schools is high, similar to the Spanish Alergológica 2005 report. In private schools, the prevalence of FA-free diets was higher than in public and subsidized schools.

For this analysis, the prevalence of FA-free diets was assessed by a positive response on the basis of a specialist's report case including all FA declared. We have found that the upward trend in the prevalence of FA-free diet as a special diet in Hortaleza District school canteens in the last year of the survey is similar to that observed in Alergólogica 2005 study for children (3). The reasons for this increase may be due to higher awareness, better diagnostic tests, changes in dietary habits, etc., but have not been established. However, we consider that the survey improved this condition specialist's medical reports as a consequence of this as a surveillance requirement, achieving a greater awareness of this condition.

These results are in line with previous studies that show an increase in the prevalence of tree nut and peanut allergies, and in severe allergic reactions induced by foods (10).

These results also indicate that the socioeconomic gradient is a factor that could influence a higher risk of developing this condition, as has been shown previously (3).

This year, the application of Regulation 1169/2011 of the EU information on food labeling of packaged foods in relation to allergens will come into effect, and the responsibility of

traders in the food industry will become a major concern. This could change Hazard Analysis Critical Control Point (HACCP) policies, as this is an individual pathology, where food security in relation to episodes caused each year is not considered 'food-borne outbreak'. Traditionally HACCP programs have been designed to control food safety, preferentially oriented to microbiological hazards.

This kind of survey could help to improve awareness on FA for all food safety stakeholder policies and, from the point of view of public health, for specialist sanitary inspectors in hygiene and food safety of all administrations, to extend information and adopt appropriate criteria when new cases of FA are presented.

School canteens represent a good source of information regarding FA trends in children.

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# Melomics music medicine (M<sup>3</sup>) to lessen pain perception during pediatric prick test procedure

To the Editor,

Melomics (1) is a research project developed at the University of Malaga, which aims at establishing a new paradigm for music medicine based on artificial intelligence and sentient computing. M<sup>3</sup> is a by-product of this project and provides the patient with tailored music (adapted to preferred or specific musical styles, and to therapeutic conditions) using a smartphone or a customized device, also with the possibility to estimate the patient's physiological state and delivering music

that positively affects that state in real time. This system can be used to prevent and treat several conditions such as anxiety, stress, chronic and acute pain, and sleep disorders. The use of this technology might improve the efficiency of the treatment and reduce the use of drugs, lessening the side effects for patients.

In pediatric ambulatory care, one of the more routinely used methods in allergy diagnosing is the skin prick test (SPT). The antigen is placed on the skin of the volar surface of the forearm and introduced into the epidermis with a standardized needle. Allergen drops are placed 2 cm or more apart to avoid false-positive reactions. A needle is passed through the drop and inserted into the epidermal surface at a low angle with the bevel facing up. The needle is removed and then withdrawn, and the solution gently wiped away with a paper tissue. Skin testing, particularly prick skin testing, is virtually painless. There is no bleeding involved, as the needle only pricks the skin to the depth of a scratch. The worst part of skin testing is that the skin test sites may be quite itchy when positive results occur. However, many children do cry during skin testing, feeling both fear and pain, which might represent a traumatic experience for this kind of patients. To date, there are not many clinical studies setting pain degree of the SPT.

On the other hand, music is a widespread tool to treat different diseases traditionally related to neurological and psychiatric disorders. However, the use of music in hospital settings has extended its field of application in the last years. In these cases, music (particularly, listening to music) reduces anxiety and pain derived from surgical or medical procedures, before and during interventions (2, 3). Music has also been used to reduce pain in absence of medical procedures, for example, in chronic pain conditions (4). A recent Cochrane Review about music and pain (5) concluded that music listening can reduce perceived pain levels and required dosages of opioids in some types of pain, for some patient populations. Also, several studies investigating pain and anxiety have been carried out in the pediatric field (6, 7). Despite the different models and techniques used in the practice of music therapy (be it psychological or neuroscientific, receptive or active), listening to music seems to be an appropriate approach to treat the pain condition, as an alternative to medication. In these cases, music is typically chosen by patients, considering the fact that music is more effective if personal preferences are followed, rather than music proposed by a therapist or a formal/informal caregiver. Music can activate some neurochemical systems linked to reward, motivation, and pleasure, but it is also tied to stress, arousal, and immunity, modulating some systems such as those of dopamine and opioids, cortisol, serotonin, etc. (8). In other cases, music is adapted by the therapist following specific criteria to relax or activate patients, in relation to the context and therapeutic target. Despite the positive effects of music therapy in lessening pain (widely reported in the literature mentioned above), there are no tools for people to easily and effectively manage their pain on a daily basis.

In an attempt to shed light on the use of music in clinical settings, this study evaluates and validates the effect of the pediatric system  ${\tt M}^3$  on the reduction of pain perception, as compared to a non-music group, on a pediatric population undergoing SPT.

Seventy-two children were included in this study and underwent SPT in the Children's Hospital of Malaga (Spain). Children were randomly assigned to either an experimental or a control group. Four children in the experimental group were discarded due to vagal reactions (2), device manipulation during the procedure (1), and probable mental deficiency (1). Therefore, the experimental group finally included 32 children.

Melomics' music constitutes a new approach in music medicine, combining advanced Artificial Intelligence and mHealth techniques. It has been designed as to be replicable and transferable to any medical unit in a straightforward way and at virtually no cost. M<sup>3</sup> is implemented as a musicstreaming system (Fig. 1): Music resides in a cloud storage, and it is made freely accessible through a Web browser (http:// melomics.com/SPT), or via an Android application (http:// melomics.com/SPTapp), so patients can use this service with any device that can connect to the Internet (be it a computer, tablet, or smartphone) and can reproduce music. An interesting aspect of this system is that music content is generated by a supercomputer (i.e., composed and synthesized) in a fully automatic way, upon the specifications of expert music therapists. This has three advantages: (i) big amounts of music can be produced in this way, what is convenient in some type of experiments where the patients are exposed to the music on a daily basis; (ii) the music is royalty free, so it can be multicast and downloaded without restrictions: worldwide, and no deals with record labels are needed; and (iii) music can be tailored to

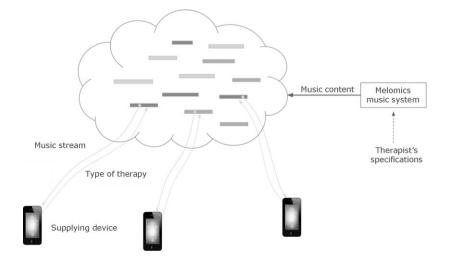


Figure 1 General description of the therapeutic system M<sup>3</sup>. A supplying device with Internet connection (either a smartphone or any conventional computer) is configured for a concrete type of therapy (skin prick test, in this case). This device demands the music to a cloudbased server or repository, which delivers music in a concrete style (as specified by a therapist, and generated by Melomics' computers). The device also includes a player, which provides the music to the patient, generally through a headphone.

basically any therapeutic need (be it relaxing, distracting, or activating), any duration and evolution of the themes, or personal preferences (particular instrumentation, type of melody, etc.)

For this study, Melomics music was generated according to two fundamental principles from the literature:

- 1 The possibility to tailor the pieces considering characteristics of children's music.
- 2 The need to create a distractive music (parametrizing the composition process in a way that makes it attractive and with variations) and to divert attention from pain and anxiety due to the SPT.

This music approach can be classified as 'music medicine' (9), since the characteristics of musical stimuli play a central role in the therapeutic approach, independently of the relationship between the patient and the therapist, commonly found in other music therapy approaches. However, in our methodology, the music therapist plays an important role in creating the music: After a contact with the medical staff, he/ she chooses the style (e.g., pop, classical), the design, and all parameters of music (rhythm course, dynamics, timbre, tonalities, duration, etc.) before the composition is done. M<sup>3</sup> composes and synthesizes the music without human intervention, using a specific algorithm, and considering the structure pre-specified by the therapist. This procedure allows to tailor the music according to the context (type of population and setting) and clinical aims. Evidence-based music therapy (10) principles were used in order to evaluate to what extent the use of M<sup>3</sup> can reduce pain perception during the SPT procedure.

During SPT, children belonging to the experimental group listened to Melomics music, whereas children in the control group did not receive any special auditory or other stimuli. The music was administered by means of a smartphone and headphones, in which M<sup>3</sup> was installed. The music was designed to be lively and appealing to children, in order to prevent their attention to focus on the procedure.

The intensity of pain experimented by children during the procedure was assessed using a linear 0–10 cm (0: no pain, 10: severe pain) VAS.

The sample was described using measures of statistical dispersion (mean and standard deviation) for quantitative variables, whereas frequency distribution was used for qualitative variables. In order to compare the experimental and control groups, the Chi-square test was used to analyze independent qualitative variables. Additionally, Student's *t*-test was used for independent quantitative variables. For the outcome variable 'presence of pain' (moderate or intense), relative risk reduction (RRR) and number needed to treat (NNT) were calculated with 95% confidence interval (CI 95%), setting a level of statistical significance at p < 0.05. Also, a quantitative and qualitative analysis of the data was done with SPSS.

Informed consent was obtained from parents of all childrens, and the research protocol was approved by the Ethical Committee of the Children's Hospital of Malaga.

Sixty-eight children aged between 5 and 14 yr (SD = 2.582) were evaluated during the experiment. In terms of the distribution by sex and age, 54.8% of the children in

Table 1 Distribution of subjects by age and sex in the two groups, and pain reported during the procedure

GROUPS	Experimental	Control	р
Age			
Male	17 (54.8%)	22 (59.5%)	0.891
Female	14 (45.2%)	15 (40.5%)	
Mean/SD	9.2/2.5	8.5/2.7	0.263
Pain (VAS)			
No pain (0-2)	22 (71.0%)	7 (18.9%)	<0.001
Moderate acute (3–10)	9 (29.0%)	30 (81.1%)	
Mean/SD	2.1/1.1	4.9/2.7	<0.001

the experimental group were male compared with 59.5% in the control group, whereas the mean age in the experimental group was 9.2 (SD 2.5) years, and 8.5 (SD 2.7) years in the control group, without statistical differences between groups (p = 0.263).

With respect to the intensity of pain, according to the VAS quantitative measure, the mean was 2.1 (SD 1.1) for children with  $\rm M^3$ , compared with a mean of 4.9 (SD 2.7), for children without music. The difference between the two groups is statistically significant (p < 0.001), with a mean difference of 2.8 (95% CI 1.8–3.8).

It also resulted that the presence of pain (VAS 3–10) was reported by 29% of children in the experimental group, compared to 81.1% in the control group (p < 0.001). Taking into consideration this qualitative measure, the values obtained for RRR and NNT were 64% (CI 95%: 39–79) and 2 (CI 95%: 1–3), respectively. All these data are summarized in Table 1.

The present study was designed to determine the effect of M<sup>3</sup> on pain perception, as compared to the standard protocol without music, on a randomly chosen pediatric population during the SPT procedure. Results implied statistically significant effects on the reduction of pain perception. Only 29% of the children using M<sup>3</sup> reported moderate or intensive pain, compared to 81% of the children without music. This means that the risk of suffering pain is 2.8 times higher with the standard protocol.

A possible explanation of these significant results could be the confirmation of the hypothesis previously mentioned: Music diverts the attention of children from pain, and consequently, reduces pain perception. It could also be that the technological support (the presence of a smartphone), and the visual stimuli could influence the results of the study. However, what is interesting in these results is the possibility of creating a tailored music catalog and a standard music distribution system, which takes into account:

- 1 The characteristics of children's preferred music, and specific sound parameters, aimed at catching children's attention.
- 2 The needs of the medical facilities where the procedure is performed.

Music, and a pleasant environment, provides neurochemical rewarding, which can lead to the activation of dopaminergic and opioid neurotransmission in the mesocorticolimbic system Letters to the Editor

and prefrontal cortical areas. Prior studies have noted that this can produce feelings of pleasure and can also affect attentional control (8).

In order to determine the real contribution of the music itself in the reduction of pain, the experimentation should cover a greater sample of children and also include control groups to compare the effects with traditional music (e.g., commercial children's music) and without music, providing an electronic device and earphones that play noise (white or pink) or no sound. On the other hand, this study is a RCT that proves a strong efficacy in reducing pain perception using a standardizable, easy to implement, and inexpensive method. In addition, this same approach can be used in a clinical setting, such as reducing anxiety before surgical interventions, alleviating sleep disorders, stress conditions, or chronic pain, etc. Another advantage is that M³ is a therapeutic tool that patients can use for free, provided that an Internet connection is available.

Despite the promising results obtained in this study, more evidence-based studies are needed to assess the therapeutic potentialities of M<sup>3</sup> and its application in clinical settings.

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#### **Conflict of interests**

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## Resveratrol plus carboxymethyl-β-glucan may affect respiratory infections in children with allergic rhinitis

To the Editor,

Social and economic costs of allergic rhinitis (AR) are impressive; AR may also significantly impact school attendance and performance, quality of life, and sleep (1).

The AR immunopathology is characterized by T-helper-2 (Th2)-dependent inflammation and Th1-response impairment. This imbalance is sustained by dysfunction of immune system: Allergic patients are lacking in allergen-specific T regulatory cells, so T helper 2 cells may polarize the immune response to allergen and produce large quantity of some interleukins, including IL-4, IL-5, and IL-13, that in turn promote IgE synthesis and eosinophil production, recruitment, and activa-

tion at nasal level. Moreover, Th2 cytokines upregulate the endothelial and epithelial expression of adhesion molecules (such as ICAM-1), which interact with other adhesion molecules (e.g., LFA-1 expressed by leukocytes) to induce the mucosal infiltration by eosinophil.

On the other hand, it is strengthened belief that allergic patients could present higher susceptibility to contract respiratory infections than non-allergic subjects. In this regard, it has been evidenced that allergic children have more numerous and severe respiratory infections than non-allergic children (2). The involved pathways may be (i) impaired immune defense because of interferon- $\gamma$  defective production (conse-