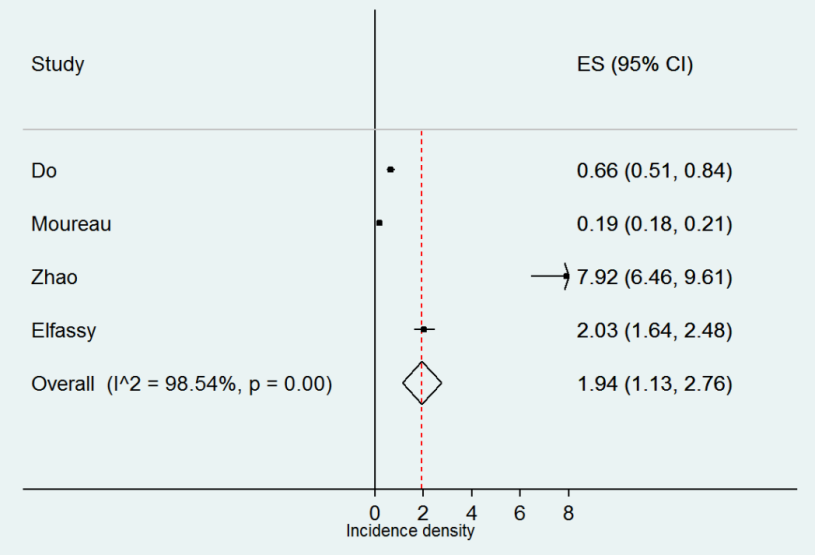
The incidence density (CI 95%) of central line-associated bloodstream infections (CLABSIs) was reported for patients undergoing intravascular therapy at home only, most commonly parenteral nutrition (Figure 3). The incidence density was 0.74 (0.27-1.21) and thus, lower than the incidence density of CRBSI among patients undergoing haemodialysis or home parenteral nutrition (Figure 2).

Figure 3. Incidence density of central line-associated bloodstream infections in patients undergoing intravascular treatment at home



The weighted incidence density (CI 95%) of all-cause BSI (instead of more specific CRBSI or CLABSI) in patients undergoing haemodialysis or home intravascular therapy was 1.94 (1.13-2.76) per 1000 catheter-days (Figure 4).

Figure 4. Incidence density of bloodstream infections in patients undergoing longterm intravascular treatment (haemodialysis or home parenteral nutrition)



The study by Santarpia et al. exemplifies the importance of outcome reporting:[54] over six years, 221 patients in two groups (see intervention below) undergoing home parenteral nutrition were followed for catheter-related sepsis. The incidence density of catheter-related sepsis was 6.8/1000 days of parenteral nutrition (≡ catheter-days) and 3.2/1000 catheter-days, respectively, which is in the range of other reports (Figure 2). On the other hand, the frequency of patients experiencing a catheter-related sepsis was 20.91%, with 15 patients (6.79%) having two or more infectious episodes during their treatment. Thus, although the risk for CRBSI seems moderate, many patients experience this complication during their therapy.

Bloodstream infections due to MRSA

Four studies reported on BSI due to methicillin-resistant *Staphylococcus aureus* in patients undergoing haemodialysis.[60, 63, 70, 78] A total of 2.65% (2.13-3.25%) of 3359 patients who were retrospectively observed, developed MRSA BSI in the report by Li et al..[60] The incidence density was 0.71 per 1000 patient-days. Fluck et al. studied the English haemodialysis database of the calendar year 2008/2009 (12 months).[63] A total of 144 MRSA BSI were identified in 17'349 patients (0.83%; 0.70-0.98%). Crowley et al. studied the English haemodialysis database for the calendar years 2009/2010 and 2010/2011, and identified 138 confirmed episodes of MRSA BSI over 24 months (77 in 2009/2010, 61 in 2010/2011).[70] The incidence among all 83'622 observed haemodialysis patients was 0.37% (0.31-0.44%). Patel et. al observed 103 patients over 12 months.[67] Ninety-three patients completed the study with an incidence of MRSA infection among carriers of 1.76 per 100 patient-months.

Interventions

Best practice intervention (multimodal strategies)

The study by Lindberg et al. measured access-related BSIs (ARBSIs) in 21 haemodialysis facilities during 28 months. Three periods were compared: 1) participating in the "Centers for Disease Control and Prevention Haemodialysis Bloodstream Infection Prevention Collaborative", 2) implementing a panel of infection prevention interventions, and 3) using positive deviance to engage staff.[76] All facilities were part of the collaborative and introduced the second and third intervention. ARBSI was defined as a positive blood culture that was either attributed to vascular access (catheter and fistula combined) or an unknown source in a haemodialysis outpatient or within one day after a hospital admission. ARBSI incidence dropped from 2.04 per 100 patient-months during the first period to 0.75 ($P = 0.03$) after employing the "Collaborative" interventions, and to 0.24 ($P < 0.01$) after adding positive deviance to the "Collaborative" interventions.

By using the "Macro-ergonomic Analysis and Design" (MEAD) method, Lewis et al. identified a number of actions in haemodialysis to form a package called the "Agency for Health Care Research and Quality Systematic Approach for Eliminating Risks" (SAFER) Initiative with nine interventions:[83]

- Provide increased environmental service resources to the dialysis unit
- Improve communication between dialysis staff and environmental services staff regarding unit cleaning
- Add antimicrobial materials to high touch areas (sinks, light switch plates, glove box holders)
- Close unit between shifts for cleaning and preparation for next shift

- Decrease distractions due to patient early entry into the dialysis unit
- Perform foot exams for at-risk patients
- Use alcohol wipes at the access site for fistula and graft patients
- Use antibiotic ointment at the access site for catheter patients
- Post monthly hospital-associated infection rates in staff areas and discuss them at monthly staff meetings

ARBSIs (1.09 vs. 1.23; $P = 0.83$) and access site infections (0.53 vs. 0.56; $P = 0.86$) as per 100 patient-months did not improve in the study unit by this strategy.

Rinke et al. conducted a trial among 520 ambulatory paediatric oncology patients.[79] Clinical staff, homecare agency nurses, and patient families 1) received training on a catheter bundle, 2) had their practice audited, and 3) were given feedback about their CLABSI rates. The mean incidence density decreased from 0.63 CLABSIs per 1000 central line-days at baseline to 0.32 CLABSIs per 1000 central line-days during the intervention period ($P = 0.005$).

Patel et al. tested a multimodal intervention strategy (surveillance and feedback, CHG-alcohol for skin antisepsis, hand hygiene surveillance, audits of vascular access care, patient education, staff education including competency assessments, and encourage permanent vascular access placement) among 17 volunteering outpatient haemodialysis facilities in the USA.[78] Pooled mean BSI and ARBSI rates were 1.09 and 0.73 events per 100 patient-months during the preintervention period, and 0.89 and 0.42 events per 100 patient-months during the intervention period, respectively. The reductions for both outcomes were significant. The study fulfilled the minimum quality assessment criteria and is of good quality.

In a prospective study by Santarpia et al., a multimodal intervention strategy to improve practice in home care parenteral nutrition reduced CRBSI significantly from 6.8/1000 days on parenteral nutrition (23/110 patients with 45 infections) to 3.2/1000 days on parenteral nutrition (9/111 patients with 15 infections) ($P < 0.001$).[54]

Catheter locks – ethanol

In a retrospective study, Lawinski et al. analysed the effectiveness of ethanol lock therapy on recurrent CRBSI compared to removing the haemodialysis catheter in a population undergoing a first CRBSI.[88] This is the largest ethanol lock study (428 patients) identified by this systematic review. There was no difference in CRBSI recurrence and other indicators between the two groups. Unfortunately, allocation to ethanol lock or catheter removal (after a first CRBSI was confirmed) was not randomized and thus, the conclusion of the outcome is not clear.

Nine patients experienced 81 CRBSI episodes (8.3 per 1000 catheter-days) before starting an ethanol lock therapy but only 9 CRBSI infections (2.7 per 1000 catheter-days: relative risk [RR], 0.325; confidence interval [CI] 95%, 0.17–0.64) thereafter in a small study by Opilla et al. in home parenteral nutrition.[56]

CRBSI incidence density decreased significantly from 10.2/1000 catheter-days to 0.9/1000 catheter-days after introducing ethanol locks in 10 children with homecare parenteral nutrition in the study by Wales et al..[68]

A study by John et al. reported significant (*P* = 0.011) CRBSI reduction from 3.53/1000 catheter-days to 1.65/1000 catheter-days after introducing ethanol lock therapy in 31 home parenteral nutrition patients.[72]

Catheter locks – taurolidine

Filiopoulos et al. compared the effectiveness of gentamicin/heparin locks and taurolidine/citrate locks in the prevention of CRBSI in haemodialysis adult haemodialysis patients. The results were compared to a historical cohort before using catheter locks.[66] The study is of low quality despite randomisation between the two lock products. There was no difference in CRBSI per 1000 catheter-days between the two lock products (2.7 vs. 3.7/1000 catheter-days); but the CRBSI incidence densities of the historic cohort were significantly higher (9.9/1000).

Taurolidine lock therapy reduced CRBSI from 2.0 CRBSI/1000 catheter-days to 0.2/1000 catheter-days in a small study by Bisseling et al. in cohort of 30 adult home parenteral nutrition patients.[62]

Similarly, Touré et al. reduced CRBSI from 6.58/1000 to 1.09/1000 catheter-days in 15 adult home parenteral nutrition patients by introducing a taurolidine lock therapy.[73]

In the study by Klek et al., 30 adult home parenteral nutrition patients were randomized into a group receiving taurolidine lock therapy (2% and 1.35%) and a group serving as controls.[87] Only one CRBSI occurred in a patient of the taurolidine lock group.

A last taurolidine lock therapy study was reported by Saunders et al.. The intervention was done among 22 adult patients undergoing home parenteral nutrition.[89] CRBSI decreased significantly from 5.71/1000 catheter-days to 0.99/1000 after introducing lock therapy.

Other intervention/comparisons

Xue et al. assessed the risk of nightly home haemodialysis (NHHD) compared to thrice weekly in-centre haemodialysis in a case-control study.[92] Sixty-one patients with NHHD were matched to 121 patients with in-centre haemodialysis. There was no significant difference of CRBSI or clinical sepsis between cases and controls (15.9% vs. 11.6%; *P* = 0.21).

No significant difference between chlorhexidine gluconate (CHG) 2% in 70% isopropylic alcohol and routine CHG solution (aqueous?) in CRBSI prevention (1/53 vs. 2/52; relative risk [RR], 0.49; CI95%, 0.05-5.25; *P* = 0.55) was observed in an Irish pilot study by McCann et al. among 105 adult haemodialysis patients.[95]

Quality assessment

A total of 15 studies were eligible for quality assessment.[54, 56, 62, 66, 68, 72, 73, 76, 78, 79, 83, 87-89, 92] One study was of good quality,[78] but all others failed predominantly on the minimal criteria but astonishingly many also on the overall score level. All studies, except one testing an ethanol or taurolidine lock therapy, were small and thus, their contribution to the knowledge base of CRBSI prevention is uncertain.

6.2.3 URINARY TRACT INFECTION

A total of 4 publications were identified,[46, 61, 97, 98] three reports contributing to the burden (Table 5),[46, 61, 98] and two studies reporting on prevention strategies.[97, 98]

Burden

Table 5 summarizes different CAUTI outcomes.

Table 5. Burden of catheter-associated urinary tract infections in outpatient care – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

Study	Year	Country	Population (type)	Population (N)	Outcome (type)	(%/ID)
Rosenheimer [46]	1998	USA	NS	NS	CAUTI, own	[1]4.5
Prasad [98]	2009	USA	Adults	13 PT	CAUTI, own	[2]2.29
Weber [61]	2009	USA	Adults	42882 CD	CAUTI, CDC	[1]1.24

[1]N/1000 catheter-days
[2]N per subject year

CDC: definition or surgical site infections using the definitions of the US Centers for Disease Control and Prevention; CAUTI: catheter-associated urinary tract infection; NS: not stated; own: own definition, specified in the report; PT: patient

Interventions

An intervention study by Cheung et al. examined the effect of periurethral cleansing before catheterization with 0.05% CHG in 20 home care patients.[97] The patients were randomized into the intervention group (12) and into the control group (8). There was no difference of urine colonisation, which was the primary outcome.

The study by Prasad et al. addressed the role of bladder colonisation with *Escherichia coli* 83972 among patients with a neurologic bladder after spinal cord injury.[98] *Escherichia coli* 83972 is a benign microorganism and the hypothesis was to test positive competition. Only 13 patients participated. Patients successfully colonised with *E. Coli* 83972 (by applying urinary catheters coated with the microorganism) had less colonisation with pathogenic bacteria. However, the small study size makes interpretation uncertain.

Quality assessment

Both studies were quality-assessed and failed by a large margin.

6.3 SETTINGS

6.3.1 HOME PARENTERAL NUTRITION

A total of 20 publications were identified, [54, 56, 62, 68, 71-74, 77, 80, 81, 85-91, 93, 94] 15 reports contributing to the burden (Table 6),[54, 68, 71, 72, 74, 77, 80, 81, 85, 86, 88, 90, 91, 93, 94] and 9 studies reporting on prevention.[54, 56, 62, 68, 72, 73, 87-89] The outcomes of the studies were any form of sepsis (BSI, clinical sepsis, CLABSI, CRBSI).

Burden

Table 6 summarizes different BSI outcomes due to home parenteral nutrition.

Table 6. Burden of bloodstream infections in home care parenteral nutrition – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

Study	Year	Country	Population (type)	Population (N)	Outcome (type)	(%/ID)
Santarpia [54]	2002	Italy	Adults	110 PT	CRBSI	[1]20.91
Wales [68]	2011	Canada	Children	9060 CD	CRBSI	[2]10.04
Gillanders [71]	2012	Australia	All	13410 CD	Sepsis	[2]2.68
John [72]	2012	USA	NS	7201 CD	CRBSI	[2]6.53
Olthof [77]	2013	Netherlands	NS	158 PT	CRBSI	[1]10.76
Cotogni [74]	2013	Italy	Adults	51308 CD	CRBSI	[2]0.35
Zhao [80]	2013	USA	Adults	12877 CD	BSI	[2]7.92
Buchman [81]	2014	USA	All	331 CT	CRBSI	[3]44.41
Touré [91]	2015	France	Adults	49134 CD	CABSI	[2]1.63
Lawinski [88]	2015	Poland	All	404808 CD	CRBSI	[2]0.87
Elfassy [86]	2015	Canada	Adults	45876 CD	BSI	[2]2.03
Szeinbach [90]	2015	USA	Adults	19104 CD	CLABSI	[2]0.58
Cotogni [85]	2015	Italy	Adults	55293 CD	CRBSI	[2]0.05
Durkin [94]	2016	USA	All	21934 CD	CRBSI	[2]3.10
Bech [93]	2016	Denmark	Adults	295 CT	CRBSI	[3]26.10

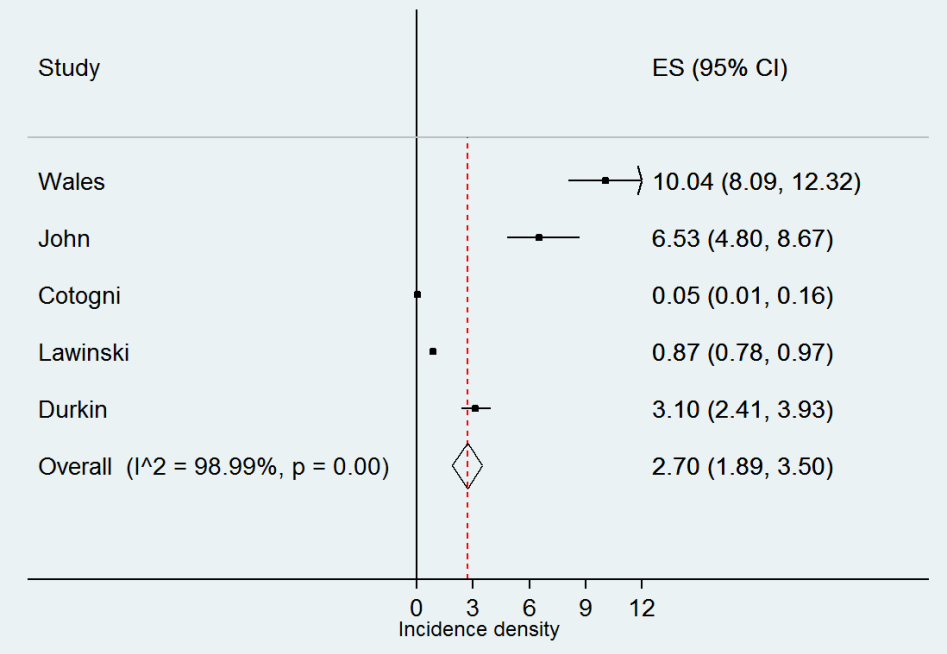
[1]N/100 patients
[2]N/1000 catheter-days
[3]N/100 catheters

BSI: bloodstream infection; CABSI: Catheter-associated bloodstream infection; CD: catheter-day; CLABSI: Central line-associated bloodstream infection; CRBSI: Catheter-related bloodstream infection; CT: catheter; ID: incidence density; NS: not stated; PM: patient month; PT: patient

Five studies reported CRBSI incidence densities (N/1000 catheter-days), which made meta-analysis possible (Figure 5).[68, 72, 74, 88, 94] The weighted CRBSI incidence density (CI 95%) for home parenteral nutrition was 2.70 (1.89-3.50) CRBSI per 1000 catheter-days, with important

variation (higher incidence density in the years 2011/2012, lower incidence densities thereafter).

Figure 5. Catheter-related bloodstream infections per 1000 catheter-days in patients undergoing home parenteral nutrition



Interventions

Best practice

In a prospective study by Santarpia et al., a multimodal best practice study in home care PN reduced CRBSI significantly from 21% (23 of 110 patients with 45 infections) to 8% (9 of 111 patients with 15 infections).[54]

Catheter locks – ethanol

In a retrospective study, Lawinski et al. analysed the effectiveness of ethanol lock therapy on recurrent CRBSI compared to removing the catheter in a population undergoing a first CRBSI.[88] This is the largest ethanol lock study (428 patients) identified by this systematic review. There was no difference in CRBSI recurrence and other indicators between the two groups. Unfortunately, allocation to ethanol lock or catheter removal (after a first CRBSI was confirmed) was not randomized and thus, the significance of the outcome is not clear.

Nine patients experienced 81 CRBSI episodes (8.3 per 1000 catheter-days) before starting an ethanol lock therapy but only 9 CRBSI infections (2.7 per 1000 catheter-days: relative risk

[RR], 0.325; confidence interval [CI] 95%, 0.17–0.64) thereafter in the study by Opilla et al. in home parenteral nutrition.[56]

CRBSI incidence density decreased significantly from 10.2/1000 catheter-days to 0.9/1000 catheter-days after introducing ethanol locks in 10 children with homecare parenteral nutrition in the study by Wales et al..[68]

A study by John et al. reported significant (*P* = 0.011) CRBSI reduction from 3.5/1000 catheter-days to 1.7/1000 catheter-days after introducing ethanol lock therapy in 31 home parenteral nutrition patients.[72]

Catheter locks – taurodlidine

Taurolidine lock therapy reduced CRBSI from 2.0 CRBSI/1000 catheter-days to 0.2/1000 catheter-days in a small study by Bisseling et al. in cohort of 30 adult home parenteral nutrition patients.[62]

Similarly, Touré et al. reduced CRBSI from 6.6/1000 to 1.1/1000 catheter-days in 15 adult home parenteral nutrition patients by introducing a taurolidine lock therapy.[73]

In the study by Klek et al., 30 adult home parenteral nutrition patients were randomized into a group receiving taurolidine lock therapy (2% and 1.4%) and one group serving as controls.[87] Only one CRBSI occurred in a patient of the taurolidine lock group.

A last taurolidine lock therapy study was reported by Saunders et al.. The intervention was done in 22 adult patients undergoing home parenteral nutrition.[89] CRBSI decreased significantly from 5.7/1000 catheter-days to 1.0/1000 after introducing lock therapy.

Quality assessment

A total of ten studies were eligible for quality assessment. [54, 56, 62, 68, 72, 73, 79, 87-89] None of the studies was of sufficient quality failing predominantly on the minimal criteria. All studies except one testing an ethanol lock therapy,[88] were small and their contribution to the knowledge base of CRBSI prevention in home parenteral nutrition is uncertain.

6.3.2 ENDOSCOPY

A total of 10 publications were identified, [84, 96, 99-106] three reports contributing to the burden (Table 6), [84, 101, 103] and 7 studies reporting on prevention.[96, 99, 100, 102, 104-106]

Burden

Table 7 summarizes reports on reports on the use of endoscopes.

Table 7. Burden of infections due to the use of endoscopes – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

Study	Year	Country	Population (type)	Population (N)	Outcome (type)	(%/ID)
Powell	2003	UK	Instruments	86 IN	Growth*	[1]17.4%
Turan	2006	Turkey	Adults	75 PT	Bacteriuria	[2]8.0%
Matveychuk [84]	2014	Israel	Adults	44 PT	BSI	[3]2.27%

*Growth after reprocessing
[1]N per 100 instruments
[2]N per 100 patients
[3]N/100 bronchoscopy procedures

BSI: bloodstream infection; IN: instrument; PT: patient

Interventions

Uno et al. tested a new protected injection needle for colonoscopy.[99] Ten patients underwent a procedure with a standard needle, 10 patients underwent a procedure using the protected needle. All needles were investigated for growth of *E. coli*. All cultures from ordinary needles grew *E. coli*, whereas only 3 new protected needles grew *E. coli*.

Sakai et al. tested the effectiveness of manual cleaning and disinfection of gastroscopes with 2%/3% glutaraldehyde in preventing hepatitis C virus (HCV) transmission.[100] Gastroscopes used for treatment of endoscopic ligation of oesophageal varices in patients with HCV infection were manually cleaned and disinfected with 3% glutaraldehyde (25), 2% glutaraldehyde (17), or 0.1% benzethonium chloride (25). Of the 25 gastroscopes in the 3% glutaraldehyde group, nine (36%) were positive for HCV before cleaning and disinfection, but all gastroscopes were negative for HCV after cleaning and disinfection.

Elackattu et al. tested the prevention of cross-contamination in fiberoptic endoscopes in an otolaryngology (ORL) outpatient clinic.[105] One-hundred endoscopes were assigned to either a protection sheath (experimental) or to germicidal immersion (control). Microbial counts were low and similar for the two groups (1/50 vs. 0/50).

Thompson et al. evaluated the infection rate associated with the use of a non-refluxing irrigation system for outpatient flexible cystoscopy.[96] The overall infection rate for flexible cystoscopy in 133 eligible patients was 3.2%, with no significant difference between the study and control groups.

Shaving pubic/genital regions before endoscopic urologic surgery had no effect on post-endoscopic urine cultures among 95 adult patients in a study by Menendez et al. [102]

In a randomized controlled trial, Gilling et al. compared the effectiveness of chlorine dioxide with ortho-phthaldehyde; 1,2–benzenedicarboxaldehyde in an automated endoscopic reprocessor for high-level disinfection of flexible cystoscopes in a population of 180 patients.[106] The urine analysis was positive in 5.4% of patients in each group, and 29% (chlorine dioxide) vs. 20% (ortho-phthaldehyde; 1,2–benzenedicarboxaldehyde) of patients had urinary leukocyturia after cystoscopy. This difference was not significant.

Quality assessment

Three studies were assessed for quality.[96, 102, 106] None of the studies was of sufficient quality.

6.3.3 HAEMODIALYSIS

A total of 42 publications were identified,[3, 45, 48, 50-52, 55, 57, 58, 60, 63, 65-67, 69, 70, 76, 78, 82, 83, 92, 95, 107-126] 21 of measuring BSI-related outcomes.[45, 48, 50-52, 55, 57, 58, 60, 63, 65-67, 69, 70, 76, 78, 82, 83, 92, 95] Thirty-seven reports contributed to the burden (Table 8),[3, 45, 48, 50-52, 55, 57, 58, 60, 63, 65-67, 69, 70, 78, 82, 107, 109-123, 126] and 10 studies reported on a prevention strategy.[66, 76, 78, 83, 92, 95, 108, 115, 123-125]

Burden

Table 8 summarizes the outcomes of different outcomes in haemodialysis, stratified into BSI outcomes, transmission of hepatitis C virus (HCV), and other outcomes.

Table 8. Burden of healthcare-associated infections in haemodialysis – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

	Study	Year	Country	Population (type)	Population (N)	Outcome (type)	(%/ID)
Bloodstream infection-related outcomes	Tokars [51]	2001	USA	Adults	4134 PM	ARBSI	[1]3.51
	Klevens [58]	2008	USA	NS	NS	ARBSI	[1]1.25
	Patel [78]	2013	USA	NS	28047 PM	ARBSI	[1]7.30
	Stevenson [50]	2000	USA	NS	39096 DS	BSI	[2]0.90
	Dopirak [52]	2002	USA	NS	142525 DS	BSI	[2]1.11
	Colville [55]	2006	Australia	NS	14528 PT	BSI	[3]1.72
	Thomson [57]	2007	UK	Adults	263 PT	BSI	[4]17.11
	Lafrance [65]	2010	Canada	Adults	621 PT	BSI	[4]11.76
	Chan [69]	2012	USA	Adults	293094 PT	BSI	[4]77.00

	Hayes [82]	2014	Canada	Adults	187 PT	BSI	[4]63.10
	Marr [45]	1997	USA	NS	16081 CD	CRBSI	[5]3.90
	Kairaitis [48]	1999	Australia	All	2613 CD	CRBSI	[5]6.51
	Filiopoulos [66]	2011	Greece	Adults	58 PT	CRBSI	[4]34.48
	Bonomo [109]	1997	USA	Adults	1316 PM	PASI	[1]3.88
	Tokars [114]	2002	USA	Adults	75535 PM	VAI	[1]3.22
	Butler [123]	2011	USA	Adults	***4132 CT	CRI	[4]1.96
	Li [60]	2009	USA	Adults	3359 PT	MRSAB	[4]2.64
	Fluck [63]	2010	UK	Adults	39476 PT	MRSAB	[4]0.31
	Patel [67]	2011	USA	Adults	93 PT	MRSAB	[4]4.30
	Crowley [70]	2012	UK	Adults	83622 PT	MRSAB	[4]0.17
Hepatitis-C	Yamaji [107]	1996	Japan	Adults	204 PT	HCV	[4]5.39 %
	Mizuno [110]	1998	Japan	NS	51 PT	HCV	[4]3.92 %
	Kobayashi [111]	1998	Japan	Adults	302 PT	HCV	[4]2.98 %
	Halfon [112]	1998	France	Adults	136 PT	HCV	[4]1.47 %
	Saxena [115]	2003	Saudi Arabia	All	189 PT	HCV	[5]6.88 %
	Izopet [118]	2005	France	NS	1077 PT	HCV	[5]0.43 %
	Girou [3]	2008	France	NS	46 PT	HCV	[4]3.85 %
	Mohamed [121]	2010	Saudi Arabia	All	36 PT	HCV	[4]0.00 %
Other outcomes	McCarthy [113]	2000	USA	Adults	17 PT	IE	[4]100 %
	Doulton [116]	2003	UK	Adults	479 PT	IE	[4]6.26 %
	Carrilho [117]	2004	Brazil	NS	813 PT	HBV	[4]9.96 %
	Sav [122]	2010	Turkey	Adults	71 PT	HBV	[4]16.90 %
	Ponce [120]	2007	Portugal	NS	4501 PM	HAI	[1]3.31
	Dalrymple [126]	2015	USA	Adults	13554 PT	HAI§	[4]28.39 %
	Nori [119]	2006	USA	Adults	**52 CT	IHM	[4]37.00 %

*Outcome BSI-related
**Patients with infective endocarditis (40 with a haemodialysis catheter)
***Patients undergoing haemodialysis but with previous peripherally inserted catheter
§Hospitalisation due to a healthcare-associated infection
[1]N/100 patient-months
[2]N/1000 dialysis sessions
[3]N/1000 patient-days
[4]N/100 patients (catheters)
[5]N/100 patients per year

ARBSI: access-related bloodstream infection; BSI: bloodstream infection; CRBSI: catheter-related bloodstream infection; CRI: catheter-related infection; CT: catheter; DS: dialysis session; HAI: healthcare-associated infection; HBV: hepatitis B virus (infection); HCV: hepatitis C virus (seroconversion); IE: infective endocarditis; IHM: in hospital mortality; MRSAB: bloodstream infection with meticillin-resistant *Staphylococcus aureus*; NS: not specified; PASI: permanent access site infection; PM: patient-month; PT: patient; VAI: vascular access infection

BSI per total of dialysis sessions was 0.9% and 1.1% as reported in two studies. [50, 52] CRBSI per 1000 catheter-days was reported by two other studies (3.50 and 6.51, respectively). [45, 48]

Incidence
BSI incidence in haemodialysis was found at 15.4 to 19.5 per 100 patient-years,[69, 82] and 0.21 to 0.31 per 1000 patient-days.[57, 65] All four studies were retrospective. Most patients started haemodialysis on a non-tunnelled CVC but may have received tunnelled catheters or fistulas later on.

Bloodstream infections due to MRSA
Four studies reported on BSI due to methicillin-resistant *Staphylococcus aureus* in patients undergoing haemodialysis.[60, 63, 70, 78] A total of 2.65% (2.13-3.25%) MRSA BSI among 3359 patients undergoing haemodialysis were reported by by Li et al. in a retrospective analysis of a former randomized trial.[60] The incidence was 0.71 per 1000 patient-days. Fluck et al. studied the English haemodialysis database for the fiscal year 2008/2009.[63] A total of 144 MRSA BSI were identified in 17'349 patients (0.83%; 0.70-0.98%) undergoing haemodialysis. Crowley et al. studied the English haemodialysis database for the fiscal years 2009/2010 and 2010/2011, and identified 138 confirmed episodes of MRSA BSI over 24 months (77 in 2009/2010, 61 in 2010/2011).[70] The frequency among all 83'622 observed haemodialysis patients was 0.37% (0.31-0.44%). Patel et. al observed 103 patients over 12 months.[67] Ninety-three patients completed the study with an incidence of MRSA infection among carriers of 1.76 per 100 patient-months.

Hepatitis-C transmission
Eight studies reported on HCV-transmission in patients undergoing haemodialysis.[3, 107, 110-112, 115, 118, 121] The studies were published in different years, and observation time varied. HCV transmission per 100 patient-months could be calculated from four of them (Table 9).

Table 9. Transmission of Hepatitis C-virus in patients undergoing haemodialysis – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

Study	Year	Country	Population (type)	Population (N)	Patient-months	Cases (N)	[1]Inc
Halfon [112]	1998	France	Adults	136 PT	1224	2	0.16
Mizuno [110]	1998	Japan	NS	51 PT	918	2	0.22
Saxena [115]	2003	Saudi Arabia	All	189 PT	13797	85	0.61
Girou [3]	2008	France	NS	46 PT	414	2	0.48

[1]Transmissions per 100 patient-months

Yamaji et al. identified 10 new HCV cases in a cohort of 204 patients.[107] The study does not reveal precise observation months. Kobayashi et al. identified 9 new HCV patients in a cohort of 302 patients that was observed up to 5 years.[111] Izopet et al. followed up 1077 sero-negative patients over 3 years, and identified 14 new cases (0.43/100 patients per year).[118] Mohamed et al. had no new cases in a cohort of 36 patients, who were observed for up to 5 years.[121]

Risk analysis

Butler et al. tested in a retrospective single centre study if previous use of peripherally inserted central catheters (PICCs) is a risk for CRBSI in haemodialysis patients.[123] The hypothesis was that PICC lines cause vasculature damage, which in turn may put the patients at risk for CRBSI. Indeed, the 38 patients of a cohort of 185 with 713 tunnelled haemodialysis catheters were more at risk for CRBSI (odds ratio [CI95%]: 2.46 [1.71–3.53]).

Schmid et al. prospectively screened haemodialysis patients for nasal and extra-nasal MRSA carriage over 7 years in Germany.[125] MRSA carriers were isolated for haemodialysis during MRSA carriage, and they were decolonised. Thirty-four carriers were identified. MRSA patients had a lower survival rate. Mortality was particularly high when MRSA decolonisation failed.

The study by Xue et al. in the US used a case-control study to assess the risk of nightly home haemodialysis (NHHD) compared to thrice weekly in-centre haemodialysis (IHD).[92] Sixty-one patients with NHHD were matched to 121 patients with IHD. The difference of CRBSI or clinical sepsis was not significant (15.9% vs. 11.6%; $P = 0.21$).

No significant difference between CHG 2% in 70% isopropylic alcohol and routine CHG solution (aqueous?) in CRBSI prevention (1/53 vs. 2/52; relative risk [RR], 0.49; CI95%, 0.05-5.25; $P = 0.55$) was observed in an Irish pilot study by McCann et al. among 105 adult haemodialysis patients.[95]

Interventions/risk analysis

Best practice

Saxena et al. investigated the impact of dedicated care on the transmission of HCV in a Saudi Arabian haemodialysis outpatient clinic.[115] Patients, identified as being HCV-positive in a retrospective analysis (5 years) were isolated, and dedicated care as well as dedicated dialysis equipment was established. A yearly seroconversion rate to HCV was identified in the retrospective analysis. After implementation of dedicated care, only 2 patients out of 189 (1.1%) showed seroconversion in the prospective 12 months surveillance.

Scheithauer et al. conducted a three-phase hand hygiene improvement study in a single centre in Germany.[124] The intervention consisted in individual and group training of hand hygiene, hand hygiene observations with feedback, and optimized placement of handrub dispensers. The study was divided into a baseline, a first intervention period targeting connection (the haemodialysis catheter with the haemodialysis machine), and a second intervention period targeting disconnection. Hand hygiene compliance increased from 30% at baseline to 45% during the first intervention and 62% during the second intervention.

The study by Lindberg et al. measured ARBSI in 2786 adult haemodialysis patients.[76] ARBSI was defined as a positive blood culture that was either attributed to the vascular access (catheter and fistula combined) or an unknown source collected from a haemodialysis patient as an outpatient or within one day after a hospital admission. An ARBSI prevention programme was established in two steps: 1) implementation of a panel of infection prevention interventions, and 2) use of positive deviance to engage staff. All participating 21

haemodialysis facilities had to participate in the “Centers for Disease Control and Prevention Haemodialysis Bloodstream Infection Prevention Collaborative”. ARBSI incidence dropped from 2.04 per 100 patient-months during preintervention to 0.75 ($P = 0.03$) after employing the prevention programme and to 0.24 ($P < 0.01$) after adding positive deviance to the Collaborative interventions.

By using the “Macro-ergonomic Analysis and Design” (MEAD) method, Lewis et al. identified a number of actions in haemodialysis to form a package called the “Agency for Health Care Research and Quality Systematic Approach for Eliminating Risks” (SAFER) Initiative with nine interventions:[83]

- Provide increased environmental service resources to the dialysis unit
- Improve communication between dialysis staff and environmental services staff regarding unit cleaning
- Add antimicrobial materials to high touch areas (sinks, light switch plates, glove box holders)
- Close unit between shifts for cleaning and preparation for next shift
- Decrease distractions due to patient early entry into the dialysis unit
- Perform foot exams for at-risk patients
- Use alcohol wipes at the access site for fistula and graft patients
- Use antibiotic ointment at the access site for catheter patients
- Post monthly hospital-associated infection rates in staff areas and discuss them at monthly staff meetings

ARBSIs (1.09 vs. 1.23; $P = 0.83$) and access site infections (0.53 vs. 0.56; $P = 0.86$) as per 100 patient-months did not improve in the study haemodialysis unit by this strategy.

Patel et al. tested a multimodal intervention strategy (surveillance and feedback, CHG-alcohol for skin antisepsis, hand hygiene surveillance, audits of vascular access care, patient education, staff education including competency assessments, and encourage permanent vascular access placement) among 17 volunteering outpatient haemodialysis facilities in the USA.[78] Pooled mean BSI and ARBSI rates were 1.09 and 0.73 events per 100 patient-months during the preintervention period and 0.89 and 0.42 events per 100 patient-months during the intervention period. The reductions for both outcomes were significant. The study fulfilled the minimum quality assessment criteria and is of good quality.

Catheter locks – taurolidine

Filiopoulos et al. compared the effectiveness of gentamicin/heparin locks and taurolidin/citrate locks in the prevention of CRBSI in haemodialysis adult haemodialysis patients. The results were compared to a historical cohort before using catheter locks.[66] The study is of low quality despite randomisation between the two lock products. There was no difference of CRBSI per 1000 catheter-days between the two lock products (2.7 vs. 3.7/1000 catheter-days); but the CRBSI incidence densities of the historic cohort were significantly higher (9.9/1000).

Quality assessment

Ten studies could be assessed for quality. [66, 76, 78, 83, 92, 95, 108, 115, 123, 125] The overall quality was rather low and none of the studies fulfilled the minimal criteria.

6.3.4 PERITONEAL DIALYSIS

A total of seven publications were identified,[108, 122, 127-131] six reports contributing to the burden (Table 9),[122, 127-131] and three studies on intervention strategies.[108, 127, 128]

Burden

Table 10 summarizes the outcomes of peritoneal dialysis.

Table 10. Burden of bloodstream infections in outpatient settings – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

Study	Year	Country	Population (type)	Population (N)	Outcome (type)	(%/ID)
MSG*	1996	UK	Adults	1236 PM	ESI	[1]4.45
Harris [128]	1996	Australia	Adults	30 PT	Peritonitis	[2]40.0
Tiong [129]	2006	Singapore	All	139 PT	Peritonitis	[2]25.9
Predari [130]	2007	Argentina	NS	7 PT	FP	[3]0.06
Sav [122]	2010	Turkey	Adults	71 PT	HBV	[2]9.9
Waness [131]	2012	Turkey	Adults	89 PT	MTP	[2]4.5

*The mupirocin study group

[1]N/100 patient-months
[2]N/100 patients
[3]N/patient-year

ESI: exit-site infection; FP: fungal peritonitis; HBV: hepatitis B virus (infection); MTP: peritonitis due to *Mycobacterium tuberculosis*; NS: not specified; PM: patient-month; PT: patient

Only two studies looked at peritonitis in settings comparable to Switzerland,[128, 129] the other studies looked at HBV, tuberculosis or exit site infections. In conclusion: all-cause peritonitis is a common complication from peritoneal dialysis, peritonitis due to fungi is rare, HBV transmission should not occur in Switzerland due to vaccinated patients, and tuberculosis is rare in Switzerland.

Interventions

The UK mupirocin study group tested the efficacy of monthly 5-day mupirocin 2% nasal ointment application to reducing nasal *Staphylococcus aureus* in patients undergoing continuous ambulatory peritoneal dialysis (CAPD).[127] A total of 267 patients out of 1144 patients from nine European centres carried nasal *Staphylococcus aureus*. They were randomly allocated either to mupirocin or placebo. Although nasal carriage in the treatment group was lower (10%) than in the control group (48%), there were no significant differences in all-cause exit-site infections, but there were significantly less infections due to *Staphylococcus aureus* in the mupirocin group (14 vs. 44; $P = 0.006$).

Harris et al tested the effectiveness of a double-bag collection system for CAPD compared to standard single-bag collection in 63 adult patients in Australia.[128] Cumulative incidence of peritonitis was 1 per 14.0 patient-months for the single-bag system and 1 per 46.5 patient-months for the double-bag system (*P* = 0.004).

There was no difference in exit-site infections among 25 CAPD patients using or leaving aside a dressing after exit-site disinfection in a UK study by Naylor et al..[108]

Quality assessment

All three prevention studies were RCTs but failed largely on the minimum criteria.[108, 127, 128]

6.3.5 HOME CARE

A total of 26 publications were identified, [46, 47, 49, 54, 56, 59, 61, 62, 68, 71-74, 77, 80, 81, 86-91, 93, 94, 97, 132] 20 reports contributing to the burden (Table 10), [46, 47, 49, 54, 59, 61, 68, 71, 72, 74, 77, 80, 81, 86, 88, 90, 91, 93, 94, 132] and 10 studies reporting on a prevention strategy . [54, 56, 62, 68, 72, 73, 87-89, 97]

Burden

Table 11 summarizes the burden of healthcare-associated infections due to delivering home care, stratified into BSI-outcomes and other outcomes.

Table 11. Burden of healthcare-associated infections in home care – Strategie NOSO Ambulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

	Study	Year	Country	Population (type)	Population (N)	Outcome (type)	(%/ID)
Bloodstream infection-related outcomes	Do [47]	1999	USA	NS	98483 CD	BSI	[1]0.66
	Zhao [80]	2013	USA	Adults	12877 CD	BSI	[1]7.92
	Elfassy [86]	2015	Canada	Adults	45876 CD	BSI	[1]2.03
	Touré [91]	2015	France	Adults	49134 CD	CABSI	[1]1.63
	Szeinbach [90]	2015	USA	Adults	19104 CD	CLABSI	[1]0.58
	Tokars [49]	1999	USA	NS	69532 CD	CRBSI	[1]0.99
	Santarpia [54]	2002	Italy	Adults	110 PT	CRBSI	[2]20.91
	Wales [68]	2011	Canada	Children	9060 CD	CRBSI	[1]10.04
	John [72]	2012	USA	NS	7201 CD	CRBSI	[1]6.53
	Olthof [77]	2013	Netherlands	NS	158 PT	CRBSI	[2]10.76
	Cotogni [74]	2013	Italy	Adults	51308 CD	CRBSI	[1]0.35
	Buchman [81]	2014	USA	All	331 CT	CRBSI	[3]44.41
	Lawinski [88]	2015	Poland	All	404808 CD	CRBSI	[1]0.87
	Durkin [94]	2016	USA	All	21934 CD	CRBSI	[1]3.10
	Bech [93]	2016	Denmark	Adults	295 CT	CRBSI	[3]26.10
	Gillanders [71]	2012	Australia	All	13410 CD	Sepsis	[1]2.68

Other outcomes	Leone [59]	2008	NS	NS	2409307 CD	ARI	[1]0.24
	Rosenheimer [46]	1998	USA	NS	NS	CAUTI	[4]4.5
	Weber [61]	2009	USA	Adults	42882 CD	CAUTI	[4]1.24
	Chenoweth [132]	2007	USA	Adults	50762 VD	VAP	[5]1.56

[1]N/1000 vascular catheter-days
[2]N/100 patients
[3]N/100 vascular catheters
[4]N/1000 urinary catheter-days
[5]N/1000 ventilator-days

ARI: access-related infection; BSI: bloodstream infection; CABSI: Catheter-associated bloodstream infection; CD: catheter-day; CLABSI: Central line-associated bloodstream infection; CRBSI: Catheter-related bloodstream infection; CT: catheter; ID: incidence density; NS: not stated; PT: patient; VAP: ventilator-associated pneumonia; VD: ventilator-days

Three and six studies reported incidence densities on BSI and CRBSI in patients undergoing intravascular therapy in home care, respectively. The weighted incidence densities (CI 95%) of BSI and CRBSI were 3.26 (1.32-5.21) and 2.33 (1.65-3.00) per 1000 catheter-days (Figures 7-8).

Figure 7. Incidence density of bloodstream infections in patients undergoing intravascular therapy in home care

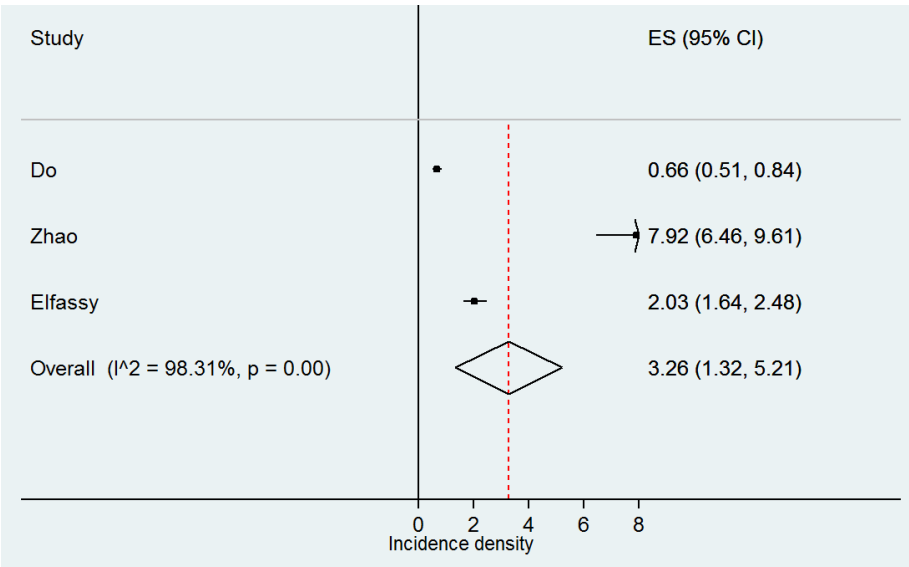
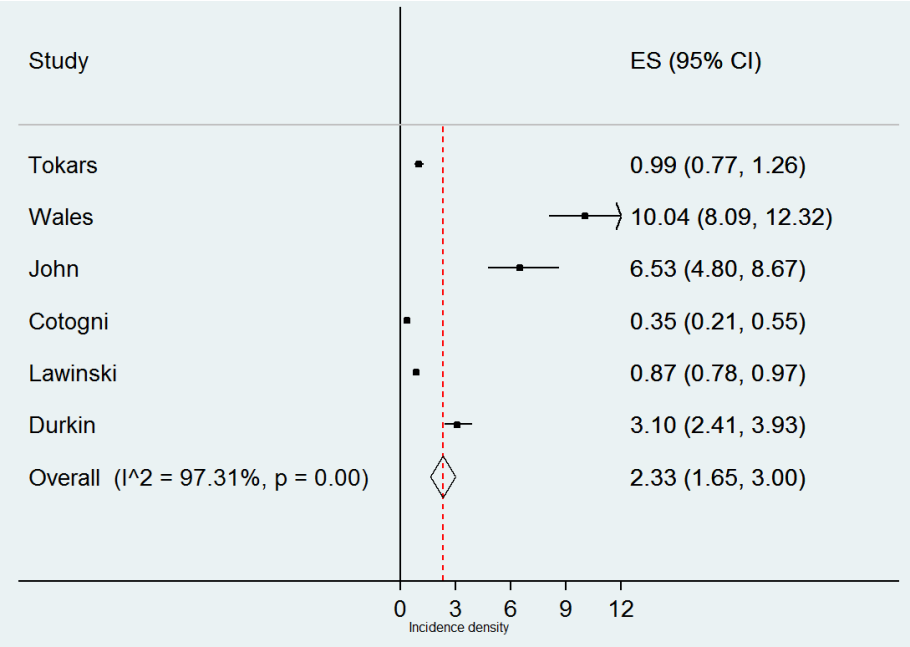


Figure 8. Incidence density of catheter-related bloodstream infections in patients undergoing intravascular therapy in home care



The incidence density (95% CI) of CRBSI as reported by 6 studies is 2.33 (1.65-3.00). However, the number of catheters getting infected in home care is high (26.1% and 44.4%, respectively), [81, 93] and 10.7% and 20.9% patients experienced a CRBSI, respectively. [54, 77]

Interventions

Best practice

In a prospective study by Santarpia et al., a multimodal best practice study in home care PN reduced CRBSI significantly from 21% (23 of 110 patients with 45 infections) to 8% (9 of 111 patients with 15 infections).[54]

An intervention study by Cheung et al. examined the effect of periurethral cleansing before catheterization with 0.05% CHG in 20 home care patients.[97] The patients were randomized into the intervention group (12) and into the control group (8). There was no difference of urine colonisation, which was the primary outcome.

Catheter locks – ethanol

In a retrospective study, Lawinski et al. analysed the effectiveness of ethanol lock therapy on recurrent CRBSI compared to removing the catheter in a population undergoing a first CRBSI.[88] This is the largest ethanol lock study (428 patients) identified by this systematic review. There was no difference in CRBSI recurrence and other indicators between the two groups. Unfortunately, allocation to ethanol lock or catheter removal (after a first CRBSI was confirmed) was not randomized and thus, the significance of the outcome is not clear.

Nine patients experienced 81 CRBSI episodes (8.3 per 1000 catheter-days) before starting an ethanol lock therapy but only 9 CRBSI infections (2.7 per 1000 catheter-days: relative risk [RR], 0.325; confidence interval [CI] 95%, 0.17–0.64) thereafter the study by Opilla et al. in home parenteral nutrition.[56]

CRBSI incidence density decreased significantly from 10.2/1000 catheter-days to 0.9/1000 catheter-days after introducing ethanol locks in 10 children with homecare parenteral nutrition in the study by Wales et al..[68]

A study by John et al. reported significant (*P* = 0.011) CRBSI reduction from 3.5/1000 catheter-days to 1.7/1000 catheter-days after introducing ethanol lock therapy in 31 home parenteral nutrition patients.[72]

Catheter locks – taurodlidine

Taurolidine lock therapy reduced CRBSI from 2.0 CRBSI/1000 catheter-days to 0.2/1000 catheter-days in a small study by Bisseling et al. in cohort of 30 adult home parenteral nutrition patients.[62]

Similarly, Touré et al. reduced CRBSI from 6.6/1000 to 1.1/1000 catheter-days in 15 adult home parenteral nutrition patients by introducing a taurolidine lock therapy.[73]

In the study by Klek et al., 30 adult home parenteral nutrition patients were randomized into a group receiving taurolidine lock therapy (2% and 1.4%) and one group serving as controls.[87] Only one CRBSI occurred in a patient of the taurolidine lock group.

The taurolidine lock therapy study reported by Saunders et al. was done among 22 adult patients undergoing home parenteral nutrition.[89] CRBSI decreased significantly from 5.7/1000 catheter-days to 1.0/1000 after introducing lock therapy.

Quality assessment

A total of 10 studies were eligible for quality assessment. [54, 56, 62, 68, 72, 73, 87-89, 97] None of the studies was of sufficient quality failing predominantly on the minimal criteria. The studies testing an ethanol or taurolidine lock therapy were small and their contribution to the knowledge base of CRBSI prevention is questionable.

6.3.6 DENTAL CARE

A total of two studies were identified.[133, 134] Ramos-Gomez et al. reported on accidental exposure to body fluids in dental care in the USA.[133] The report documents 1'212'071 visits and 428 accidental exposures at four study sites during a 63-month observation period. Dental students and dental assistants had the highest rates of exposure. Syringe needle injuries were the most common type of exposure, while giving injections, cleaning instruments after procedures and drilling were the activities most frequently associated with exposures. Barbosa et al. investigated the development of post-extraction bacteraemia after prophylactic use of CHG.[134] A total of 210 patients were randomly allocated to four groups, one control and three using different methods of CHG-application. Peripheral venous blood samples were

collected at baseline, and 30 seconds and 15 minutes after completion of the tooth extraction. Bacteraemia at 15minutes was significantly higher in the control group than in the CHG groups (23% versus 4%; *P* = 0.005).

6.3.7 OTHERS

A total of eight studies could not have been attributed to any of the above-mentioned topics.[135-142]

Paediatrics: Cohen et al. investigated 50 stethoscopes and 42 otoscopes from paediatricians working in 12 community clinics in Israel. [135] All stethoscopes and 90% of the otoscope handles were colonised with bacteria with staphylococci being the most common pathogen (and of which 54.4% and 45.2% were *S. aureus*, respectively).

Ophthalmology: Lam et al. used agar imprints of the dominant hand of 36 ophthalmologists working in an outpatient clinic in Hongkong.[136] They measured hand contamination before and after patient care. Of 108 imprints, 107 (99.1%) were positive, yielding 15 separate organisms. Gram-negative bacilli were the most common flora, followed by Gram-positive cocci and fungi.

Cystic fibrosis: Festini et al. tested inanimate surfaces and sinks of a cystic fibrosis outpatient clinic monthly over 4 years in Italy.[137] Of 460 environmental specimens, 36.3% were positive for respiratory pathogens (23% of rooms' inert surfaces, 49.5% of sinks). *Achromobacter xylosoxidans* was found in 0.8% of surface samples. *Pseudomonas aeruginosa* was isolated in 22.8% samples. The estimated risk for each non-colonised patient of coming in contact with *P. aeruginosa* on the surfaces at each visit was 5.4‰. Genotyping of a sample of environmental strains revealed a genetic relation between environmental and clinical isolates in most cases.

Diabetic foot clinic: Lagace-Wiens et al. investigated the potential of MRSA transmission in a diabetic foot clinic in the USA.[138] A total of 5103 new patients were admitted during the ten year study period of which 91 had MRSA. Analysis of trends revealed a low-potential, clinic-attributable incidence and a total clinic incidence that was comparable with regional and hospital MRSA rates.

Outpatient setting (non specified): MRSA was also the outcome of interest in a study by Lautenbach et al..[139] They identified eight consecutive outpatients who presented with a skin or soft tissue infection due to MRSA. Of seven household members, three were found to be colonized with MRSA. The mean duration of MRSA colonization among index cases was 33 days (range 14-104), while mean duration of colonization among household cases was 54 days (range 12-95).

Policlinic: Meyer et al. monitored decolonisation of 32 patients colonized with MRSA in Germany.[140] All patients could be decolonised but some needed 2 or more cycles and systemic antibiotics.

Blood pressure cuffs: Matsuo et al. tested blood pressure cuffs for bacterial growth.[141] Fifty-eight tests were performed on the interior of blood pressure cuffs from an outpatient clinic in

Japan. The MRSA contamination rate was 31.4 % and no growth was detected after washing or disinfecting the cuffs.

Antibiotics: Hopkins et al. tested a urinary tract infection clinical practice guideline addressing prescribers of an ambulatory urgent care practice in the USA.[142] The guideline increased the number of appropriate choice of antibiotics to treat uncomplicated UTI from 41/82 to 66/82.

6.4 OUTBREAKS

A total of 33 outbreak reports were identified,[143-173] six in the context with endoscopy, [143, 150, 156, 160, 164, 172] and 16 in haemodialysis.[144-149, 152-154, 157, 158, 161-163, 165, 173]

Table 12. Outbreaks in outpatient care – Strategie NOSOAmbulant: Systematic review on the prevention of healthcare-associated infections in outpatient care

Report	Year	Setting	Country	Cases	Pathogen	Source
Radcliffe [168]	2013	dental clinic	USA	5	HBV	patients/staff
Blanc [143]	1997	endoscopy	Switzerland	35	*P. aeruginosa*	bronchoscope
Srinivasan [150]	2003	endoscopy	USA	39	*P. aeruginosa*	bronchoscopy
Cetre [156]	2005	endoscopy	France	117	enterobacteriaceae	bronchoscope
CDC [160]	2008	endoscopy	USA	6	HCV	staff
Gutelius [164]	2010	endoscopy	USA	6	HCV	anasethetist
Ross [172]	2015	endoscopy	USA	32	MDRE	duodenoscopy
CDC [151]	2003	haematology	USA	99	HCV	multidose vial
Abe [159]	2007	haematology	USA	10	*B. cepacia*	multidose vial
Mendes [169]	2013	haematology	Brazil	31	RSV	community
Jochimsen [144]	1998	haemodialysis	Canada	10	HCV	WHO valve
Le Pogam [174]	1998	haemodialysis	France	4	HCV	not found
Katsoulidou [146]	1999	haemodialysis	UK	9	HCV	not found
Kokubo [148]	2002	haemodialysis	Japan	11	HCV	not found
Furusyo [153]	2004	haemodialysis	Japan	5	HCV	patients/staff
Macedo [157]	2005	haemodialysis	USA	99	HCV	not found
Savey [158]	2005	haemodialysis	France	22	HCV	patients/staff
CDC [161]	2009	haemodialysis	USA	9	HCV	not found
Thompson [163]	2009	haemodialysis	USA	7/5/3/7	HCV	patients/staff
Muleta [173]	2016	haemodialysis	USA	6	HCV	not found
Hutin [145]	1999	haemodialysis	USA	6	HBV	multidose vial
Wang [147]	1999	haemodialysis	USA	10	GNB	WHO valve
Price [149]	2002	haemodialysis	USA	78	polymicrobial	not found
CDC [152]	2004	haemodialysis	USA	42	*M. tuberculosis*	single HCW
Souza [154]	2004	haemodialysis	Brazil	35	*B. cepacia*	water system
Rao [162]	2009	haemodialysis	USA	2	*P. curvatum*	water system
Baraboutis [165]	2010	haemodialysis	Greece	2	*S. agalactiae*	patient/staff

Sydnor [167]	2012	haemotology	USA	12	HPV3	patients
Chu [170]	2014	oncology	USA	51	RSV	visitors
Dobbs [171]	2014	oncology	USA	14	*P. aeruginosa*	staff
Comstock [155]	2004	pain clinic	USA	71	HCV	Reuse of needles/syringes
Comstock [155]	2004	pain clinic	USA	31	HBV	Reuse of needles/syringes
Wong [166]	2010	pain clinic	USA	9	*K. pneumoniae*	multidose vial
CDC [151]	2003	private office	USA	38	HBV	single physician
CDC [151]	2003	private office	USA	12	HCV	staff

HBV: hepatitis B virus; HCV: hepatitis C virus; GNB: Gram-negative bacteria; MDRE: Multidrug-resistant *E. Coli*; RSV: respiratory syncytial virus

6.5 INFECTION PREVENTION AND CONTROL GUIDELINES

Bloodstream infections

Six guidelines for BSI/CRBSI were identified. The most recent available guidelines published by CDC in collaboration with HICPAC in 2011 (*Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011*) addresses both in- and outpatient settings, including homecare, and it replaces the guidelines published for the same purpose in 2002. However, the cited evidence in the guidelines is weak.

Dental care

A surprisingly high number of guidelines and recommendations (21) were identified. In United States, *Guidelines for Infection Control in Dental Health-Care Settings* were published by CDC in 2003 and supplemented in 2016 by a guide summarizing the principles and basic elements of IPC in this setting (*Summary of Infection Prevention Practices in Dental Settings*) with a companion edition of an assessment checklist (*Infection Prevention Checklist for Dental Settings*). In Canada, the Royal college of Dental Office of Ontario published extensive guidelines in 2010 (*Infection prevention and control in the dental office*). Based on this document, the College of Dental Surgeons of British Columbia offered the most recent version in 2012. Australian Dental Association published a detailed guideline document in 2015. Other national policies exist in other countries such as China, United Arab Emirates, India, Malaysia and the UK. They all focus on standard precautions, equipment reprocessing (disinfection and sterilization), and waste management. Only a few documents dedicate separate chapters in blood-borne infection prevention (hepatitis B and C, HIV).

Endoscopy

The *Guideline for Reprocessing Flexible Gastrointestinal Endoscopes* exists since 2003 as a multi-society collaboration guided by the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Healthcare Epidemiology of America (SHEA) and was updated in 2011. An extensive guidebook was also published at a regional level in Italy in 2006 (*Reprocessing degli endoscopi, Servizio Sanitario Regionale Emilia - Romagna*). In 2010, the Swiss societies of gastroenterology, lung diseases, infection prevention and control, and

endoscopy workers published a joint guideline about the correct retreatment of flexible endoscopes.[175]

Haemodialysis
In 2001, the CDC has published a handbook with detailed background information about blood borne infections and their prevention. However, this document lacks cleaning, sterilization and disinfection, as well as IPC prevention in haemodialysis catheters. An extensive illustrative guidebook including all these aspects was published by APIC in 2010. More recently, the US national healthcare safety network (NHSN) has published an assessment tool for haemodialysis settings that participate in the Outpatient Dialysis Center Practices Survey. The third available guideline comes from the Department of Health in Hong Kong. Two review articles were identified. Karkar et al. aimed to summarize existing IPC policies and guidelines regarding hand hygiene, vascular access, catheter-related and blood-borne infection prevention in haemodialysis.[176-178] Kallen et al. summarized major IPC topics in haemodialysis such as HBV, HCV, influenza, BSI and decolonization (of MRSA).[179, 180]

Surgery
IPC guidelines for surgical procedures were developed internationally by WHO and nationally in USA (CDC), UK (NHS), France (Société Française d'Hygiène Hospitalière). Although many SSI surveillance systems such as US NHSN and the German Ambu-KISS include outpatient settings, guidelines do not focus specifically on outpatients. Specific surgery IPC guidance however, was published in Germany, in the UK, and by the Pennsylvania Patient Safety Authority.

7 DISCUSSION

This is the first systematic review of its kind about the burden and prevention of HAI in outpatient care. Although almost 8000 titles and abstracts were identified, most articles were comments, reviews or qualitative work, which were exclusion criteria. Intervention studies eligible for quality assessment were of low to very low quality. Only two studies fulfilled both the minimal criteria and the overall score. The evidence base as reported here includes 156 studies, most of them observational. Only two publications from Switzerland were identified. Due to the short time of the project, it was not possible to perform an extensive search for unpublished data in Switzerland. The Swiss Society for Hospital Hygiene (SSHH) may have known about local projects in outpatient care; the main surveillance and intervention projects from Swissnoso are all in inpatient care.

7.1 Burden of healthcare-associated infections in outpatient care

In ambulatory surgery the range for deep or organ-space SSI is 0.13% to 3.85% (median 1.19%). The proportions for superficial SSI are higher (7.81% and 8.63%, respectively). The range of interventions is large, and often the type of surgery is not indicated. However, ambulatory surgery (other than incisions and excisions in general practice) is generally elective and clean. The median SSI incidence of 1.19% is similar to inpatient outcomes.[181] However, the overall weighted SSI incidence of 0.69% (0.55%-0.84%) is rather low. The

incidence for superficial SSI was high with an incidence of 8.6% in one Australian study in primary care.[31] However, it is not clear if this is generalizable. The same study investigated risk factors and found that excisions from lower legs and feet ($P = 0.009$) and thighs ($P = 0.005$), excisions of basal cell carcinoma ($P = 0.006$) or squamous cell carcinoma ($P = 0.002$), and diabetes ($P < 0.001$) were independent risk factors for wound infection. The study was not very large but sufficiently powered and the findings suggest that more information is needed to assess the quality of surgical interventions in primary care but also that there is room to define a prevention strategy for surgical primary care interventions. A second study identified a high incidence of superficial SSI occurring in a small cohort of outpatient hernia repair. However, this was a small study and given the size, any conclusion is uncertain.[39] SSI prevention strategies in outpatient care follow the same principles as prevention strategies in inpatient care. Given a rather low overall incidence but little information available from primary care, the latter may be a focus for interventions, because such interventions may be performed by non-surgeons and in settings, which may be less equipped for surgery.

Bloodstream infections (catheter-associated or –related, or not) or clinical sepsis were the most measured outcome in outpatient care. The studies can be best stratified by clinical setting: 1) haemodialysis, 2) home parenteral nutrition, and 3) other settings (homecare other than administration of parenteral nutrition, oncology, cardiology). Incidence densities as per patient-months or catheter-days, and infections per patients were the most common reported dimensions. The incidence density of CRBSI in longterm intravascular treatment was 1.82 (1.37-2.28) per 1000 catheter-days, which is comparable to reports from inpatient settings. However, the incidence of CRBSI in longterm intravascular treatment was 20.97 (8.76-33.18) per 100 patients. Thus, although the outcome is relatively rare compared to the duration of treatment, a large number of patients experience CRBSI because of the long duration of such treatments. This is in contrast to patients in acute care, where the incidence density is similar but due to the short duration of treatment, only few patients experience a CRBSI. The incidence density (CI 95%) of CLABSIs in patients undergoing intravascular therapy at home was lower (0.74 [0.27-1.21]) than the incidence density of CRBSI (1.82 [1.37-2.28)]. Usually, CRBSI-rates are lower than CLABSI-rates because “catheter-relation” (the catheter is the proven source for BSI) is a subset of “catheter-association” (a catheter was in place during BSI, but although there is no other potential source, formal relation to the catheter is lacking). Most likely, the reason for this difference is due to the fact that the two studies in home parenteral nutrition are retrospective,[90, 89] while the studies on other therapy indications (with lower risk than parenteral nutrition) were prospective.[60, 78]
Results in homecare parenteral nutrition were reported most commonly as CRBSI per catheter-days with a large range from 0.05/1000 to 10.04/1000 catheter-days but a weighted incidence density of 2.7 (1.89-3.5) per 1000 catheter-days, which is quite similar to inpatient settings.[182] The median incidence density of 0.63/1000 catheter-days in the population of “other” settings that included 6 studies in homecare, two in outpatient oncology, and one in cardiology, is considerably lower of what is known in acute care. One of the two identified Swiss studies reported an incidence density of 1.28 CRBSI/1000 catheter-days in outpatients with pulmonary hypertension treated with continuous iloprost. The reasons for this are not clear but most likely and despite the longer duration of catheters, the limited number of catheter handling may be responsible for this outcome.[183] Parenteral nutrition is a significant risk for CRBSI,[184] and thus, interventions to prevent CRBSI in this patient group may be advisable.

The reported outcomes in haemodialysis are more heterogeneous. All five incidence studies reported very high numbers of patients suffering from one or more BSI (42.23%!).[57, 65, 66, 69, 82] This means that BSI (and in particular CRBSI) is a common event during longterm haemodialysis and as a consequence, resources in this patient group may be well invested. CRBSI incidence densities in patients with a haemodialysis catheter were high as well (3.9/1000 and 6.5/1000 catheter-days, respectively).[45, 48] The incidence of MRSA bacteraemia in this patient group is between 0.17% and 4.30%, which is also high. In summary, BSI and particularly CRBSI is an important adverse outcome, particularly in haemodialysis patients and focusing on CRBSI prevention in this patient group may be advisable.

Patients in haemodialysis not only suffer from BSI but also are at risk for HCV transmission. Nine reports reported about this adverse outcome.[3, 107, 110-112, 115, 118, 121, 174] The incidence of HCV-transmission varies but in some reports is relatively high.[3, 107, 110-112, 115, 118, 121, 174] The reports come from different countries, among others two from France.[3, 118] The incidence as per 100 patient-months in the reports by Girou et al. and Izopet et al. were 0.48 and 0.04, respectively. This is a log10 difference, and does not allow clear conclusion. Interestingly, unspecified peritonitis from peritoneal dialysis was high in the identified two reports (25.9% and 40%, respectively).[128, 129] We are not aware about numbers in Switzerland but given the narrow spectrum of interventions in small studies of low quality, information in this relatively large population in Switzerland may be of interest.

Thirty-three outbreak reports were identified. The settings, countries and pathogens varied. A worrying number of 9 reports on HCV transmissions among haemodialysis patients were identified. This finding is worth mentioning. HCV appears to be a serious risk in the haemodialysis population.

7.2 Prevention strategies

Only a small proportion (35) of the identified studies tested the effectiveness of an intervention. Among those, only two articles fulfilled the minimal criteria as well as the minimal score of the quality assessment. One was an American RCT that found no difference between the use of petrolatum and mupirocin ointments in the treatment of patients after dermatologic surgery;[42] and the other study was a non-controlled before-and-after study testing a multimodal quality improvement intervention among haemodialysis patients.[78] Although studies not meeting the minimum criteria should not be part of the final evidence-base according to ICROMS, we still summarized the findings if the studies met the inclusion criteria. Thus, the conclusions on HAI prevention strategies in outpatient care must be made with caution. The low quality of the intervention studies of this systematic review is not surprising. In the SIGHT project, which summarized findings in acute care settings, only 92 studies out of 47’948 titles and abstracts were of sufficient quality.[13]

Ten studies were RCTs comparing medical products. The majority were small trials with poor reporting on sequence generation and allocation to the study groups. Seven applied a multimodal quality improvement strategy, five measuring ARBSI or CRBSI,[54, 76, 78, 79, 83] one measuring hand hygiene compliance,[124] and one measuring HCV transmission.[115] The settings were diverse: haemodialysis,[76, 78, 83, 115, 124] home parenteral nutrition,[54] and oncology.[79] Together, it can be concluded that multimodal strategies aiming at behaviour

change in patient care work similarly in outpatient as well as in inpatient care.[185] All other intervention studies looked mainly at technology. Four studies investigated the effectiveness of ethanol lock therapy[56, 68, 72, 88] and five studies tested the effect of taurolidine lock therapy[62, 66, 73, 87, 89] in CRBSI prevention, mostly in parenteral nutrition. Given the small size of the studies and the limitation in quality, we cannot conclude that the use either of ethanol or taurolidine locks in home intravenous therapy must be recommended for CRBSI prevention. All other studies testing technology investigated individual interventions and thus, we cannot draw the conclusion to recommend any single intervention reported by any of the studies.

Most interventions in endoscopy tested some technology in the prevention of pathogen transmission. Generally, the most important part in HAI-prevention in endoscopy is retreatment after use of all (flexible) endoscopes. In 2010, the Swiss societies of gastroenterology, lung diseases, infection prevention and control, and endoscopy workers published a joint guideline about the correct retreatment of flexible endoscopes.[175]

7.3 Guidelines and recommendations

Identifying guidelines and recommendations was not the major objective of this report. However, all discussed outcomes are addressed by one or more guidelines, either directly or indirectly. The highest number of recommendations was found for dental care, which contrasts the low number of articles in this field. Most other guidelines about endoscopes or the prevention of BSI are general documents that assume that the prevention measures for HAI are not dependent on the setting but best practice. The only recent guideline identified for Switzerland was about endoscope (reprocessing) and was issued by the Swiss societies of gastroenterology, lung diseases, infection prevention and control, and endoscopy workers. Thus, what is lacking are not necessarily prevention strategies, but implementation documents explaining, how best practice can be established e.g. primary care.

7.4 Conclusions

The identified reports and studies were overall quite heterogeneous and generally of low quality. Most information comes from haemodialysis, home parenteral nutrition, and home intravenous therapy for the outcome (catheter-related) bloodstream infection, but also from SSI. The incidence of BSI among haemodialysis patients is high, but also is important in parenteral nutrition and home care. The incidence of SSI cannot be directly compared to inpatients because surgical procedures are different. Of note, the one study looking at SSI in general practices found quite a high number. Hepatitis C transmissions have been identified for both incidence reports and outbreak reports. The publications though are rather old and it is not clear if the findings are applicable to Switzerland. A small number of studies emphasized the importance of accurate cleaning and disinfection in reprocessing endoscopes. This topic has been addressed already by a joint guideline in Switzerland. There is almost no information from Switzerland. Although countries such as the USA and UK where most of the studies were performed are high-income countries, organisation of outpatient care is different from Switzerland; and thus, findings may not be applicable to Switzerland.

Based on the findings of this systematic review the following may considered first steps in addressing HAI burden and prevention in Swiss outpatient settings:

- Some surveillance strategy should be established to observe healthcare-associated infections in outpatient care in Switzerland, e.g. small surgery in private practice, or bloodstream infection in home infusion therapy
- Given the sparse data on catheter-associated urinary tract infections in home care, a surveillance strategy should be established
- Guidelines should be issued for all homecare and outpatient intravenous therapy in collaboration with the different stakeholders (societies), particularly for the use of home parenteral nutrition and outpatient antibiotic therapy

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