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SYSTEMATIC REVIEW

The right interface for the right patient in noninvasive ventilation: a systematic review

Paola Pierucci [a,b], Andrea Portacci[a], Giovanna Elisiana Carpagnano [a], Paolo Banfi[c], Claudia Crimi [d], Giovanni Misseri[e] and Cesare Gregoretti [f]

[a]Cardiothoracic Department, Respiratory and Critical care, Unit Bari Policlinic University Hospital, Bari, Italy; [b]Section of Respiratory Diseases, Department of Basic Medical Science Neuroscience and Sense Organs, University of Bari 'Aldo Moro', Bari, Italy; [c]Department of respiratory rehabilitation, IRCCS Fondazione Don Carlo Gnocchi, Milano, Italy; [d]Respiratory Medicine Unit, "Policlinico-Vittorio Emanuele San Marco" University Hospital, Catania, Italy; [e]Fondazione Instituto "G. Giglio" Cefalu', Palermo, Italy; [f]Department of Surgical, Oncological and Oral Science (Di.Chir.On. S.), University of Palermo, Italy and Fondazione Istituto "G.Giglio" Cefalù', Palermo, Italy

ABSTRACT

Introduction: Research in the field of noninvasive ventilation (NIV) has contributed to the development of new NIV interfaces. However, interface tolerance plays a crucial role in determining the beneficial effects of NIV therapy.

Areas covered: This systematic review explores the most significant scientific research on NIV interfaces, with a focus on the potential impact that their design might have on treatment adherence and clinical outcomes. The rationale on the choice of the right interface among the wide variety of devices that are currently available is discussed here.

Expert opinion: The paradigm 'The right mask for the right patient' seems to be difficult to achieve in real life. Ranging from acute to chronic settings, the gold standard should include the tailoring of NIV interfaces to patients' needs and preferences. However, such customization may be hampered by issues of economic nature. High production costs and the increasing demand represent consistent burdens and have to be considered when dealing with patient-tailored NIV interfaces. New research focusing on developing advanced and tailored NIV masks should be prioritized; indeed, interfaces should be designed according to the specific patient and clinical setting where they need to be used.

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1. Introduction

Since the first trial of positive pressure non-invasive ventilation (NIV) [1], significant improvement in equipment technology has occurred. Adherence to NIV treatment mainly depends on patient comfort, which ultimately contributes to improving clinical outcomes. Therefore, patients need to be provided with interfaces ensuring ease of use. In this context, respiratory physicians, physiotherapists and nurses play a pivotal role in providing the best possible care for each individual patient as far as the choice of the optimal NIV interface is concerned. There is now a growing body of literature evaluating and comparing different devices used in specific clinical settings [2–11]. This review, will explore the rationale behind the choice of NIV interfaces and discuss their distinctive characteristics that need to be considered before starting NIV. Given the interest and widespread use of non-invasive respiratory support during the COronaVIrus Disease 19 (COVID-19), we will also review some of the emerging interfaces found to be useful in this pandemic time. Finally, we will highlight some practical considerations when choosing NIV interfaces in acute settings when compared to long-term home care NIV therapy.

2. Concerning interfaces and NIV

In this systematic review, we searched articles published on Pubmed and Medline Electronic until July 31th 2021. For this purpose, two independent authors (P. P. and A. P.) performed the research using the following keywords: "Noninvasive ventilation" "NIV", "pressure support ventilation", "PSV", "Noninvasive positive pressure ventilation", "NIPPV" and "Continuous positive pressure ventilation", "CPAP". We then combined each term with: "interface", "nasal mask", "oral mask"," oronasal mask", "total face mask", "nasal pillows", "helmet", "hybrid mask", "mouthpiece", "custom mask" or "made to measure mask". Discrepancies in selections were solved by consensus, with the help of the third author (G. E.C.). We also checked references of relevant articles to find potential articles not retrieved by the databases search. We excluded articles in languages other than English, duplicates and non-relevant articles. The manuscript follows the Prisma 2020 statement guidelines. Table 1 shows the flow diagram of all the studies included [12] and the Prisma-P checklist was added as the

CONTACT Paola Pierucci paola.pierucci@policlinico.ba.it Cardiothoracic Department, Respiratory and Critical Care Unit, Bari Polyclinic University Hospital; 'Aldo Moro' Bari University school of medicine Piazza G Cesare 12 70121 Bari, Italy

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Article highlights

- There are many different interfaces commercially available, and sometimes the choice of the right interface may become challenging. This manuscript aims to provide an accurate literature review to help the clinician in the day to day clinical practice.
- In order to understand the peculiarity of each interface all the technical aspects are described in full details either the actual constitution parts or the manufacturing of the interface or the details related to the setting and use in practice.
- The acute and the chronic setting are the two clinical scenarios where interface and NIV become necessary.In the acute setting, Fiberoptic bronchoscopy procedure may be required, therefore helmets, total or full face, or oro-nasal interfaces may be preferred.
- In the chronic setting other NIV interfaces may be instead more comfortable to initiate NIV with, such as small nasal interface, mouthpiece, oral or hybrid interfaces.
- Many pitfalls and new opportunities are described in the present manuscript to help the clinician disentangle in difficult clinical scenario and to provide with the right interface choice.
- A patient-centered perspective is always advisable when choosing an interface. New research focusing on developing advanced and tailored NIV masks should be prioritized, and interfaces should be designed according to the specific clinical setting where they need to be used.

supplementary material. At the end of the search, 152 articles were selected for the final paper. Although 28 of them were only accessible to the reader as abstracts, we included all of them in the final draft to avoid a possible selection bias.

2.1. Interfaces definition and overview

Several types of interfaces are commercially available, classified according to the design of the device and the anatomical structures to which it relates. All the interfaces may be used both during Noninvasive Ventilation (NIV) and simple Continuous Positive Airway Pressure (CPAP) in acute or home-care settings.

The common term *mask* refers to an interface enclosing:

- the whole nose (*full nasal mask)* (Figure 1A)
- only the nostrils *(nasal plugs, nasal cushions, or nasal pillows-NP)* (Figure 1B and 1C)
- only the mouth (*mouthpiece, oral mask)* (Figure 2)
- the nose and the mouth, with full nose cover *(oro-nasal mask)* (Figure 3A)
- the mouth and the nose, without full nose cover *(hybrid mask)* (Figure 3B and C)
- the nose, the mouth and the eyes *(total full face and integral mask)* (Figure 4A and B)
- the whole head and the neck *(hoods or helmets)* (Figure 5A and B)

Most interfaces are made of 2 parts: a rigid exoskeleton and a soft cushion for skin contact. The two components are often detachable, simplifying the cleaning process and allowing the replacement of damaged parts [13]. As for the anchor system, although there is still a wide use of hooks or plastic elements to fix velcro fasteners, magnetic attachments have been developed; these features are particularly beneficial for patients with reduced mobility of the upper limbs. Materials commonly used for the interface frame are thermoplastic, polyvinyl chloride or carbonate polymers.

Cushions are made and filled with soft materials to allow the best comfort to the patient and minimize unintentional air leaks. While older cushions were filled with air, more recent models are made of silicone, hydrogel, polypropylene or polyvinyl chloride [13] and some of them are equipped with a memory foam system to guarantee an even softer touch on the patient's skin. In addition, a cloth-made mask has also been designed, both for daytime and nighttime NIV. The advantage of this new mask design lays in a more comfortable interface, with inflatable cloth cushions guaranteeing less pressure/rubbing on patients' skin and possibly reducing skin breakdown.

Interfaces can be found either in a vented configuration (with intentional air leaks vented through slots or holes in the masks, without an expiratory valve) or a non-vented configuration (with an expiratory valve wherever placed in the circuit) [14]. Usually, a 'blue' or 'white/orange' mask swivel connector allows the distinction between the non-vented or vented configuration, respectively. From now on,

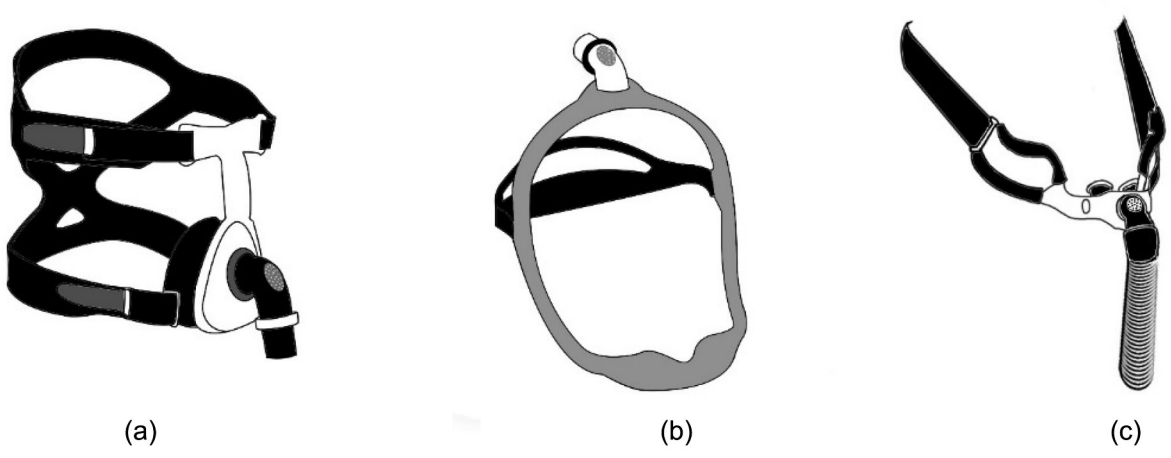
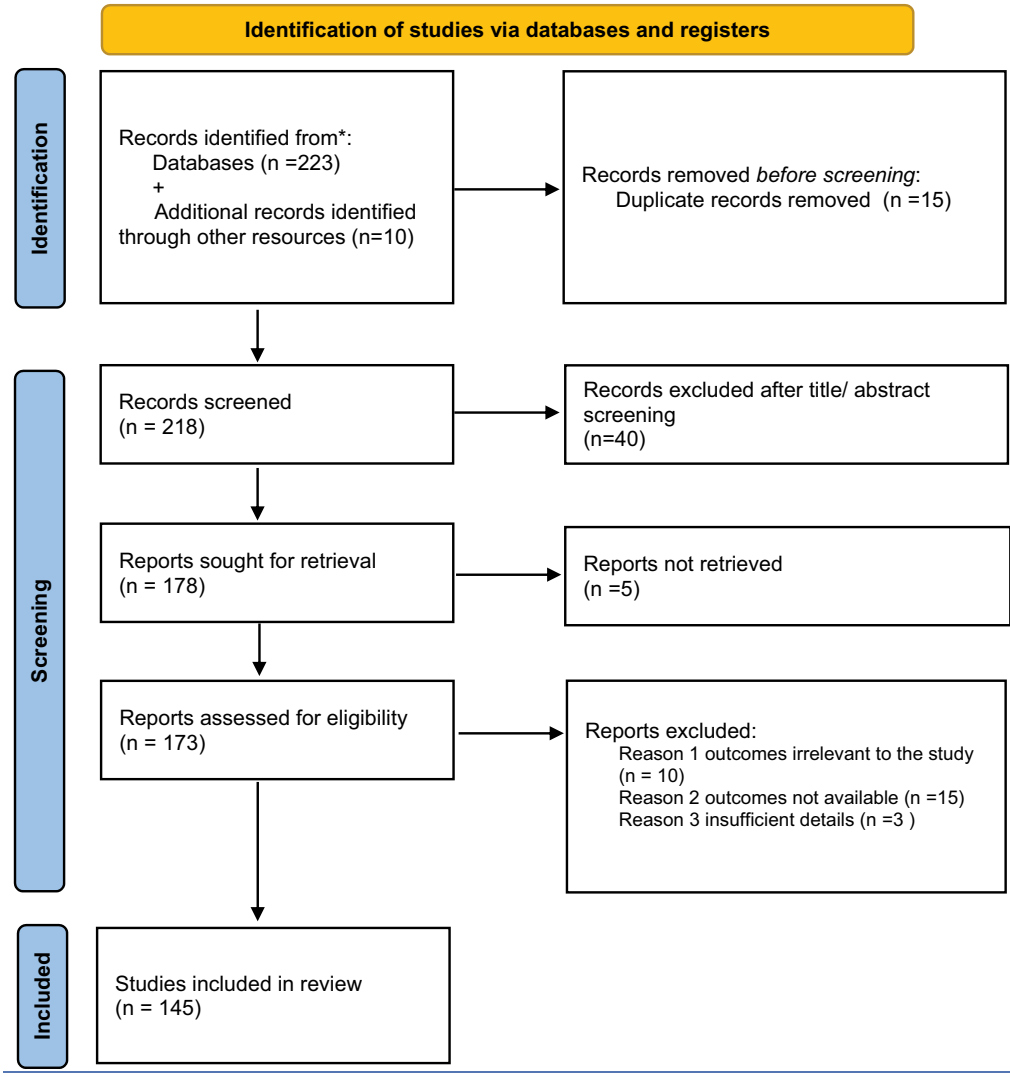


Figure 1. Nasal masks A vented nasal mask, B nasal pillows and C vented nasal cushions.

Table 1. Prisma flow diagram of all studies included in the review.



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/

Figure 2. A mouthpiece.

the paper will refer to 'Leaks' as intentional (through the vented system) or unintentional (inadvertent leaks from any source) (Figure 1 - Figure 5).

Table 2 summarizes the advantages and disadvantages of the use of each interface.

2.1.1 Nasal mask, pillows and cushions

- (Figure 1): this type of interface is commonly prescribed for both NIV and CPAP [16]. Two small cushions allow better nares sealing, significantly reducing unintentional air leaks [13]. As such interfaces have smaller sizes, patients are less likely to experience claustrophobia. Speaking, eating, coughing and expectorating are only moderately influenced by the use of these interfaces. The vented configuration is available in different shapes and sizes.

2.1.2. Mouthpiece

(Figure 2): mouthpieces are among the most suitable interfaces for patients needing intermittent daytime NIV [7,17,18], especially for patients with neuromuscular

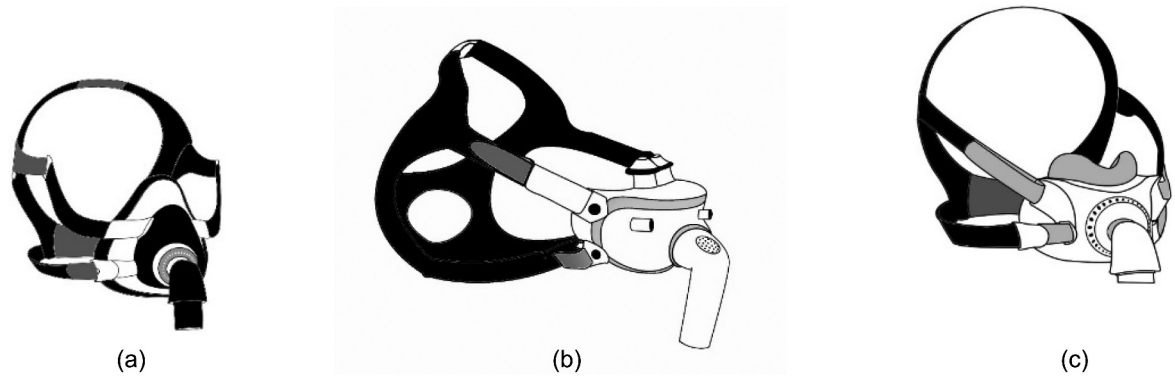


Figure 3. Oronasal Masks. A Oronasal vented mask, B Hybrid vented mask with pillows, C Hybrid vented mask last generation.

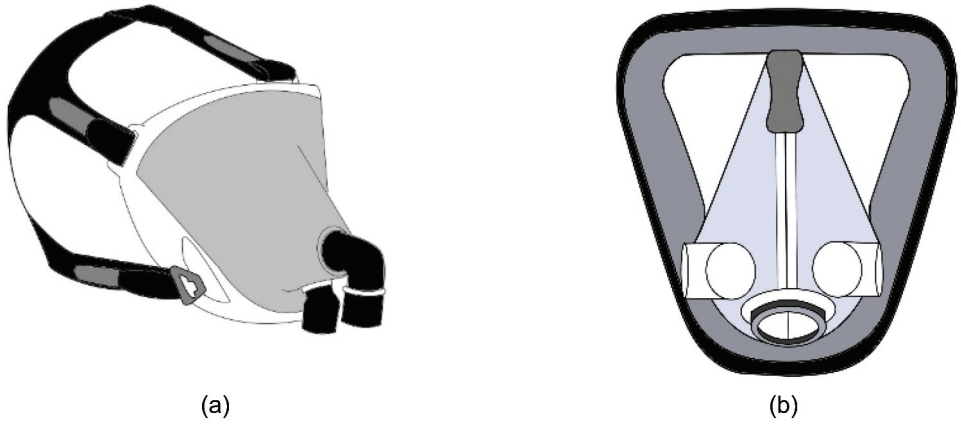


Figure 4. A Full face non vented mask with double separated inspiration and expiration tube .Figure 4 B Full face non vented Mask for FOB.

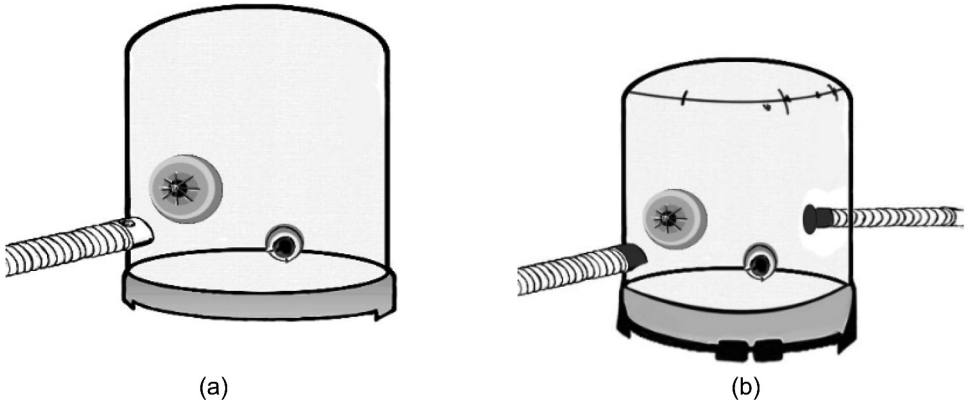


Figure 5. A helmet CPAP and B helmet NIV.

disorders. This interface is made of two parts: the mouthpiece itself and a single limb. Mouthpieces can be built with a 15 mm angle, with a 22 mm angle or they come as straw-type mouthpieces, which are supported by a rigid frame for prompt use according to patients' needs. A mouthpiece circuit can be a simple 'open' circuit or a dedicated flexible circuit. The rigid part of the mouthpiece is held in place with the lips and/or teeth. Patients usually trigger the NIV breath creating a slight negative pressure [19]. Alternatively, the 'kiss trigger' (®Philips Respironics Murrysville, USA) [20] allows patients to start the inspiratory phase only by touching the mouthpiece with their lips. In case the 'kiss trigger' is not available, the use of a backup rate is always advisable [21].

2.1.3. Oral mask

Oval-shaped interface, with a soft part that needs to be placed between teeth and lips

2.1.4. Oronasal mask

- (Figure 3A): these interfaces are suitable for both acute and chronic settings. These interfaces cover both nose

Table 2. Advantages and disadvantages of all interfaces.

INTERFACES	ADVANTAGES	DISADVANTAGES
Nasal masks (i.e Nasal Pillows, Cushion covering nose)[15,98,103,108]	• small size • allow speaking, coughing and eating without NIV interruption • less claustrophobia compared to the other interfaces • prolonged time of use up to 24 h a day • allow better opening of the retro-palatal space • NP allows to wear glasses	• mouth leaks • nasal discomfort, dryness and eventually bleeding • not suitable for high PEEP use • patients may need to have handy nasal decongestion medications
Oronasal masks [7,30,61]	• lower air leaks compared to nasal interfaces • suitable to deliver higher inspiratory and expiratory pressure use compared to nasal interfaces	• more likelihood of face and nose bridge lesions compared to nasal masks • may generate claustrophobia • does not allow speaking, coughing and eating compared to nasal masks • risk of jaw displacement • risk of vomiting and aspiration • may generate aerophagia
Mouthpieces[10,111]	• allow easily speaking, eating and secretion without NIV interruption • absence of skin breakdowns, claustrophobia and eye irritations	• may generate patient/ventilator asynchronies and nuisance alarms • may generate transient oxygen desaturation and hypoventilation due to prompt disconnection • May cause orthodontic deformities • Not suitable for night-time ventilation
Hybrid oronasal mask vented [108]	• Lack of skin breakdown on nose bridge allow to wear glasses	• less likelihood of claustrophobia compared to the others oronasal interfaces • does not allow speaking coughing and eating • same other aforementioned complications of oronasal interfaces
Full face [30]	• lack of skin breakdown on nose bridge compared to the others oronasal interfaces	• may generate claustrophobia • risk of jaw displacement • risk of vomiting and aspiration • eye dryness • same other aforementioned complications of oronasal interfaces
Helmet CPAP or NIV [37,80,81]	• absence of nasal and facial skin breakdown • aerophagia • lower unintentional leaks • allow more hours on NIV • use of higher PEEP compared to the other interfaces	• eye dryness • may be too noisy • increased dead space and CO_2 retention • higher likelihood of patient ventilator asynchrony • need dedicated settings • underarm or neck breakdown if used with armpit braces • requires team experience

and mouth. They can be vented or non-vented, and different shapes and sizes are available.

2.1.5. Hybrid Mask

- (Figure 3B and C): covers only mouth and nostrils, leaving the upper part of the face and the nasal bridge free from mask pressure. In addition, patients' visual field is not hampered by the interface itself. These characteristics (Table 2) offer a higher comfort level. When compared to first-generation hybrid masks (Figure 3A), the newer generation (Figure 3B) seems to allow more comfort and higher level of applied inspiratory pressure and PEEP (unpublished data). Hybrid masks can be vented or non-vented, and different shapes and sizes are available.

2.1.6. Total Facemask

- (Figure 4A): covers the whole face contour avoiding pressure nasal ulcers by distributing its pressure on the face perimeter. Total face masks are very easy to use. These interfaces ensure better leak management and lead to greater acceptance among patients who are intolerant to other NIV interfaces [22]. Vented or non-vented configurations are available. Total face masks may be equipped with swivel connectors with two ports (one for the inlet and one for the outlet of the respiratory circuit) (Figure 4A) [23]. Another possible option is a dedicated port for nasogastric /feeding tube insertion. A specific type of interface is designed with two halves surrounding a central hole for the passage of the fiberoptic bronchoscope (Figure 4B). These two parts are only attached at the top; therefore, the mask can be easily opened or closed from the bottom, allowing to switch to NIV promptly without removing the probe [24].

2.1.7. Helmet

(Figure 5A and 5B): this interface consists of a transparent cylindrical polyvinyl chloride cover and a plastic collar (plastic ring). In order to secure the interface, two-arm braces are connected to the collar and anchored just beneath the armpits. A 'brace-free' model allows the helmet to be secured to the patient via a hard-base ring

(placed underneath an inflatable cushion) which seals the helmet around the patient's head and neck. The air flow generated by the ventilator inflates the membrane, creating a soft cushion with a sealing effect, and improving tolerance to the interface. The cylindrical transparent part of the helmet is equipped with ports for the inspiratory and expiratory circuits and, in some models, with an anti-suffocation valve. A small manometer or an additional port for external devices insertion (feeding tube, probes, bronchoscope etc.) can also be present. There are two different types of helmets: CPAP helmets (Figure 5A), which are slightly bigger and allow the use of CPAP settings [25], and the smaller NIV helmets (Figure 5B) used for bilevel ventilation [26].

2.2. Technical aspect for NIV interface choice

Although alternative modalities of noninvasive supports may be used in clinical practice [27,28], the research in the field of NIV has focused its attention on modern interfaces suited for every patient's need. Choosing the proper type of interface is crucial to avoid NIV failure.

2.2.1. Interface shape and characteristics

Some of the mid-long term issues with NIV masks are related to the failed match between anatomical patients' features and interface structure [29]. Therefore, spending some time looking for the proper interface shape is highly suggested. Skin breakdown and pressure ulcers may often occur during NIV use, both in acute and home care settings [30–33]. The most critical area is the nasal bridge, where the skin and thin subcutaneous layers may be pressed between the nasal bone and the interface. This, in turn, may lead to hypo-perfusion of the tissues, eventually generating skin breakdown, ulcers and skin necrosis [34]. When prolonged NIV is required, hydrocolloid wound care dressing, foam dressings, or gel cushions can help to mitigate interface pressure on the skin. A mask rotation strategy could also be applied to change the points of high pressure [35,36]. Skin and interfaces hygiene is also important. The use of alternative interfaces such as a helmet, a total face mask or a hybrid mask which skip the nasal bridge can avoid pressure lesions on this site [37–42].

2.2.2. Unintentionalse leaks and noise

Unintentional air leaks management is the most critical issue during NIV use. Modern ventilators are provided with algorithms for unintentional leak compensation [43] to avoid patient-ventilator asynchrony and eventually NIV failure [43]. Patients usually complain about the tightness of the interface or the excessive pressure delivered by the ventilator. In case NIV is delivered with vented masks, their better intrinsic compensation for unintentional leaks [44,45] can limit the tightening of the interface to the patients. Unintentional leaks may cause noises, eye irritation, and sleep fragmentation [46]. Patients with chronic respiratory failure are more prone to a difficult adaptation to NIV, because of their perception of higher anxiety levels and dyspnea [47,48]. In these cases, the correct timing to start NIV may be difficult to be recognized [49,50].

2.2.3. Costs

It has been reported that helmet use in patients with Acute Respiratory Distress Syndrome (ARDS) can reduce Intensive Care Unit (ICU) length of stay and costs compared to face masks [36]. However, NIV delivered via helmets has been demonstrated to have no advantages in term of clinical gas exchange improvements when compared to NIV delivered via masks [51]. Cost considerations for the use of new materials, handcrafting and research in new technologies should always be weighed in new interface development.

2.2.4. Masks' dead space and CO_2 rebreathing

While the effectiveness of new interfaces has been proven [22,52,53], the relationship between mask's dead space and CO_2 retention within the mask has yet to be clarified. Several studies have assessed the role of interfaces in CO_2 washout [23,36,54–61]. The first data on the influence of mask's dead space on pulmonary mechanics were reported on newborns [54,55], whose differences in respiratory rate (RR), tidal volume (Vt) and work of breathing (WOB) were described according to different CO_2 washout methods. In adult patients, Navalesi et al. found in stable hypercapnic patients that $PaCO_2$ was significantly lower with a full-face mask or nasal plugs than with a nasal mask ($p < 0.01$) [36]. Later, in a bench study using CPAP on an experimental lung model, Taccone et al. demonstrated how the helmet might be considered as a "semiclosed environment", where CO_2 amount comes from CO_2 production while the flow of fresh gas is ongoing in the helmet [56]. According to this model, when the helmet is used in CPAP mode delivered by an ICU ventilator with a double limbs circuit, it causes higher CO_2 retention compared to other masks. Two different hypotheses could explain this phenomenon. First of all, the internal gas volume of the helmet remains stable compared to the tidal volume exhaled. Secondary, CPAP mode in ICU ventilator does not guarantee an adequate replacement of fresh gas flow in the helmet, as the flow generated within this ventilatory mode equals the patient's minute ventilation. High gas flow (greater than 40L/min) is required to maintain a low inspired partial pressure of CO_2 during helmet CPAP when delivered with a Venturi system or rotameters [62]. As a matter of fact, an ICU ventilator with a double-limb circuit should not be used to deliver helmet CPAP. In addition, Taccone et al. also found that a 33% reduction in the helmet volume does not affect the amount of CO_2 rebreathing at steady state [56]. Two other physiologic studies confirmed these data regarding CO_2 rebreathing with ICU ventilators [61,63]. A new helmet set up with a single limb vented circuit has been demonstrated to be able to use CPAP without a significant increase in CO_2 rebreathing [61,64].

The term "mask's dead space" has been discussed in many studies: Saatci et al. defined it as "dynamic apparatus dead space", emphasizing the influence of inspiratory/expiratory flow over mask's dead space. Moreover, they demonstrated how little the dead space/tidal volume ratio is affected by

different masks type [58]. Fraticelli and coworkers underlined the inadequacy of the term "mask's dead space", confirming its non-significative role in pulmonary mechanics [59]. Finally, Fodil and colleagues, using a fluid dynamic model, demonstrated for the first time the difference between "interface gas volume" and "effective dead space" by testing 3 types of masks:

a. The oronasal masks, which showed almost no difference between effective dead space and interface gas volume;

b. The helmet interface, in which the volume appears greater than the dead space;

c. The face integral mask, in which the ratio between interface gas volume and effective dead space is similar to the helmet.

This study, although recognizing a possible rebreathing effect using the helmet or a total face mask, also argues that CO_2 retention is greatly reduced at lower tidal volumes, considering 'probably questionable' the choice of a NIV interface based on 'mask's dead space' logic [60]. Furthermore, the aforementioned studies refer to the use of the helmet during CPAP without considering the possible dead space washout with other ventilation modes [23,65].

The addition of flow-by (namely the continuous basal flow circulating inside the circuit) may increase CO_2 washout. Signori et al. [23] in a bench study found that a total face mask with separate ports for inflow and outflow gas at the mask swivel scales down CO_2 rebreathing. Further studies are needed to confirm the clinical relevance of this mask setting.

2.2.5. Expiration port position in vented mask

In vented configuration, Schettino et al. suggested that an expiratory port located on the mask could perform better in CO_2 washout than a port located in the respiratory circuit close to the mask swivel (ie Whisper Swivel II system Philips Respironics Murrysville, USA) [66]. In addition, Saatci and colleagues demonstrated that, in a vented configuration, combining positive end-expiratory pressure (PEEP) and an expiratory port embedded in the mask could minimize rebreathing [58].

2.3. NIV interfaces in the acute setting

It is still highly questionable which NIV interface should be considered the best in the acute setting [67]. As a matter of fact, the setting of care strongly influences the choice of interface [68]. Helmets have been considered as one of the most useful NIV interface in acute respiratory failure. Total face and oronasal masks have been widely used in the acute setting and found to be non-inferior in terms of comfort, side effects and gas exchange improvement compared to the helmet in the acute setting [69–76]. These interfaces are easily fitted to patients and are very practical in the emergency setting. Unfortunately, however, skin breakdowns [30,77], claustrophobia [29], jaw displacement and risk for vomiting and aspiration are frequently reported by patients using face masks. In the case of nasal mask use, nasal obstruction or bleeding, mouth breathing and oral leaks can reduce NIV effectiveness, thus increasing the risk of NIV failure.

The helmet represents a possible alternative device, since it has been found to be non-inferior in terms of gas exchange improvement compared to the total face mask, even in hypercapnic patients, in acute settings [74]. Although the interfaces used during NIV in the treatment of viral pneumonia-related acute hypoxemic respiratory failure were rarely described and specified[78], the helmet has been demonstrated to be effective in ARDS and hypoxic respiratory failure [79], in severe COVID-19 pneumonia [80–84], in weaning from endotracheal intubation [85] and in hypercapnic respiratory failure [74]. Since the helmet can minimize skin ulcers, aerophagia and unintentional leaks, it should be preferred in these settings of care. However, on the other hand, the large amount of 'dead space' can induce a significant delay between the patient's trigger and the effective activation of the ventilator during bi-level ventilation, leading to asynchrony [61] and potential NIV failure [86]. When the helmet is coupled with neurally-adjusted ventilatory assist (NAVA) mode, it allows better patient-ventilator coordination and increases NIV acceptance and tolerance [87,88] while reducing asynchrony. Helmet drawbacks also encompass nuisance related to the helmet air flow and the painful pressure of the armpit braces, limiting the use of this interface [89]. The latter problem could be overcome by opting for a new 'brace-free' helmet. This helmet type reduces the pressure rise time (namely, the time that the ventilator takes to reach the set pressure) by reducing the upward swings during the delivery of positive pressure, eventually improving patient-ventilator interaction, if compared to conventional helmets [90,91]. It is also worth remembering that helmets use always requires training and experience [92], both for physician, physiotherapist and nurses (Table 2). During the COVID 19 pandemic, awake prone positioning in spontaneous breathing [93] and helmet CPAP use [94] have been demonstrated to be extremely successful in improving gas exchanges in severely hypoxemic patients. However, although helmets may reduce aerosolization compared to other interfaces, they are susceptible to becoming a reservoir of virus particles [78] . Therefore, extra-precaution needs to be ensured by healthcare providers when dismissing the helmet after use, in order to contain droplet dispersion and infection risks among healthcare workers [95].

Moreover, during the COVID-19 pandemic, the increased need for noninvasive respiratory support devices has led also to converting commercial surface full face snorkeling masks into interfaces that can be used to apply CPAP therapy [96].

2.4. NIV interfaces in the chronic setting

The use of long-term NIV in home care setting requires different strategies for interface choice. While the acute setting requires clinicians to achieve the best clinical result with the shortest NIV trial, in the chronic scenario this perspective is inverted. As a result, keeping a steady balance between the clinical improvement and the patient's adherence to NIV is essential to carefully identify the most suitable interface to use. Some NIV masks have been proven to be effective and well tolerated in long-term settings and for specific diseases. For instance, a comprehensive review focuses on RCT on mask use in the chronic setting found there is no difference in the efficacy or tolerance of oronasal or nasal masks [97]. A few of them will be described in the following paragraphs.

2.4.1. Obstructive Sleep Apnea Syndrome (OSAS) and Obesity Hypoventilation Syndrome (OHS)

In OSAS/OHS patients, a nasal vented mask is often the first choice [17], not only for better patients' adherence but also for the efficacy in opening the retro-palatal space without affecting jaw and tongue position. In a recent meta-analysis, Lebret et al. did not find any significant difference in gas exchanges or NIV adherence in OHS patients, confirming a prominent role of nasal masks for NIV in home settings [98]. Nevertheless, oral and oronasal masks represent good alternatives to nasal interfaces. Oral masks have been proven to be very similar to nasal masks in terms of generated pressure [97], CPAP/NIV adherence and an Epworth Sleepiness Scale improvement (ESS) [99]. Possible explanations for these results are reduced tongue displacement during sleep and the forward displacement of the jaw. Unfortunately, there is no evidence of oral mask usefulness during NIV, both in OSAS and OHS patients. Oronasal masks can be effective in presence of mouth leaks or when higher CPAP/NIV pressures are required. A major drawback of most oronasal masks in OSAS/OHS patients is the backward jaw and tongue displacement [100], eventually leading to higher CPAP levels compared to nasal masks to avoid the persistence of apnoea/hypopnoea [101]. Nasal pillows represent another viable option. Nasal pillows can be as effective as other types of interfaces and are associated with greater acceptance and comfort for the patient, independently from the titrated PEEP [102–105]. Unfortunately, data on longer follow up in OSAS/OHS patients using nasal pillows are still lacking, leaving unsolved concerns about the adherence to CPAP/NIV therapy using this interface for a longer treatment period.

2.4.2. Neuromuscular diseases

When choosing an interface for patients suffering from neuromuscular disorders, it is always important to consider the length of NIV use during the day. For patients who need only night-time NIV, an oronasal mask is frequently chosen, especially when concomitant apneas/hypopneas are diagnosed [106,107]. Besides, in case of a daytime NIV, nasal masks, nasal pillows/cushions and hybrid masks can be alternatively used, since interface rotation can minimize possible side effects arising after a long NIV trial [5,108]. Daytime use of mouthpiece has also been well described in end-stage Duchenne muscular dystrophy [109] as well as post-polio syndrome [110] and kyphoscoliosis [111]. Despite all its possible advantages, the use of the mouthpiece can induce salivation, gag reflex, gastric distension and vomiting [7]. Moreover, the mouthpiece can cause orthodontic deformities after some years of prolonged use [112]. Air leaks and alarm activation represent another important drawback. Mouthpiece use is frequently associated with excessive air leaks and for this reason, it can bring a higher rate of patient/ventilator asynchrony or lead to the elicitation of NIV alarms, causing nuisance and discomfort to the patient. Lip seals, nasal clips or plugs can be used to decrease the impact of mouth and nose leaks [110]. In addition, during mouthpiece use, a lower pressure alarm and a prolonged apnoea time are needed to correct possible noises due to alarm activation [20]. The study by Nardi and coworkers confirms that mouthpiece ventilation (MPV) can be effective as long as the patient remains connected to the mouthpiece. However, transient oxygen desaturation and hypoventilation due to disconnection from the ventilator may occur without inducing unpleasant sensations in the patients [113]. Some concerns still remain about mouthpiece use during night-time MPV [110]. Using a mouth seal can help avoid the risk of losing mouthpiece control in patients with open-mouth sleep (Table 2). Lastly, but not less importantly, in some patients with neuromuscular disease (NMD) and amyotrophic lateral sclerosis (ALS) inspiratory pressure effects and the use of an oronasal interface may promote obstructive events [114].Therefore, initiation of NIV using an oronasal interface may be associated with treatment-induced upper airway obstruction in a subset of patients. Since both expiratory positive airway pressure (EPAP) and the the amount of Delta inspiratory positive pressure applied to the airways (Δ pressure support PS or IPAP depending on machine setting) appear to play a causative role, careful titration of ventilator settings is recommended [115]. This can have significant negative consequences for some patients, such as those with ALS. It has been shown that the persistence of treatment-induced upper airway obstruction during NIV in this population results in reduced survival rates [116].

2.4.3. Chronic Obstructive Pulmonary Disease (COPD)

The choice of NIV interface in long-term NIV for COPD patients is still an unsolved issue. Despite clinical data showing no substantial differences between NIV interfaces for all the major outcomes [98], there are no globally accepted criteria for a standardized approach [117]. Data from international surveys show a clear positive trend in the use of oronasal and total face masks over the nasal interface [4]. These results are in contrast with the broader use of the nasal mask reported by the 2005 Eurovent Survey [118], suggesting a change of attitude of clinicians towards the use of NIV interfaces[11]. Many authors link this phenomenon to much broader use of the so-called 'High-Intensity' NIV, which was firstly described by Windisch et al. in 2009 [119]. According to their description, high-intensity NIV aims to reach normocapnia using the assist/control pressure mode with a progressive increase of Inspiratory Positive Airway Pressure (IPAP) and respiratory rate. According to these principles, high-intensity NIV is able to reach greater average levels of IPAP compared to 'low-intensity' NIV without any loss of treatment adherence by the patient but with higher levels of unintentional leakages [120,121]. Considering the higher levels of inspiratory pressure and the consequent increase of mouth and unintentional leakages with the use of this ventilation approach, it is easier to understand why high-intensity NIV is believed to be one of the most relevant influencers of the trend change in NIV interface choice [11]. Oronasal and total face masks can easily prevent mouth leakages, also distributing evenly the greater inspiratory pressure generated by a high-intensity NIV. Despite this data, many problems concerning high-intensity NIV and mask choices remain unsolved. As previously stated, the lack of a scientific consensus about standardized criteria of NIV interface selection leaves too much variability, both for

everyday clinical choices and for trial assessments. Secondary, only a few data are available on the physiologic effects of interfaces during nocturnal high intensity NIV trials [122]. Lastly, the long-term interface impact on adherence and efficacy of high-intensity NIV has still to be established.

2.4.4. Interfaces used during fiberoptic bronchoscopy (FOB)

NIV interfaces specifically conceived for FOB would be extremely helpful, leading to safer and easier procedures.

NIV during FOB has already been established to be feasible and safe in hypoxemic patients [123] and in acute exacerbated COPD [124], offering better results compared with the use of oxygen alone [39,54].

Considering the aforementioned data from the literature, it is clear that the interest in FOB procedures during NIV has grown exponentially during these years. Unfortunately, only few studies focused their attention on the NIV interface problem. As a matter of fact, NIV masks are frequently adapted for bronchoscopy without having a specific design or structure for endoscopic purposes. Research in the field of NIV interfaces for FOB is moving on, offering an array of clues for future clinical research. In their randomized study, Maitre et al. connected a full face mask to two different sources: the first carried oxygen only, while the second used a high-speed flow to generate positive pressure [125]. Thanks to this system, the bronchoscope can easily pass through the interface prong without any substantial pressure loss during the endoscope passage. Nevertheless, several other options are available when FOB is needed in patients undergoing an NIV trial. Heunks et al. proposed using a total face mask equipped with a plastic cylinder for the bronchoscope passage [126]. Furthermore, there are commercially available specific holed elbows for NIV interfaces, furnished with a sealing membrane for an easier passage of the bronchoscope without excessive air leaks [127]. Apart from full face masks, other NIV interfaces have been tested for endoscopic procedures. Chiner et al. evaluated the feasibility of FOB using a nasal mask in patients with acute respiratory failure [22]. Antonelli and colleagues obtained interesting results performing bronchoalveolar lavage (BAL) using the helmet in patients with acute respiratory failure [128] [129]. Recently, a new type of mask has been described as a specific tool for endoscopic manoeuvers during NIV. The design of this interface includes two halves surrounding a central hole for the passage of FOB. These two parts are only joined at the top; therefore, the mask can be easily opened or closed from the bottom, allowing a rapid passage to NIV without moving the probe. Moreover, two lateral connectors are present for the ventilator circuit or bag ventilation. This mask has been proposed during FOB [24], for fiberoptic intubation [130] and even during transesophageal echocardiography [130] with good results. (Figure 4B)

2.5. NIV interface choice: pitfalls and opportunities

Different factors are involved in patient and physician choice of NIV interfaces[131]:

2.5.1. Compliance

patients' tolerance to NIV is often suboptimal in acute setting [68,127,132]. As for the home setting, a few studies have investigated compliance or adherence to NIV [133,134]. Several factors may negatively impact the compliance or adherence in an NIV trial and interface is considered the most common factor.

2.5.2. Cognitive and behavioural dysfunctions

Anxiety, claustrophobia and cognitive impairment [135] may often be noticed during NIV nursing and initiation [29,135,136]. They have been recognized as predictors of poor NIV adaptation [137], frequently leading to asynchronies or NIV interruption [138].

2.5.3. Reducing facial coverage

nasal masks, nasal pillows and hybrid masks have the undoubtful advantage of sparing mouth coverage during CPAP/NIV treatment. One limit of such interface is that some of them do not allow high pressure delivery, on the other hand, the enhanced patients' tolerance both in acute and chronic settings represent undoubtedly an asset For example, smaller nasal masks may allow patients to wear eyeglasses without any visual impairment [139].

2.5.4. Length of interface use

The time-response effect of NIV treatment is deeply related to NIV interfaces. Considering the NIV starting at the time when the interface is placed on the patient's face, a mask-on-time trial between 2 hours and 24 hours in acute settings seems to reduce in-hospital mortality in acute hypercapnic respiratory failure (AHRF) in COPD [140,141]. This time interval can be considered the best for NIV and mask acceptance. On the contrary, NIV failure can occur for longer trials[68], as discomfort and intolerance can be too heavy a burden to bear for patients. This is the case of patients with acute hypoxemic respiratory failure, for whom the risk of failure due to the loss of interface tolerance is potentially higher because they need NIV for a prolonged time [45]. The same could happen in patients undergoing long-term, round-the-clock home care ventilation[10].

2.5.5. Considerations when choosing an NIV mask

Currently there is still an open debate on which interface for an NIV trial should be considered the best [67]. As a matter of fact, there are several features to be considered when choosing a NIV interface [16,59]:

- type of interface (nasal, oral, oronasal, hybrid, total face, nasal pillows, helmet, mouthpiece);
- acute or home care setting and disease features (i.e. hypercapnic neuromuscular vs chronic hypercapnic respiratory failure vs AHRF; patients' face contours and personal preference [142];
- breathing pattern;
- unintentional leaks
- costs;
- materials;
- patients preference;

- type of ventilator mode [143] and circuit configuration (vented vs non-vented mask)[144];
- clinician expertise.

As the comfort of interfaces is one of the crucial issues concerning NIV compliance, custom masks may represent a possible solution. In the late 80', 29 neuromuscular patients with chronic respiratory failure with nocturnal ventilation, given NIV and nasal mask were treated at home using a made-to-measure mask by modelling silicon paste onto the patient's face for at least one year [145]. These interfaces faithfully reproduced the patient's facial anatomy, ensuring a perfect adhesion of the mask with greater comfort and tolerability. Tsuboi et al. evaluated the effect on gas exchanges of a custom-made nasal mask during intermittent positive pressure ventilation [146]. In their study, the custom mask was prepared, asking the patient to breathe through a mouthpiece, while keeping their eyes closed and their nares sealed. Then, a cast of alginate was used to create the mask exoskeleton, which was finally used to obtain a resin nasal mask. In clinical settings, this new interface (called F-mask) was found to improve gas exchanges and alveolar ventilation, reduce dead space and air leaks and support even higher pressures than a 'standard' CPAP nasal mask. Interestingly, the authors underlined that this new crafting technique for the NIV mask was even more affordable, because of reduced production costs and frequency of repairs needed. The made-to-measure mask has now limited use, mainly focused on paediatric patients with facial deformities [147,148].

Following the idea of a custom NIV interface, Willow et al. have recently proposed the use of 3D printers [149]. In their feasibility study with adult volunteers, skin sensors were used to track patients' facial contours. Then, following the digital face frame, a selective laser sintering overlapped several polyamide layers to create the rigid part of the mask. Despite the lack of relevant clinical information, this new interface model guarantees reduced air leakage while providing a good comfort level. However, the higher production costs and the relevant amount of time needed to complete a single mask are issues that are still to be solved. Moreover, there is a lack of scientific evidence to support the use of this type of interface compared to others. High quality research is urgently needed in order to understand whether this new concept of NIV interface may offer more advantages compared to a standard mask with a reasonable cost-effectiveness ratio.

3. Conclusions

The paradigm 'the right mask for the right patient' seems to be difficult to achieve in real life. According to various clinical situations, moving from acute to chronic settings, the gold standard should be to tailor NIV interfaces to patients' needs and preferences. However, this may be hampered by economic issues. As a matter of fact, high production costs and the increasing demand represent consistent burdens and have to be considered when dealing with tailored NIV interfaces. New research focusing on developing advanced and tailored NIV masks should be prioritized, and interfaces should be designed according to the specific clinical setting where they need to be used. A patient-centered perspective is always advisable when developing a new interface. Pressure sensors, new materials for cushions, modern exoskeleton shapes and other technological tools will play a pivotal role in improving NIV interfaces' comfort and tolerability [149–152]. Alongside, an environment-centered perspective should also be implemented. As healthcare is becoming increasingly influenced by the green economy, research on new materials and devices must take into account environmental factors for future choices.

4. Expert opinion

The paradigm 'The right mask for the right patient' seems to be difficult to achieve in real life, and adherence to NIV treatment mainly depends on patient comfort, which ultimately contributes to improving clinical outcomes. Therefore, patients need to be provided with interfaces ensuring ease of use. In this context, respiratory physicians and physiotherapists play a pivotal role in providing the best possible care for each individual patient as far as the choice of the optimal NIV interface is concerned. Several types of interfaces are commercially available, classified according to the design of the device and the anatomical structures to which it relates. The common term *mask* refers to an interface enclosing: the whole nose (*full nasal mask*),only the nostrils *(nasal plugs, nasal cushions, or nasal pillows-NP*), only the mouth (*mouthpiece, oral mask*), the mouth and the nose, without full nose cover *(hybrid mask*),the nose and the mouth, with full nose cover *(oro-nasal mask*),the nose, the mouth and the eyes *(total full face and integral mask*), the whole head and the neck *(hoods or helmets)*. It is still highly questionable which NIV interface should be considered the best in the acute setting. As a matter of fact, the setting of care strongly influences the choice of interface. Helmets have been considered as one of the most useful NIV interface in acute respiratory failure. Total face and oronasal masks have been widely used in the acute setting and found to be non-inferior in terms of comfort, side effects and gas exchange improvement compared to the helmet in the acute setting. These interfaces are easily fitted to patients and are very practical in the emergency setting. While the acute setting requires clinicians to achieve the best clinical result with the shortest NIV trial, in the chronic scenario this perspective is inverted. As a result, keeping a steady balance between the clinical improvement and the patient's adherence to NIV is essential to carefully identify the most suitable interface to use. Some NIV masks have been proven to be effective and well tolerated in long-term settings and for specific diseases. For instance, a comprehensive review focused on RCT on mask use in the chronic setting found there is no difference in the efficacy or tolerance of oronasal or nasal masks. Ranging from acute to chronic settings, the gold standard should include the tailoring of NIV interfaces to patients' needs and preferences. However, such customization may be hampered by issues of economic nature. High production costs and the increasing demand represent consistent burdens and have to be considered when dealing with patient-tailored NIV interfaces. New research focusing on developing advanced and tailored NIV masks should be prioritized; indeed, interfaces should be designed according to the specific patient and clinical setting where they need to be used. Pressure sensors, new materials

for cushions, modern exoskeleton shapes and other technological tools will play a pivotal role in improving NIV interfaces' comfort and tolerability. Alongside, an environment-centered perspective should also be implemented. As healthcare is becoming increasingly influenced by the green economy, research on new materials and devices must take into account environmental factors for future choices.

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ORCID

Paola Pierucci http://orcid.org/0000-0002-0201-0486
Giovanna Elisiana Carpagnano http://orcid.org/0000-0001-7931-4704
Claudia Crimi http://orcid.org/0000-0002-9088-5214
Cesare Gregoretti http://orcid.org/0000-0002-1442-1426

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a X	Identify the report as a protocol of a systematic review
Update	1b NA	If the protocol is for an update of a previous systematic review, identify as such
Registration	2NA	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3aX	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3bX	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4NA	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5aX	Indicate sources of financial or other support for the review
Sponsor	5bX	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5cX	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6X	Describe the rationale for the review in the context of what is already known
Objectives	7X	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8X	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9X	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10X	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11aX	Describe the mechanism(s) that will be used to manage records and data throughout the review

Selection process	11bX	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11cX	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12NA	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13X	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14X	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15aNA	Describe criteria under which study data will be quantitatively synthesised
	15bNA	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15cNA	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15dX	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16X	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17NA	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**