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HELP-VDL: study protocol for a multicentre, open, randomised, controlled clinical trial comparing the use of the head-elevated laryngoscopy position and the use of a videolaryngoscope to facilitate orotracheal intubation in a patient population without predictable difficulty of intubation

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036570
Article Type:	Protocol
Date Submitted by the Author:	08-Jan-2020
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Keywords:	Adult anaesthesia < ANAESTHETICS, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Adult surgery < SURGERY

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HELP-VDL: study protocol for a multicentre, open, randomised, controlled clinical trial comparing the use of the head-elevated laryngoscopy position and the use of a videolaryngoscope to facilitate orotracheal intubation in a patient population without predictable difficulty of intubation

Abbreviated title : Head-elevated position and videolaryngoscope for intubation

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Key words: Anaesthesia, General - Intubation, Intratracheal - Equipment and Supplies - Randomised Controlled Trial

Word count: 3274

ABSTRACT

Introduction: Tracheal intubation remains an everyday challenge for anaesthesiologists, even in patients without suspected difficulty of mask ventilation or tracheal intubation. The ideal patient positioning and the use of videolaryngoscopy remain controversial in such patients. Thus, this trial aims at comparing the efficacy for orotracheal intubation of the sniffing position or head-elevated laryngoscopy position (HELP), in association with a videolaryngoscope (McGrath Mac videolaryngoscope), the video screen of which is either switched on or off.

Methods and analysis: The HELP-VDL trial is a prospective, randomised, parallel, multicentre, open study of 240 adult patients undergoing tracheal intubation under general anaesthesia. Patients will be randomly allocated into four groups: sniffing position plus standard Macintosh laryngoscope, sniffing position plus McGrath Mac videolaryngoscope, HELP plus standard Macintosh laryngoscope, and HELP plus McGrath Mac videolaryngoscope. The primary outcome is the proportion of orotracheal intubations that do not require the assistance of a third party (as requested by the operator). The secondary outcomes include intubation duration, quality of visualization of the glottis, glottis visualization score, adjunctive manoeuvres and alternative techniques used, occurrence of oesophageal intubation, failure of tracheal intubation, incidence of arterial oxygen desaturation, perception of a difficult intubation, score on the Intubation Difficulty Scale, cooperation of the members of the anaesthesia team, evolution of vital signs, and frequency and severity of intubation complications. Data will be analysed on the intention-to-treat principle and a per-protocol basis.

Ethics and dissemination: The HELP-VDL trial has been approved by an independent ethics committee for all study centres. Participant recruitment began in October 2019. The results will be published in international peer-reviewed medical journals.

Trial registration number: NCT03987009

STRENGTHS and LIMITATIONS of this STUDY

- The primary outcome was pragmatically chosen to represent the clinical relevance of the difficulty of tracheal intubation.
- The risk of selection and allocation bias will be reduced through the use of computer-generated randomisation and allocation concealment.
- Only patients without predictable difficulty of intubation will be included since the indication for videolaryngoscopy is disputable in this population.
- The head-elevated position is not amenable to the blinding of patients, clinical or research staff; consequently, this is an open study.
- The study uses the McGrath Mac videolaryngoscope, and the results will not be readily extended to all videolaryngoscopes since there are major differences between them.

INTRODUCTION

Airway management remains an important determinant of morbidity and mortality in anaesthesia, despite progress in recognizing factors predictive of difficult mask ventilation and intubation. Many recommendations have been published regarding the practice of intubation in anaesthesia. Our study focuses on two topics that remain under discussion: the position of the patient's head and the use of a videolaryngoscope.

Most anaesthesiologists place the patient in the sniffing position (supine torso with neck flexed forward and head extended), a position named "sniffing" by analogy to a position would adopt to breathe perfume. However, Adnet et al. questioned this position based on magnetic resonance imaging of eight healthy young volunteers positioned either with their heads in a neutral position or in extension or with their heads and necks on a pillow. They showed that the sniffing position does not allow the alignment of the three important axes (mouth, pharynx and larynx) in awake patients with normal airways and anatomy,[1] The locution "head-elevated laryngoscopy position" (HELP) was coined by Levitan et al.;[2] it is also sometimes referred to as the "ramped position", but the latter term refers specifically to one of the devices used to obtain the HELP. The HELP, i.e., raising the head and neck so that “an imaginary horizontal line should connect the patient’s sternal notch with the external auditory meatus”,[3] facilitates the alignment of the oral, pharyngeal and laryngeal axes during difficult laryngoscopy,[4] This position can be achieved with a combination of hospital pillows and/or a stack of blankets or by using a dedicated device such as the Troop Elevation Pillow (Mercury Medical, Clearwater, FL, USA), the Pi’s Pillow (American Eagle Medical, NY, USA), and the Oxford Head Elevating Laryngoscopy Pillow (Alma Medical, Oxford, UK). The AirPal RAMP™ mattress was chosen in this trial because it has two compartments: the first one steers the patient towards the sniffing position, and the second one provides the HELP and allows adjusting the height of the compartments to the patient’s morphology. The HELP has been proven to be a better position for intubation in obese[4-7] and lean patients.[7] In patients with an expected difficult intubation, positioning the patient in the HELP compared to the sniffing position led to a higher rate of successful endotracheal intubation and improved laryngeal view,[8] However, a

multicentre trial performed in critically ill adults showed that the HELP may worsen glottic view and increase the number of laryngoscopy attempts required for successful intubation.[9] Furthermore, the HELP has not been studied in patients without expected difficult intubation.

Videolaryngoscopy is a major advance in airway management. A recent Cochrane Systematic Review concluded that videolaryngoscopy eased laryngeal views and reduced difficult viewings and intubation difficulty.[10] However, its place is still debated: first line or rescue in cases of suspected airway difficulty. Its systematic use means discarding the standard Macintosh laryngoscope,[11] the discarding of which has not been supported by clinical studies, in particular those of Wallace et al.[12] and Thion et al.[13] We choose to use the McGrath Mac videolaryngoscope in this trial since this apparatus has the advantage of being almost identical to the classic Macintosh laryngoscope, which still remains a reference for many anaesthesiologists. Conversely, this means that the results of our study will not be readily generalizable to all videolaryngoscopes since there are major differences between videolaryngoscopes, such as angled blade videolaryngoscopes, videolaryngoscopes with a guide channel, the LMA-CTrach, and the Macintosh blade geometry videolaryngoscopes.

The main purpose of this study is to show whether the combination of HELP and videolaryngoscopy reduces the need for a third party to assist the anaesthesiologist in performing tracheal intubation. This main outcome is original since it reflects "real life" much more than criteria usually used in studies on tracheal intubation, *i.e.*, time to intubate or number of attempts, etc., which have little clinical relevance. A few more seconds or two or even three attempts have a very limited clinical impact, and failure to intubate is too rare to be used as the principal criterion of evaluation when the study bears on patients with a "normal" airway.

METHODS AND ANALYSIS

Trial design

The HELP-VDL trial is an investigator-initiated, national, multicentre, randomised, parallel-group, open clinical trial with allocation of patients scheduled to undergo orotracheal intubation for general anaesthesia to receive a combination of two factors: position (sniffing or HELP) and a McGrath laryngoscope (with or without video). The trial is to be conducted at five Parisian private nonprofit tertiary medical centres.

Participant eligibility and consent

Trial site investigators will identify consecutive eligible patients from the listed criteria. Eligible patients will receive written and oral information and will be included after investigators have obtained informed written consent.

Inclusion criteria

Patients with American Society of Anesthesiology (ASA) physical status I to III, who are 18 to 89 years old and scheduled for elective surgical procedures that require orotracheal intubation for general anaesthesia will be enrolled in the study.

Non-inclusion criteria

Pregnant or lactating women will be excluded as will patients with anticipated difficult mask ventilation[14] or anticipated difficult intubation (Arné score ≥ 11),[15] patients requiring a rapid induction sequence, patients requiring the use of a double-lumen tube, and patients having a contra-indication to one of the drugs required by the protocol.

Allocation and blinding

Patients will be randomised into four groups:

- Group A: sniffing position plus McGrath Mac videolaryngoscope with its screen deactivated to mimic a plain laryngoscope (R−V−);

- Group B: HELP plus McGrath Mac videolaryngoscope with a deactivated video screen (R+V−);

- Group C: sniffing position plus a McGrath Mac videolaryngoscope with an activated video screen (R−V+); and

- Group D: HELP plus a McGrath Mac videolaryngoscope with its video screen activated (R+V+).

To ensure group comparability, a plan of randomisation will be used. Randomisation stratified by centre with a 1:1:1:1 ratio will be performed by investigators just before induction of anaesthesia. Randomisation will be performed using a password protected IWRS system managed by an independent CRO (Clinfile, Vélizy-Villacoublay, France). To preclude an investigator guessing the last member of a block, a randomised sequence of blocks of 4, 8 or 12 patients will be generated for each centre. Investigators are blinded to the size of each balanced block.

Each patient will be given a unique patient number, and a randomisation number (patient code) will be computer generated.

Each procedure is recorded on videotape, with the recording person at the patient's feet. This video will be used to evaluate the primary outcome and some secondary outcomes. Thus, the patient's position, sniffing position or HELP, cannot be blinded to the outcome assessors, unlike the activation or not of the videolaryngoscope screen. Similarly, the patient can remember the position in which he or she was placed. Under these conditions, this is an open study.

Interventions

Figure 1 outlines the trial procedures, and Table 1 shows the schedule for enrolment, intervention, and assessments.

Preoperative period

Inclusion and non-inclusion criteria will be verified during a pre-anaesthesia visit; the criteria will be confirmed by the anaesthesiologist in charge of the patient at the time of the anaesthesia.

Patients will receive complete, loyal information on the study at the time of the pre-anaesthetic visit. At this occasion, a written notice of information and a consent form will be handed over to the patient. This form should be completed by the patient (first and last names, signature, and date) and the investigator or his/her representative (first and last names, signature, and date) before the beginning of any

trial−specific procedure. Two originals will be signed: one for the patient and one for the investigator.

Experienced anaesthesiologists who will receive a specific training as to the study procedures prior to the beginning of the trial will perform the laryngoscopies and tracheal intubation. An observer, placed at the feet of the patient and consequently unable to see if the screen of the videolaryngoscope is activated, will videotape the preoxygenation and intubation sequence. The recording will be terminated as soon as intubation is completed or when failure to intubate is declared. The patient's authorization to use the recording will be obtained at the time of consent. In addition, an independent assistant will review all recordings ensuring proper blurring of the patients' face and removal of any spoken indication that could hinder the blindness of the outcome assessor.

Study-specific technical notes have been developed describing how the recordings should be made, downloaded, erased from the recorder, blurred and cleared of spoken indications prior to being transferred for outcome scoring.

Intraoperative period

Patients will have standard monitoring in the operating room, *i.e.,* heart rate, non-invasive blood pressure, pulse oximetry, capnography, bispectral index, and quantitative measurement of neuromuscular block. A peripheral venous line will be established.

The proper functioning of the AirPal RAMP™ mattress (Rapid Airway Management Positioner, AirPal®-Patient Transfer Systems, PA 18034, USA) will be checked before the patient enters the operating room; then, the AirPal RAMP™ will be deflated. The patient will be placed in the supine position and then positioned in either the sniffing position or HELP according to randomisation. The AirPal mattress has two distinct inflatable compartments; when inflated, the lower one corresponds to an 8 cm high pillow (sniffing position), while the upper one, when inflated, ensures that the patient is in the HELP with the external auditory meatus at the same level as the suprasternal notch.

Following adequate preoxygenation using 100% oxygen via a face mask for at least 3 minutes to reach an end-tidal oxygen fraction ≥ 90%, anaesthesia will be induced via an intravenous injection of propofol and sufentanil or remifentanil. Atracurium or rocuronium will be administered for neuromuscular blockade. Bag-mask ventilation will be continued with 100% oxygen until muscle relaxation is confirmed (no response to a train of four nerve stimulations). The bispectral index should be less than

60; if not, an additional bolus dose of propofol will be administered. The anaesthesiologist will choose either a 3 or a 4 blade size for the McGrath Mac laryngoscope and will generally use a tracheal tube size with an internal diameter of 7 mm (women) or 7.5 mm (men). At any time and whatever the circumstances, the anaesthesiologist may ask the anaesthetist nurse to apply external laryngeal pressure, use a stylet, change the plastic blade or use a metal blade, change the intubation technique (insertion of a laryngeal mask or Fastrach LMA™, fibroscopy, trans-tracheal oxygenation, and even tracheostomy), activate the screen of the videolaryngoscope, or interrupt anaesthesia.

After tracheal intubation, the upper cushion is deflated, which leaves the patients of the R+ groups in the same position (head raised 8 cm above the table level) as those in the R− groups. The deflation of the pillow is not video recorded. Anaesthesia is then continued according to the routine procedures of the anaesthesia department.

Postoperative period

The research completion visit will take place no more than three days after surgery, if surgery was performed on a Friday, and usually on the first postoperative day. Two questions are asked with four possible answers. To the question “Are you hoarse?”, four responses are possible: no hoarseness; hoarseness noticed only by the patient; hoarseness obvious for the observer; and aphonia.[16] To the question “Do you have a sore throat?”, four responses are possible: no; mild (pain when swallowing); moderate (permanent pain increasing with swallowing); and severe (pain interfering with diet and requiring analgesia).[17]

Outcomes measures

Primary outcome measure

The primary outcome is the proportion of orotracheal intubations for which it is necessary to resort, upon request of the operator, to the assistance of a third party.

Secondary outcomes measures

Secondary outcomes include the intubation duration (from the passage of the incisors to the first capnogram), the quality of visualization of the glottis (Cormak and Lehane's score modified by Yentis),[18]

percentage of glottic opening (POGO),[19] the resorting to adjunctive manoeuvres and alternative techniques, the occurrence of oesophageal intubation, the failure of tracheal intubation, the incidence of arterial oxygen desaturation ($SpO_2 < 92\%$), the perception of a difficulty in intubation (using a numerical scale from 0 for "no difficulty" to 10 for "extreme difficulty") and the Intubation Difficulty Scale score.[20] The cooperation between the various members of the anaesthesia team (scale adapted by Kraus from Ellyson & Dovidio[21]), the evolution of vital signs (heart rate and blood pressure), the frequency and severity of intubation complications (especially lip or dental injury, sore throat and hoarseness; as recorded by a blinded observer during the scheduled postoperative visit).

Statistical analysis and sample size calculation

The intent-to-treat approach is considered the primary analysis. A bilateral p less than 0.05 will be considered significant. If more than 10% of the cases are considered to be major protocol violations, a per-protocol analysis will be performed on the cases with no or minor protocol violations. In such a case, the results of both analyses will be provided and discussed in the statistical report.

Global scores and subscores for scales will be calculated according to the results of the French validation of these scales. Since the cooperation scale adapted by Kraus has not been validated in France, it will be validated using our study data prior to starting the statistical analysis proper.

Descriptive summaries will be provided globally and for each group. For continuous variables, counts, mean and 95% confidence limits obtained using bootstrapping methods will be provided. For discrete variables, counts, percentages and confidence limits obtained using a bootstrap method will be provided. Ordinal variables will be considered continuous.

For the primary outcome, the comparison between groups will be used a Chi² test or an exact Fisher test depending on the validity. As the centre will be a potential cofounding factor, this variable will be tested using a multinomial regression multivariate.

For the secondary outcomes, continuous variables will be compared between groups using a Permanova+ procedure. Pseudo−analysis of variance uses a procedure to partition dissimilarity matrices that are calculated using Euclidean distances for continuous variables and simple matching for discrete ones. The Permanova+ procedure provides a pseudo F ratio, which is tested using a permutation

paradigm. Discrete variables will be compared between groups using a Chi² test or an exact Fisher test between groups.

All statistical analysis will be performed using the Software SAS® 9.4 (SAS Institute INC., USA).

Missing values

Missing data will not be replaced. Mixed models can be used in the analysis of repeated data to avoid deleting subjects with any missing values.

Sample size estimation

Two small pilot studies in our department, in which the type of laryngoscope was not controlled (n=15 for each study), showed that the operator had to resort to the help of a third party in 5 (33%) intubations with the HELP and in 6 (40%) intubations in the sniffing position. It is hypothesised that resorting to the help of a third party will occur in 50% of the cases in the R−V− group, 33% in the R−V+ and the R+V− groups and in slightly more than 10% in the R+V+ group, which would indicate an actual synergy of the two factors. This leads to an effect size of approximately 0.2, which has an alpha risk of 0.05 and a beta risk of 0.8, and an attrition rate inferior to 10% leads to a total sample size of 240.

Data registration

The study data presented in Table 1 will be recorded in an electronic database from 3 sources:

− direct entry by the staff in an electronic case report form (eCRF) available in the operating room or at the operator's desk;

− entry by an independent scorer reviewing the videotapes once blurred and edited from cues that could break the blindness of the scorer; a predefined scoring sheet has been developed that will be used as a source document; and

− direct entry in the eCRF of the scores obtained on the postoperative visit.

From the eCRF, the trial database will be established. Data collection will be monitored by trained research coordinators.

Patient withdrawal

A participant who no longer agrees to participate in the clinical trial can withdraw the informed consent at any time without need of further explanation. Participants who will withdraw from the study will be followed up, according to routine clinical practice in each participating centre. To conduct the intention-

to-treat analyses with as little missing data as possible, the investigator may ask the participant which aspects of the trial he/she wishes to withdraw from (participation in the remaining follow-up assessments, use of already collected data). Whenever possible, the participant will be asked for permission to obtain data for the primary outcome measure. All randomised patients will be reported, and all data available with consent will be used in the analyses.

Safety

Every serious adverse event related to the studied procedure, expected or unexpected, will be reported within 24 hours by the investigator to the sponsor on a 'Serious adverse event' form on which the date of occurrence, criterion of severity, intensity, relationship with the study evaluated and the outcome will be indicated. The period in which serious adverse events should be reported begins from the day of the written informed consent to the end of the follow-up. Whenever a serious adverse event persists at the end of the study, the investigator will follow the patient until the event is considered resolved. The management of serious adverse events will follow regulations and good clinical practices.

Data handling and retention

Data will be handled according to French law. All original records (including consent forms, reports of suspected unexpected serious adverse reactions and relevant correspondences) will be archived at trial sites for 15 years. The clean trial database file will be anonymised and maintained for 15 years.

Patient and public involvement

Patients and public are not involved in any of the phases of this study.

ETHICS AND DISSEMINATION

Ethics

Ethics approval was sought and obtained for the HELP-VDL trial from the Ethical Committee Ile de France V on November 6th, 2018, with the reference number 18.09.11.39700 CAT 2. Written informed consent is required from patients to enter the study. The HELP-VDL trial is registered at ClinicalTrials.gov with the trial identification number NCT03987009.

Recruitment of patients to HELP-VDL commenced in July 2019. We expect to complete recruitment in one year.

Dissemination

The Consolidated Standards of Reporting Trials (CONSORT) to guide protocol and study design will be followed (Additional File 1).[22 23] All dissemination will involve aggregate data only and be undertaken using the CONSORT 2010 statement: updated guidelines for reporting parallel-group randomised trials[24] and the template for intervention description and replication checklist.[25]

Publication plan

Scientific presentations and reports corresponding to the study will be written under the responsibility of the coordinating investigator of the study with the agreement of the principal investigators and the methodologist. The coauthors of the report and the publications will be the investigators and clinicians involved, on a pro rata basis of their contribution in the study, as well as the biostatistician and associated researchers. All trial sites will be acknowledged, and all investigators at these sites will appear with their names under 'the HELP-VDL investigators' in an appendix to the final manuscript. Rules on publication will follow international recommendations.[26]

CONCLUSION

The HELP-VDL trial will answer several questions: what are the respective contributions of the McGrath Mac videolaryngoscope and the head-elevated laryngoscopic position on intubation ease in a population with no suspicion of a risk of difficult mask ventilation or intubation? Is the combination of both factors synergistic in such patients? A partial answer has been published in paediatric patients; Kim et al. compared the HELP to a position with the head remaining horizontal and reported that

videolaryngoscopy with the McGrath device provides a better visualization of the glottis and easier intubation.[27]

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FIGURE LEGEND

Figure 1. Trial procedures.

ADDITIONAL FILE 1

SPIRIT Checklist–Recommendations for Interventional Trials

DATA STATEMENT

Data will be available in the Dryad repository.

AUTHOR CONTRIBUTIONS

MLG, JT, and MF contributed to the conception and design of the research protocol.

ZC, GD, JO, MLG provided critical input pertaining to the design of the trial interventions and procedures; they will make substantial contributions to the acquisition of data and of their interpretation.

MF wrote the first draft of the protocol and this manuscript. JT designed the statistical analysis plan. All authors (MLG, ZC, GD, JO, JT, and MF) critically revised and modified the protocol and the article. They all approved the final version to be published. They all agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work will be appropriately investigated and resolved.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

COMPETING INTERESTS STATEMENT

The authors declare that they have no competing interests.

PATIENT CONSENT

Required

ACKNOWLEDGEMENTS

This work was sponsored by the Clinical Research Department of Foch Hospital.

Table1. Schedule for enrolment, intervention, and assessments

	STUDY PERIOD				
	Enrolment	Intervention			
TIMEPOINT	Preoperative visit*	Before anaesthesia	During anaesthesia	After anaesthesia	Completion visit**
ENROLMENT:					
Eligibility	X				
Informed consent	X				
Demographic characteristics	X				
Allocation		X			
INTERVENTIONS:					
Sniffing position and McGrath Mac videolaryngoscope			X		
Sniffing position and McGrath Mac videolaryngoscope with a masked screen			X		
HELP and McGrath Mac videolaryngoscope			X		
HELP and McGrath Mac videolaryngoscope with a masked screen			X		
ASSESSMENTS:					
Proportion of orotracheal intubations for which it is necessary to use the assistance of a third party required by the operator (Primary outcome)			X		
Intubation time			X		
Visualization of the glottis			X		
Adjunctive manoeuvres and alternative techniques			X		
Oesophageal intubation, failure and complications of tracheal intubation			X		
Arterial oxygen desaturation			X		
Difficulty in intubation (numerical scale and Intubation Difficulty Scale)			X		
Kraus-adapted scale of cooperation			X		
Evolution of vital signs			X		
Hoarseness					X
Sore throat					X
Adverse events			X		X

*: Preoperative visits are performed within the 2 weeks before the day of anaesthesia

**: Completion visits are usually performed on the first postoperative day, but no later than three days after surgery (if surgery was performed on a Friday)".

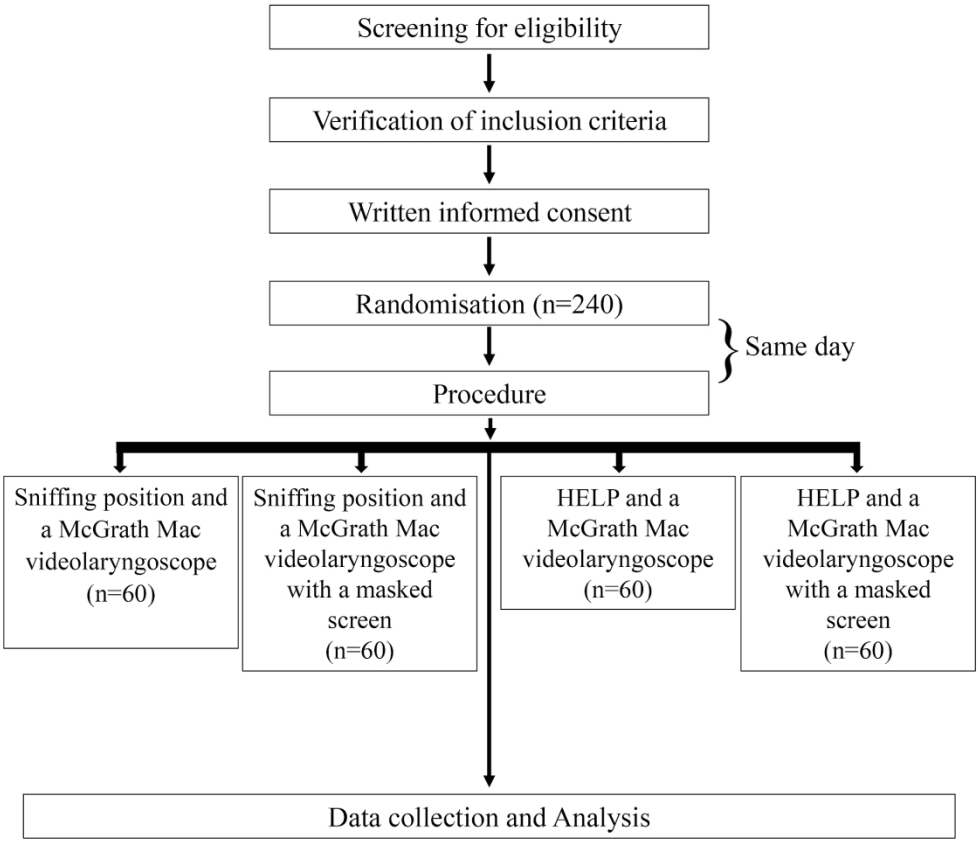

Figure 1

180x180mm (300 x 300 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	ItemNo	Description	Page
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name.	2
	2b	All items from the World Health Organization Trial Registration Data Set	-
Protocol version	3	Date and version identifier	-
Funding	4	Sources and types of financial, material, and other support	19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	19
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	5; 9-10
Trial design	8	Description of trial design including type of trial	6

		(eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	

Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9-10 Table 1
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 1 Figure 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	10
Recruitment	15	Strategies for achieving adequate participant	NA

		enrolment to reach target sample size	

Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6-7
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	6-7
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Open study 7
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA

Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9-10 Table 1
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to	11

		promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	10-11
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	NA
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA

Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	12
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA

Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Obtained
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Clinical trials web site
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised	All MD investigators

		surrogates, and how (see Item 32)	6
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Protected eCRF 11
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Statistician
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	13
	31b	Authorship eligibility guidelines and any intended use of professional writers	13
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Upon request

Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Upon request
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

INTERVENTION STUDY PROTOCOL WITH MINIMAL RISKS AND CONSTRAINTS

Promotor Code: 2017011F

N° ID-RCB : 2017-A03408-45

HELP-VDL: study protocol for a multicentre, open, randomised, controlled clinical trial comparing the use of the head-elevated laryngoscopy position and the use of a videolaryngoscope to facilitate orotracheal intubation in a patient population without predictable difficulty of intubation

HELP-VDL

Version n° 2 –08/10/2019

SYNOPSIS

Principal Investigator: DR MORGAN LE GUEN
Multicenter study: 3: Hôpital Foch, Fondation Ophtalmologique Adolphe de Rothschild, Institut Mutualiste Montsouris
Number of patients: 240 (60 in each group)
Promotor : Hôpital Foch – Délégation à La Recherche Clinique (DRCI)
Contact : Mme Elisabeth HULIER-AMMAR
Tél : 00 33 1 46 25 11 75 / e-mail : e.hulier-ammar@hopital-foch.com

STUDY RATIONALE

Airway management remains an important determinant of morbidity and mortality in anaesthesia despite progress in the recognition of difficult mask ventilation and intubation factors.

1. The patient's position

The position of the patient is of utmost importance. This position must allow the axes of the larynx to be aligned with the operator's visualization axis. The visual axis can be represented by a straight line passing through the lower end of the upper incisors and the posterior edge of the arytenoid cartilage. The extension of the neck as well as an extension of the facial mass brings the laryngeal and visual axes closer together. This configuration of the head is called the "sniffing position". During dorsal decubitus positioning, the placement of a cushion under the back of the neck and an extension of the head (about 20°) allows this configuration to be obtained (Jackson's amended position). However, Adnet et al. questioned this position using magnetic resonance imaging. A more pronounced position, the "HELP position", consists of raising the head and neck so that the external auditory canal is at the same level as the supra-sternal trough. This patient position is achieved either by placing folded fields under the patient or by using a specially developed compressed air mattress to facilitate patient positioning: the AirPal RAMP™ (Rapid Airway Management Positioner) mattress produced by AirPal®-Patient Transfer Systems, Inc. (Center Valley, Pennsylvania 18034, USA, www.airpal.com). The "HELP position" has shown its interest in obese patients and in patients with difficult intubation criteria. Some studies have shown the benefits of the HELP position in patients with no known risk of difficult intubation but without using the AirPal RAMP™ mattress.

2. The use of a video laryngoscope

The use of a video laryngoscope is becoming more common in anaesthesia, especially for the management of patients at risk of difficult airway management. The videolaryngoscope provides better visualization of the glottic orifice. Its purchase cost is moderate and the cost of consumables is compatible with current practice. The McGrath® Mac video laryngoscope was selected for routine use.

3. The hypotheses of this research

The main hypothesis of this study is that there is a synergy between the use of patient positioning on the AirPal RAMP™ mattress, the two inflated cushions (bringing the external auditory canal to

the same level as the supra-sternal "HELP position" trough), and the use of a McGrath® Mac video laryngoscope.

It will also be confirmed in the present study that each of the components of this dual procedure provides a significant advantage for the position compared to the conventional position as obtained by inflating only the lower cushion, and for the video laryngoscope compared to the use of a conventional laryngoscope without a camera.

GENERAL INFORMATION ABOUT THE TRIAL

Indications: Patients requiring tracheal intubation during general anaesthesia.

Methodology: Multicentre, randomised, open research

Main objective: To determine if there is synergy (significant interaction term) between the use of the HELP position (head elevated 8 cm above the table plane) obtained with the AirPal medical device RAMP™ and the use of a videolaryngoscope with respect to ease of tracheal intubation.

Secondary Objectives :

- To confirm the value of using the HELP position obtained using the AirPal RAMP™ device compared to traditional positioning on the quality of intubation.
- Confirm the value of using a video laryngoscope compared to a traditional laryngoscope without a video camera on the quality of intubation.
- Evaluate the behaviour of the anaesthetic team. The attitude of the different members of the anaesthetic team is determined from the video/audio recording of the intubation (role of each, timing).
- Evaluate the impact of the use of each device on the haemodynamic consequences of intubation.
- Evaluate the impact of the combined use of the HELP position and videolaryngoscopy on the frequency and severity of the usual complications of intubation: post-operative pharyngeal pain and hoarseness.

Inclusion Criteria:

- Patients managed by the Anaesthesia Services of participating hospitals.
- Male or female over 18 and under 90 years of age
- Should be given general anaesthesia with oral intubation using a standard intubation tube
- Can be contacted directly by telephone in the case of patients undergoing outpatient surgery
- Having signed a consent form
- Be affiliated with a Health Insurance plan.

Criteria for non-inclusion:

- Pregnant or breastfeeding women
- Patients with predicted difficulty with mask ventilation or intubation as assessed by the

physician performing the pre-inclusion clinical examination (Arne score ≥ 11) or the physician managing the patient in the operating room.

- Patients for whom the surgical procedure requires the installation of a double-lumen tube
- Patients requiring rapid sequence induction
- Patients for whom induction cannot be achieved by the sequence sufentanil, propofol, atracurium or rocuronium.
- Being deprived of liberty or under guardianship.

ORGANISATION OF THE STUDY

- Inclusion visit with verification of inclusion and non-inclusion criteria and signing of consent after a period of reflection deemed sufficient by the patient.
- Confirmation by the anaesthetist in charge of the patient's anaesthesia, of the presence of inclusion criteria and the absence of non-inclusion criteria
- Intubation (with audio/video recording)
- Follow-up visit and end of research done the day after the intervention (no later than 3 days after the intervention for patients included on Fridays)

STATISTICAL CONSIDERATIONS

Sample size estimation

Two small pilot studies in our department, in which the type of laryngoscope was not controlled (n=15 for each study), showed that the operator had to resort to the help of a third party in 5 (33%) intubations with the HELP and in 6 (40%) intubations in the sniffing position. It is hypothesised that resorting to the help of a third party will occur in 50% of the cases in the R−V− group, 33% in the R−V+ and the R+V− groups and in slightly more than 10% in the R+V+ group, which would indicate an actual synergy of the two factors. This leads to an effect size of approximately 0.2, which has an alpha risk of 0.05 and a beta risk of 0.8, and an attrition rate inferior to 10% leads to a total sample size of 240.

Statistical analysis

The intent-to-treat approach is considered the primary analysis. A bilateral p less than 0.05 will be considered significant. If more than 10% of the cases are considered to be major protocol violations, a per-protocol analysis will be performed on the cases with no or minor protocol violations. In such a case, the results of both analyses will be provided and discussed in the statistical report.

Global scores and sub-scores for scales will be calculated according to the results of the French validation of these scales. Since the cooperation scale adapted by Kraus has not been validated in France, it will be validated using our study data prior to starting the statistical analysis proper. Descriptive summaries will be provided globally and for each group. For continuous variables, counts, mean and 95% confidence limits obtained using bootstrapping methods will be provided. For discrete variables, counts, percentages and confidence limits obtained using a bootstrap method will be provided. Ordinal variables will be considered continuous.

For the primary outcome, the comparison between groups will be used a Chi² test or an exact Fisher test depending on the validity. As the centre will be a potential cofounding factor, this variable will be tested using a multinomial regression multivariate.

For the secondary outcomes, continuous variables will be compared between groups using a Permanova+ procedure. Pseudo−analysis of variance uses a procedure to partition dissimilarity matrices that are calculated using Euclidean distances for continuous variables and simple matching for discrete ones. The Permanova+ procedure provides a pseudo F ratio, which is tested using a permutation paradigm. Discrete variables will be compared between groups using a Chi² test or an exact Fisher test between groups.

All statistical analysis will be performed using the Software SAS® 9.4 (SAS Institute INC., USA).

EXPECTED DURATION OF THE TRIAL

Inclusion period: 12 months from first inclusion

Study participation period for a patient: 48 hours as a general rule (maximum 4 days when the anaesthesia takes place on Fridays)

Overall duration of the trial including follow-up period: 12 months

QA

Data Collection: The following data will be collected, if applicable and available in the context of patient management:

- Demographic data (date of birth, gender)
- Clinical data (weight, height)
- The type of surgery
- A clinical examination to assess the risk of mask ventilation or difficult intubation (Arne's score)
- Date and time of intervention
- Intubation data (blade size, tube diameter, intubation parameters, glottic exposure,
- Overall assessment of the difficulty of intubation
- Adverse events in the operating room
- Pharyngeal complications at D+1 of intubation

Data Management

Patients will be identified in the study by an inclusion number.

Medical data will be collected in an electronic CRF by the investigating physician. Access to the CRF will be restricted to authorized persons in charge of the protocol.

Quality Control:

A Clinical Research Associate (CRA) from the Foch Hospital, Promoter, will be in charge of the follow-up of the study, the verification of the consent forms, the quality control of the collected data...

REGULATORY

Committee for the Protection of Individuals - Ile de France V: Favourable opinion obtained on November 6th, 2018

CNIL: Commitment to Reference Methodology 001 (MR001) on 06/02/2017

BMJ Open

HELP-VDL: study protocol for a multicentre, open, randomised, controlled clinical trial comparing the use of the head-elevated laryngoscopy position and the use of a videolaryngoscope to facilitate orotracheal intubation in a patient population without predictable difficulty of intubation

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036570.R1
Article Type:	Protocol
Date Submitted by the Author:	05-May-2020
Complete List of Authors:	Le Guen, Morgan; Hopital Foch, Department of Anesthesiology Coppere, Zoé; Fondation Ophtalmologique Adolphe de Rothschild, Department of Anaesthesiology Dufour, Guillaume ; Institut Mutualiste Montsouris, Department of Anaesthesiology Ouattara, Jonathan ; Groupe hospitalier Paris Saint-Joseph, Department of Anaesthesiology Trichereau, Julie; Hopital Foch, Research Unit Fischler, Marc; Hopital Foch, Anesthesia
Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Surgery
Keywords:	Adult anaesthesia < ANAESTHETICS, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Adult surgery < SURGERY

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HELP-VDL: study protocol for a multicentre, open, randomised, controlled clinical trial comparing the use of the head-elevated laryngoscopy position and the use of a videolaryngoscope to facilitate orotracheal intubation in a patient population without predictable difficulty of intubation

Abbreviated title: Head-elevated position and videolaryngoscope for intubation

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Key words: Anaesthesia, General - Intubation, Intratracheal - Equipment and Supplies - Randomised Controlled Trial

Word count: 3318 words for the main body

ABSTRACT

Introduction: Tracheal intubation remains an everyday challenge for anaesthesiologists, even in patients without suspected difficult airways. The ideal positioning of the patient's head (flat, raised a few centimetres on a cushion in the sniffing position (SP), or raised to achieve horizontal alignment between the external acoustic meatus and the sternal angle) and the use of videolaryngoscopy remain controversial. This trial aims to compare the efficacy for orotracheal intubation of the SP or the head-elevated laryngoscopy position (HELP), which has been shown to improve laryngeal visualization and the intubation condition particularly in obese patients, in combination with a McGrath Mac videolaryngoscope whose video screen is either on or off (Video or NoVideo).

Methods and analysis: The HELP-VDL factorial trial is a prospective, randomised, parallel, multicentre, open study of 240 adult patients undergoing tracheal intubation under general anaesthesia. Patients will be allocated into four groups: SP-NoVideo, HELP-NoVideo, SP-Video, and HELP-Video. The primary outcome is the proportion of orotracheal intubations that do not require the assistance of a nurse anaesthetist. The secondary outcomes include the intubation duration, the first intubation success rate, the quality of visualization of the glottis, the glottis visualization score, adjunctive manoeuvres and alternative techniques used, the occurrence of oesophageal intubation, failure of tracheal intubation, the incidence of arterial oxygen desaturation, the perception of a difficult intubation, the score on the Intubation Difficulty Scale, cooperation among the members of the anaesthesia team, the evolution of vital signs, and the frequency and severity of intubation complications. Data will be analysed on the intention-to-treat principle and a per-protocol basis.

Ethics and dissemination: Ethics approval was obtained from the Ethical Committee Ile de France V (Paris, France). Participant recruitment began July 3rd, 2019. The results will be submitted for publication in peer-reviewed journals. Trial registration number: ClinicalTrials.gov (NCT03987009).

STRENGTHS and LIMITATIONS of this STUDY

- The primary outcome was pragmatically selected to represent the clinical relevance of the difficulty of tracheal intubation.
- The risk of selection and allocation biases will be reduced through the use of computer-generated randomisation and allocation concealment.
- Only patients without predictable difficulty of intubation will be included since the indication for videolaryngoscopy is disputable in this population.
- The head-elevated position is not amenable to the blinding of patients or clinical or research staff; consequently, this is an open study.
- The study uses the McGrath Mac videolaryngoscope, and the results will not be readily extended to all videolaryngoscopes since major differences exist between them.

INTRODUCTION

Airway management remains an important determinant of morbidity and mortality in anaesthesia despite progress in recognizing factors that are predictive of difficult mask ventilation and intubation.[1] Many recommendations have been published regarding the practice of intubation in anaesthesia.[2 3] Our study focuses on two topics that remain under discussion: the position of the patient's head and the use of a videolaryngoscope.

Although the position with the head flat is used by some anaesthesiologists, most place the patient in the sniffing position (SP, a supine torso with the neck flexed forward and the head extended). However, this choice has been questioned since this position does not allow alignment of the three important axes (the mouth, pharynx and larynx) in awake volunteers with normal airways and anatomy as shown by magnetic resonance imaging.[4] A more elevated head position with the back tilted at 25 degrees by breaking the operating table at the hips has been proposed, which improves the laryngeal view,[5] facilitates tracheal intubation in surgical patients,[6 7] and decreases airway-related complications in patients undergoing emergent tracheal intubation outside of the operating room.[8] This proposed position led to a position called bed-up-head-elevated (BUHE), which has been proposed as the standard intubation position for all patients.[9] A similar position with the head and neck raised, the "head-elevated laryngoscopy position" (HELP), is specified by an anatomical marker—an imaginary horizontal line should connect the patient's sternal notch with the external auditory meatus.[10] The HELP has been proven to be a better position for intubation in obese[11-14] and lean patients.[14] In patients with an expected difficult intubation, positioning the patient in the HELP compared to the SP led to a higher rate of successful endotracheal intubation and an improved laryngeal view.[15] A similar result has been reported when novices perform intubation on a simulator configured to have a difficult airway.[16] However, a systematic review and meta-analysis of randomized clinical trials showed no favourable aspects of the ramped position compared to the sniffing position,[17] while more favourable results have been reported in non-randomized clinical trials.[13 14] This contrast renders the effectiveness of the HELP controversial. The HELP can be achieved with a combination of hospital pillows and/or a stack of blankets[18] or by using a dedicated device such as the Troop Elevation Pillow (Mercury Medical, Clearwater, FL, USA), Pi's Pillow (American Eagle Medical, NY, USA), and the Oxford Head

Elevating Laryngoscopy Pillow (Alma Medical, Oxford, UK). The AirPal RAMP™ mattress was selected in this trial because it has two compartments: the first compartment steers the patient towards the sniffing position, and the second compartment provides the HELP and allows adjustment of the height of the compartments to the patient's morphology.

Videolaryngoscopy represents a major advance in airway management. A recent Cochrane Systematic Review concluded that videolaryngoscopy eased laryngeal views and reduced difficult visualization and intubation difficulty.[19] However, its role is still debated as a first-line method or a rescue strategy in cases of suspected airway difficulty. Systematic use of videolaryngoscopy entails discarding the standard Macintosh laryngoscope,[20] which has not been supported by clinical studies, especially those of Wallace et al.[21] and Thion et al.[22] We selected the McGrath Mac videolaryngoscope (Covidien/Medtronic, Minneapolis, MN, USA) for this trial since this apparatus has the advantage of being almost identical to the classic Macintosh laryngoscope, which still remains a reference for many anaesthesiologists. Conversely, this choice implies that the results of our study will not be readily generalizable to all videolaryngoscopes since major differences exist between videolaryngoscopes, such as hyperangulated-blade videolaryngoscopes, videolaryngoscopes with a guide channel, and Macintosh blade-geometry videolaryngoscopes.

The main purpose of this study, which will be carried out under real-world conditions, is to show whether combining the HELP and videolaryngoscopy reduces the need for a nurse anaesthetist to assist the anaesthesiologist in performing tracheal intubation. This main outcome is original since it reflects "real life" much more than criteria usually used in studies on tracheal intubation, *i.e.*, time to intubate or number of attempts, etc., which have little clinical relevance. A few more seconds or two or even three attempts have a very limited clinical impact, and failure to intubate is too rare to be used as the principal criterion of evaluation when the study bears on patients with a "normal" airway.

METHODS AND ANALYSIS

Trial design

The HELP-VDL trial is an investigator-initiated, multicentre, randomised, parallel-group, open factorial clinical trial with allocation of patients scheduled to undergo orotracheal intubation for general anaesthesia to groups subjected to a combination of two factors: position (sniffing or HELP) and a McGrath Mac videolaryngoscope (with or without using the video screen, with the latter corresponding to direct laryngoscopy). The trial will be conducted at five Parisian private nonprofit tertiary medical centres.

Participant eligibility and consent

Trial site investigators will identify consecutive eligible patients from the listed criteria. Eligible patients will receive written and oral information and will be included after investigators have obtained informed written consent.

Inclusion criteria

Patients with American Society of Anesthesiologists (ASA) physical status classes of I to III who are 18 to 89 years old and scheduled for elective surgical procedures that require orotracheal intubation for general anaesthesia will be enrolled in the study.

Non-inclusion criteria

Pregnant or lactating women will be excluded as will patients with anticipated difficult mask ventilation[23] or anticipated difficult intubation (Arné score $\geq$ 11),[24] patients requiring a rapid sequence induction, patients requiring the use of a double-lumen tube, patients scheduled for a surgical procedure involving the mouth or the upper airway, and patients with a contra-indication to one of the drugs required by the protocol.

Allocation

Patients will be randomised into four groups in this factorial trial at a 1:1:1:1 ratio:

- Group A: the SP plus a McGrath Mac videolaryngoscope with its screen deactivated to mimic a plain laryngoscope (SP-NoVideo);

- Group B: the HELP plus a McGrath Mac videolaryngoscope with a deactivated video screen (HELP-NoVideo);

- Group C: the SP plus a McGrath Mac videolaryngoscope with an activated video screen (SP-Video); and

- Group D: the HELP plus a McGrath Mac videolaryngoscope with its video screen activated (HELP-Video).

To ensure group comparability, a plan of randomisation will be used. Centralised randomisation using fixed-size blocks will be performed by the biostatistician of the Research Unit of the Promotor using SAS® v9.4 (SAS France, 77257 Brie Comte Robert, France). Each patient will be given a unique patient number and a randomisation number (patient code) when the investigator connects to an Interactive Web Response System managed by an independent Contract Research Organization (Clinfile, 78146 Vélizy-Villacoublay, France) using a protected password just before the induction of anaesthesia.

Blinding

Each procedure is recorded on videotape, with the recording person at the patient's feet. This video will be used to evaluate the primary outcome and some secondary outcomes. Thus, the patient's position, SP or HELP, cannot be blinded to the outcome assessors, unlike the activation or not of the videolaryngoscope screen. Similarly, the patient can remember the position in which he or she was placed. Under these conditions, this is an open study.

Interventions

Figure 1 outlines the trial procedures, and Table 1 shows the schedule for enrolment, interventions, and assessments.

Preoperative period

Inclusion and non-inclusion criteria will be verified during a pre-anaesthesia visit; the criteria will be confirmed by the anaesthesiologist in charge of the patient at the time of the anaesthesia.

Patients will receive complete, reliable information on the study at the time of the pre-anaesthetic visit. At this occasion, a written notice of information and a consent form will be handed over to the patient. This form should be completed by the patient (first and last names, signature, and date) and the investigator or his/her representative (first and last names, signature, and date) before the beginning of any trial-specific procedure. Two originals will be signed: one for the patient and one for the investigator.

Three persons are required to run the procedure: an anaesthesiologist with a specific training pertaining to the study procedures prior to the beginning of the trial, a nurse anaesthetist who will help the anaesthesiologist in case of difficulty, and an observer at the feet of the patient who will be unable to see whether the screen of the videolaryngoscope is activated and will videotape the preoxygenation and intubation sequence. The recording will be terminated as soon as intubation is completed or when failure to intubate is declared. The patient's authorization to use the recording will be obtained at the time of consent. In addition, an independent assistant will review all recordings ensuring proper blurring of the patients' face and removal of any spoken indication that could hinder the blindness of the outcome assessor.

Study-specific technical notes have been developed describing how the recordings should be made, downloaded, erased from the recorder, blurred and cleared of spoken indications prior to being transferred for outcome scoring.

Intraoperative period

In all cases, the patient will receive care during the induction and intubation periods from a physician anaesthetist and a nurse anaesthetist as is usual in the hospitals where the protocol takes place. Patients will have standard monitoring in the operating room, *i.e.,* heart rate, non-invasive blood pressure, pulse oximetry, capnography, bispectral index, and quantitative measurement of neuromuscular block. A peripheral venous line will be established.

The proper functioning of the AirPal RAMP™ mattress (Rapid Airway Management Positioner, AirPal®-Patient Transfer Systems, PA 18034, USA) will be checked before the patient enters the operating room; then, the AirPal RAMP™ will be deflated. The patient will be placed in the supine

position and then positioned in either the SP or the HELP according to randomisation. The AirPal mattress has two distinct inflatable compartments; when inflated, the lower one corresponds to an 8-cm-high pillow (sniffing position), while the upper one, when inflated, ensures that the patient is in the HELP with the external auditory meatus at the same level as the suprasternal notch.

Following adequate preoxygenation using 100% oxygen via a face mask for at least 3 minutes to reach an end-tidal oxygen fraction ≥ 90%, anaesthesia will be induced via an intravenous injection of propofol and sufentanil or remifentanil. Atracurium or rocuronium will be administered for neuromuscular blockade. Bag-mask ventilation will be continued with 100% oxygen until muscle relaxation is confirmed (no response to a train of four nerve stimulations). The bispectral index should be less than 60; if not, an additional bolus dose of propofol will be administered. The anaesthesiologist will choose either a 3 or a 4 blade size for the McGrath Mac laryngoscope and will generally use a tracheal tube size with an internal diameter of 7 mm (women) or 7.5 mm (men). At any time and whatever the circumstances, the anaesthesiologist may ask the anaesthetist nurse to apply external laryngeal pressure, use a stylet, change the plastic blade or use a metal blade, change the intubation technique (insertion of a laryngeal mask or Fastrach LMA™, fibroscopy, trans-tracheal oxygenation, and even tracheostomy), activate the screen of the videolaryngoscope, or interrupt anaesthesia.

After tracheal intubation, the upper cushion is deflated, which leaves the patients in the R+ groups in the same position (the head raised 8 cm above the table level) as those in the R− groups. The deflation of the pillow is not video recorded. Anaesthesia is then continued according to the routine procedures of the anaesthesia department.

Postoperative period

The research completion visit will take place no more than three days after surgery, if surgery was performed on a Friday, and usually on the first postoperative day. Two questions are asked with four possible answers. To the question “Are you hoarse?”, four responses are possible: no hoarseness; hoarseness noticed only by the patient; hoarseness obvious for the observer; and aphonia.[25] To the question “Do you have a sore throat?”, four responses are possible: no; mild (pain when swallowing); moderate (permanent pain increasing with swallowing); and severe (pain interfering with diet and requiring analgesia).[26]

Outcomes measures

Primary outcome measure

The primary outcome is the proportion of orotracheal intubations for which the assistance of a third party (a nurse anaesthetist) is necessary upon request of the operator.

Secondary outcomes measures

Secondary outcomes include the intubation duration (from passage of the incisors to the first capnogram), the first intubation success rate, the quality of visualization of the glottis (Cormak and Lehane's score modified by Yentis),[27] the percentage of glottic opening (POGO),[28] the use of adjunctive manoeuvres and alternative techniques, the occurrence of oesophageal intubation, failure of tracheal intubation, the incidence of arterial oxygen desaturation (SpO_2 < 92%), the perception of a difficult intubation (using a numerical scale ranging from 0 for "no difficulty" to 10 for "extreme difficulty"), the Intubation Difficulty Scale score,[29] cooperation among the various members of the anaesthesia team (using a scale adapted by Kraus from Ellyson & Dovidio[30]), the evolution of vital signs (heart rate and blood pressure), the frequency and severity of intubation complications (especially lip or dental injury, sore throat and hoarseness as recorded by a blinded observer during the scheduled postoperative visit).

Statistical analysis and sample size calculation

The intent-to-treat approach is considered the primary analysis. However, if more than 10% of the cases are considered to suffer from major protocol violations (for example, failure to comply with the inclusion criteria or shifting a patient from the right randomization arm to another arm), a secondary per-protocol analysis will be performed on the cases with no or minor protocol violations.

Global scores and subscores for scales will be calculated according to the results of the French validation of these scales. Since the cooperation scale adapted by Kraus has not been validated in France, it will be validated using our study data prior to starting the statistical analysis proper.

For the primary outcome, the comparison between groups will be performed using a Chi-squared test or the Fisher exact test depending on the validity. Then, a logistic multivariate regression will be performed

as follows: the need for nurse anaesthetist help (primary outcome) will be considered the dependent variable, and position (SP or HELP) and videolaryngoscope (video function on or off) will serve as the independent variables. We will add an interaction term between position and videolaryngoscope in the model to measure the influence of the synergy. As the centre will be a potential cofounding factor, this variable will be tested using multinomial multivariate regression.

For the secondary outcomes, continuous variables will be compared between groups using a Permanova+ procedure. Pseudo−analysis of variance uses a procedure to partition dissimilarity matrices that are calculated using Euclidean distances for continuous variables and simple matching for discrete ones. The Permanova+ procedure provides a pseudo F ratio, which is tested using a permutation paradigm. Discrete variables will be compared between groups using the Chi-squared test or the Fisher exact test.

Descriptive summaries will be provided for the overall group and for each group. Continuous variables will be presented as the mean ± standard deviation or as the median [interquartile range] according to their normal or non-normal distribution. Categorical variables will be presented as a number (percentage).

All statistical analyses will be performed using the Software SAS® 9.4 (SAS Institute INC., USA). A 2-sided p value less than 0.05 will be considered significant.

Missing values

Missing data will not be replaced.

Sample size calculation

Previous observations from our centre led us to consider that the need for help from a nurse anaesthetist could be reduced by 50% when the procedure is performed in the HELP with a videolaryngoscope compared to the SP with a videolaryngoscope without its video function turned on. Then, to observe a 50% reduction in the main outcome with an alpha risk of 0.05 and a beta risk of 0.8, and an attrition rate below 10%, 60 patients are required per group, resulting in a total of 240 patients.

Data registration

The study data presented in Table 1 will be recorded in an electronic database from 3 sources:

− direct entry by the staff in an electronic case report form (eCRF) available in the operating room or at the operator's desk;

− entry by an independent scorer reviewing the videotapes once blurred and edited from cues that could break the blindness of the scorer; a predefined scoring sheet has been developed that will be used as a source document; and

− direct entry in the eCRF of the scores obtained on the postoperative visit.

From the eCRF, the trial database will be established. Data collection will be monitored by trained research coordinators.

Patient withdrawal

A participant who no longer agrees to participate in the clinical trial can withdraw the informed consent at any time without need of further explanation. Participants who will withdraw from the study will be followed up according to routine clinical practice in each participating centre. To conduct the intention-to-treat analyses with as little missing data as possible, the investigator may ask the participant which aspects of the trial from which he/she wishes to withdraw (participation in the remaining follow-up assessments, use of already collected data). Whenever possible, the participant will be asked for permission to obtain data for the primary outcome measure. All randomised patients will be reported, and all data available with consent will be used in the analyses.

Safety

All the investigators are aware of the French regulation rules and know how to record any adverse events regardless of the severity on the eCRF. This study is registered as Class 2 Research according to French law. This class corresponds to research with minimal risks and constraints. In this case, in accordance with article L1123-10 of the Public Health Code, the safety of the research participants will be ensured in the same manner as usually ensured in the context of care. Adverse events and incidents occurring in the context of this research will thus be reported according to the usual channels for health vigilance, such as:

- The circuit of material vigilance in connection with the local correspondent of material vigilance of the investigator centre;

- The pharmacovigilance circuit in connection with the Pharmacovigilance Centre on which the investigating centre depends;

- The biovigilance circuit in connection with the local biovigilance correspondent of the investigating centre.

Finally, adverse events will not be reported to the ethical committee according to the law.

Data handling and retention

Data will be handled according to French law. All original records (including consent forms, reports of suspected unexpected serious adverse reactions and relevant correspondences) will be archived at trial sites for 15 years. The clean trial database file will be anonymised and maintained for 15 years.

Patient and public involvement

Patients and public are not involved in any of the phases of this study.

ETHICS AND DISSEMINATION

Ethics

Ethics approval was sought and obtained for the HELP-VDL trial from the Ethical Committee Ile de France V (Paris, France) on November 6th, 2018, with the reference number 18.09.11.39700 CAT 2. Written informed consent is required from patients to enter the study. The HELP-VDL trial is registered at ClinicalTrials.gov with the trial identification number NCT03987009.

Participant recruitment began July 3rd, 2019. We expect to complete recruitment in one year.

Dissemination

The Consolidated Standards of Reporting Trials (CONSORT) to guide protocol and study design will be followed.[31 32] All dissemination will involve aggregate data only and be undertaken using the CONSORT 2010 statement: updated guidelines for reporting parallel-group randomised trials[33] and the template for intervention description and replication checklist.[34]

Publication plan

Scientific presentations and reports corresponding to the study will be written under the responsibility of the coordinating investigator of the study with the agreement of the principal investigators and the methodologist. The coauthors of the report and the publications will be the investigators and clinicians involved, on a pro rata basis of their contribution in the study, as well as the biostatistician and associated

researchers. All trial sites will be acknowledged, and all investigators at these sites will appear with their names under 'the HELP-VDL investigators' in an appendix to the final manuscript. Rules on publication will follow international recommendations.[35]

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FIGURE LEGEND

Figure 1. Trial procedures.

DATA STATEMENT

Data will be available in the Dryad repository.

AUTHOR CONTRIBUTIONS

MLG, JT, and MF contributed to the conception and design of the research protocol.

ZC, GD, JO, and MLG provided critical input pertaining to the design of the trial interventions and procedures and will make substantial contributions to the acquisition and interpretation of the data.

MF wrote the first draft of the protocol and this manuscript. JT designed the statistical analysis plan.

All authors (MLG, ZC, GD, JO, JT, and MF) critically revised and modified the protocol and the article. They all approved the final version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work will be appropriately investigated and resolved.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. Hospital Foch, who supported the study, has no role in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether Hospital Foch will have ultimate authority over any of these activities.

COMPETING INTERESTS STATEMENT

The authors declare that they have no competing interests.

PATIENT CONSENT

Required.

ACKNOWLEDGEMENTS

This work was sponsored by the Clinical Research Department of Foch Hospital.

Table1. Schedule for enrolment, interventions, and assessments

	STUDY PERIOD				
	Enrolment	**Intervention**			
TIMEPOINT	Preoperative visit*	Before anaesthesia	During anaesthesia	After anaesthesia	Completion visit**
ENROLMENT:					
Eligibility	X				
Informed consent	X				
Demographic characteristics	X				
Allocation		X			
INTERVENTIONS:					
Sniffing position and McGrath Mac videolaryngoscope			X		
Sniffing position and McGrath Mac videolaryngoscope with a masked screen			X		
HELP and McGrath Mac videolaryngoscope			X		
HELP and McGrath Mac videolaryngoscope with a masked screen			X		
ASSESSMENTS:					
Proportion of orotracheal intubations for which the assistance of a nurse anaesthetist is required by the operator (primary outcome)			X		
Intubation time			X		
First intubation success rate					
Visualization of the glottis			X		
Adjunctive manoeuvres and alternative techniques			X		
Oesophageal intubation, failure and complications of tracheal intubation			X		
Arterial oxygen desaturation			X		
Difficulty with intubation (numerical scale and Intubation Difficulty Scale)			X		
Kraus-adapted scale of cooperation			X		
Evolution of vital signs			X		
Hoarseness					X
Sore throat					X
Adverse events			X		X

*: Preoperative visits are performed within the 2 weeks before the day of anaesthesia

**: Completion visits are usually performed on the first postoperative day but no later than three days after surgery (if surgery was performed on a Friday).

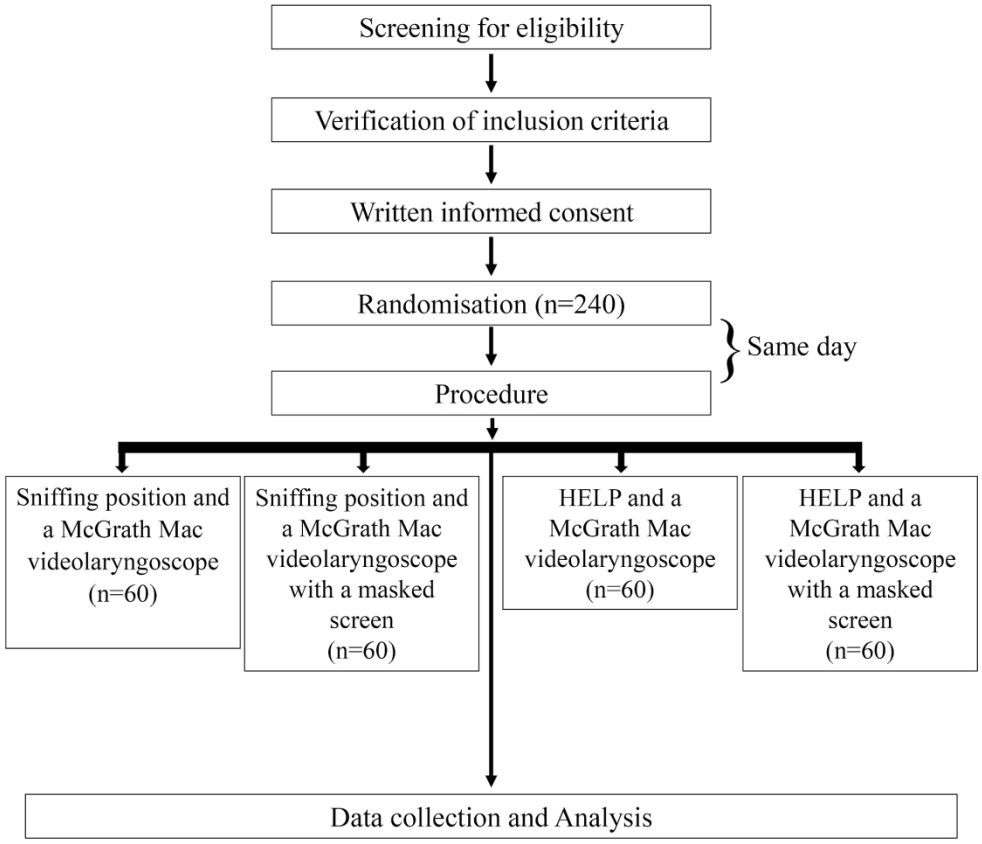

Figure 1

180x180mm (300 x 300 DPI)

BMJ Open

HELP-VDL: study protocol for a multicentre, open, randomised, controlled clinical trial comparing the use of the head-elevated laryngoscopy position and the use of a videolaryngoscope to facilitate orotracheal intubation in a patient population without predictable difficulty of intubation

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-036570.R2
Article Type:	Protocol
Date Submitted by the Author:	22-May-2020
Complete List of Authors:	Le Guen, Morgan; Hopital Foch, Department of Anesthesiology Coppere, Zoé; Fondation Ophtalmologique Adolphe de Rothschild, Department of Anaesthesiology Dufour, Guillaume ; Institut Mutualiste Montsouris, Department of Anaesthesiology Ouattara, Jonathan ; Groupe hospitalier Paris Saint-Joseph, Department of Anaesthesiology Trichereau, Julie; Hopital Foch, Research Unit Fischler, Marc; Hopital Foch, Anesthesia
Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Surgery
Keywords:	Adult anaesthesia < ANAESTHETICS, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Adult surgery < SURGERY

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HELP-VDL: study protocol for a multicentre, open, randomised, controlled clinical trial comparing the use of the head-elevated laryngoscopy position and the use of a videolaryngoscope to facilitate orotracheal intubation in a patient population without predictable difficulty of intubation

Abbreviated title: Head-elevated position and videolaryngoscope for intubation

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Key words: Anaesthesia, General - Intubation, Intratracheal - Equipment and Supplies - Randomised Controlled Trial

Word count: 3318 words for the main body

ABSTRACT

Introduction: Tracheal intubation remains an everyday challenge for anaesthesiologists, even in patients without suspected difficult airways. The ideal positioning of the patient's head (flat, raised a few centimetres on a cushion in the sniffing position (SP), or raised to achieve horizontal alignment between the external acoustic meatus and the sternal angle) and the use of videolaryngoscopy remain controversial. This trial aims to compare the efficacy for orotracheal intubation of the SP or the head-elevated laryngoscopy position (HELP), which has been shown to improve laryngeal visualization and the intubation condition particularly in obese patients, in combination with a McGrath Mac videolaryngoscope whose video screen is either on or off (Video or NoVideo).

Methods and analysis: The HELP-VDL factorial trial is a prospective, randomised, parallel, multicentre, open study of 240 adult patients undergoing tracheal intubation under general anaesthesia. Patients will be allocated into four groups: SP-NoVideo, HELP-NoVideo, SP-Video, and HELP-Video. The primary outcome is the proportion of orotracheal intubations that requires the assistance of a nurse anaesthetist. The secondary outcomes include the intubation duration, the first intubation success rate, the quality of visualization of the glottis, the glottis visualization score, adjunctive manoeuvres and alternative techniques used, the occurrence of oesophageal intubation, failure of tracheal intubation, the incidence of arterial oxygen desaturation, the perception of a difficult intubation, the score on the Intubation Difficulty Scale, cooperation among the members of the anaesthesia team, the evolution of vital signs, and the frequency and severity of intubation complications. Data will be analysed on the intention-to-treat principle and a per-protocol basis.

Ethics and dissemination: Ethics approval was obtained from the Ethical Committee Ile de France V (Paris, France). Participant recruitment began July 3rd, 2019. The results will be submitted for publication in peer-reviewed journals. Trial registration number: ClinicalTrials.gov (NCT03987009).

STRENGTHS and LIMITATIONS of this STUDY

- The primary outcome was pragmatically selected to represent the clinical relevance of the difficulty of tracheal intubation.
- The risk of selection and allocation biases will be reduced through the use of computer-generated randomisation and allocation concealment.
- Only patients without predictable difficulty of intubation will be included since the indication for videolaryngoscopy is disputable in this population.
- The head-elevated position is not amenable to the blinding of patients or clinical or research staff; consequently, this is an open study.
- The study uses the McGrath Mac videolaryngoscope, and the results will not be readily extended to all videolaryngoscopes since major differences exist between them.

INTRODUCTION

Airway management remains an important determinant of morbidity and mortality in anaesthesia despite progress in recognizing factors that are predictive of difficult mask ventilation and intubation.[1] Many recommendations have been published regarding the practice of intubation in anaesthesia.[2 3] Our study focuses on two topics that remain under discussion: the position of the patient's head and the use of a videolaryngoscope.

Although the position with the head flat is used by some anaesthesiologists, most place the patient in the sniffing position (SP, a supine torso with the neck flexed forward and the head extended). However, this choice has been questioned since this position does not allow alignment of the three important axes (the mouth, pharynx and larynx) in awake volunteers with normal airways and anatomy as shown by magnetic resonance imaging.[4] A more elevated head position with the back tilted at 25 degrees by breaking the operating table at the hips has been proposed, which improves the laryngeal view,[5] facilitates tracheal intubation in surgical patients,[6 7] and decreases airway-related complications in patients undergoing emergent tracheal intubation outside of the operating room.[8] This proposed position led to a position called bed-up-head-elevated (BUHE), which has been proposed as the standard intubation position for all patients.[9] A similar position with the head and neck raised, the "head-elevated laryngoscopy position" (HELP), is specified by an anatomical marker—an imaginary horizontal line should connect the patient's sternal notch with the external auditory meatus.[10] The HELP has been proven to be a better position for intubation in obese[11-14] and lean patients.[14] In patients with an expected difficult intubation, positioning the patient in the HELP compared to the SP led to a higher rate of successful endotracheal intubation and an improved laryngeal view.[15] A similar result has been reported when novices perform intubation on a simulator configured to have a difficult airway.[16] However, a systematic review and meta-analysis of randomized clinical trials showed no favourable aspects of the ramped position compared to the sniffing position,[17] while more favourable results have been reported in non-randomized clinical trials.[13 14] This contrast renders the effectiveness of the HELP controversial. The HELP can be achieved with a combination of hospital pillows and/or a stack of blankets[18] or by using a dedicated device such as the Troop Elevation Pillow (Mercury Medical, Clearwater, FL, USA), Pi's Pillow (American Eagle Medical, NY, USA), and the Oxford Head

Elevating Laryngoscopy Pillow (Alma Medical, Oxford, UK). The AirPal RAMP™ mattress was selected in this trial because it has two compartments: the first compartment steers the patient towards the sniffing position, and the second compartment provides the HELP and allows adjustment of the height of the compartments to the patient's morphology.

Videolaryngoscopy represents a major advance in airway management. A recent Cochrane Systematic Review concluded that videolaryngoscopy eased laryngeal views and reduced difficult visualization and intubation difficulty.[19] However, its role is still debated as a first-line method or a rescue strategy in cases of suspected airway difficulty. Systematic use of videolaryngoscopy entails discarding the standard Macintosh laryngoscope,[20] which has not been supported by clinical studies, especially those of Wallace et al.[21] and Thion et al.[22] We selected the McGrath Mac videolaryngoscope (Covidien/Medtronic, Minneapolis, MN, USA) for this trial since this apparatus has the advantage of being almost identical to the classic Macintosh laryngoscope, which still remains a reference for many anaesthesiologists. Conversely, this choice implies that the results of our study will not be readily generalizable to all videolaryngoscopes since major differences exist between videolaryngoscopes, such as hyperangulated-blade videolaryngoscopes, videolaryngoscopes with a guide channel, and Macintosh blade-geometry videolaryngoscopes.

The main purpose of this study, which will be carried out under real-world conditions, is to show whether combining the HELP and videolaryngoscopy reduces the need for a nurse anaesthetist to assist the anaesthesiologist in performing tracheal intubation. This main outcome is original since it reflects "real life" much more than criteria usually used in studies on tracheal intubation, *i.e.*, time to intubate or number of attempts, etc., which have little clinical relevance. A few more seconds or two or even three attempts have a very limited clinical impact, and failure to intubate is too rare to be used as the principal criterion of evaluation when the study bears on patients with a "normal" airway.

METHODS AND ANALYSIS

Trial design

The HELP-VDL trial is an investigator-initiated, multicentre, randomised, parallel-group, open factorial clinical trial with allocation of patients scheduled to undergo orotracheal intubation for general anaesthesia to groups subjected to a combination of two factors: position (sniffing or HELP) and a McGrath Mac videolaryngoscope (with or without using the video screen, with the latter corresponding to direct laryngoscopy). The trial will be conducted at five Parisian private nonprofit tertiary medical centres.

Participant eligibility and consent

Trial site investigators will identify consecutive eligible patients from the listed criteria. Eligible patients will receive written and oral information and will be included after investigators have obtained informed written consent.

Inclusion criteria

Patients with American Society of Anesthesiologists (ASA) physical status classes of I to III who are 18 to 89 years old and scheduled for elective surgical procedures that require orotracheal intubation for general anaesthesia will be enrolled in the study.

Non-inclusion criteria

Pregnant or lactating women will be excluded as will patients with anticipated difficult mask ventilation[23] or anticipated difficult intubation (Arné score $\geq$ 11),[24] patients requiring a rapid sequence induction, patients requiring the use of a double-lumen tube, patients scheduled for a surgical procedure involving the mouth or the upper airway, and patients with a contra-indication to one of the drugs required by the protocol.

Allocation

Patients will be randomised into four groups in this factorial trial at a 1:1:1:1 ratio:

- Group A: the SP plus a McGrath Mac videolaryngoscope with its screen deactivated to mimic a plain laryngoscope (SP-NoVideo);

- Group B: the HELP plus a McGrath Mac videolaryngoscope with a deactivated video screen (HELP-NoVideo);

- Group C: the SP plus a McGrath Mac videolaryngoscope with an activated video screen (SP-Video); and

- Group D: the HELP plus a McGrath Mac videolaryngoscope with its video screen activated (HELP-Video).

To ensure group comparability, a plan of randomisation will be used. Centralised randomisation using fixed-size blocks will be performed by an independent biostatistician not involved in the trial, from the Research Unit of the Promotor using SAS® v9.4 (SAS France, 77257 Brie Comte Robert, France). Each patient will be given a unique patient number and a randomisation number (patient code) when the investigator connects to an Interactive Web Response System managed by an independent Contract Research Organization (Clinfile, 78146 Vélizy-Villacoublay, France) using a protected password just before the induction of anaesthesia.

Blinding

Each procedure is recorded on videotape, with the recording person at the patient's feet. This video will be used to evaluate the primary outcome and some secondary outcomes. Thus, the patient's position, SP or HELP, cannot be blinded to the outcome assessors, unlike the activation or not of the videolaryngoscope screen. Similarly, the patient can remember the position in which he or she was placed. Under these conditions, this is an open study.

Interventions

Figure 1 outlines the trial procedures, and Table 1 shows the schedule for enrolment, interventions, and assessments.

Preoperative period

Inclusion and non-inclusion criteria will be verified during a pre-anaesthesia visit; the criteria will be confirmed by the anaesthesiologist in charge of the patient at the time of the anaesthesia.

Patients will receive complete, reliable information on the study at the time of the pre-anaesthetic visit. At this occasion, a written notice of information and a consent form will be handed over to the patient. This form should be completed by the patient (first and last names, signature, and date) and the investigator or his/her representative (first and last names, signature, and date) before the beginning of any trial-specific procedure. Two originals will be signed: one for the patient and one for the investigator.

Three persons are required to run the procedure: an anaesthesiologist with a specific training pertaining to the study procedures prior to the beginning of the trial, a nurse anaesthetist who will help the anaesthesiologist in case of difficulty, and an observer at the feet of the patient who will be unable to see whether the screen of the videolaryngoscope is activated and will videotape the preoxygenation and intubation sequence. The recording will be terminated as soon as intubation is completed or when failure to intubate is declared. The patient's authorization to use the recording will be obtained at the time of consent. In addition, an independent assistant will review all recordings ensuring proper blurring of the patients' face and removal of any spoken indication that could hinder the blindness of the outcome assessor.

Study-specific technical notes have been developed describing how the recordings should be made, downloaded, erased from the recorder, blurred and cleared of spoken indications prior to being transferred for outcome scoring.

Intraoperative period

In all cases, the patient will receive care during the induction and intubation periods from a physician anaesthetist and a nurse anaesthetist as is usual in the hospitals where the protocol takes place. Patients will have standard monitoring in the operating room, *i.e.,* heart rate, non-invasive blood pressure, pulse oximetry, capnography, bispectral index, and quantitative measurement of neuromuscular block. A peripheral venous line will be established.

The proper functioning of the AirPal RAMP™ mattress (Rapid Airway Management Positioner, AirPal®-Patient Transfer Systems, PA 18034, USA) will be checked before the patient enters the operating room; then, the AirPal RAMP™ will be deflated. The patient will be placed in the supine

position and then positioned in either the SP or the HELP according to randomisation. The AirPal mattress has two distinct inflatable compartments; when inflated, the lower one corresponds to an 8-cm-high pillow (sniffing position), while the upper one, when inflated, ensures that the patient is in the HELP with the external auditory meatus at the same level as the suprasternal notch.

Following adequate preoxygenation using 100% oxygen via a face mask for at least 3 minutes to reach an end-tidal oxygen fraction ≥ 90%, anaesthesia will be induced via an intravenous injection of propofol and sufentanil or remifentanil. Atracurium or rocuronium will be administered for neuromuscular blockade. Bag-mask ventilation will be continued with 100% oxygen until muscle relaxation is confirmed (no response to a train of four nerve stimulations). The bispectral index should be less than 60; if not, an additional bolus dose of propofol will be administered. The anaesthesiologist will choose either a 3 or a 4 blade size for the McGrath Mac laryngoscope and will generally use a tracheal tube size with an internal diameter of 7 mm (women) or 7.5 mm (men). At any time and whatever the circumstances, the anaesthesiologist may ask the anaesthetist nurse to apply external laryngeal pressure, use a stylet, change the plastic blade or use a metal blade, change the intubation technique (insertion of a laryngeal mask or Fastrach LMA™, fibroscopy, trans-tracheal oxygenation, and even tracheostomy), activate the screen of the videolaryngoscope, or interrupt anaesthesia.

After tracheal intubation, the upper cushion is deflated, which leaves the patients in the R+ groups in the same position (the head raised 8 cm above the table level) as those in the R− groups. The deflation of the pillow is not video recorded. Anaesthesia is then continued according to the routine procedures of the anaesthesia department.

Postoperative period

The research completion visit will take place no more than three days after surgery, if surgery was performed on a Friday, and usually on the first postoperative day. Two questions are asked with four possible answers. To the question “Are you hoarse?”, four responses are possible: no hoarseness; hoarseness noticed only by the patient; hoarseness obvious for the observer; and aphonia.[25] To the question “Do you have a sore throat?”, four responses are possible: no; mild (pain when swallowing); moderate (permanent pain increasing with swallowing); and severe (pain interfering with diet and requiring analgesia).[26]

Outcomes measures

Primary outcome measure

The primary outcome is the proportion of orotracheal intubations for which the assistance of a third party (a nurse anaesthetist) is necessary upon request of the operator.

Secondary outcomes measures

Secondary outcomes include the intubation duration (from passage of the incisors to the first capnogram), the first intubation success rate, the quality of visualization of the glottis (Cormak and Lehane's score modified by Yentis),[27] the percentage of glottic opening (POGO),[28] the use of adjunctive manoeuvres and alternative techniques, the occurrence of oesophageal intubation, failure of tracheal intubation, the incidence of arterial oxygen desaturation (SpO_2 < 92%), the perception of a difficult intubation (using a numerical scale ranging from 0 for "no difficulty" to 10 for "extreme difficulty"), the Intubation Difficulty Scale score,[29] cooperation among the various members of the anaesthesia team (using a scale adapted by Kraus from Ellyson & Dovidio[30]), the evolution of vital signs (heart rate and blood pressure), the frequency and severity of intubation complications (especially lip or dental injury, sore throat and hoarseness as recorded by a blinded observer during the scheduled postoperative visit).

Statistical analysis and sample size calculation

The intent-to-treat approach is considered the primary analysis. However, if more than 10% of the cases are considered to suffer from major protocol violations (for example, failure to comply with the inclusion criteria or shifting a patient from the right randomization arm to another arm), a secondary per-protocol analysis will be performed on the cases with no or minor protocol violations.

Global scores and subscores for scales will be calculated according to the results of the French validation of these scales. Since the cooperation scale adapted by Kraus has not been validated in France, it will be validated using our study data prior to starting the statistical analysis proper.

For the primary outcome, the comparison between groups will be performed using a Chi-squared test or the Fisher exact test depending on the validity. Then, a logistic multivariate regression will be performed

as follows: the need for nurse anaesthetist help (primary outcome) will be considered the dependent variable, and position (SP or HELP) and videolaryngoscope (video function on or off) will serve as the independent variables. We will add an interaction term between position and videolaryngoscope in the model to measure the influence of the synergy. As the centre will be a potential cofounding factor, this variable will be tested as an independent variable in the model.

For the secondary outcomes, continuous variables will be compared between groups using a Permanova+ procedure. Pseudo−analysis of variance uses a procedure to partition dissimilarity matrices that are calculated using Euclidean distances for continuous variables and simple matching for discrete ones. The Permanova+ procedure provides a pseudo F ratio, which is tested using a permutation paradigm. Discrete variables will be compared between groups using the Chi-squared test or the Fisher exact test.

Descriptive summaries will be provided for the overall group and for each group. Continuous variables will be presented as the mean ± standard deviation or as the median [interquartile range] according to their normal or non-normal distribution. Categorical variables will be presented as a number (percentage).

All statistical analyses will be performed using the Software SAS® 9.4 (SAS Institute INC., USA). A 2-sided p value less than 0.05 will be considered significant.

Missing values

Missing data will not be replaced.

Sample size calculation

Previous observations from our centre showed that the operator had to resort to the help of a nurse anaesthetist in 50% of the cases when intubation was performed without video function. We assume that the need for help could be reduced by 50% when the procedure is performed using the video function turned on. Thus, to observe a 50% reduction in the main outcome with an alpha risk of 0.05 and a beta risk of 0.8, and an attrition rate below 10%, 60 patients are required per group, resulting in a total of 240 patients.

Data registration

The study data presented in Table 1 will be recorded in an electronic database from 3 sources:

− direct entry by the staff in an electronic case report form (eCRF) available in the operating room or at the operator's desk;

− entry by an independent scorer reviewing the videotapes once blurred and edited from cues that could break the blindness of the scorer; a predefined scoring sheet has been developed that will be used as a source document; and

− direct entry in the eCRF of the scores obtained on the postoperative visit.

From the eCRF, the trial database will be established. Data collection will be monitored by trained research coordinators.

Patient withdrawal

A participant who no longer agrees to participate in the clinical trial can withdraw the informed consent at any time without need of further explanation. Participants who will withdraw from the study will be followed up according to routine clinical practice in each participating centre. To conduct the intention-to-treat analyses with as little missing data as possible, the investigator may ask the participant which aspects of the trial from which he/she wishes to withdraw (participation in the remaining follow-up assessments, use of already collected data). Whenever possible, the participant will be asked for permission to obtain data for the primary outcome measure. All randomised patients will be reported, and all data available with consent will be used in the analyses.

Safety

All the investigators are aware of the French regulation rules and know how to record any adverse events regardless of the severity on the eCRF. This study is registered as Class 2 Research according to French law. This class corresponds to research with minimal risks and constraints. In this case, in accordance with article L1123-10 of the Public Health Code, the safety of the research participants will be ensured in the same manner as usually ensured in the context of care. Adverse events and incidents occurring in the context of this research will thus be reported according to the usual channels for health vigilance, such as:

- The circuit of material vigilance in connection with the local correspondent of material vigilance of the investigator centre;

- The pharmacovigilance circuit in connection with the Pharmacovigilance Centre on which the investigating centre depends;

- The biovigilance circuit in connection with the local biovigilance correspondent of the investigating centre.

Finally, adverse events will not be reported to the ethical committee according to the law.

Data handling and retention

Data will be handled according to French law. All original records (including consent forms, reports of suspected unexpected serious adverse reactions and relevant correspondences) will be archived at trial sites for 15 years. The clean trial database file will be anonymised and maintained for 15 years.

Patient and public involvement

Patients and public are not involved in any of the phases of this study.

ETHICS AND DISSEMINATION

Ethics

Ethics approval was sought and obtained for the HELP-VDL trial from the Ethical Committee Ile de France V (Paris, France) on November 6th, 2018, with the reference number 18.09.11.39700 CAT 2. Written informed consent is required from patients to enter the study. The HELP-VDL trial is registered at ClinicalTrials.gov with the trial identification number NCT03987009.

Participant recruitment began July 3rd, 2019. We expect to complete recruitment in one year.

Dissemination

The Consolidated Standards of Reporting Trials (CONSORT) to guide protocol and study design will be followed.[31 32] All dissemination will involve aggregate data only and be undertaken using the CONSORT 2010 statement: updated guidelines for reporting parallel-group randomised trials[33] and the template for intervention description and replication checklist.[34]

Publication plan

Scientific presentations and reports corresponding to the study will be written under the responsibility of the coordinating investigator of the study with the agreement of the principal investigators and the methodologist. The coauthors of the report and the publications will be the investigators and clinicians involved, on a pro rata basis of their contribution in the study, as well as the biostatistician and associated

researchers. All trial sites will be acknowledged, and all investigators at these sites will appear with their names under 'the HELP-VDL investigators' in an appendix to the final manuscript. Rules on publication will follow international recommendations.[35]

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FIGURE LEGEND

Figure 1. Trial procedures.

DATA STATEMENT

Data will be available in the Dryad repository.

AUTHOR CONTRIBUTIONS

MLG, JT, and MF contributed to the conception and design of the research protocol.

ZC, GD, JO, and MLG provided critical input pertaining to the design of the trial interventions and procedures and will make substantial contributions to the acquisition and interpretation of the data.

MF wrote the first draft of the protocol and this manuscript. JT designed the statistical analysis plan.

All authors (MLG, ZC, GD, JO, JT, and MF) critically revised and modified the protocol and the article. They all approved the final version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work will be appropriately investigated and resolved.

FUNDING

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. Hospital Foch, who supported the study, has no role in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether Hospital Foch will have ultimate authority over any of these activities.

COMPETING INTERESTS STATEMENT

The authors declare that they have no competing interests.

PATIENT CONSENT

Required.

ACKNOWLEDGEMENTS

This work was sponsored by the Clinical Research Department of Foch Hospital.

Table1. Schedule for enrolment, interventions, and assessments

	STUDY PERIOD				
	Enrolment	**Intervention**			
TIMEPOINT	Preoperative visit*	Before anaesthesia	During anaesthesia	After anaesthesia	Completion visit**
ENROLMENT:					
Eligibility	X				
Informed consent	X				
Demographic characteristics	X				
Allocation		X			
INTERVENTIONS:					
Sniffing position and McGrath Mac videolaryngoscope			X		
Sniffing position and McGrath Mac videolaryngoscope with a masked screen			X		
HELP and McGrath Mac videolaryngoscope			X		
HELP and McGrath Mac videolaryngoscope with a masked screen			X		
ASSESSMENTS:					
Proportion of orotracheal intubations for which the assistance of a nurse anaesthetist is required by the operator (primary outcome)			X		
Intubation time			X		
First intubation success rate					
Visualization of the glottis			X		
Adjunctive manoeuvres and alternative techniques			X		
Oesophageal intubation, failure and complications of tracheal intubation			X		
Arterial oxygen desaturation			X		
Difficulty with intubation (numerical scale and Intubation Difficulty Scale)			X		
Kraus-adapted scale of cooperation			X		
Evolution of vital signs			X		
Hoarseness					X
Sore throat					X
Adverse events			X		X

*: Preoperative visits are performed within the 2 weeks before the day of anaesthesia

**: Completion visits are usually performed on the first postoperative day but no later than three days after surgery (if surgery was performed on a Friday).

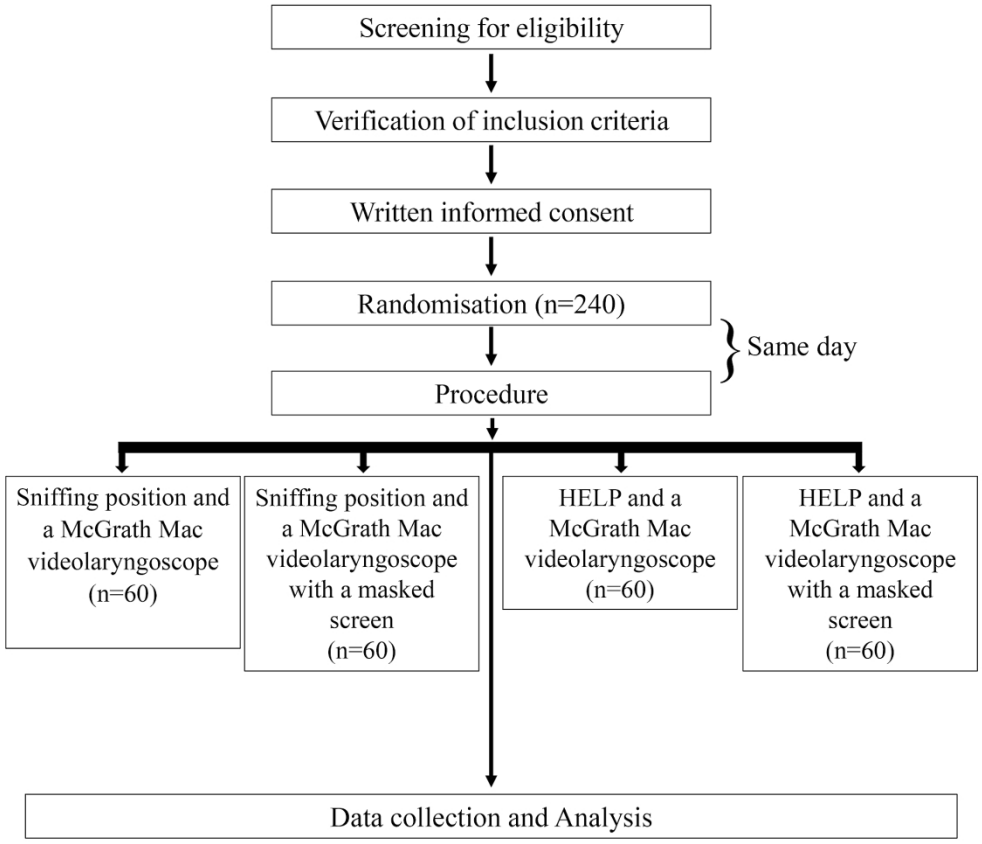

Figure 1

180x180mm (300 x 300 DPI)