BMJ Open

Is the equimolar mixture of oxygen and nitrous oxide (EMONO) associated with audiovisuals effective in reducing pain and side effects during peripheral venous access placement in children? Protocol for a single-centre randomised controlled trial from Italy

Stefano Maiandi ,[1] Greta Ghizzardi,[1] Valeria Edefonti,[2,3] Roberta Giacchero,[4] Maura Lusignani,[5] Maria Lorella Giannì [6,7]

To cite: Maiandi S, Ghizzardi G, Edefonti V, *et al*. Is the equimolar mixture of oxygen and nitrous oxide (EMONO) associated with audiovisuals effective in reducing pain and side effects during peripheral venous access placement in children? Protocol for a single-centre randomised controlled trial from Italy. *BMJ Open* 2023;**13**:e067912. doi:10.1136/bmjopen-2022-067912

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-067912).

Received 16 September 2022
Accepted 31 May 2023

For numbered affiliations see end of article.

Correspondence to
Dr Stefano Maiandi;
stefano.maiandi@asst-lodi.it

ABSTRACT

Introduction Nurses frequently place a peripheral venous catheter during children's hospitalisation. Many studies suggest treatment of venipuncture-related pain. The administration of an equimolar mixture of oxygen and nitrous oxide (EMONO) is employed for pain control; however, no studies have analysed the association between EMONO and audiovisuals.

The purpose of the study is to evaluate the effect of EMONO administration when combined with audiovisuals (EMONO+Audiovisual) versus EMONO alone on perceived pain, side effects and level of cooperation during peripheral venous access placement in children aged 2–5 years.

Methods and analysis The first 120 eligible children admitted to the paediatric ward of the Lodi Hospital and presenting the indication for peripheral venous access will be enrolled. Sixty children will be randomly assigned to the experimental group (EMONO+Audiovisual) and 60 to the control group (EMONO alone).

The Face, Legs, Activity, Cry, Consolability scale will be used to assess pain in the children aged 2-years old; pain in the children aged 3–5 years will be assessed using the Wong-Baker scale. The cooperation throughout the procedure will be measured using the Groningen Distress Rating Scale.

Ethics and dissemination The Milan Area 1 Ethics Committee approved the study protocol (Experiment Registry No. 2020/ST/295). The trial results will be presented at conferences and published in peer-reviewed journals.

Trial registration number NCT05435118.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Validated tools for data collection contribute to results' reliability.
⇒ The intervention is economically sustainable and generally available to all, as parents commonly own the non-pharmacological device used (smartphone to watch the audiovisuals).
⇒ The monocentric study design could limit the generalisability of the results. The nature of the intervention does not permit a double-blind study design.

INTRODUCTION

Children experience numerous episodes of pain resulting from care procedures during illness. In these children, the consequences of lack of protection from pain can result in prolonged stressful situations.[1 2] Inadequate pain control can cause anxiety in children,[3–5] which may increase the perception of pain during procedures,[6] altering the relationship with healthcare providers and reducing therapeutic compliance.[7] The perceived pain may also cause the child to fear facing subsequent procedures.[8]

Peripheral venous catheter (PVC) placement is the most frequently performed procedure during hospitalisation, representing a primary source of pain.[9 10] The literature reports that more than 80% of hospitalised children undergo PVC placement at least once for both clinical (such as hydration infusions, intravenous administration of therapies, and blood transfusions) and preventive purposes.[11] The Equimolar Mixture of Oxygen and Nitrous Oxide (EMONO) is a valuable tool for managing pain.[1 12] This gas inhalation is indicated for short-term procedural pain treatment in adults and children.[13]

The mixture, contained in premixed cylinders, is delivered during the respiratory act, based on current lung volume, at least 3 min before the procedure. The mixture speed of action makes it an ideal pain management tool for a full range of care procedures.[14 15] The mode of EMONO action is not known yet. Experts believe that the analgesic effects are due to supraspinal centres' stimulation, with consequent endorphin release in spinal cord neurons and inhibition of transmission of pain signals to higher brain levels.[16 17]

EMONO-related side effects are all minor, are mainly gastrointestinal or affect the central nervous system; examples of the most prevalent ones are nausea, vomiting, dizziness or euphoria. The incidence of side effects is between 4.4% and 37%.[1 14 18] As indicated in a recent Consensus Conference[19] and in the literature,[1 18] the safety level and the low incidence of complications guaranteed by EMONO allow it to be administered by properly trained nursing staff.[20]

Literature suggests that combining medication drugs with non-pharmacological tools can enhance the analgesic effect of pharmacological principles. Non-pharmacological tools might help reducing anxiety and short-term procedural pain.[5 21] In particular, an Italian experience suggests that watching audiovisuals improves pain management and promotes child's cooperation during the procedure.[22] Cooperation is the ability to be subjected to a procedure without external restriction to avoid sudden movements and guarantee procedure safety.[23–25] Watching audiovisuals, such as cartoons,[7] or videos on online platforms, such as Youtube or Youtube Kids, is considered a passive distraction, as the child is only partially engaged in managing the distractive means.[26] Thus, the association between EMONO and distractive audiovisual content could strategically lead to improved outcomes during painful procedures in children. However, there is no available literature regarding improving EMONO effects on perceived pain, side effects and cooperation levels, when administered with audiovisuals.

This project aims to evaluate the extent of the effect of EMONO administration when combined with audiovisual vs EMONO alone on perceived pain, side effects and level of cooperation during peripheral venous access placement in children aged 2–5 years.

STUDY OUTCOMES

Primary outcome measures

The primary outcome measures are pain and cooperation. Cooperation will be measured with the Groningen Distress Rating Scale,[27–29] pain through the Face, Legs, Activity, Cry, Consolability (FLACC)[30] and the Wong-Baker[31] scales. Details on instruments used are reported in the 'Measure' section.

Secondary outcome measures

The secondary outcome measures are related to the presence (or absence) of side effects throughout the procedure. Symptoms will be collected using an ad hoc instrument, as reported in the 'Measure' section.

METHODS AND ANALYSIS

Study setting and timeline

The study will be conducted in the paediatric ward, at Lodi Hospital, Lombardy, Italy.

The first 120 eligible children between 2 and 5 years and 364 days of age admitted to the paediatric ward and presenting the indication for peripheral venous access placement will be enrolled. The team will recruit eligible subjects 24/7. Patient recruitment will begin in August 2023 and will last about 16 weeks.

Participants: inclusion/exclusion criteria

Children will be enrolled after parental or legal guardian written consent to participate in the study. Children's parents or legal guardians must own a smartphone/tablet connected to the internet.

Children younger than 2 years and older than 5 years plus 364 days or whose parents or legal guardians do not consent to participate will be excluded from the study. Children presenting contraindications for EMONO administration (including the administration of intranasal drugs) with a facial pathology or malformations that would prevent proper face mask application and adherence will not be eligible for recruitment. Children with a tracheostomy, oxygen therapy or need for emergency treatment will also be excluded.

Study design and interventions

This study is a randomised, open-label, controlled trial comparing the experimental group (EMONO+Audiovisual) versus the control group (EMONO alone) on perceived pain, level of cooperation and side effects during the peripheral venous access placement procedure. The EMONO used in the study will be AirLiquide Kalinox in 5 L cylinders with a demand valve; the company supplying the product is not a study sponsor and is not involved in the research project. AirLiquide collaborated with Lodi Hospital exclusively in the initial stages of implementing EMONO in the standard care practice. Venous access will be performed using BD Saf-T-Intima devices sized from 20 G to 24 G. The choice of the needle size will depend on the vein gauge, the availability of venous supply, and the nurse's discretion. The BD company is neither a study sponsor nor it is involved in the research project implementation.

Study conductance

The use of EMONO will take place per internal procedure in use at Lodi Hospital. The EMONO is administered based on a doctor's prescription by trained nursing staff. The training course consists of a theoretical part that will last at least 2 hours and will be carried out by professionals experienced in using EMONO, followed by at least 3 EMONO supervised administration procedures.

Four trained nurses from the paediatric ward will be employed; the principal investigator (PI) (SM) will coordinate the study conduction. The involved personnel will meet to reach a prestudy consensus on intervention delivery and criteria for data collection.

The researchers will welcome eligible children and their parents or legal guardians in a dedicated room, and the nurse will explain the peripheral venous access placement procedure. The PI will provide parents or legal guardians with comprehensive information about the study; parents or legal guardians will have the chance to ask any questions and take all the needed time to decide if signing the informed consent. On agreement to participation, fasting will be prescribed by the referent physician for EMONO administration. Specifically, the fasting time to be observed consists of 6 hours of abstaining from solid foods and milk, 4 hours from breast milk and 1 hour from clear liquids (water, fruit juice without pulp, carbonated drinks and clear tea).

Before starting the procedure, researchers will record the child's level of cooperation to have a baseline score. At the beginning of the procedure, a peripheral SpO_2 monitor will be placed, and the nurse will choose an appropriate face mask for the child. The child will take a supine position on the crib, and the nurse in charge will apply the EMONO inhalation face mask with an on-demand valve for at least 3 min before starting the procedure.

Being the standard treatment, EMONO will be delivered to all enrolled children (in the control and experimental arms). Parents or legal guardians of children in the experimental group will own a smartphone/tablet connected to the Internet. The device will be used to show the experimental-arm children a video on the Youtube or Youtube Kids app during EMONO administration. In the absence of child's favourite videos at hand, the child will be provided with a list of videos to choose from; this guarantees that videos are prevetted and consistent across the intervention group, thus reducing variability from this source. The video should last for the entire procedure; therefore, parents will be advised to choose a video of a minimum length of 5 min. Researchers will record any issues with the video playback (eg, video freeze-up) on the study logbook. In the case of persistent playback issues during the procedure, the data collection will be interrupted, and the patient will be excluded from the final analysis.

Researchers will invite and educate the children to independently ensure and maintain the correct face mask position. If the child's age is unsuitable for guaranteeing the proper face mask position, the parent, legal guardian or healthcare professional will support her/him. If the child is unable, the parent or the legal guardian will ensure the proper phone/tablet position for watching and listening to the contents. This process will take place at least 3 min before starting the procedure and will last until procedure's conclusion, when EMONO's administration will be discontinued.

Measures

Cooperation throughout the procedure will be measured using the Groningen Distress Rating Scale.[27–29] The Groningen Distress Rating Scale consists of a five-point Likert scale: the minimum score describes the calm and cooperative child; the maximum score represents the uncooperative child with a panic attitude. Pain assessment in the children aged 2 years old will be conducted through the FLACC[30] scale, whereas assessment in children aged 3–5 years old will be based on the Wong-Baker scale.[31] The FLACC scale consists of five items referring to two body districts (face and legs), the overall behaviour of the child, and crying and consolability. Each item can achieve a score from 0 to 2. The Wong-Baker scale allows the child to describe the pain level by choosing from one of six proposed faces ranging from a happy face at 0 (corresponding to the absence of pain) to a crying face at 10 (representing the worst pain ever experienced), with four intermediate faces representing 2 points each.

The incidence of retching (ie, an involuntary phenomenon due to contraction of the diaphragmatic and abdominal muscles that precedes or accompanies vomiting[32]) and vomiting (ie, the forced emission of gastric contents from the mouth[33]) will be collected by employing an ad hoc tool whose total score ranges from 0 to 3. Specifically, 0 indicates the absence of symptoms, 1 the presence of symptoms that do not require medical intervention or treatment, 2 the presence of symptoms requiring medical evaluation but not treatment and 3 indicates the presence of symptoms requiring medical intervention and treatment. We created this ad hoc tool due to the absence of a validated instrument for assessing the symptoms of interest.

Except for the Groningen Distress Rating Scale (administered also before the procedure starts), researchers will administer each scale once to collect data during the procedure.

Data collection: quality management and storage

Researchers will collect data during the procedure; no further follow-ups are planned. Data for each measurement will be reported on paper and then recorded electronically. All paper-collected data will be marked with a study identification number to prevent participant identification and kept in locked storage. Only the PI will have access to the data.

Adverse events

Patients' safety will be monitored during the procedure by nurse staff who will look at unexpected clinical manifestations. According to the Lodi Hospital procedure, a pulse oximeter will also be applied to each child when the EMONO administration starts and kept until the end of the procedure. Participant's parents or legal guardians will receive a study information sheet containing explicit details regarding healthcare professionals to contact in case of adverse events.

Analyses

We will use descriptive statistics for summarising the study participants' sociodemographic, clinical and care characteristics. A χ^2 test will be used to assess potential differences in the proportions between the two groups for the following variables: age, sex, previous venipunctures, previous venipunctures during hospitalisation, the calibre of venous access, level of cooperation (Groningen Distress Rating Scale), number of attempts at peripheral venous access placement and incidence of vomiting. The Kruskal-Wallis test will allow to describe differences in the distribution of pain (as detected by the two scales) in the experimental and control groups. All the statistical analyses will be performed using the current version of the R software.[34] We will consider a $p<0.05$ as significant.

A sensitivity analysis will be performed between preprocedure and postprocedure data collected with the Groningen Distress Rating Scale.

Power and sample size

The primary outcomes are perceived pain and cooperation detected during peripheral venous access placement as measured according to the corresponding score. A sample size of 48 subjects allows detection of an effect size on cooperation W of 0.5 (large) using a χ^2 test with 4 df (df=(5–1) times (2–1)=4) 80% power and a significance level (alpha) of 0.05. If the effect size W is 0.3 (medium level), 133 subjects guarantee 80% power in a 4 df χ^2 test with a significance level (alpha) of 0.05.

The effect size (W) was used by Cohen (1988) because it does not depend on the sample size, with the suggestion of the effect size cut-offs of 0.1 (small), 0.3 (medium) and 0.5 (large) as rough guidelines to help calculate sample sizes in studies. For this study, a total of120 subjects will allow for an effect size between medium and large with a drop-out of about 20% and the usual assumptions of alpha=0.05 and power=0.80.

Blinding and randomisation

Patients will be randomly assigned to the intervention or the control group with an allocation ratio of 1:1 until the desired sample size is reached. The PI will create the randomisation list through the 'random' function of Microsoft Excel 2010. Sequentially numbered opaque sealed envelopes will contain the allocation group: 60 for the experimental group (EMONO+Audiovisual) and 60 for the control group (EMONO alone).

The nature of the intervention does not allow blindness to be applied: the nurse and the enrolled subjects will be aware of the allocated treatment, and the nurse will report the observed data during the procedure. However, blinding will be enforced in the data entry phase as it will be performed by research assistants, who will not be aware of the subject's assigned group.

Patient and public involvement

This study has been designed to identify a well tolerated, child-centred intervention which also involves parents.

A deep literature search and assessment of children/parents' priorities, experiences and preferences have guided the development of the research question and outcome measures, although patients have not been directly involved in the study design.

Children will be our source of data on the topic. For this reason, we would like to disseminate the study results to children's parents or legal guardians by publishing the manuscript in an open-access journal. Patients have not previously assessed the burden related to the intervention; however, findings from the literature have reported that the intervention adopted in this study should not cause any burden or discomfort to patients.

ETHICS AND DISSEMINATION

The Milan Area 1 Ethics Committee approved the study protocol (Experiment Registry No. 2020/ST/295). The study was also registered on ClinicalTrials.gov (registration number NCT05435118). The researchers will provide parents or legal guardians with all information related to the study. Procedural pain treatment will be provided to all children participating in the study in the experimental and control groups through the administration of EMONO. As specified in the informed consent, equal treatment will be adopted for all the children, even in case of dissent to participate in the study. Also, children can withdraw from the study at any time.

The results of the study may be presented at conferences and will be published in peer-reviewed journals.

DISCUSSION

The study emphasises the importance of procedural pain treatment in the paediatric setting. As children may experience adverse consequences from failure to treat pain,[35–37] proper pain treatment is pivotal to guaranteeing a better hospitalisation experience. This study investigates the effects of combining EMONO with distractive devices compared with EMONO alone in children undergoing peripheral venous access placement.

The study involves the administration of EMONO by trained nurses, who are most frequently close to hospitalised children. The choice of EMONO derives from its ease of use, speed of action and low side effects incidence. The study could have investigated additional side effects, such as nausea and dizziness; however, we believed it is unlikely that these symptoms are reported in a reliable way by the youngest children enrolled and for this reason we excluded them from the list of available side effects to be reported.

The choice of distractive means (YouTube or YouTube Kids) will be undertaken because of the spreading availability of smartphones and a free corporate Wi-Fi network which allows access to online content. In addition, the parent can deliver the distractive tool without involving a healthcare provider.

The study sample was designed to include the most vulnerable paediatric age group. However, we had included children above 2 years of age because smartphone exposure for children younger than that age is not recommended.[38 39] The freedom to choose which video to use is motivated by the desire to increase the audiovisual tool's distractive power and meet every child's preferences.

Whether the hypothesis of increased cooperation during the procedure is confirmed, children may cease to face body restraint by a second nurse during the PVC procedure, making the experience less traumatic.

Although the literature offers many studies on the efficacy of audiovisual tools in reducing pain,[40–42] we want to proceed by administering EMONO as usual care in our research. EMONO is safe, and it would not be ethical not to distribute it to children. For this reason, even though results from a study comprehending a third arm with audiovisual alone would be feasible, we would not suggest this option.

Author affiliations
[1]Healthcare Professions Directorate – ASST di Lodi, Lodi, Italy
[2]Department of Clinical Sciences and Community Health, Branch of Medical Statistics, Biometry and Epidemiology, "G.A. Maccacaro," University of Milan, Milano, Italy
[3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy
[4]Pediatric, ASST Lodi, Lodi, Italy
[5]Department of Biomedical Sciences for Health, University of Milan, Milano, Italy
[6]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neonatal Intensive Care Unit, Milano, Italy
[7]Department of Clinical Sciences and Community Health, University of Milan, Milano, Italy

Acknowledgements A special thanks to Dr Gambarana of the Pharmacy and all the nurses and doctors in the Paediatrics Department of the ASST of Lodi, and heartfelt thanks to patient advisers.

Contributors SM, RG and MLG designed the study, VE developed the statistical analysis, GG and ML revised the protocol.

Funding This study was partially funded by Italian Ministry of Health, Current research IRCCS.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Consent obtained from parent(s)/guardian(s).

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Stefano Maiandi http://orcid.org/0000-0002-4772-0676
Maria Lorella Giannì http://orcid.org/0000-0003-3901-9131

REFERENCES

1 Annequin D, Carbajal R, Chauvin P, *et al*. Fixed 50% nitrous oxide oxygen mixture for painful procedures: A French survey. *Pediatrics* 2000;105:E47.
2 Cohen LL. Behavioral approaches to anxiety and pain management for pediatric venous access. *Pediatrics* 2008;122 Suppl 3:S134–9.
3 Ballard A, Khadra C, Adler S, *et al*. Efficacy of the Buzzy® device for pain management of children during needle-related procedures: a systematic review protocol. *Syst Rev* 2018;7:78.
4 Chan E, Hovenden M, Ramage E, *et al*. Virtual reality for pediatric needle procedural pain: two randomized clinical trials. *J Pediatr* 2019;209:160–7.
5 McMurtry CM, Pillai Riddell R, Taddio A, *et al*. Far from «just a poke»: common painful needle procedures and the development of needle fear. *Clin J Pain* 2015;31(10 Suppl):S3–11.
6 Cook LS. Needle Phobia. *Journal of Infusion Nursing* 2016;39:273–9.
7 L Cassidy, G J Reid, P J McGrath, D K. A randomized double-blind, placebo-controlled trial of the EMLA patch for the reduction of pain associated with Intramuscular injection in four to six-year-old children. *Acta Paediatrica* 2001;90:1329–36.
8 McCarthy AM, Kleiber C. A conceptual model of factors influencing children's responses to a painful procedure when parents are distraction coaches. *J Pediatr Nurs* 2006;21:88–98.
9 Waitt C, Waitt P, Pirmohamed M. Intravenous therapy. *Postgrad Med J* 2004;80:1–6.
10 Friedrichsdorf SJ, Postier A, Eull D, *et al*. Pain outcomes in a US children's hospital: A prospective cross-sectional survey. *Hosp Pediatr* 2015;5:18–26.
11 Zempsky WT. Optimizing the management of peripheral venous access pain in children: evidence, impact, and implementation. *Pediatrics* 2008;122 Suppl 3:S121–4.
12 Tunstall ME. Obstetric analgesia. the use of a fixed nitrous oxide and oxygen mixture from one cylinder. *Lancet* 1961;2:964.
13 Gérardin M, Couec M-L, Grall-Bronnec M, *et al*. PHEDRE trial protocol - observational study of the prevalence of problematic use of Equimolar mixture of oxygen and nitrous oxide (EMONO) and Analgesics in the French sickle-cell disease population. *BMC Psychiatry* 2015;15:281.
14 Abdelkefi A, Abdennebi YB, Mellouli F, *et al*. Effectiveness of fixed 50% nitrous oxide oxygen mixture and EMLA cream for insertion of central venous catheters in children. *Pediatr Blood Cancer* 2004;43:777–9.
15 Heinrich M, Menzel C, Hoffmann F, *et al*. Self-administered procedural analgesia using nitrous oxide/oxygen (50:50) in the pediatric surgery emergency room: effectiveness and limitations. *Eur J Pediatr Surg* 2015;25:250–6. 10.1055/s-0034-1371716 Available: http://www.thieme-connect.de/products/ejournals/issue/10.1055/s-005-29214
16 Tobias JD. Applications of nitrous oxide for procedural sedation in the pediatric population. *Pediatr Emerg Care* 2013;29:245–65.
17 Duarte LTD, Duval Neto GF, Mendes FF. Nitrous oxide use in children. *Rev Bras Anestesiol* 2012;62:451–67.
18 Onody P, Gil P, Hennequin M. Safety of inhalation of a 50% nitrous oxide/oxygen premix: a prospective survey of 35 828 administrations. *Drug Saf* 2006;29:633–40.
19 on behalf of the Procedural Sedation Analgesia Consensus working group, Sforzi I, Bressan S, *et al*. The development of a consensus conference on pediatric procedural sedation in the emergency department in italy: from here where to? *Ital J Pediatr* 2020;46.
20 Gall O, Annequin D, Benoit G, *et al*. Adverse events of Premixed nitrous oxide and oxygen for procedural sedation in children. *The Lancet* 2001;358:1514–5.
21 Sinha M, Christopher NC, Fenn R, *et al*. Evaluation of non pharmacologic methods of pain and anxiety management for laceration repair in the pediatric emergency Department. *Pediatrics* 2006;117:1162–8.
22 Bagnasco A, Pezzi E, Rosa F, *et al*. Distraction techniques in children during Venipuncture: an Italian experience. *J Prev Med Hyg* 2012;53:44–8.
23 Hull K, Clarke D. Restraining children for clinical procedures: a review of the issues that continue to challenge children's nursing. *Br J Nurs* 2010;19:346–50.
24 Brenner M, Treacy MP, Drennan J, *et al*. Nurses' perceptions of the practice of restricting a child for a clinical procedure. *Qual Health Res* 2014;24:1080–9.
25 Crellin D, Sullivan TP, Babl FE, *et al*. Analysis of the validation of existing behavioral pain and distress scales for use in the procedural setting. *Paediatr Anaesth* 2007;17:720–33.
26 MacLaren JE, Cohen LL. A comparison of distraction strategies for Venipuncture distress in children. *J Pediatr Psychol* 2005;30:387–96.
27 Doumit M, Belessis Y, Stelzer-Braid S, *et al*. Diagnostic accuracy and distress associated with oropharyngeal suction in cystic fibrosis. *Journal of Cystic Fibrosis* 2016;15:473–8.
28 Humphrey GB, Boon CM, van Linden van den Heuvell GF, *et al*. The occurrence of high levels of acute behavioral distress in children

and adolescents undergoing routine Venipunctures. *Pediatrics* 1992;90(1 Pt 1):87–91.
29 Herd DW, McAnulty KA, Keene NA, *et al*. Conscious sedation reduces distress in children undergoing voiding Cystourethrography and does not interfere with the diagnosis of Vesicoureteric reflux: a randomized controlled study. *AJR Am J Roentgenol* 2006;187:1621–6.
30 Merkel SI, Voepel-Lewis T, Shayevitz JR, *et al*. The FLACC: a behavioral scale for scoring postoperative pain in young children. *Pediatr Nurs* 1997;23:293–7.
31 Wong DL, Baker CM. Pain in children: comparison of assessment scales. *Pediatr Nurs* 1988;14:9–17.
32 Katsouda M, Provatenou E, Arapostathis K, *et al*. The Greek version of the gagging assessment scale in children and adolescents: Psychometric properties, prevalence of gagging, and the association between gagging and dental fear. *Int J Paediatr Dent* 2017;27:145–51.
33 Schlegelmilch M, Punja S, Jou H, *et al*. Observational study of pediatric inpatient pain, nausea/vomiting and anxiety. *Children (Basel)* 2019;6:65.
34 Lafaye de Micheaux P, Drouilhet R, Liquet B. The R software. In: *The R software*. New York, NY: Springer, 2013.
35 Chambers CT, Craig KD, Bennett SM. The impact of maternal behavior on children's pain experiences: an experimental analysis. *J Pediatr Psychol* 2002;27:293–301.
36 Hamilton JG. Needle Phobia: a neglected diagnosis. *J Fam Pract* 1995;41:169–75.
37 Koutantji M, Pearce SA, Oakley DA, *et al*. Children in pain: an investigation of selective memory for pain and psychological adjustment. *Pain* 1999;81:237–44.
38 Park JH, Park M. Smartphone use patterns and problematic Smartphone use among preschool children. *PLoS One* 2021;16:e0244276.
39 Bozzola E, Spina G, Ruggiero M, *et al*. Media devices in pre-school children: the recommendations of the Italian pediatric society. *Ital J Pediatr* 2018;44.
40 Bergomi P, Scudeller L, Pintaldi S, *et al*. Efficacy of non-pharmacological methods of pain management in children undergoing Venipuncture in a pediatric outpatient clinic: A randomized controlled trial of audiovisual distraction and external cold and vibration. *J Pediatr Nurs* 2018;42:e66–72.
41 Guinot F, Mercadé M, Oprysnyk L, *et al*. Comparison of active versus passive audiovisual distraction tools on children's behaviour, anxiety and pain in Paediatric dentistry: a randomised crossover clinical trial. *Eur J Paediatr Dent* 2021;22:230–6.
42 Chow CHT, Van Lieshout RJ, Schmidt LA, *et al*. Systematic review: audiovisual interventions for reducing preoperative anxiety in children undergoing elective surgery. *J Pediatr Psychol* 2016;41:182–203.