Appendix D: Clinical evidence tables

Study	Brandt 2008-1[13]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=39,589)
Countries and setting	Conducted in Germany; Setting: Data from 44 hospitals in Germany.
Line of therapy	Adjunctive to current care
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People undergoing hip replacement surgery
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People who have had primary hip joint replacement
Exclusion criteria	None detailed
Recruitment/selection of patients	The data utilised for this analysis came from the 2000-2004 KISS surveillance in Germany.
Age, sex and family origin	Age - --: Not detailed. Sex (M:F): Not detailed. Family origin: Not reported
Indirectness of population	No indirectness
Interventions	(n=17,657) Intervention 1: Ultra clean-air theatres . HEPA-filtered laminar airflow ventilation (vertical). Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Mixed airflow area 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: vertical laminar (n=10,966) Intervention 2: Conventional air flow theatres. HEPA-filtered conventional turbulent ventilation. Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Academic or government funding (German national nosocomial infection surveillance system (KISS) is supported by the German Federal Ministry of Health)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES Protocol outcome 1: Deep surgical site infection at 1 month - Actual outcome: Severe surgical site infection at Unclear; OR; 1.63 (95%CI 1.06 to 2.52, Comments: Adjusted OR: multivariate analysis including: sex, age, NNIS risk index variables (ASA score, wound class, duration of operation), frequency of this operative procedure in the hospital, number of hospital beds, academic status of hospital, long term participation in KISS.); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: No mention of space suits; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	Brandt 2008-2[13]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=9,396)
Countries and setting	Conducted in Germany; Setting: Data from 18 hospitals in Germany.
Line of therapy	Adjunctive to current care
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People undergoing knee replacement surgery
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People who have had primary knee replacement surgery
Exclusion criteria	None detailed
Recruitment/selection of patients	The data utilised for this analysis came from the 2000-2004 KISS surveillance in Germany.
Age, sex and family origin	Age - --: Not detailed. Sex (M:F): Not detailed. Family origin: Not reported
Interventions	(n=5,993) Intervention 1: Ultra clean-air theatres . HEPA-filtered laminar airflow ventilation (vertical). Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Mixed airflow area 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: vertical laminar (n=3,403) Intervention 2: Conventional air flow theatres. HEPA-filtered conventional turbulent ventilation. Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Academic or government funding (German national nosocomial infection surveillance system (KISS) is supported by the German Federal Ministry of Health)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES

Protocol outcome 1: Deep surgical site infection at 1 month
- Actual outcome: Severe surgical site infection at Unclear; OR; 1.76 (95%CI 0.8 to 3.85, Comments: Adjusted OR: multivariate analysis including: sex, age, NNIS risk index variables (ASA score, wound class, duration of operation), frequency of this operative procedure in the hospital, number of hospital

beds, academic status of hospital, long term participation in KISS.); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: No mention of space suits; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	Breier 2011-1[14]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=33,463)
Countries and setting	Conducted in Germany; Setting: Data from 48 hospitals in Germany.
Line of therapy	Adjunctive to current care
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People undergoing hip replacement
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People who have had primary hip joint replacement due to arthrosis
Exclusion criteria	Revision joint replacement surgeries were not included in the analysis.
Recruitment/selection of patients	The data utilised for this analysis came from the KISS surveillance 2004-2009 in Germany.
Age, sex and family origin	Age - --: Not detailed. Sex (M:F): 13158/20305. Family origin: Not reported
Indirectness of population	No indirectness
Interventions	(n=23,017) Intervention 1: Ultra clean-air theatres . Laminar airflow system. Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Mixed airflow area (Subgroup data available if required). 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Mixed type (n=10,466) Intervention 2: Conventional air flow theatres. Non laminar flow ventilation systems installed from 1990 and 2004. . Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Academic or government funding (German national nosocomial infection surveillance system (KISS) is supported by the German Ministry of Health)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES Protocol outcome 1: Deep surgical site infection at 1 month	

- Actual outcome: Severe surgical site infection at Unclear; OR; 1.1 (95%CI 0.56 to 2.17, Comments: Adjusted for sex, age, duration of operation, ASA score); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: Space suits not mentioned; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	Breier 2011-2[14]
Study type	Non randomised study
Number of studies (number of participants)	1 (n=7749)
Countries and setting	Conducted in Germany; Setting: Data from 41 hospitals in Germany.
Line of therapy	Adjunctive to current care
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People who have undergone hip replacement due to trauma
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People who have had primary hip joint replacement due to trauma
Exclusion criteria	Revision joint replacement surgeries were not included in the analysis.
Recruitment/selection of patients	The data utilised for this analysis came from the KISS surveillance in Germany.
Age, sex and family origin	Age - --: Not reported. Sex (M:F): 2090/5659. Family origin: Not reported
Indirectness of population	No indirectness
Interventions	(n=6,513) Intervention 1: Ultra clean-air theatres . Laminar airflow system. Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Mixed airflow area 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Mixed type (n=1,236) Intervention 2: Conventional air flow theatres. Non laminar flow ventilation systems installed from 1990 and 2004. . Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Academic or government funding (German national nosocomial infection surveillance system (KISS) is supported by the German Ministry of Health)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES Protocol outcome 1: Deep surgical site infection at 1 month	

- Actual outcome: Severe surgical site infection at Unclear; OR; 1.28 (95%CI 0.67 to 2.43, Comments: Adjusted for sex, age, duration of operation, ASA score); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: Space suits not mentioned; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	Breier 2011-2[14]
Study type	Non-randomised study
Number of studies (number of participants)	1 (n=20,554)
Countries and setting	Conducted in Germany; Setting: Data from 38 hospitals in Germany.
Line of therapy	Adjunctive to current care
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People undergoing knee prosthesis procedures
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People who have had primary knee joint replacement
Exclusion criteria	Revision joint replacement surgeries were not included in the analysis.
Recruitment/selection of patients	The data utilised for this analysis came from the KISS surveillance in Germany.
Age, sex and family origin	Age - --: Not detailed. Sex (M:F): 6559/13995. Family origin: Not reported
Indirectness of population	No indirectness
Interventions	(n=14,456) Intervention 1: Ultra clean-air theatres . Laminar airflow system. Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Mixed airflow area (Specific laminar flow size data available if required). 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Mixed type (n=6,098) Intervention 2: Conventional air flow theatres. Non laminar flow ventilation systems installed from 1990 and 2004. . Duration During joint replacement surgery. Concurrent medication/care: Background treatment dependent on local policy in the hospital and a person's specific clinical needs. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Academic or government funding (German national nosocomial infection surveillance system (KISS) is supported by the German Ministry of Health)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES	

Protocol outcome 1: Deep surgical site infection at 1 month - Actual outcome: Severe surgical site infection at Unclear; OR; 0.95 (95%CI 0.37 to 2.41, Comments: Adjusted for sex, age, duration of operation, ASA score); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Key confounders: Space suits not mentioned; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	Dale 2009[18]
Study type	Non-randomised study
Number of studies (number of participants)	1 (n=97,344)
Countries and setting	Conducted in Norway; Setting:
Line of therapy	Part of comparison
Duration of study	Follow up (post intervention): 0-20 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People who underwent primary total hip replacement
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People who underwent primary total hip replacement.
Exclusion criteria	In order to have homogeneous subgroups concerning type of fixation, 4,392 hybrids and 3,727 reversed hybrids were excluded. 3,730 arthroplasties had incomplete data on fixation method or were registered with different brands of cement for different components, and were also excluded. 1,689 additional THAs were excluded because of missing values for other adjustment variables.
Recruitment/selection of patients	Norwegian Arthroplasty Register (NAR) data utilised. From September 15th 1987 to January 1st 2008.
Age, sex and family origin	Age - --: Not detailed. Sex (M:F): 70% male, 30% female. Family origin: Not detailed
Indirectness of population	No indirectness
Interventions	(n=45,620) Intervention 1: Ultra clean-air theatres . Laminar flow ventilation. Duration During joint replacement surgery. Concurrent medication/care: Background treatment depended on local hospital guidelines. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not stated / Unclear (n=48,338) Intervention 2: Conventional air flow theatres. Reported as ordinary airflow ventilation. Duration During joint replacement surgery. Concurrent medication/care: Background treatment depended on local hospital guidelines. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES	

Protocol outcome 1: Return to theatre at within 3 months - Actual outcome: Revision due to infection at within 1 year of surgery; RR; 1.3 (95%CI 1.1 to 1.5, Comments: Adjusted risk ratio estimates for sex, age, diagnosis, type of prosthesis, duration of operation, antibiotic prophylaxis systemically, and type of fixation); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Key confounders: No mention of space suits; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Deep surgical site infection at 1 month; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	Fitzgerald jr 1992[20]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=5,868)
Countries and setting	Conducted in USA; Setting: Wayne State University School of Medicine, Detroit, USA. All procedures performed by one group of surgeons with standardised protocols.
Line of therapy	Adjunctive to current care
Duration of study	Follow up (post intervention): 1 year to 8 years.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Primary hip or knee joint replacement
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Age, sex and family origin	Age - --: Not detailed. Sex (M:F): Define. Family origin: Not detailed
Indirectness of population	No indirectness
Interventions	(n=2,848) Intervention 1: Ultra clean-air theatres . Horizontal ultra clean-air theatre. Duration During joint replacement surgery. Concurrent medication/care: Prophylactic antibiotic therapy utilised. Traffic in theatre controlled. . Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: horizontal laminar (n=3,202) Intervention 2: Conventional air flow theatres. Conventional ventilated operating room with turbulent airflow. Duration During joint replacement surgery. Concurrent medication/care: Prophylactic antibiotic therapy utilised. Traffic in theatre controlled. . Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES Protocol outcome 1: Deep surgical site infection at 1 month - Actual outcome: Deep surgical site infection at From 1 to 8 years follow-up; Group 1: 8/2848, Group 2: 10/3202 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,	

Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study (subsidiary papers)	Lidwell 1982[35] (Lidwell 1987[33])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=8136)
Countries and setting	Conducted in Sweden, United Kingdom; Setting: Hospitals in England (11), Scotland (4), and Sweden (4)
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 4 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People undergoing total hip or knee joint replacement
Stratum	Overall
Subgroup analysis within study	Post-hoc subgroup analysis: People administered prophylactic antibiotics
Inclusion criteria	People undergoing total hip or knee joint replacement.
Exclusion criteria	None detailed
Recruitment/selection of patients	Recruited from 1974 until 1979.
Age, gender and ethnicity	Age - --: Not detailed. Gender (M:F): Not detailed. Ethnicity: Not detailed
Further population details	
Indirectness of population	No indirectness
Interventions	(n=1279) Intervention 1: Ultra clean-air theatres . Ultra-clean air operating theatres. . Duration Operative period. Concurrent medication/care: Conventional clothing. All people in this subgroup were given prophylactic antibiotics. . Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable (Mixed). (n=2968) Intervention 2: Conventional air flow theatres. Operating theatre with positive-pressure air supply.. Duration During surgery. Concurrent medication/care: Conventional operating-room clothing. Prophylactic antibiotics utilised. . Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable (Mixed). (n=3922) Intervention 3: Ultra clean-air theatres . Ultra-clean air operating theatres. . Duration Operative period. Concurrent medication/care: Some hospitals utilised body exhaust ventilated suits for the operation. Prophylactic antibiotics given as decided by surgeon. . Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not stated / Unclear

	(n=4133) Intervention 4: Conventional air flow theatres. Operating theatre with positive-pressure air supply.. Duration During surgery. Concurrent medication/care: Conventional operating-room clothing. Prophylactic antibiotic use decided by surgeon. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable (n=2863) Intervention 5: Ultra clean-air theatres . Ultra-clean air operating theatres. . Duration Operative preiod. Concurrent medication/care: Everyone in this group was given prophylactic antibiotics. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not stated / Unclear
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES: ANTIBIOTICS & CONVENTIONAL CLOTHING versus CONVENTIONAL AIR FLOW THEATRES: ANTIBIOTICS

Protocol outcome 1: Deep surgical site infection at 1 month
- Actual outcome: Confirmed sepsis at at a median of 2.5 years; Group 1: 9/1279, Group 2: 24/2968
Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES

Protocol outcome 1: Deep surgical site infection at 1 month
- Actual outcome: Confirmed sepsis at at a median of 2.5 years; Group 1: 3922/23, Group 2: 4133/63
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High, Other 1 - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES: ANTIBIOTICS & ANY CLOTHING versus CONVENTIONAL AIR FLOW THEATRES: ANTIBIOTICS

Protocol outcome 1: Deep surgical site infection at 1 month
- Actual outcome: Confirmed sepsis at at a median of 2.5 years; Group 1: 2863/10, Group 2: 2968/24
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - High; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre

study	at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	**Namba 2012[46]**
Study type	Non-randomised study

Number of studies (number of participants)	1 (n=30,491)
Countries and setting	Conducted in USA; Setting: 46 medical centres in six regions in the United States. Data from Kaiser Permanente Total Joint Replacement Registry (TJRR)
Line of therapy	Part of comparison
Duration of study	Follow up (post intervention): 1 year postoperative follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People who underwent total hip replacement
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Primary elective total hip replacements
Exclusion criteria	None detailed
Recruitment/selection of patients	All primary elective THRs registered in the TJRR from 1st April 2001 until 30th December 2009 2001 and 30 December 2009
Age, sex and family origin	Age - Mean (SD): 65.5 (11.8). Sex (M:F): 13017/17474. Family origin: Not detailed
Indirectness of population	No indirectness
Interventions	(n=8,478) Intervention 1: Ultra clean-air theatres . Laminar flow operating theatres. Duration During THR surgery. Concurrent medication/care: Background treatment was local orthpaedic centre policy. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not stated / Unclear (n=22,013) Intervention 2: Conventional air flow theatres. No details, defined as not laminar flow. Duration During THR surgery. Concurrent medication/care: Background treatment was local orthpaedic centre policy. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Academic or government funding (No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article).
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES Protocol outcome 1: Deep surgical site infection at 1 month - Actual outcome: Deep surgical site infection	

at 1 year postoperatively; HR; 1.08 (95%CI 0.77 to 1.53, Comments: Univariate Cox's proportional hazard regression model. All variables found to be independently associated with the outcome were included in the multivariable Cox models but laminar flow was not. Factors investigated: age, sex, race, body mass index (BMI), weight, diabetic status, ASA score, diagnosis (osteoarthritis, rheumatoid arthritis, post-traumatic arthritis, osteonecrosis, and other), yearly volumes for hospitals, surgeon annual volume, surgeon arthroplasty fellowship training status, unilateral or bilateral procedure, anaesthesia (epidural, general, spinal, other), infection prophylaxis, use of a body exhaust system, surgical approach and duration of surgery); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	**Pedersen 2010[53]**
Study type	Non randomised study
Number of studies (number of participants)	1 (n=80,756)

Countries and setting	Conducted in Denmark; Setting: All orthopedics departments performing total hip replacement, including private hospitals from Jan 1st 1995 to Dec 31st 2008. Danish Hip Arthroplasty Registry data
Line of therapy	Part of comparison
Duration of study	Other: Data on surgery undertaken Jan 1st 1995 and Dec 31st 2008.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People who underwent total hip athroplasty
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People undergoing primary total hip arthrosplasty
Exclusion criteria	None detailed
Recruitment/selection of patients	Nationwide clinical database of all primary THAs performed in Denmark
Age, sex and family origin	Age - Other: median group 70-79. Sex (M:F): 33925/46831. Family origin: Not detailed
Indirectness of population	No indirectness
Interventions	(n=72,423) Intervention 1: Ultra clean-air theatres . Laminar air flow ventilation. Duration During joint replacement surgery. Concurrent medication/care: Followed local orthopaedic department policy. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not stated / Unclear (n=8,333) Intervention 2: Conventional air flow theatres. Conventional ventilation. Duration During joint replacement surgery. Concurrent medication/care: Followed local orthopaedic department policy. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES

Protocol outcome 1: Deep surgical site infection at 1 month
- Actual outcome: Revision due to infection at Median follow-up: 4.6 years (0-14); RR; 0.9 (95%CI 0.7 to 1.14, Comments: Adjusted for type of anaesthesia, ossification prophylactic treatment, duration of surgery, fixation technique, previous surgery to same hip, primary diagnosis for THA, Charlson co-morbidity index, age, sex, calendar year of surgery.
);
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover

- Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	Pinder 2016[54]
Study type	Non-randomised study
Number of studies (number of participants)	1 (n=114,967)
Countries and setting	Conducted in United Kingdom; Setting: 184 NHS hospitals were surveyed
Line of therapy	Part of comparison
Duration of study	Follow up (post intervention): Outcome follow-up was 90 days after surgery
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People undergoing hip arthroplasty
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People undergoing hip arthroplasty
Exclusion criteria	Hospitals where <20 hemiarthroplasties performed annually, elective hospitals, children's hospitals, treatmen centres, non orthpaedic hospitals.
Recruitment/selection of patients	Questionnaires sent to 184 NHS hospitals who conduct orthopaedic trauma surgery
Age, sex and family origin	Age - Other: Not detailed. Sex (M:F): Not detailed. Family origin: Not detailed
Indirectness of population	No indirectness
Interventions	(n=73,112) Intervention 1: Ultra clean-air theatres . Laminar flow ventilation utilised throughout the study period for hemiarthroplasty. Duration During hemiarthroplasty. Concurrent medication/care: Dependent on the hospital policy. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not stated / Unclear (n=12,497) Intervention 2: Conventional air flow theatres. Plenum ventilation throughout the study period.. Duration During hemiarthroplasty surgery. Concurrent medication/care: Dependent on the hospital policy. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	No funding (No funding from a commercial entity.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES Protocol outcome 1: Deep surgical site infection at 1 month - Actual outcome: Surgical Site Infection at Within 90 days; OR; 1.45 (95%CI 1.17 to 1.8) ( ) , Comments: Confounding variables adjusted for in analysis	

though it is unclear what these factors were. The following factors were mentioned: age, sex, Charlson co-morbidity index, socio-economic deprivation, and number of trauma operations performed.; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge

Study	Song 2012[59]
Study type	RCT (randomised; Parallel)
Number of studies (number of participants)	1 (n=6,848)
Countries and setting	Conducted in South Korea; Setting:
Line of therapy	Part of comparison
Duration of study	Follow up (post intervention): At least 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: People who underwent total knee arthroplasty of total hip arthroplasty
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People who underwent total knee arthroplasty of total hip arthroplasty. All hospitals must have had 1 full-time infection control practitioner on staff.
Exclusion criteria	People having preoperative antibiotics for infections.
Recruitment/selection of patients	26 hospitals participating in the Korean Nosocomial Infections Surveillance System (KONIS).
Age, sex and family origin	Age - --: Not detailed. Sex (M:F): Not detailed. Family origin: Not detailed
Indirectness of population	No indirectness
Interventions	(n=4,188) Intervention 1: Ultra clean-air theatres . High-efficiency particulate air HEPA-filtered laminar airflow ventilation. Duration Airflow during joint replacement surgery. Concurrent medication/care: Antimicrobial prophylaxis administered. . Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not stated / Unclear 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not stated / Unclear (n=2,086) Intervention 2: Conventional air flow theatres. Conventional turbulent ventilation with HEPA-filtered air. Duration Airflow during joint replacement surgery. Concurrent medication/care: Parenteral antimicrobial prophylactic antibiotics were administered. Indirectness: No indirectness Further details: 1. Size of the vertical laminar airflow area:: Not applicable 2. Theatre use: Not stated / Unclear 3. Type of ultra clean air flow system: Not applicable
Funding	Academic or government funding (The Korean Nosocomial Infections Surveillance System is supported by a grant from the Korean Centers for Disease Control and Prevention.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ULTRA CLEAN-AIR THEATRES versus CONVENTIONAL AIR FLOW THEATRES Protocol outcome 1: Deep surgical site infection at 1 month	

- Actual outcome: Severe surgical site infection at 1 year after surgery; OR; Not significant, Comments: Stepwise multiple logistic model used. Risk factors with a p value of less than 0.1 were included in the initial model. p values of less than 0.5 were considered statistically significant in multivariate analysis. Factors included: surgeries performed each month, OR airflow, sex, preoperative hospital stay, diabetes, anaesthesia, revision surgery, duration of surgery, trauma, other infections. ; Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Mortality at 30 day ; Quality of life at 1 month; Superficial surgical site infection at 1 month; Return to theatre at within 3 months; Hospital readmissions at within 90 days; Length of stay at time until hospital discharge