ART AND (HEARING) SCIENCE

Auditory Effects of Antiretroviral Exposure

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3. **Potential Conflicts of Interest**
   a. I am a member of the **International Ototoxicity Management Group**, which will be discussed during this presentation.

SEMINAR AGENDA

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HIV AND ITS MANAGEMENT

02

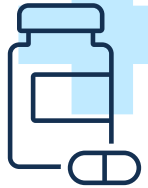
AUDITORY EFFECTS OF HIV & ART

03

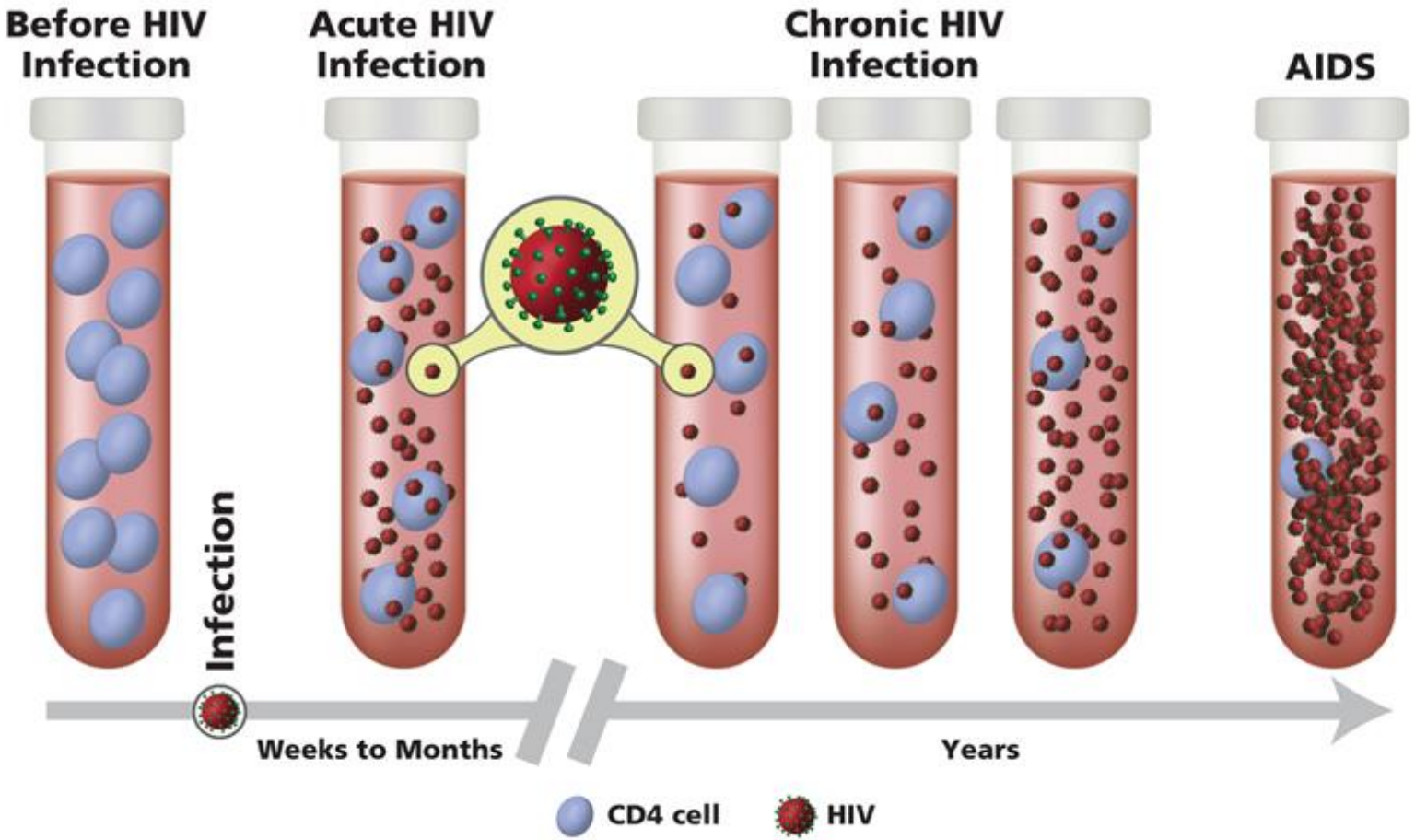
OTOTOXICITY MANAGEMENT

01

HIV AND ITS MANAGEMENT

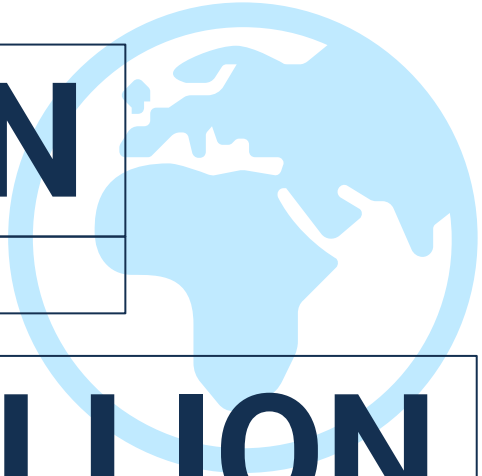


HIV Progression



37.7 MILLION

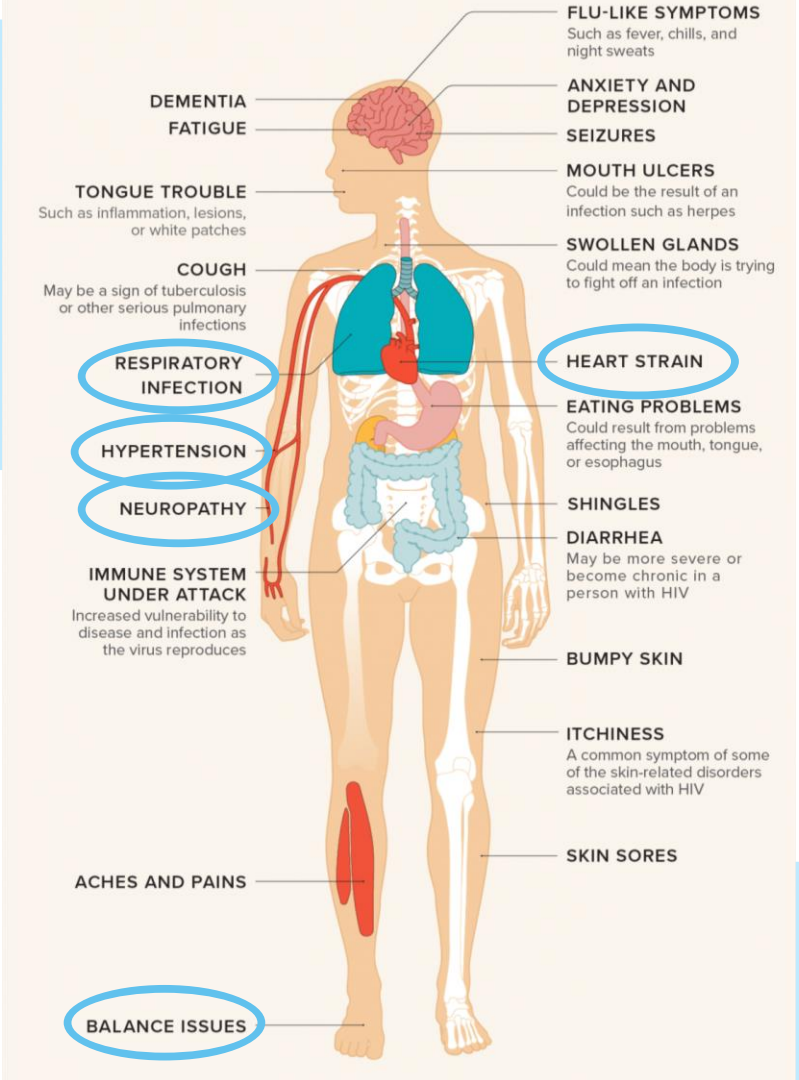
people living with HIV globally



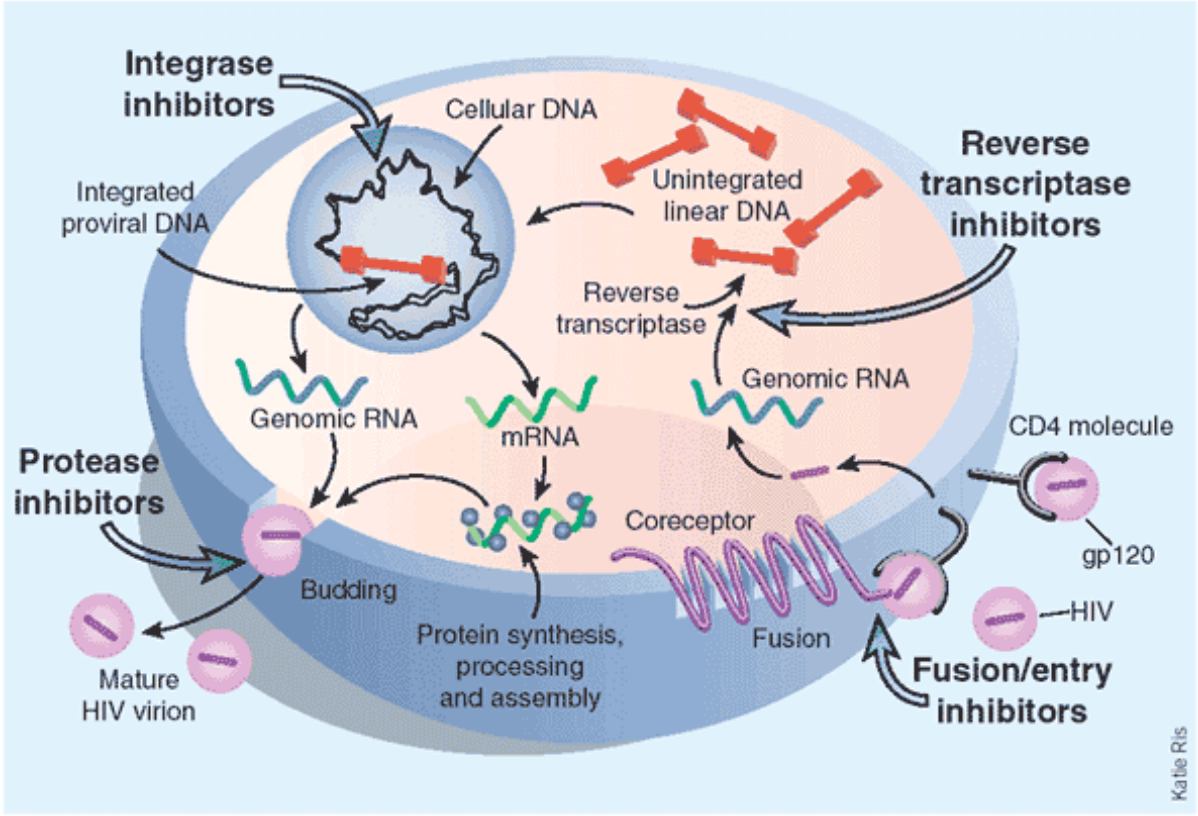
27.5 MILLION

people taking antiretroviral therapy

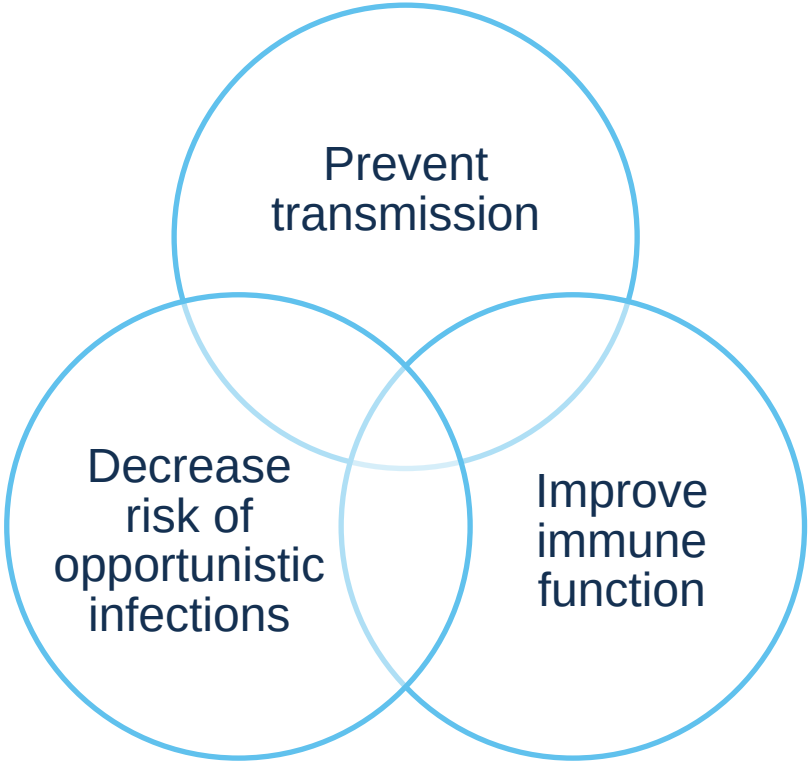
HIV'S EFFECTS ON THE BODY

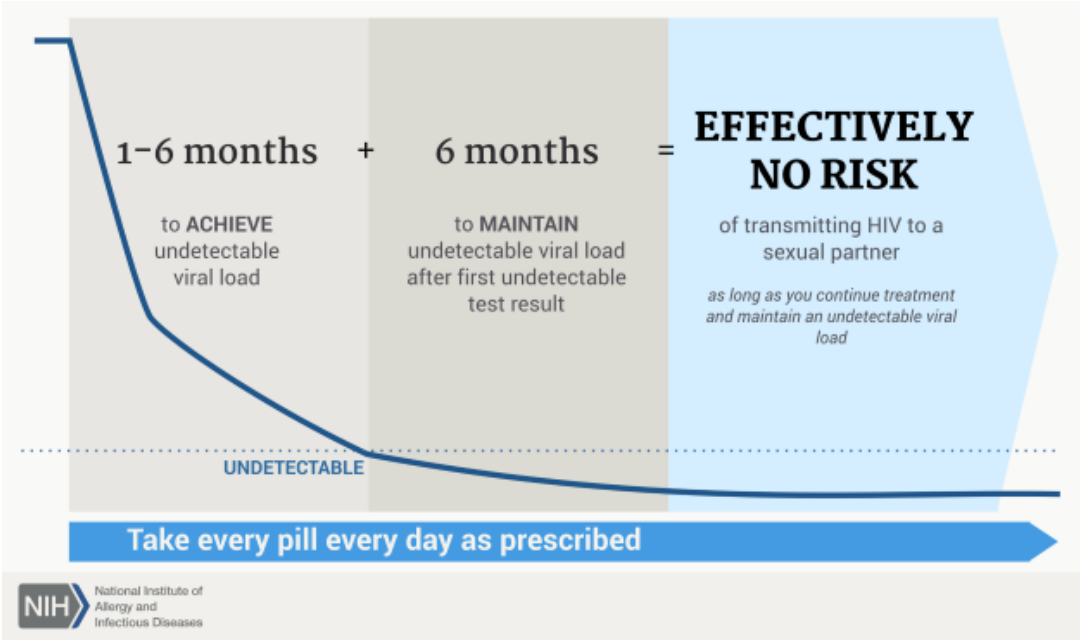


HOW DOES ANTIRETROVIRAL THERAPY WORK?



WHAT ARE THE GOALS OF ART?



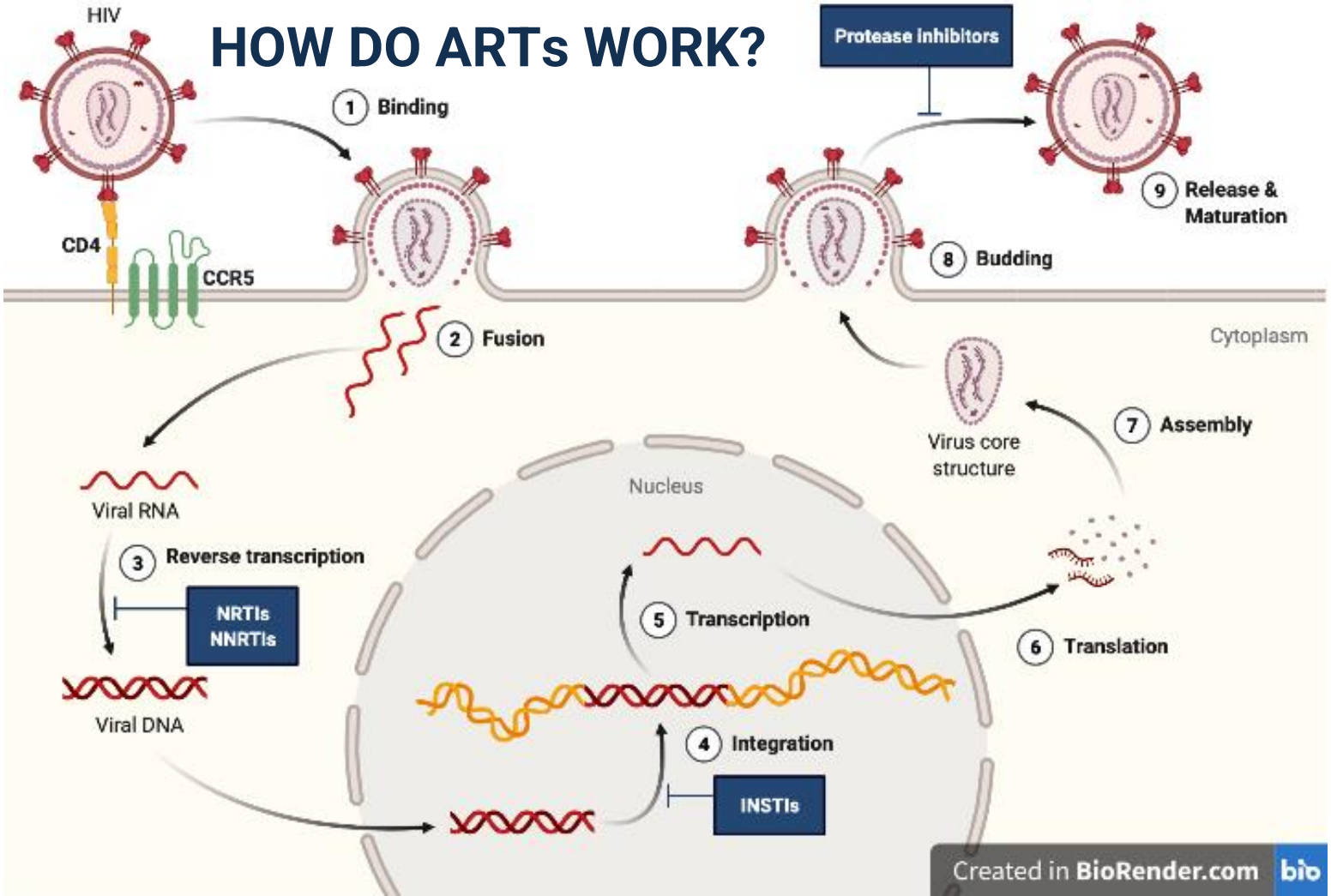


COMMON ANTIRETROVIRAL DRUGS

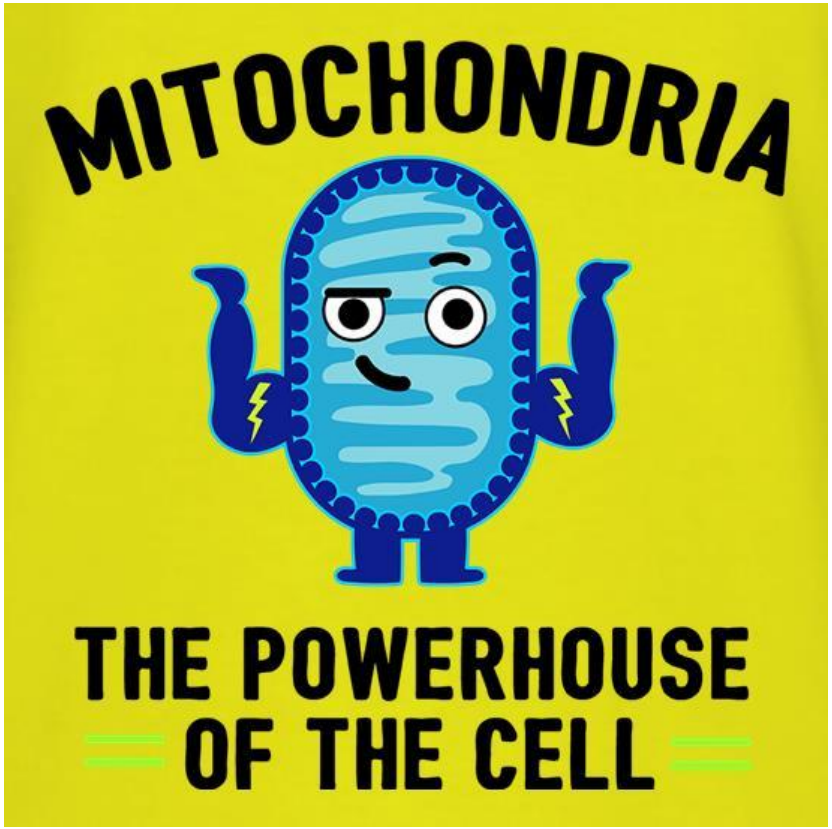



NRTI	NNRTI	INSTI	PI
❑ **Emtricitabine** ❑ Tenofovir disoproxil fumarate ❑ **Tenofovir alafenamide** ❑ Zidovudine	❑ Doravirine ❑ Efavirenz ❑ Rilpivirine	❑ **Bictegravir** ❑ Cabotegravir ❑ **Dolutegravir** ❑ Raltegravir	❑ Atazanavir ❑ Darunavir ❑ Lopinavir ❑ Ritonavir ❑ Cobicistat

HOW DO ARTs WORK?



ART EFFECTS ON MITOCHONDRIA



1. ARTs disrupts the production of mitochondrial polypeptides and leads to increased ROS production
2. ROS are disruptive throughout the body and exacerbate many conditions, including HL
3. Mitochondrial damage has been shown to drive:
    - Age-Related HL (Kim et al., 2019),
    - Noise-Induced HL (Van Laer et al., 2006),
    - Congenital hearing loss (Kokotas et al., 2007),
    - Ototoxic hearing losses (Estivil et al., 1998; Gurtler et al., 2005).

IMPACTS OF ART EXPOSURE DURING PREGNANCY

COGNITIVE DEVELOPMENT

Variable reports of both global and specific cognitive developmental delays

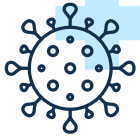
LANGUAGE DEVELOPMENT

Increased language delay in ART-exposed children, with greater risk from cART than AZT monotherapy

AUDITORY FUNCTION

Mixed reports of increased hearing screening failures and auditory dysfunction beginning at birth

OTHER USES FOR ANTIRETROVIRAL DRUGS



COVID-19

HEPATITIS

02

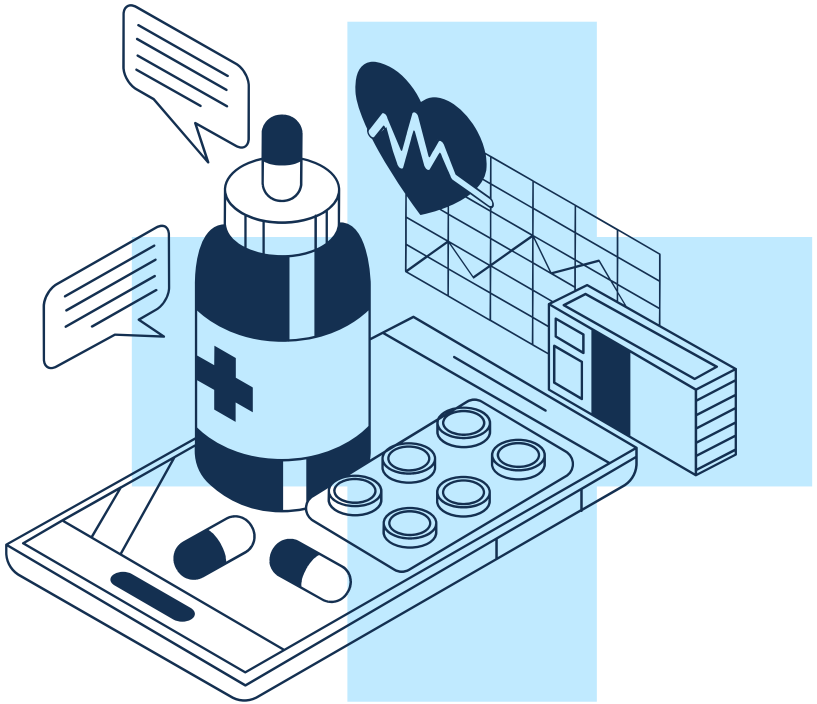
AUDITORY EFFECTS OF HIV & ART

OTOTOXICITY

Damage to the audiovestibular system as a result of a drug or chemical exposure. Symptoms may include:

- Hearing loss
- Tinnitus
- Balance disturbances

Cochleotoxicity or vestibulotoxicity may be used to refer to toxicity only to the cochlea or vestibular system, respectively.



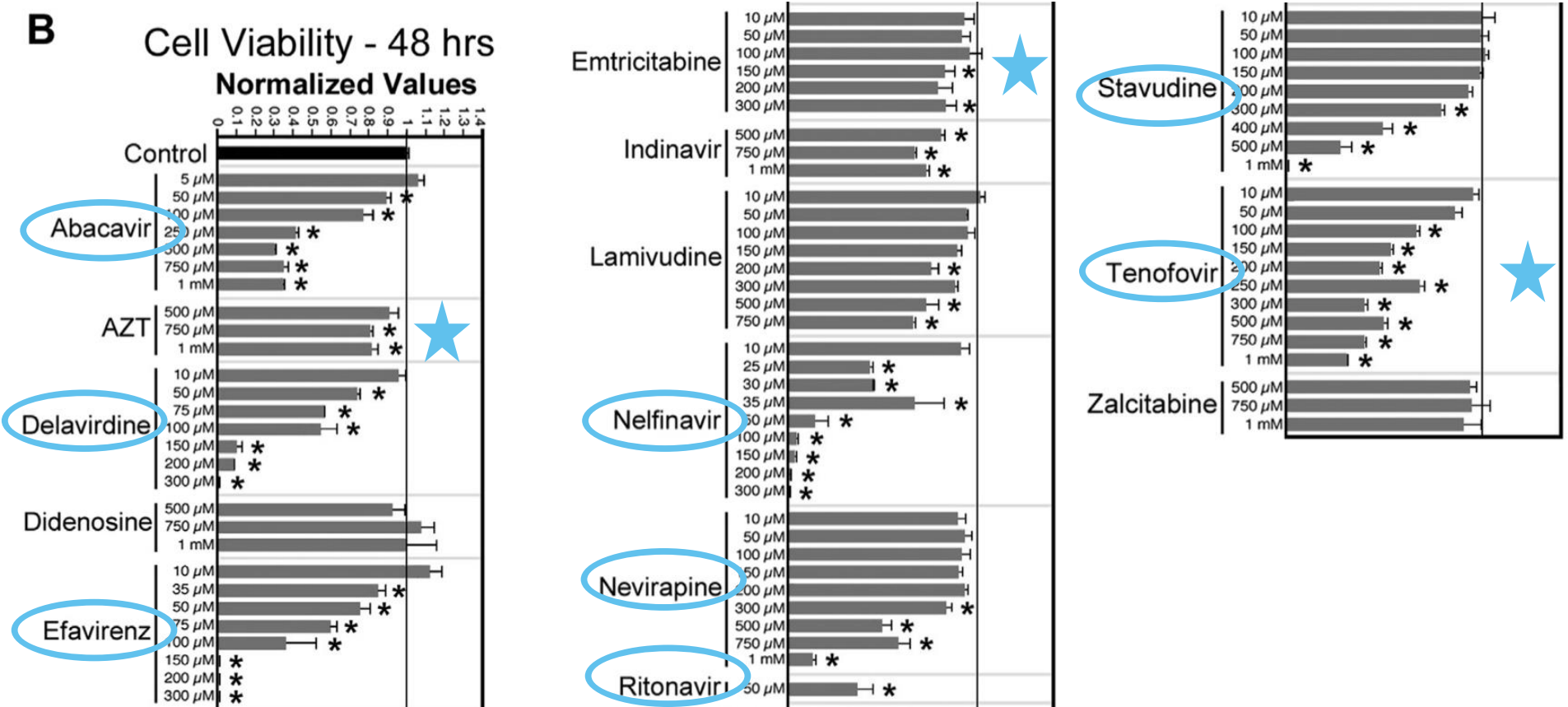
AUDITORY IMPACTS OF HIV IN ADULTS

1. Adults with HIV have greater incidence of HL that those without, as measured by both low and high frequency PTA (Torre et al., 2015)
   a. This is seen across countries, though the incidence varies from 9-26% (Khoza-Shangase, 2018; Matas et al., 2017; Millar et al., 2020; Van der Westhuizen et al., 2013)
   b. Other groups (Buckey et al., 2019; Torre et al., 2017) report no effects of HIV on auditory thresholds
2. People with HIV had longer ABR Wave I, III, and V latencies, prolonged ABR I-V interpeak latency, and a prolonged P300 latency (Matas et al., 2017)
   a. Those with AIDS had a decreased middle latency Pa amplitude when compared to HIV and non-HIV groups.
3. Mixed findings related to DPOAE
   a. Decreased amplitudes over time (Buckey et al., 2019)
   b. No difference (Torre et al., 2014)

AUDITORY IMPACTS OF HIV IN CHILDREN

1. Fasunla et al., 2019
    a. Relationship between HIV viral load and HL in teens
    b. 20% of teens with HIV had HL
2. Romero et al., 2017
    a. 86.67% of children exposed to HIV during pregnancy and breastfeeding present with abnormal results on the SSW and 60% abnormal on Simplified Auditory Processing Test

ART DRUG EFFECTS ON OHCs



WHEN YOU SEE A CLAIM THAT A COMMON DRUG OR VITAMIN "KILLS CANCER CELLS IN A PETRI DISH,"

KEEP IN MIND:

SO DOES A HANDGUN.

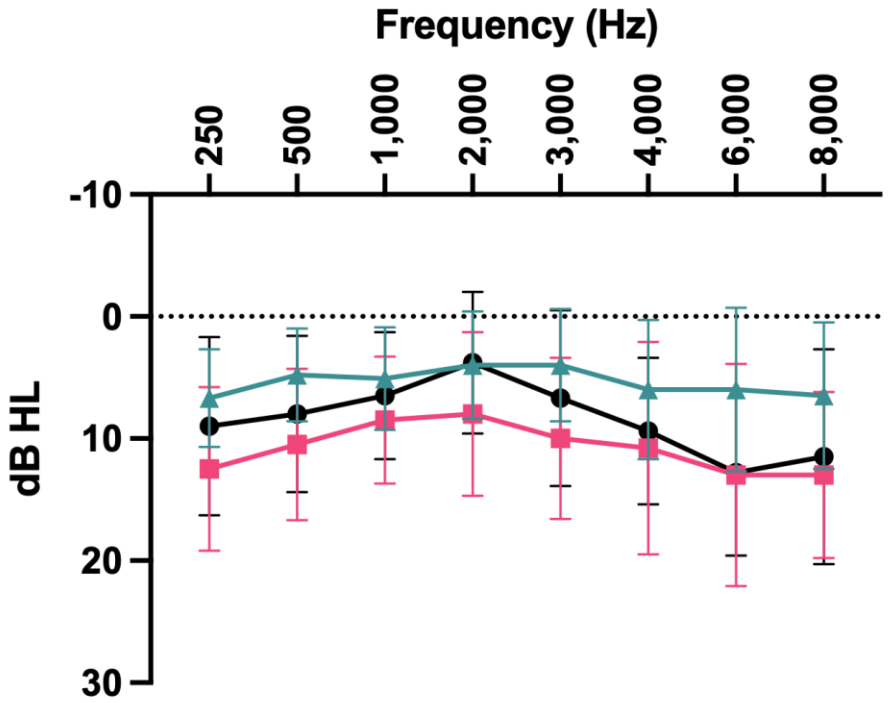
AUDITORY IMPACTS OF ART

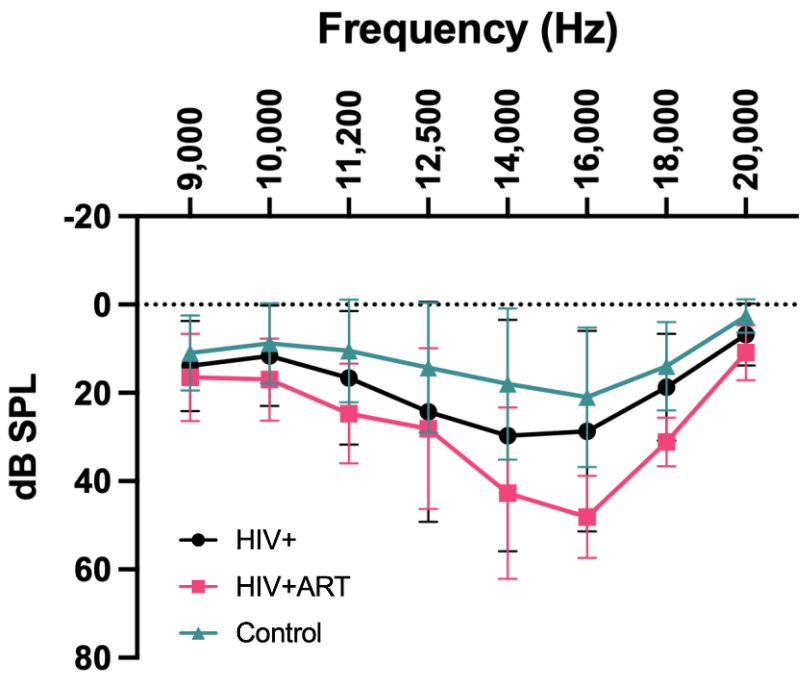




1. Marra et al., 1987
    a. 2.2 OR of HL in pts on ART
2. Bektas et al., 2008
    a. No differences in ABR or DPOAE threshold after 12 weeks of AZT+3TC exposure
3. Khoza-Shangase, 2018
    a. More self-reported hearing difficulty after 6 mos of ART
4. Minhas et al., 2018
    a. TDF+3TC+EFV caused no change in hearing over 6-month period in ART naïve pts.

AUDITORY IMPACTS OF ART

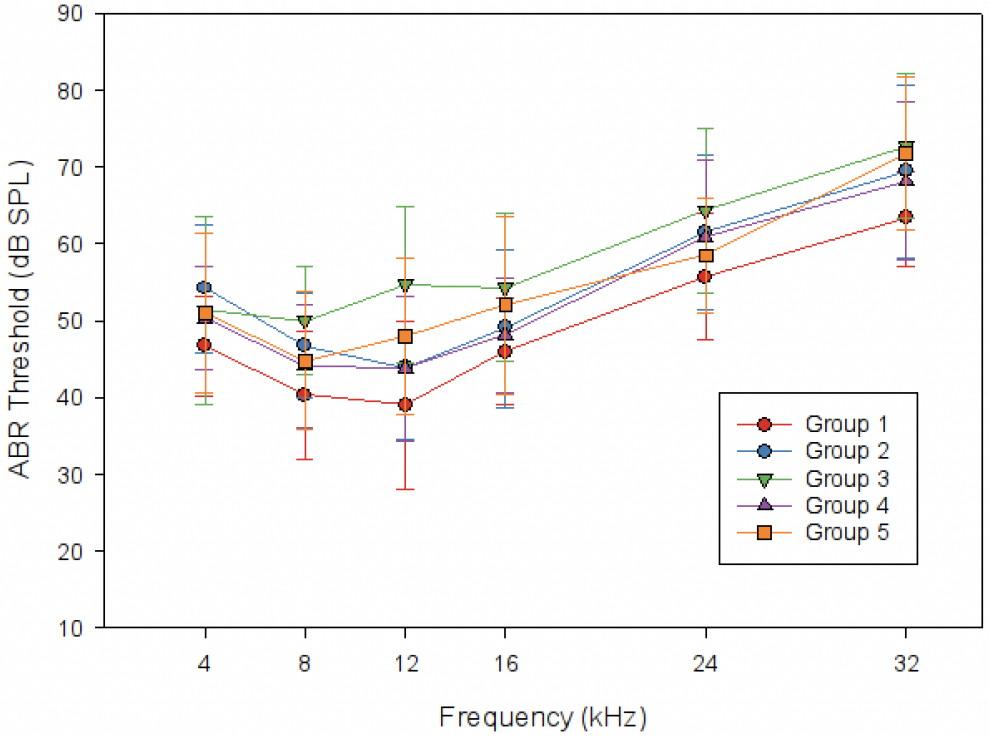


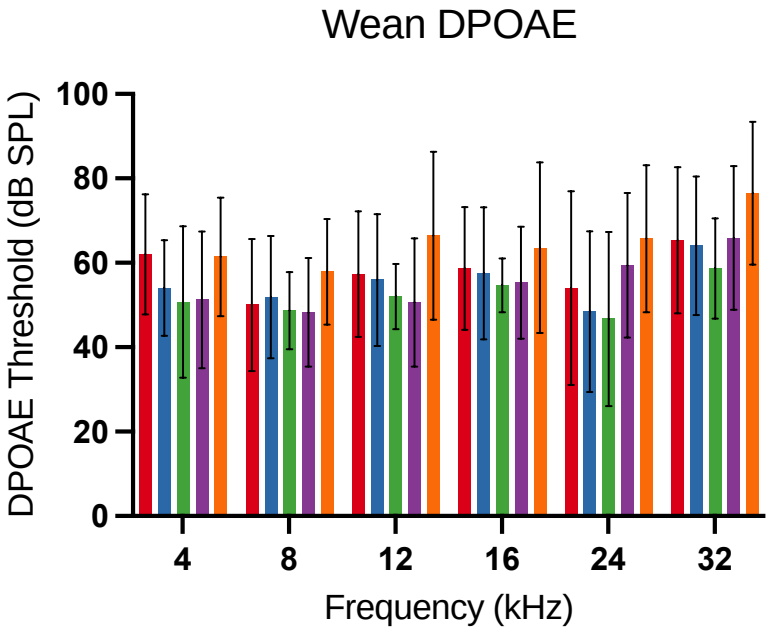


AUDITORY IMPACTS OF ART DURING PREGNANCY

1. Poblano et al., 2004
    a. Sig. delays in ABR I latency and I-III interpeak latency for PHEU exposed to AZT or AZT+3TC
2. Fasunla et al. 2014
    a. *in utero* exposure to HIV more likely to result in failed hearing screening and confirmed HL on ABR
    b. Sig. relationship between maternal viral load during pregnancy and HL
    c. Did not control for whether or not mothers were taking ART
3. Fasunla et al., 2018
    a. Children exposed to ART *in utero* and born HIV- have higher ABR thresholds at birth than unexposed
    b. Thresholds worsened over first 9 months of life
4. Torre et al., 2017
    a. No specific ART drug was related to an increased likelihood of hearing screening failure using **DPOAE, AABR, or both**
    b. Incredibly wide range of variability in auditory outcomes, even after adjusting for factors like birth weight, gestational age, and other drug exposures during pregnancy
    c. Lower OR for TDF exposure in 1st trimester than other ARTs

AUDITORY IMPACTS OF ART DURING PREGNANCY (PRE-CLINICAL)





AUDITORY IMPACTS OF ART DURING PREGNANCY

1. Torre et al., 2020
    a. PHEU young adults were more likely to have impaired WIN with otherwise normal cognition than HIV+ young adults
    b. Association b/w longer HAART use and impaired WIN in HIV+ young adults

SYNERGISTIC INTERACTIONS

1. PLWH are at greater risk for opportunistic infections like TB and MRSA (Cenizal et al., 2008) and certain forms of cancer that can be treated with platin-based chemotherapy (Quatan et al., 2005)
2. Multiple factors related to HIV and ARTs suggest that these patients may be at greater risk for HL from these therapies.
3. **Noise** + ART (Bektas et al., 2008)
   a. After 1hr 105 dB SPL noise, higher DPOAEs in ART group than control. Still no difference in ABR threshold
4. **Kanamycin** + ARTS (DeBacker et al., in press)
   a. Mice exposed to ARTs during pregnancy and breastfeeding had significantly greater aminoglycoside-induced HL than controls
   b. This difference was worst for animals exposed to cocktails containing tenofovir and efavirenz.
5. **Aminoglycosides** + ART (Harris et al., 2012)
   a. 70% of patients with HIV developed aminoglycoside-induced HL vs. 42% of HIV- patients






03

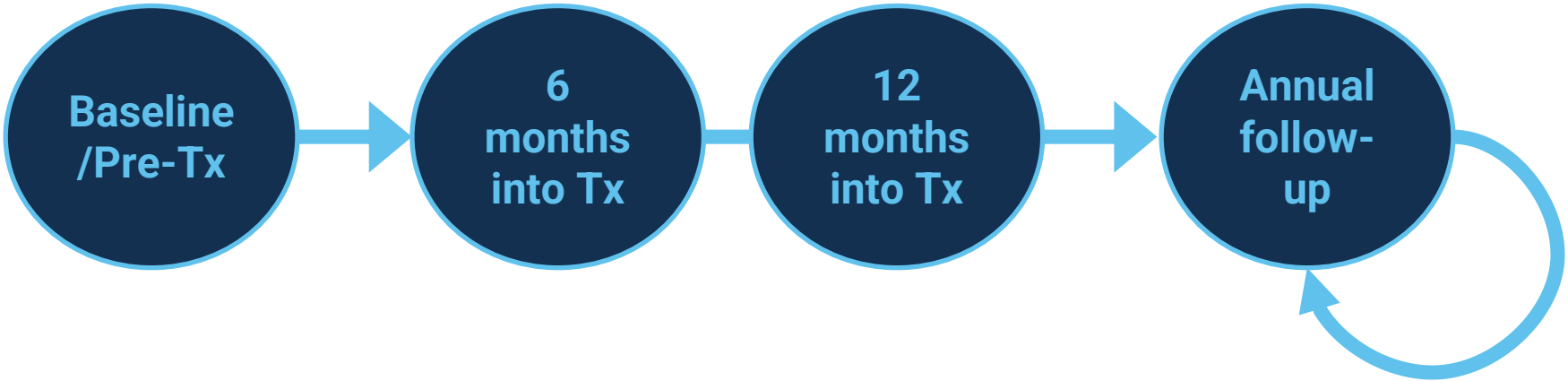
OTOTOXICITY MANAGEMENT

MONITORING HIV-RELATED OTOTOXICITY

HIGH FREQUENCIES

SPEECH IN NOISE

ABR



CURRENT OTOTOXICITY MANAGEMENT GUIDELINES

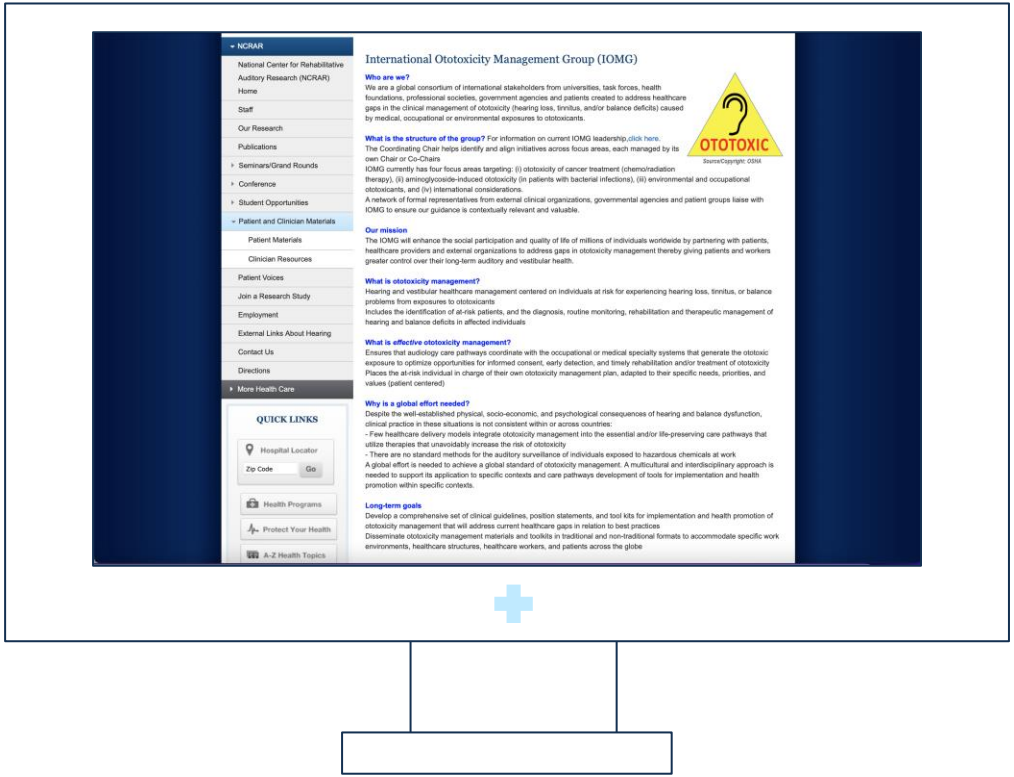
- ASHA, 1993
- AAA, 2013
- HPCSA, 2018

INTERNATIONAL OTOTOXICITY MANAGEMENT GROUP (IOMG)

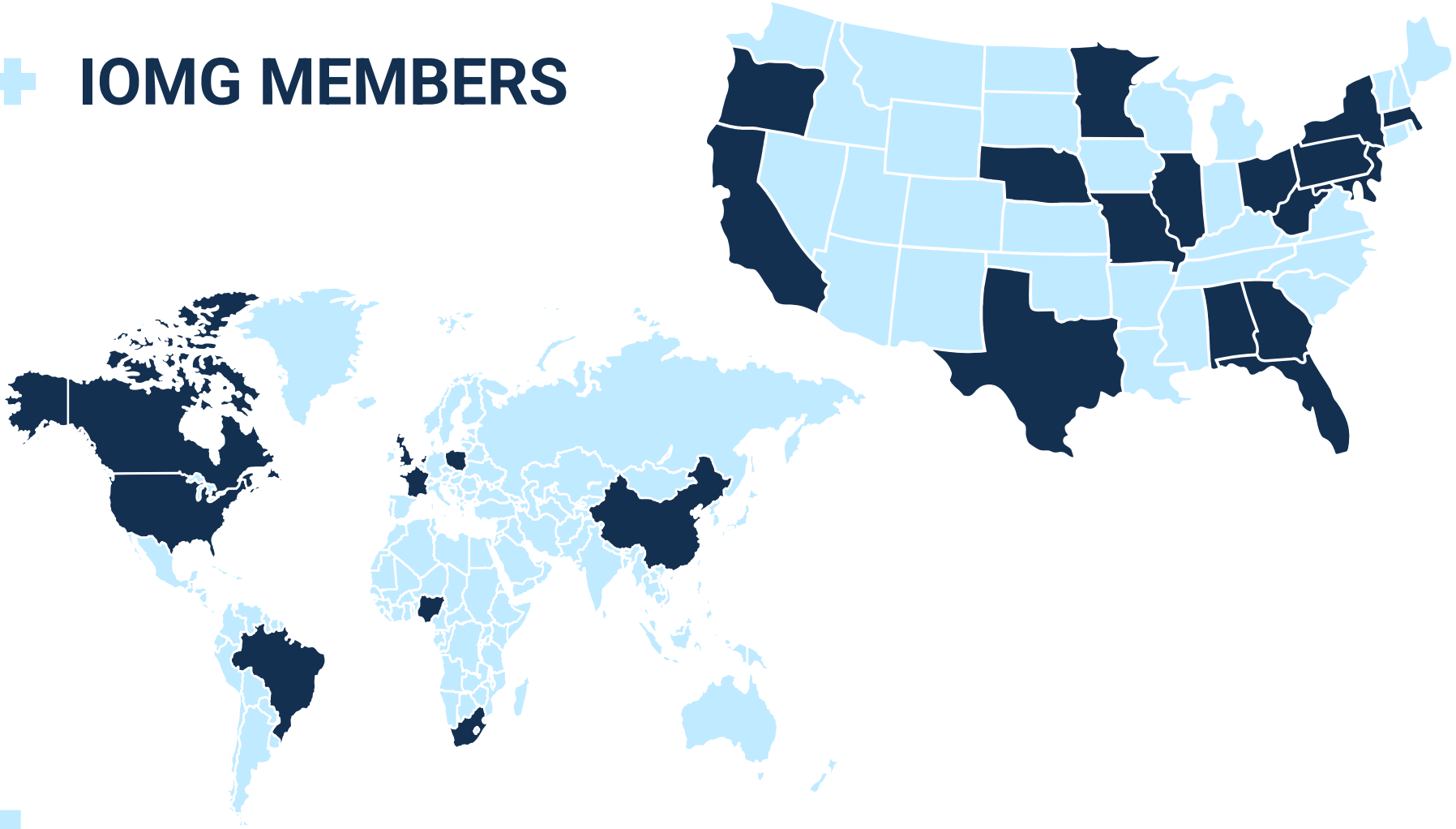
Join us!

Learn more and indicate interest at:

https://go.usa.gov/xzX2g



IOMG MEMBERS



QUESTIONS?

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