The Importance of Pathogen Genomics to US Public Health

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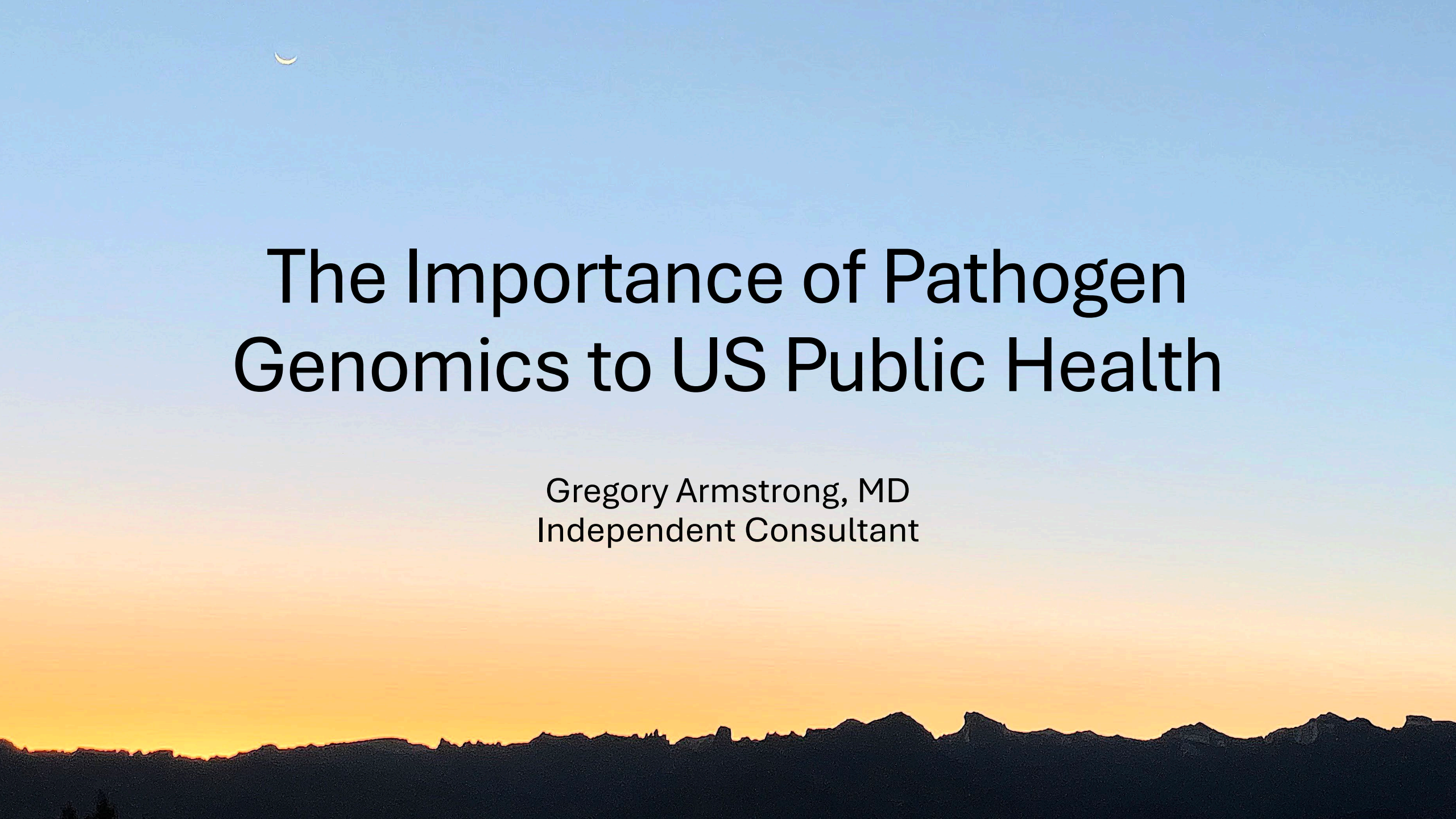
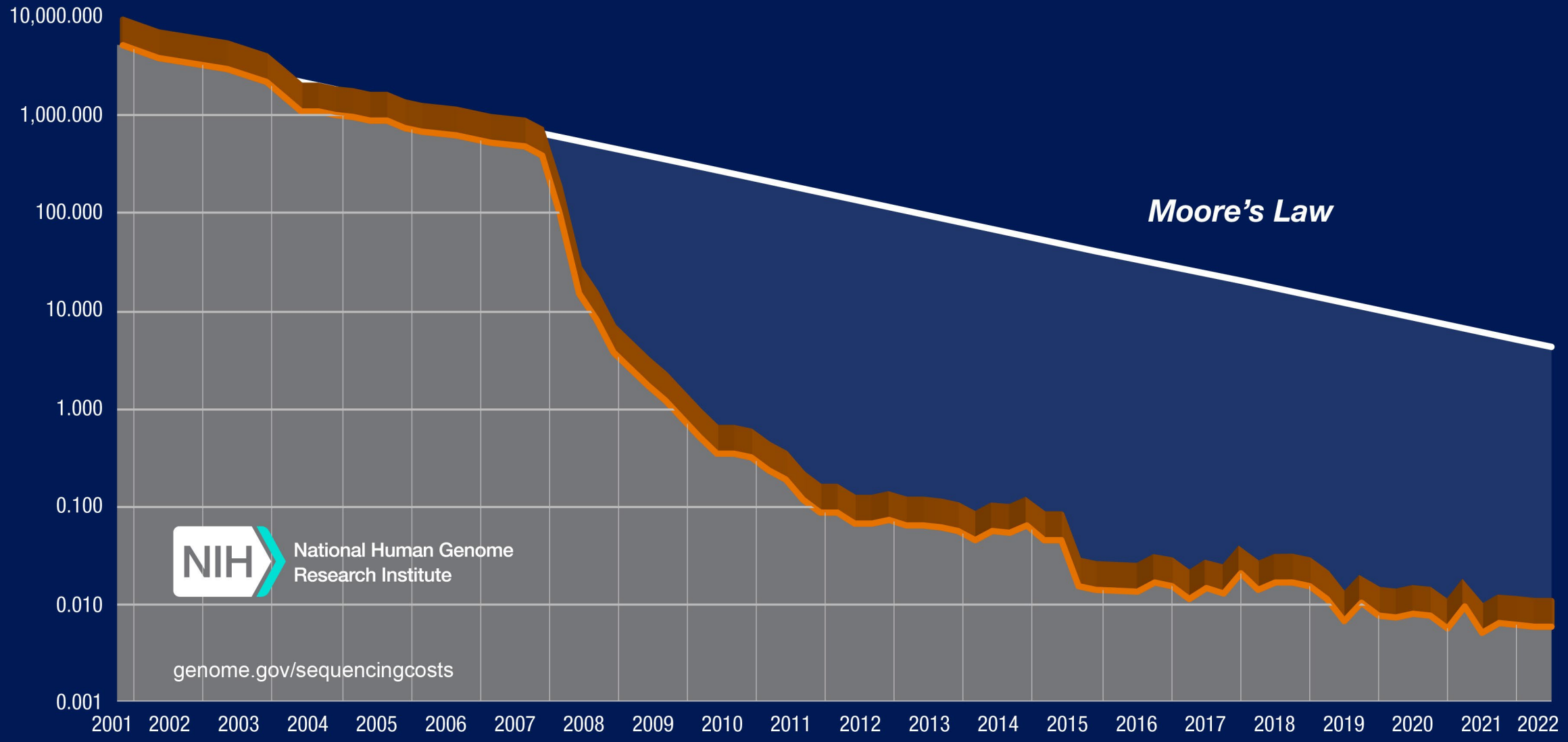


Disclosures

- Previously employed by US CDC, including as Director of the Advanced Molecular Detection Program
- Non-profit consulting (ongoing):
  - Task Force for Global Health (with funding from BMGF)
  - Theiagen Global Health Initiative (volunteer board member)
- Private sector consulting (past):
  - Merck
  - ClearLabs
  - Ginkgo Bioworks

Cost per Raw Megabase of DNA Sequence



Implications of High-Throughput Sequencing for Pathogen Genomics

- Research settings
  - Earliest uses
  - Transformed the understanding of
    - Microbial evolution
    - Epidemiology (“genomic epidemiology”)
- Public health settings
  - Early 2010’s: first uses in public health
  - Provides actionable information
    - Directly
    - Indirectly (e.g., through better “situational awareness”)
- Clinical settings

  (now in early phases)

Why is This Useful in Public Health?

(examples to follow)

- High-resolution sub-typing of pathogens
- Finding outbreaks
- Investigating outbreaks
- Inferring phenotype (including AMR)
- Informing development of vaccines, therapeutics and diagnostics
- Providing a more granular picture of epidemiology

High-Resolution Subtyping of Pathogens

- Legacy subtyping systems
  - PFGE (pulsed-field gel electrophoresis)
  - MLST (multi-locus sequence typing)
  - RFLP (restriction fragment length polymorphisms)
  - Spoligotyping, MIRU-VNTR
  - MEE (multi-locus enzyme electrophoresis)
  - Others
- Genomics provides a single technology to replace these
- Compared with these, whole-genome sequencing:
  - Provides (usually much) higher resolution
  - May be more expensive
  - Usually takes longer

Outbreak Detection

- Bacterial foodborne illness
  - PulseNet (clinical cases, run by CDC)
  - GenomeTrakr (food, environmental samples, run by FDA)
  - USDA
  - NCBI/Pathogens
- COVID-19; example: outbreak linked to a gymnastics events
- Tuberculosis
- Many other examples

Outbreak Investigation

- Used routinely in outbreaks
- Utility
  - Determining which cases are part of the outbreak
  - Linking to the source of the outbreak (e.g., to the food source in foodborne outbreaks, or to a cooling tower in a *Legionella* outbreak)
  - Elucidating transmission pathways (esp. with rapidly evolving viruses)
  - Providing evidence for or against transmission in healthcare settings (or other closed settings)

Determining Phenotype, Particularly AMR

- *Mycobacterium tuberculosis*
  - Now in use routinely in some locations for first-line drug susceptibility testing
  - Second-line drug susceptibility determination is more variable
- Malaria
  - Antimalarial resistance
  - Detectability by rapid tests (i.e., HRP-2 deletions)
- HIV
  - Antiviral resistance

Development of Vaccines, Therapeutics, and Diagnostics

- SARS-CoV-2
  - Vaccines
  - Monoclonal antibodies
  - Diagnostics
- Influenza—“sequence-first” approach
- Pertussis vaccine

Providing a More Granular Understanding of the Epidemiology—Better “Situational Awareness”

- SARS-CoV-2
  - Variant emergence
  - Vaccine breakthrough
- Hepatitis A

Some Other Considerations (part 1)

- Pathogens and Sequencing techniques are highly varied
  - Viruses, bacteria, eukaryotic pathogens
  - Whole-genome vs. targeted sequencing
- Cost issues
  - Sample collection
  - Sequencing (costs may be decreasing again; automation is improving)
  - Bioinformatics
  - Obtaining “metadata” (epidemiological and clinical data)
  - Data integration, analysis, visualization

Some Other Considerations (part 2)

- Integrating genomic and epidemiologic data
- Workforce development
  - Microbiologists
  - Bioinformaticians
  - Epidemiologists

Summary

- Pathogen genomics has implications across the spectrum of infectious diseases of public health importance
- The field is still young and rapidly evolving