Study Protocol and Statistical Analysis Plan

Effect of Hearing Aid Labeling on Speech Understanding Measures

Version 1.0

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Protocol Title

Effect of Hearing Aid Labeling on Speech Understanding Measures

1 Background

The purpose of this study is to investigate the placebo effect of labeling hearing aids as "OTC" (over-the-counter) or "Prescriptive" for inexperienced and experienced hearing aid users with mild to moderate hearing loss.
Previous interest in placebo effects for hearing aid research have centered around labeling devices as "digital" vs. "conventional" (Bentler et al. 2003) and "new" vs. "old" (Dawes et al. 2011, 2013). These studies found that participants had strong preferences for devices labeled as "digital" and "new" even when all variables between conditions were equal besides the label. In addition to the effect of labeling, Rakita et al. (2021) have shown that end users are also susceptible to placebo effects stemming from the language used by the hearing aid fitter. Specifically, it was found that when the participants were given a positive narrative for hearing aid expectations, they performed better in behavioral measurements (i.e. lower SNRs via the QuickSIN) and anticipated needing less time to get used to the hearing aids as compared to a negative narrative. These findings have shown that placebo effects are measurable in hearing aid research and do have an impact not only on device preference but also hearing performance.
The recent release of FDA guidelines for OTC hearing aids has created an urgency to understand the impact of these devices on the hearing aid market. Device labeling has been proven to influence consumer preference in hearing aid research, but the specific effect of labeling devices as "OTC" or "Prescriptive" has not been previously investigated; therefore, it is worthwhile for Sonova to pursue this investigation in order to understand the impact of OTC labeling on consumer behavior and perceptions.

2 Objectives

The primary objective is to investigate the effect of hearing aid labeling on objectively measured speech understanding in noise for inexperienced and experienced hearing aid users with mild to moderate hearing loss.

3 Description of the investigational device

The Audéo P is a hearing aid on the Paradise platform and is worn with the processor behind the ear with the receiver in the ear canal. The microphone(s) pick(s) up sound waves, convert(s) them into an electrical signal which is sent to the Digital Signal Processor (DSP), which is part of the hybrid. The DSP applies the amplification to the electrical signal, which means that the amplitude of the signal gets modified. The modified electrical signal is forwarded to the external receiver, which is held in the ear canal with the aid of an earpiece. The external receiver converts the electrical signal into an acoustic signal and submits it to the ear drum. An integrated Bluetooth antenna enables the hearing aid to also receive digital signals (e.g. streamed music), which will be processed in the same way.
The overall intended purpose of the device is to amplify and transmit sound ot the ear and thereby compensate for impaired hearing.

4 Design of the clinical investigation

This investigation is a single-center, randomized, double-blinded crossover study with two treatment conditions. Treatment conditions include an OTC device condition, wherein the participant believes they are wearing an OTC device, and a prescriptive device condition, wherein the participant believes they are wearing a hearing aid that has been programmed prescriptively for their hearing loss. There will be two arms of the study; one group of participants will be new users, who have never worn or owned a hearing aid, and the other group will consist of experienced hearing aid users, defined as having worn hearing aids for at least six months.

During the investigation, the participants will be told which condition they are in because the aim of this investigation is to measure bias. That being said, the investigators will use pre-planned scripts when conversing with the participants in the study to ensure that factors relating to the bias are equitable for the participants, notwithstanding the bias the participants may or may not have prior to the study appointment. The QuickSiN test will be scored by a sub-investigator who will be blinded to the condition in order to minimize tester bias. Because this investigation follows a cross-over design, participants will be randomly assigned to one of two possible orders for exposure to the two treatment arms to counteract potential order effects.

5 Risks and benefits of the investigational device and clinical investigation

There are minimal risks associated with both the investigational device and participating in the clinical investigation. Identified risks are no greater than those associated with the daily use and wear of approved, available hearing aids. The device used presents non-significant risk per FDA.
The benefits of participating in the investigation include the possibility of hearing sounds that have not been previously heard, such as speech and environmental sounds, which may improve communication in daily life. Subjects may experience the benefit of personal satisfaction for participating in research to improve hearing instrument technology. Subjects will also be compensated for their time in participating in this study.
There are no known or anticipated risks to subject hearing ability associated with participation in this study. All sounds used in this study will be presented at safe listening levels. While using hearing aids, the following are possible occurrences:

- Cerumen impaction
- Ear discomfort, pain or soreness
- Sweat or moisture accumulation in the ear canal or pinna
- A feeling of pressure or fullness in the ear
- Itching, blisters, or sores in the ear canal or pinna
- Headache
- Redness of tissue

The research personnel will review these risks with the subjects and answer any questions they have. Hearing aids are not a significant risk investigational device as defined in the FDA 21 CFR 812.3(m).

6 Endpoints

Primary endpoint:

- Quick Speech-in-Noise (QuickSiN) benefit score. QuickSiN is an adaptive test of an individual's ability to understand speech in noise. The test adapts the relative levels of noise and speech to determine the signal-to-noise ratio (SNR) at which the individual can correctly identify 50% of key words. This test was independently developed and validated and is available for use by clinicians and researchers (Killion, et al., 2004).

7 Inclusion and Exclusion Criteria

Subjects fulfilling all of the following inclusion criteria are eligible for the investigation:

- Adults and adolescents 18-95 years of age
- Target recruitment is for 15 first-time hearing aid users and 15 experienced hearing aid users
- Mild to moderate (N1-N3) bilateral hearing loss
- Fluent in English; ability to read and write in English
- Willing and able to provide informed consent

Participants must meet the eligibility criteria for OTC hearing aids per the FDA. New-to-hearing aid participants must not have prior hearing aid experience, defined as never owning their own devices. Experienced hearing aid participants must have at least 6 months of hearing aid use with their own devices

The presence of any one of the following exclusion criteria will lead to the exclusion of the subject:

- Self-reported ear-related pathology (otorrhea w/in 90 days, dizziness, sudden hearing loss or worsening of hearing w/in 90 days, otalgia)
- Visible deformity of the ear
- Chronic, severe tinnitus
- Unilateral hearing loss
- Cognitive impairment

8 Measurements and procedures

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15 inexperienced users and 15 experienced hearing aids users will be recruited for this study. They will be told they are participating in a research study comparing two sets of hearing aids. One set of hearing aids will be labeled as "OTC" devices, while the other will be labeled as "Prescriptive" devices. Definitions for OTC hearing aids and prescriptive hearing aids will be provided to the participants verbally; however, all the participants will see are two identical hard shell hearing aid cases with a physical label on them that say "OTC" and "Prescriptive." The participants will complete the QuickSIN for both conditions (OTC and prescriptive) in order to assess if there is a labeling effect on objective speech understanding performance in noise.

Data will be captured at the time of testing. Data will be stored electronically on a Sonova-owned server and will be analyzed after all participants have completed all investigation tasks and appointments. Any computing code generated to conduct the analysis will be stored with the data following the analysis.

There will be two researchers involved in this study. One researcher will speak with the participants, place the hearing aids in their ears, and administer the questionnaires. The other researcher will score the objective testing while blinded to the condition.

9 Statistical design and analysis

An a priori power analysis was conducted in G*Power3 for the primary objective. The primary objective will be measured for two groups (experienced and inexperienced) via repeated measures of the QuickSIN for two conditions (OTC and prescriptive). A repeated measures, within and between factors ANOVA, using a medium effect size (f= .55) and alpha of .05, would require a sample of 14 participants per group (inexperienced and experienced) for a total of 28 participants to achieve a power of .95.

Speech-in-noise (i.e. QuickSiN) data for the primary objective from all subjects will be analyzed. Participants will be grouped by hearing aid experience (either inexperienced or experienced) as a part of these analyses. For the primary objective and its associated endpoint (QuickSiN benefit), two lists will be presented for each condition in order to expect a 1.8 dB critical difference between the conditions with a 80% confidence level. The principal investigator will conduct the analysis of the primary endpoint after data has been collected from all participants for all test conditions.

10 Investigation Duration

This investigation is scheduled to last approximately 10 weeks. Each participant's duration will be one day of testing.

11 Data handling and management

Electronic or paper based CRFs will be used to capture the participant data. If electronic, subjective questionnaires will be available in the EDC system and the participant will be able to read question and choose answer. If paper based subjective questionnaires are used, the participant will answer each question and the results will be transferred to the EDC by the investigator. Objective data will either be entered in directly to the EDC system, or transferred from a paper based CRF into the EDC system.

All CRFs are kept current to reflect the subject's status at each phase during the course of study. Participants cannot be identified in the CRF by name or initials and birth date but an appropriate coded identification is used. All study team members are authorized for the CRF entries and it is assured that any authorized person can be identified both for pCRFs and eCRFs. If pCRFs are used, the investigator's initials and subject ID are documented and data are entered into an electronic file for analysis by the respective investigator and data will be monitored by the assigned monitor. In case of a self-evident corrections, either the subject does it by himself or the investigator undertakes the correction by crossing out the word/sentence with a single horizontal line and by adding the correction including his personal identifier and the date.

The results for the audiometer-based objective measure will be taken from the computer used to complete the test and imported into the EDC system or transferred via an excel or csv file. Real Ear Measurements will be imported from the verification system and stored as an excel file.

The pCRFs/eCRFs are only available to the local study team and to the monitor of the study.
In the case of an audit or a serious adverse event, the CRFs may need to be de-anonymized and sent to the governing body (i.e FDA) or insurance company.
Any paper-based data will be stored in a locked filing cabinet at the investigation site. All electronic data will be stored on an access-restricted server owned, operated, and maintained by Sonova USA. Servers used to store data in this investigation are physically located in the US. Permission to access data will be limited to study manager, monitor, PI, and essential research staff, as designated by the principal investigator.
During data collection of the investigation, physical copies of the data will be compiled and digitized by the study manager/investigator on a daily basis. Data will be reviewed for mis-entries or inaccuracies as each data set is entered.
The extent and nature of monitoring appropriate for the clinical investigation including the strategy for source data verification (SDV) are based on considerations such as the objective, design, complexity, size critical data points and endpoints of the clinical investigation. A de-tailed plan for monitoring arrangements is provided separately from this CIP.

12 Amendments to the CIP

Any necessary amendments to the CIP will be communicated to the study manager/sponsor.
A new version of the CIP will be written, with the necessary changes and justification, and the PI will be trained on the amendments. The amended CIP will go through the approval process and necessary signatures obtained from the study manager/sponsor, PI, and statistician. The amended CIP will be uploaded to the eQMS system as an additional revision.

13 Deviations from clinical investigation plan

Deviations from the CIP to protect the rights, safety and well-being of human participants under emergency circumstances may proceed without prior approval of the sponsor and the EC – such deviations will be documented and reported to the sponsor representative (Study Manager) and the EC as soon as possible. Apart from that the investigator is not allowed to deviate from this CIP unless that deviation does not influence the investigation data.

14 Device accountability

Sonova, in its capacity as sponsor, will maintain a log of all investigational devices, including the date of shipment from Sonova to the site, serial number, receiving study site, and date returned to Sonova.

The site will maintain a log of the devices provided by Sonova, including the date of receipt,serial number, date of fitting, participant identification, date of return to site by participant, and date returned to Sonova. Sonova will provide each site a template with which to record such information.

If a device needs to be replaced due to a device deficiency, the PI or sub-investigator will add the new device serial number, date of receipt, and date of return of the defective device on the Device Accountability Log.

In the case of a device deficiency, the Adverse Event-Device Deficiency form will be completed by the study manager and the PI or sub-investigators together.

15 Informed consent process

Informed consent will be obtained from participants prior to any study participation in accord-ance with the IRB guidelines. The participants will be granted sufficient time to read through the consent in full and ask any questions they have before signing. After the participant signs the consent form, the researcher will sign and provide a copy to the participant. This process will take place in a private office located in the Phonak Audiology Research Center (PARC).

Informed Consent will only be obtained by investigation participants who can provide informed consent themselves before enrollment.

16 Adverse events, adverse device effects and device deficiencies

Device deficiencies and all **adverse events (AE)** including all **serious adverse events (SAE)** are collected, fully investigated and documented in the source document and appropriate case report form (CRF) during the entire investigation period, i.e. from participant's informed con-sent until the last protocol-specific procedure, including a safety follow-up period (ISO-14155, 2020). Documentation includes dates of event, treatment, resolution, assessment of serious-ness and causal relationship to device and/or investigation procedure.
Information on AEs is systematically collected during the regular investigation visits, and phone calls (if applicable).
The investigator(s) will follow-up on a biweekly basis with any participant experiencing an AE until either a) the participant reports resolution of the AE or b) 8 weeks have passed since the participant's final visit. If, however, the participant's condition worsens throughout the 8 week follow-up period, the investigator will continue to follow-up biweekly until the AE is resolved or the participant's condition stabilizes over an 8 week period.
The reporting of Serious Adverse Events and Device Deficiencies follows the Regulation (EU) 2017/745 and the MDCG 2020-10/1 Safety Reporting in Clinical Investigations of Medical Devices under Regulation (EU) 2017/745.
The causality assessment of the SAE will be conducted according to MDCG 2020-10/1 Safety Reporting in Clinical Investigations of Medical Devices under Regulation (EU) 2017/745.

17 Vulnerable populations

This investigation will not include any vulnerable populations.

18 Suspension or premature termination of the clinical investigation

The study will be terminated if the majority of the participants are not able to wear the devices for the study visit.
The study will be terminated if the participants or researchers are exposed to safety risks other than those outlined in this document.
The study may be terminated in the event natural disasters, widespread outbreak of illness, compromised structure of the investigation site, etc. that would make continuation of the study

impossible or impractical. The study will be suspended within 5 days of determination that the study or device put participants at an unreasonable risk.
If a participant is suspended, terminated, or withdraws from the study, their data can be traced with their unique study identification number.
According to the FDA, follow-up is required for participants who experience Serious Adverse Events. Follow up will be conducted by the study manager and/or the PI until the nature of the event is resolved.

19 Publication policy

The clinical investigation will be registered in clinicaltrials.gov, a publicly accessible database, as required by U.S. regulations.
The results of the clinical investigation will be published on clinicaltrials.gov no later than one calendar year following the final participant appointment.
An internal report of the results of this investigation will be completed and uploaded to eQMS.