Appendix 1. Evidence table for LCA studies

Study reference	Journal	Study characteristics	Methods	Data collection	Outcomes	Interpretation	Comments
Sherman (2012)	Anesthesia & Analgesia Journal information The "The Global Standard in Anesthesiology," provides practice-oriented, clinical research you need to keep current and provide optimal care to your patients. Brings peer reviewed articles on the latest advances in drugs, preoperative preparation, patient monitoring, pain management, pathophysiology, and many other timely topics. Critical review: Peer reviewed, not a specific LCA journal.	Type of study: LCA Objective: To perform an initial life cycle assessment on 5 anesthetic drugs – sevoflurane, desflurane, isoflurane, N_2O and propofol – to inform clinician drug selection on this basis. LCA-method: Attributional LCA Setting and country: Hospital in the US Facility: Yale-New Haven Hospital Years of data collection: - Surgical discipline(s): Anaesthesia Funding and conflict of interest: No funding mentioned. The authors state no conflicts of interest.	Goal and scope[1]: To compare the environmental impacts of 5 anaesthetic drugs to inform clinicians in drug selection. Functional unit(s)[2]: 1 minimum alveolar concentration (MAC), or MAC-equivalent for propofol, for maintenance anesthesia for an average 70 kg adult patient for 1 hour (1 MAC-h) System boundaries: Cradle to grave Included stages: Raw material extraction, production, transport, drug delivery, disposal Stated excluded components: Baseline energy requirement for the anaesthesia machine (considered to be constant for all drugs), basic disposables (such as: endotracheal tubes, circuits, CO_2 absorbents) were considered to be equivalent. Inventory database: EcoInvent Allocation: No Normalization & Weighting: No	An LCA was conducted to compare the environmental impact of 5 types of anaesthetic drugs – sevoflurane, desflurane, isoflurane, N_2O and propofol – to inform clinician drug selection on this basis. The functional unit was 1 minimum alveolar concentration (MAC), or MAC-equivalent for propofol, for maintenance anesthesia for an average 70 kg adult patient for 1 hour (1 MAC-h). Included stages in the life cycle of the drug were raw material extraction, production, transport (to health care facilities), drug delivery (to the patient) and disposal. Besides that, the waste gas of the agent in the atmosphere and N_2O release were considered (O_2/air admixture and N_2O/O_2 admixture for administration were considered). Data collection on transport, drug transportation, energy requirements and disposal was specific to the Yale-New Haven Hospital. EcoInvent was used as primary data source. When data regarding the drugs was unavailable in EcoInvent, proxies that best matched the production characteristics of the drug were used. Characterization methods:	1. Climate Change The results on climate change are only graphically reported in Figure 1 (Sherman, 2012). The figure shows two graphs, whereas panel A shows the results on the life cycle (as mentioned before) of the drug, agent release and N_2O release and panel B shows nonwasted anaesthetic gas emissions (life cycle) from drug manufacturing, transport, drug delivery and disposal. Considering the N_2O/O_2 admixture, desflurane has the biggest impact with approximately 56,000 g CO_2e including agent release and N_2O release, followed by sevoflurane with 46,000 g CO_2e, isoflurane 24,000 g CO_2e and propofol. The emissions of propofol can not be depicted from the figure (too small). When choosing for the O_2/air admixture, desflurane has the greatest impact followed by isoflurane and sevoflurane. Regarding the life cycle, desflurane has the biggest impact of 700 g CO_2e, followed by sevoflurane (430 g CO_2e), isoflurane (200 g CO_2e) and propofol (25 g CO_2e).	Overall desflurane has the greatest impact on the outcome climate change. Propofol is the best choice considering this outcome. The admixture of O_2/air instead of NO_2/O_2 is the better environmental choice. The biggest hotspot of the GHG emissions is the N_2O release, followed by agent release and lastly the life cycle of the agent. When choosing for the O_2/air admixture, desflurane has the greatest impact followed by isoflurane and sevoflurane. The change in impact between isoflurane and sevoflurane when using the O_2/air mixture instead of NO_2/O_2 is attributable to the higher GWP for isoflurane and conversely the higher gas flow requirements for sevoflurane when using N_2O/O_2 (more N_2O is used). Considering the lifecycle of the agents, for desflurane the greatest hotspot is the agent manufacturing, followed by delivery of the drug to the patient (electricity required for volatilization) and N_2O manufacturing. Sevoflurane and isoflurane have more similar profiles, with the greatest hotspot being N_2O manufacturing, followed by agent manufacturing and packaging. GHG impacts of	Authors conclusion The results reiterate previous published data, while providing the life cycle data on the anaesthetic drugs. Clinicians should consider the full environmental and human health impacts from anaesthetic use. Limitations study There is uncertainty regarding the synthesis of propofol and the volatile drugs and results should be carefully interpreted. It is not clear whether the manufacturing process of the disposables used for propofol administration is included in the analysis.

Study reference	Journal	Study characteristics	Methods	Data collection	Outcomes	Interpretation	Comments
			Impacts reported: Yes Contribution analysis: Yes Scenario analysis: Yes Comparative analysis: Yes Sensitivity analysis: No Uncertainty analysis: No Variance analysis: No	Sulbaeck et al. 2010, IPCC	2. Waste No results in this study. 3. Medicine residue in water No results in this study. 4. Human toxicity No results in this study. 5. Ozone Depletion No results in this study.	propofol are comparatively quite small and most of it is attributable to the drug delivery to the patient (energy needed to operate the syringe pump) and waste management.	
Thiel (2018)	American Journal of Public Health (AJPH) Journal information The American Journal of Public Health is a peer-reviewed public health journal published by the American Public Health Association that covers health policy and public health. The journals' stated mission is "to advance public health research, policy, practice, and education". Critical review: Peer reviewed, not a specific LCA journal.	Type of study: LCA Objective: To determine the carbon footprint of various sustainability interventions used for laparoscopic hysterectomy. LCA-method: Hybrid-LCA Setting and country: Hospital USA Facility: Magee-Womens Hospital of the University of Pittsburgh Medical Center (UPMC) Years of data collection: 2016 Surgical discipline(s): Obstetrics & Gynaecology, Anaesthesiology Funding and conflict of interest: None stated.	Goal and scope[1]: To examine the efficacy of interventions to reduce GHG emissions in the OR with the goal to improve the emission rate of the healthcare sector and thereby human health. Functional unit(s)[2]: One laparoscopic hysterectomy System boundaries: Cradle to grave, intraoperative period Included stages: Production, transport, energy use, pharmaceuticals, reuse, disposal Stated excluded components: Infrastructure including machines and building; chemical manufacturing and cleaning of products; hot water use Inventory database: EcoInvent, USLCI Allocation: Impacts of resuable materials and	A hybrid LCA was conducted to examine the efficacy of sustainable interventions to reduce GHG emissions in the OR. Baseline emissions for laparoscopic hysterectomy were calculated from an average of 17 hysterectomies extracted from a previous study in the USA (Thiel, 2017). Further data was obtained from EIO-LCA and EcoInvent. Life cycle GHGs were calculated for interventions regarding anaesthetics (type of anaesthetic), surgical materials and energy. To model anaesthetic interventions, an average anaesthetic duration of 150 minutes was assumed. The outcome measure was climate change. Characterization methods: TRACI	1 Climate Change The baseline case is an average of the combination of anaesthetic approaches used in each of the 17 laparoscopic hysterectomies. This resulted with anaesthesia in 562 kg CO_2e and without anaesthesia in 402 kg CO_2e. Using desflurane only, resulted in an emission of 762 kg CO_2e, desflurane with NO_2 in 757 kg CO_2e, sevoflurane with NO_2 in 416 kg CO_2e, sevoflurane only in 410 kg CO_2e and propofol only in 402 kg CO_2e. 2. Waste No results in this study. 3. Medicine residue in water No results in this study. 4. Human toxicity No results in this study. 5. Ozone Depletion No results in this study.	Volatile anaesthetics have a greater environmental impact compared to intravenous anaesthetics. The use of N_2O increases this impact and should be avoided if possible. If a volatile anaesthetic should be used, sevoflurane seems to be the most environmentally sound choice.	Authors conclusion Available interventions can be used with promising results to reduce the carbon footprint. Limitations study Uncertainty due to limited or lack of LCA data in healthcare. One location included in calculations, poor generalizability. More interventions possible than studied.

Study reference	Journal	Study characteristics	Methods	Data collection	Outcomes	Interpretation	Comments
			equipment were apportioned based on estimated lifespan/number of uses. Normalization & Weighting: No Impacts reported: Yes Contribution analysis: Yes Scenario analysis: Yes Comparative analysis: Yes Sensitivity analysis: No Uncertainty analysis: No Variance analysis: No				
McGain (2021)	Anesthesiology Journal information ANESTHESIOLOGY is the official journal of the American Society of Anesthesiologists. Their mission is promoting scientific discovery and knowledge in perioperative, critical care and pain medicine to advance patient care. Critical review: Peer reviewed, not a specific LCA journal.	Type of study: LCA Objective: To examine the carbon dioxide equivalent emissions associated with general anaesthesia, spinal anaesthesia and combined (general and spinal) anaesthesia during total knee replacement. LCA-method: Attributional LCA Setting and country: Hospital Australia Facility: Williamstown Hospital, Western Health, Melbourne, Australia Years of data collection: 2019 Surgical discipline(s): Anaesthesia	Goal and scope[1]: To aim to quantify the carbon dioxide equivalent emissions of general and spinal and combined anaesthesia to reduce GHG production and reduce the threat of climate change in healthcare. Functional unit(s)[2]: All anaesthesia for a total knee replacement. System boundaries: Cradle to grave Included stages: Raw material extraction, production, transport, drug usage phase, disposal Stated excluded components: HVAC and surgical equipment data. Inventory database:	An LCA was conducted to examine the carbon dioxide equivalent emissions associated with general anaesthesia (propofol and sevoflurane), spinal anaesthesia and combined (general and spinal) anaesthesia during total knee replacement. The functional unit was all anaesthesia for a total knee replacement. Anaesthesia data were obtained from 30 patients undergoing total knee replacement in an Australian hospital. Data from literature and databases such as EcoInvent and Australian Life Cycle Inventory were used. The outcome measures were climate change and waste. Characterization methods: -	1. Climate Change Three hours of propofol at 700 mg/h will result in less than 50 g CO_2e. The average/mean duration of spinal and combined anaesthesia were approximately 40 and 30 minutes more than general. This leads to increased energy use (0.8 and 0.6 kg CO_2e) and oxygen use (0.6 kg CO_2e). Spinal anaesthetic of shorter duration will result in a decrease of 1.4 kg CO_2e. The total emissions of general anaesthesia were 14.9 kg CO_2e (95% CI, 9.7 to 22.5); spinal anaesthesia 16.9 kg CO_2e (95% CI, 13.2 to 20.5); and combination anaesthesia 18.5 kg CO_2e (95% CI, 12.5 to 27.3). The average anaesthesia duration times were: general 161 (113 to 193) min, spinal 200 (168 to 288)	The study shows total intravenous anaesthesia has the lowest environmental impact compared to general anaesthesia with sevoflurane, spinal anaesthesia and the two combined. The latter are comparable. Great contributors are the agent itself, single-use products and energy-use. International comparisons show reusables are a good alternative for single-use products when using a renewable energy sources (e.g. nuclear/wind/solar energy).	Authors conclusion Carbon footprints for knee replacement anaesthesia (general, spinal, combined) were similar, with significant overlap between the CIs. Limitations study Small study with 30 samples, however possibly not more needed. One centre, difficult to generalize results. Lack of other anaesthetics (e.g. desflurane, intravenous anaesthesia separately).

Study reference	Journal	Study characteristics	Methods	Data collection	Outcomes	Interpretation	Comments
		Funding and conflict of interest: In-kind support (no cash funding) was provided solely from Western Health Anaesthesia Department sources (Melbourne, Australia). The authors declare no conflict of interest.	EcoInvent, the Australian Life Cycle Inventory Allocation: No Normalization & Weighting: No Impacts reported: Yes Contribution analysis: Yes Scenario analysis: No Comparative analysis: Yes Sensitivity analysis: Yes Uncertainty analysis: Yes, Monte Carlo analysis Variance analysis: No		min, combination 189 (128 to 241) min. Electricity for the patient air warmer was responsible for at least 2.46 kg CO_2e for all approaches. Total single-use plastics, glass and so forth were responsible for 3.5 (general), 3.4 (spinal) and 4.3 (combination) CO_2e. The majority was from single-use plastics. Pharmaceuticals beyond gases were responsible for 1.2 to 1.3 CO_2e (7 to 8%). For general anaesthesia, sevoflurane was responsible for an average of 4.7 kg CO_2e (32%), range 2.7 to 8.6 kg CO_2e. The patient who received propofol represented the minimum of 8.4 kg CO_2e in the general anaesthesia group. In the combination group sevoflurane contributed for 3.1 kg CO_2e (17%), range 0.6 to 10 kg CO_2e. Fro spinal and combination anesthesia, washing an sterilizing reusable gowns, plastic spinal trays and so forth contributed for 4.5 kg and 4.0 kgCO_2e, respectively. Oxygen use was important for spinal, resulting in 2.8 kg CO_2e (16%) with flow rates from 6 to 10 l/min (compared to 0.5 to 3.1 l/min for general and combination).		

Study reference	Journal	Study characteristics	Methods	Data collection	Outcomes	Interpretation	Comments
					International comparisons were made by changing energy sources. Australia and China are more coal reliant, where the European Union (and UK) are more dependent on nuclear and hydro/wind/solar sources. This modelling changed the CO_2e for washing and sterilizing reusable equipment and electricity for patient warming. In the EU spinal anaesthesia has a carbon footprint of approximately 60% (9.9/16.9 CO_2e) of that in Australia. The general anaesthesia in Australia (total intravenous) is less than the EU average (8.4 kg vs. 11.9 kg CO_2e). The minimum for spinal anaesthesia in Australia is higher than the EU average (14.7 vs 9.9 kg CO_2e), due to high carbon intensity electricity required to clean reusable anaesthesia equipment. 2. Waste The total masses of single-use equipment were: general anaesthesia (mean 996 g; interquartile range 873 to 1,033 g; range 725 to 1,392 g), spinal anaesthesia (mean 997 g; interquartile range 934 to 1,076 g; range 885 to 1,184 g) and combination anaesthesia (mean 1,237g; interquartile		

Study reference	Journal	Study characteristics	Methods	Data collection	Outcomes	Interpretation	Comments
					range 1,100 to 1,285 g; range 1,009 to 1,678 g). The majority of the waste was from total plastics: average for general anaesthesia 783/996 g (78%); spinal 729/997 g (73%); and combination 932/1,237 (75%). Glass was the next most discarded material. 3. Medicine residue in water No results in this study. 4. Human toxicity No results in this study. 5. Ozone Depletion No results in this study.		
Hu (2021)	Resources, conservation & recycling Journal information Contributions from research, which consider sustainable management and conservation of resources. The journal emphasizes the transformation processes involved in a transition toward more sustainable production and consumption systems. Emphasis is upon technological, economic, institutional and policy aspects of specific resource management practices. Critical review: Peer reviewed article, LCA mentioned in scope of journal.	Type of study: LCA Objective: To estimate the carbon footprint of sevoflurane, isoflurane, desflurane and intravenous propofol and to provide evidence of the potential impact of Vapour Capture Technology. LCA-method: Attributional LCA Setting and country: UK Facility: - Years of data collection: 2018 Surgical discipline(s): Anaesthesia	Goal and scope[1]: The carbon footprint of general anaesthetics at the national level is presented to inform policy. Functional unit(s)[2]: 1 minimum alveolar concentration hour (MAC-h), or MAC-h equivalent for propofol. System boundaries: Cradle to grave Included stages: Raw material extraction, manufacturing, packaging, use, waste gases Stated excluded components: Transport, energy consumptions of using general anaesthetics in the	A life cycle inventory was conducted to calculate the carbon footprint of general anaesthetics. Thereby the potential impact of Vapour Capture Technology was provided. The functional unit for the general anaesthetics in the LCI analysis was 1 minimum alveolar concentration hour (MAC-h), or MAC-h equivalent for propofol. Values of 2.2%, 1.2% and 6.7% respectively for sevoflurane, isoflurane and desflurane were used as basis of the modelling. Raw material extraction, manufacturing, packaging, transport, use and disposal were included in the analysis. Ecoinvent was used as an inventory database. Since information on synthesizing general	1. Climate Change The results on climate change are graphically shown in figure 2-4 (Hu, 2021). Three different scenarios are studied: 1. Fresh gas flow of 1L (UK) or 2L (US)/min, % gas flow O_2/N_2O = 40/60 2. Fresh gas flow of 1L (UK) or 2L (US)/min, % gas flow O_2/N_2O = 100/0 3. Fresh gas flow of 0.5L/min, % gas flow O_2/N_2O = 100/0 Desflurane has the highest carbon footprint in all scenarios, however sevoflurane is close in scenario 1. Propofol has the lowest carbon footprint, half of this is due to energy used to manufacturing the syringes. Scenario 2 (eliminating NO_2) leads to lower carbon footprints for	Propofol use results in a low carbon footprint. It can be reduced by using renewable energy in the manufacturing process. Influence from propofol drug waste (e.g. urine excretion in sewerage water) has not been studied. Desflurane has the highest GWP and leads to a high carbon footprint compared to isoflurane and sevoflurane. Using low fresh gas flow rates, avoid using tetrafluoroethylene as raw material to synthesize IAGs and to avoid using NO_2 for isoflurane and sevoflurane leads to a lower carbon footprint. Sevoflurane has a lower carbon footprint compared to isoflurane when using method-B for the manufacturing	Authors conclusion Both isoflurane and sevoflurane have a smaller life-cycle carbon footprint compared to desflurane in all scenarios. It is optimal to use a low fresh gas flow rate, avoid using tetrafluoroethylene as raw material to synthesize IAGs and to avoid using NO_2 when using isoflurane or sevoflurane. VCT reduces carbon footprint of IAGs. Limitations study Not all inventory data was available, so assumptions has been made and data should be interpreted with caution.

Study reference	Journal	Study characteristics	Methods	Data collection	Outcomes	Interpretation	Comments
		Funding and conflict of interest: HX, TT and MK were funded from the Innovate UK to the University of Exeter and SageTech Medical Equipment Ltd. The study was conducted independently and without the intervention of SageTech Medical Equipment Ltd.	OR, disposables from inhalational anaesthetic gases (IAG) use (assumed to be equal). Waste from propofol use. Inventory database: EcoInvent Allocation: No Normalization & Weighting: No Impacts reported: Yes Contribution analysis: Yes Scenario analysis: Yes Comparative analysis: Yes Sensitivity analysis: No Uncertainty analysis: No Variance analysis: No	anaesthesic agents was not publicly available, two methods were modelled for the manufacturing process of the drugs. Method 'A': relatively older processes and method 'B': newer processes in manufacturing. Synthesis of propofol liquid was included. Transportation was assumed to be similar, and therefore excluded from the analysis, as was energy consumption for using general anaesthetics in the OR, the use of disposables and propofol end of life waste. For the Vapour Capture Technology effect, it was assumed that IAG can only be recycled once. Two stages were employed: 1) IAG is used for 1 MAC-h, 70% is recycled and 2) recycled drug with manufactured drug is used for another MAC-h. Results are shown for US and UK scenarios; general scenario where NO_2 is used as a carrier gas and two scenarios were it is not used. The outcome measure was climate change. Characterization methods: -	isoflurane and sevoflurane compared to scenario 1, however desflurane increases due to the high GWP. In scenario 3 the carbon footprint is lowest for all IAGs. The manufacturing process with method-B (lower impact) has a lower carbon footprint compared to method-A (higher impact) for all three anaesthetic gases. Reduction of the carbon footprint for the production of sevoflurane can be achieved by avoiding the use of tetrafluoroethylene (84% reduction). For isoflurane and desflurane these differences are smaller. For sevoflurane and isoflurane scenario 3, with method-B results in the lowest carbon footprint. Using method-A in all scenarios leads to a higher carbon footprint for sevoflurane compared to isoflurane, which is attributable to the manufacturing process. The US method (fresh gas flow of 2L/min), leads to a higher impact for sevoflurane compared to isoflurane. When changing this to 1L/min or 0.5L/min, combined with method-B, the carbon footprint of sevoflurane is lower than that of isoflurane. Using Vapour Capture Technology	process (avoid using tetrafluoroethylene) and using low fresh gas flow rates (0.5 or 1 L/min).	

Study reference	Journal	Study characteristics	Methods	Data collection	Outcomes	Interpretation	Comments
					(VCT) results in lower carbon footprints for all anaesthetic gases. When using a fresh gas flow rate of 0.5L/min, with method-B as the manufacturing process, the carbon footprint is comparable to that of propofol. However, when the manufacturer of propofol uses renewable energy the carbon footprint can be cut by half. Overall, the biggest hotspot for desflurane and isoflurane is the waste IAG, for sevoflurane the manufacturing process and for propofol drug administration. <u>2. Waste</u> No results in this study. <u>3. Medicine residue in water</u> No results in this study. <u>4. Human toxicity</u> No results in this study. <u>5. Ozone Depletion</u> No results in this study.		

[1]Goals and scope: 'Phase of life cycle assessment in which the aim of the study, and in relation to that, the breadth and depth of the study is established'

[2]Functional unit: Quantified description of the function of a product or process that serves as the reference basis for all calculations regarding impact assessment.