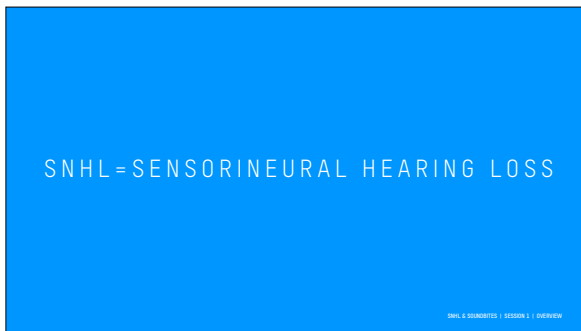


1

Hi, and welcome to the online learning course SNHL and Soundbites. I'm Barry Seifer. I'll tell you more about me in a moment but first I'd like to explain those two words and what you'll learn in this session and the following four videos.



2

The course is about SNHL, which is the abbreviation for sensorineural hearing loss, the medical term for inner ear hearing loss.



3

SNHL is the major form of hearing loss, so SNHL is commonly called hearing loss.



4

Soundbites is the trademark for the biomedical product of the hearing preservation formula known as ACEMg in medical research journals. I'll use the terms interchangeably in these talks.

A blue slide with a table of contents for Session 1. The table has three columns: session, title, and topics. The first row shows session 1, title 'overview', and topics: founders, research, development, and real-world evidence. The rest of the table is empty. In the bottom right corner, there is a small white text "SNHL & SOUNDBITES | SESSION 1 | OVERVIEW".

session	title	topics
1	overview	<ul style="list-style-type: none">• founders• research• development• real-world evidence

5

There are five sessions in this course. In this overview I'll introduce the project's two founders, one of whom is me, and summarize the thirty-six-year medical R&D story in about 12 minutes. I'll end this talk with a summary of the real-world clinical data demonstrating ACEMg's evidence of effectiveness.

A blue slide with a table of contents for Session 2. The table has three columns: session, title, and topics. The first row shows session 1, title 'overview', and topics: founders, research, development, and real-world evidence. The second row shows session 2, title 'the snhl problem', and topics: major cause, common belief; scope, scale, and consequences; and who suffers and how. The rest of the table is empty. In the bottom right corner, there is a small white text "SNHL & SOUNDBITES | SESSION 1 | OVERVIEW".

session	title	topics
1	overview	<ul style="list-style-type: none">• founders• research• development• real-world evidence
2	the snhl problem	<ul style="list-style-type: none">• major cause, common belief• scope, scale, and consequences• who suffers and how

6

Session 2, the SNHL problem, covers the hearing loss problem in detail. You'll learn about the major cause and common belief. I'll use global health data to explain the problem's scale and consequences, and who suffers and how.

session	title	topics
1	overview	<ul style="list-style-type: none"> founders research development real-world evidence
2	the snhl problem	<ul style="list-style-type: none"> major cause, common belief scope, scale, and consequences who suffers and how
3	how sound becomes hearing	<ul style="list-style-type: none"> hearing anatomy, physiology and biochemistry

7

In Session 3 you'll learn the anatomy, physiology and biochemistry of hearing, focusing on the inner ear.

session	title	topics
1	overview	<ul style="list-style-type: none"> founders research development real-world evidence
2	the snhl problem	<ul style="list-style-type: none"> major cause, common belief scope, scale, and consequences who suffers and how
3	how sound becomes hearing	<ul style="list-style-type: none"> hearing anatomy, physiology and biochemistry
4	when auditory transduction goes wrong	<ul style="list-style-type: none"> hearing loss pathogenesis and pathophysiology ACEMg development, mechanisms of action, preclinical and clinical data

8

In Session 4 you'll learn the pathogenesis and pathophysiology of hearing loss, how the ACEMg formula emerged from about two decades of basic research, and how ACEMg works – its mechanisms of action – along with some preclinical and clinical data.

session	title	topics
1	overview	<ul style="list-style-type: none"> founders research development real-world evidence
2	the snhl problem	<ul style="list-style-type: none"> major cause, common belief scope, scale, and consequences who suffers and how
3	how sound becomes hearing	<ul style="list-style-type: none"> hearing anatomy, physiology and biochemistry
4	when auditory transduction goes wrong	<ul style="list-style-type: none"> hearing loss pathogenesis and pathophysiology ACEMg development, mechanisms of action, preclinical and clinical data
5	ACEMg becomes Soundbites	<ul style="list-style-type: none"> translational research timeline RWE/RWD Study

9

In Session 5, if you're curious, you can learn about the sixteen-year translational research journey from laboratory to product to market.

▸ founders

TMH & SOURCES | SESSION 1 | OVERVIEW

10

I'll start by introducing myself and my late colleague, friend, co-founder, mentor and chief scientist Dr. Joe Miller.



11

I'm on the left driving a moped. Dr. Joe Miller, the ACEMg inventor, is my passenger. In 2010 Joe and I cofounded the company to move ACEMg out of his medical school lab and into the market. I became the company's CEO.

make a difference in public health

TMH & SOURCES | SESSION 1 | OVERVIEW

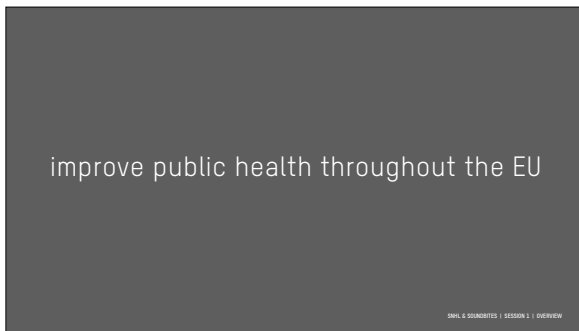
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We were California natives and University of California at Berkeley grads living in Ann Arbor, Michigan. We shared a hardwired desire to make a difference in public health.



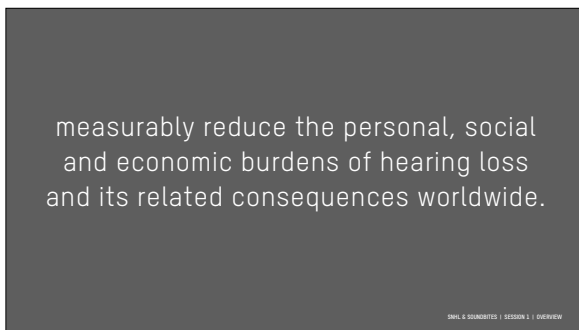
13

The photo was taken in Amsterdam after the European government awarded a four-year medical innovation grant to our ACEMg project in 2012, and where I had moved to become a Principal Investigator.



14

The grant's objective was to make ACEMg available throughout the EU, to help improve public health among the fast-growing aging population.



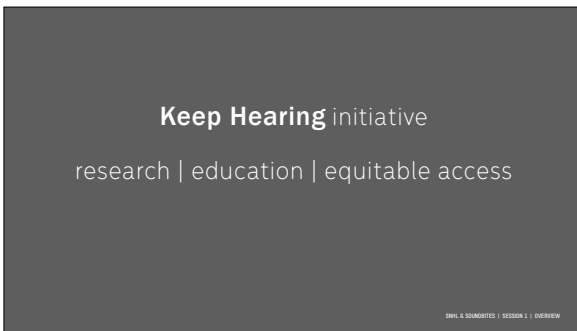
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For us, this was an important step toward achieving the long-term goal stated in our grant application: Measurably reduce the personal, social and economic burdens of hearing loss and its related consequences worldwide. You'll learn how ambitious that goal is in Session 2.



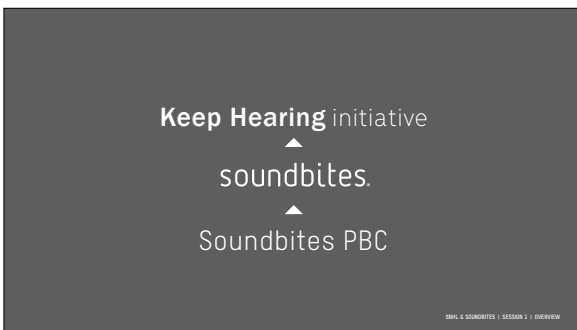
16

Along the way, the ACEMg formula became Soundbites softgel capsules, the first oral preventive care for hearing. ACEMg came to test market in the Netherlands in July 2017, a few months after Joe died. I promised to finish the project.



17

In 2018 Joe's family and friends formed the Keep Hearing initiative nonprofit to continue research and education on hearing loss and ACEMg, aiming for broad awareness and equitable access. I'm the Impact Director for the Keep Hearing initiative.



18

Soundbites Public Benefit Corporation was formed in 2019 to become the nonprofit's major donor by marketing Soundbites under a license from the University of Michigan, the owner of the nine issued ACEMg patents.



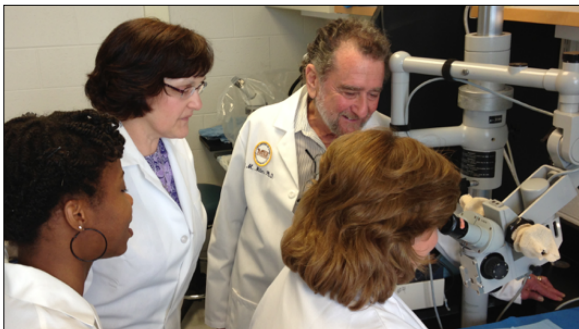
19

Now let's go back to the beginning of the story, the research.



20

The Soundbites company grew out of three decades of Joe Miller's research at the Kresge Hearing Research Institute at the University of Michigan Medical School. The research started in 1987.



21

Joe was the Institute's director, shown here with his lab team in 2010.

auditory neuroscience

SMALL & SOUNDBITES | SESSION 1 | OVERVIEW

22

His research is in the field of auditory neuroscience, which studies inner ear biology and cellular biochemistry.

free radicals in inner ear biology

SMALL & SOUNDBITES | SESSION 1 | OVERVIEW

23

The focus turned out to be unstable oxygen molecules called free radicals, which are fundamental to metabolic energy production in inner ear cell mitochondria, the power plants of cells throughout the body.



inner ear ROS is our central topic

SMALL & SOUNDBITES | SESSION 1 | OVERVIEW

24

Collectively, oxygen free radicals are reactive oxygen species, or ROS. Inner ear ROS is our central topic.

hearing preservation in the organ of Corti

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

25

Joe's motivation was hearing preservation in the organ of Corti, the hearing organ in the cochlea, the inner ear. The organ of Corti's job is to change sound waves into electric impulses that the brain interprets as hearing in a process called auditory transduction. I'll cover that topic in Sessions 3 and 4.

human hearing cells don't regrow

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

26

His goal was to help keep cochlear cells healthy and alive because even though these cells are commonly called hair cells, they don't regrow in humans. Their dysfunction is experienced as hearing loss. Hearing loss was a big problem when he started the research, and it's an even bigger problem today, as we'll learn in Session 2.

90%+

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

27

SNHL accounts for more than 90% of all hearing loss, so when someone says they have hearing loss, the chances are better than 9 in 10 they're talking about SNHL.

noise, mainly

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

28

Noise accounts for the vast majority of hearing loss.

noise-induced hearing loss = NIHL

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

29

It's sometimes called noise-induced hearing loss, or NIHL.

>90% hearing loss = NIHL

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

30

Noise accounts for more than 90% of inner ear hearing loss.

human hearing cells can last a lifetime

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

31

Human hearing cells can last a lifetime. There's no biological reason for humans to lose their hearing. But clearly we do, and noise exposure is most often the reason.

noise hastens hearing cell aging

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

32

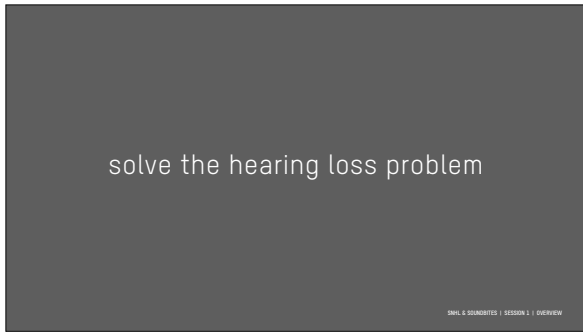
Noise hastens hearing cell aging, causing hearing loss and contributing to incurable neurological disorders like tinnitus and dementia.

NIHL ≈90% less hearing loss

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

33

Said another way, eliminating noise exposure would cut hearing loss by about 90%. Hearing loss is caused in other ways, too, but the root cause of almost all types of hearing loss is the same.



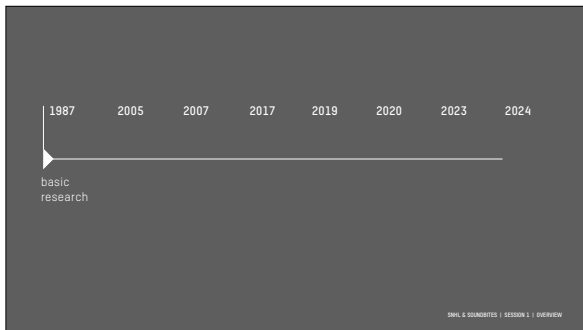
34

Joe aimed to solve the hearing loss problem.



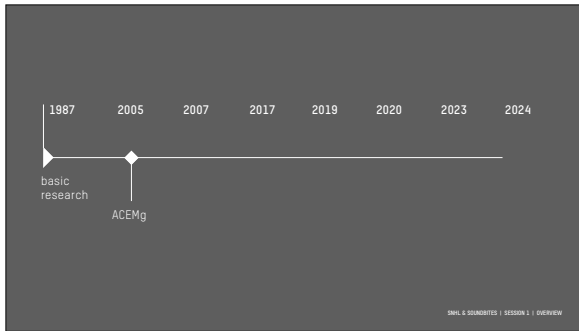
35

Let's look at how he went about it.



36

It took about sixteen years, from 1987 to 2003, to understand the inner ear biochemistry, pathogenesis, and pathophysiology underlying SNHL.



37

With that understanding, it took a relatively short two years to identify ACEMg as a potential solution.

ACEMg = vitamins, A, C, and E + Mg

38

ACEMg is a micronutrient biomedicine formula. The abbreviation stands for vitamins A, C, and E, and the mineral magnesium, or Mg.



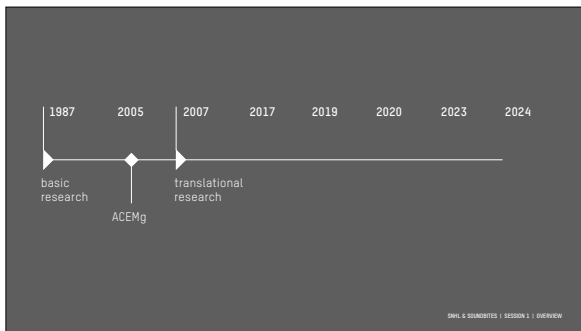
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The peer-reviewed paper disclosing ACEMg to the medical research community was published in 2007. ACEMg was demonstrated to significantly block the initiating biological events leading to SNHL, a significant scientific achievement.



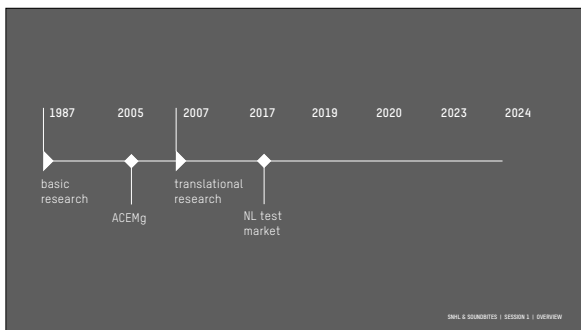
40

The discovery made the CBS evening news.



41

Then, like virtually all candidate therapeutics, ACEMg disappeared into translational medicine, the research process aimed at demonstrating that a candidate therapeutic is statistically better than the current standard of treatment.



42

The grant from the European government provided a boost from 2012 to 2016. That chapter ended in 2017 with the Soundbites test market in the Netherlands from the home base in Amsterdam.



43

Amsterdam hosts the annual Amsterdam Dance Event, called ADE, a week-long conference and nonstop party for the electronic dance music scene, or EDM. About a hundred EDM festivals start at about 10 pm and go all night, each night. EDM fans are mainly the young adults currently most at risk for hearing loss early in life, a key research group for us.



44

We collaborated with Netherlands universities and dance festival producers, aiming to collect real-world data from festival attendees on the effectiveness of Soundbites. Real-world data from real world-evidence studies informs public health.



45

Here's how we started.



46

We collected anecdotal real-world data from a pop-up EDM event we produced on a ferry transporting fans to an overnight music festival during ADE. We ferried several thousand EDM fans. The one-minute aftermovie is available in the extra documents.



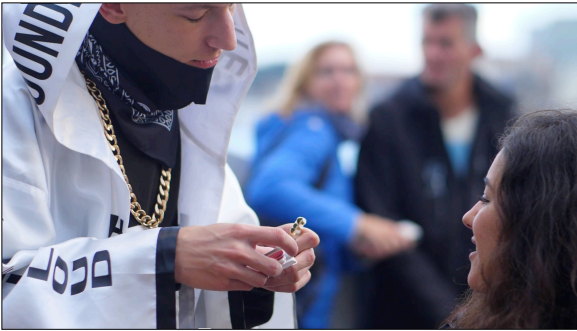
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The event was called the Soundbites Sessions. It had plenty of EDM attitude.



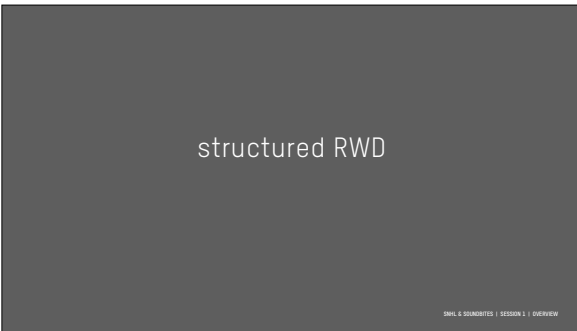
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EDM events are loud, and so was ours. The slogan was life is loud.



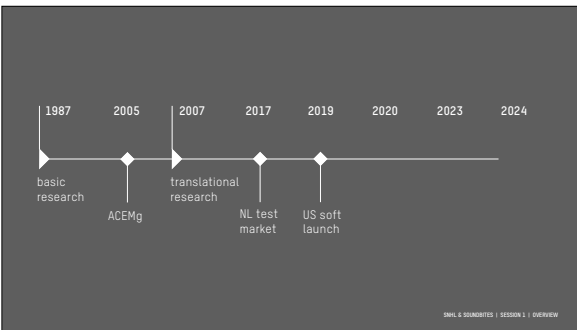
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We handed out Soundbites softgel capsules to the fans, who were on the ferries for about ten minutes. But our staff worked all night. Accidentally, our ferry party staff provided the most useful anecdotal data. They noticed Soundbites worked when the protection wore off. They asked if they could take more. We learned that Soundbites appeared to work faster and better than we had imagined.



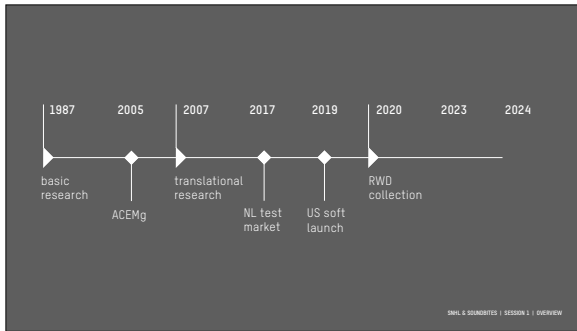
50

This insight motivated us to aim for structured, statistically-reliable real world data from a real-world evidence study conducted under a strict protocol. The project returned to the U.S. before we could conduct that study in Europe.



51

U.S. distribution of Soundbites softgels started at the end of 2019, a few months before Covid shut the world down. Very few people knew about Soundbites because we were still focused on research.



52

In 2020 Chicago-based audiologist Dr. Lori Halvorson heard about us from a colleague who'd known us for more than a decade. She expressed interest in collecting real-world data by making Soundbites available to her patients.

otoacoustic emissions (OAE) examinations

SMAIL & SOUNDBITES | SESSION 1 | OVERVIEW

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Importantly, Dr. Halvorson had been conducting otoacoustic emissions examinations for many years in the normal course of her clinical practice.

OAE exams measure auditory function objectively

SMAIL & SOUNDBITES | SESSION 4 - WHEN AUDITORY TRANSDUCTION DOES WRONG

54

OAE examinations measure auditory function of outer hair cells (OHC) in the cochlea objectively.

retrospective (no treatment) RWD = control

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

55

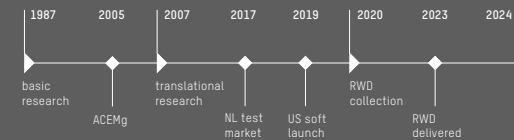
Historic, or retrospective OAE data could function as the control group, providing objective data that tested the conventional wisdom that untreated hearing loss is progressive.

retrospective (no treatment) RWD = control
prospective RWD = treatment

SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

56

Access to patients previously diagnosed with SNHL who had several years of annual OAE examination data who then started taking Soundbites made it feasible to define a treatment group aimed at objectively assessing the potential impact of the ACEMg intervention on progressive hearing loss.



SNHL & SOUNDBITES | SESSION 1 | OVERVIEW

57

The study took two years. Dr. Halvorson shared the real-world dataset with the research team under a data-sharing agreement in the second half of 2023.

N=190 total

SNDL & SOUNDBITES | SESSION 4 - WHEN AUDITORY TRANSDUCTION GOES WRONG

58

A total of 190 patients in two groups participated in the study.

N=97 no treatment

N=190 total

SNDL & SOUNDBITES | SESSION 4 - WHEN AUDITORY TRANSDUCTION GOES WRONG

59

Five years of no-treatment data on 97 patients tested the hypothesis that untreated hearing loss gets progressively worse.

N=97 no treatment

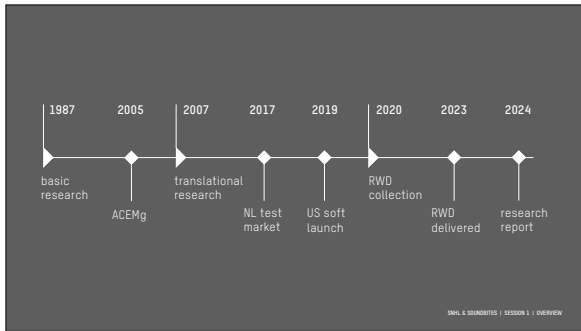
N=93 ACEMg treatment

N=190 total

SNDL & SOUNDBITES | SESSION 4 - WHEN AUDITORY TRANSDUCTION GOES WRONG

60

Impact of the ACEMg treatment was provided by 93 patients who had at least two years of previous annual OAE exams and then started taking ACEMg as Soundbites softgel capsules for two years.



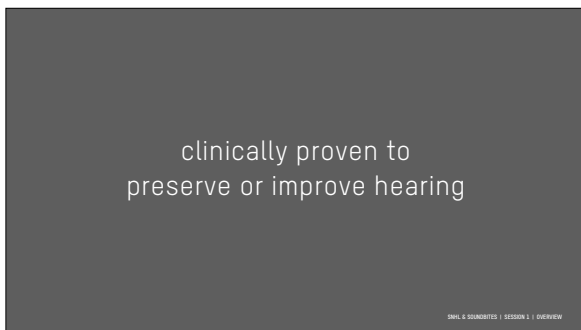
61

The Keep Hearing nonprofit received an IRB exemption allowing analysis of the secondary data. We prepared a manuscript.



62

Here's what we found.



63

The study demonstrated Soundbites was clinically proven to preserve or improve hearing.

OAE scores increased or remained unchanged for 75.3%, or 70 of the 93 patients who took Soundbites

SINEL & SOUNDBITES | SESSION 4 - WHEN AUDITORY TRANSDUCTION GOES WRONG

64

OAE scores remained unchanged or improved for 75.3 %, or 70 of the 93 patients who took Soundbites daily for two years.

OAE scores didn't change for 35 of 93 Soundbites patients. Hearing was preserved.

SINEL & SOUNDBITES | SESSION 4 - WHEN AUDITORY TRANSDUCTION GOES WRONG

65

OAE scores didn't change for 35 of the Soundbites patients. Hearing was preserved.

OAE scores didn't change for 35 of 93 Soundbites patients. Hearing was preserved.

OAE scores increased for 35 of 93 Soundbites patients. Hearing improved.

SINEL & SOUNDBITES | SESSION 4 - WHEN AUDITORY TRANSDUCTION GOES WRONG

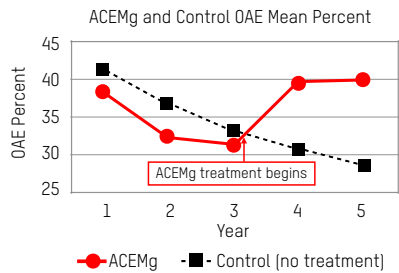
66

OAE scores increased for 35 of the Soundbites patients. Hearing improved. Most of the improvement happened within the first six months, and continued with daily use.

OAE scores decreased for 71 of the 97 untreated patients

67

In stark contrast, OAE scores decreased for 73.2%, or 71 of the 97 untreated patients.



68

This chart visualizes the findings. The black line confirms the common belief that hearing loss progresses without intervention.

The red line shows what happened when patients with two previous annual OAE exams starting taking ACEMg as Soundbites immediately following their third annual OAE exam. The research report is available in the extra documents.

Soundbites helps preserve cognitive health and reduces dementia risk

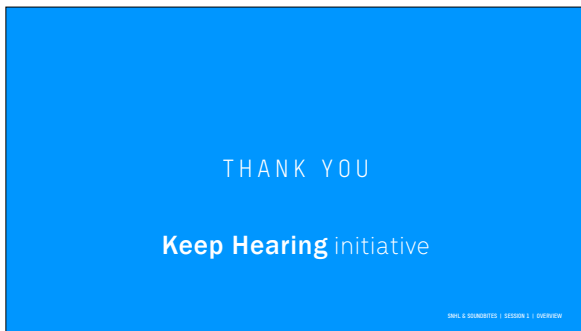
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Moreover, real-world data support the claim that Soundbites helps preserve cognitive health and reduces dementia risk because hearing loss is known to hasten cognitive dysfunction, a disability strongly correlated with hearing loss. I'll cover this topic in Session 2.



70

For avoidance of doubt, Soundbites does not grow new inner ear hair cells. That's currently impossible.



71

Thank you. I hope you'll continue the course and I look forward to sharing it with you.