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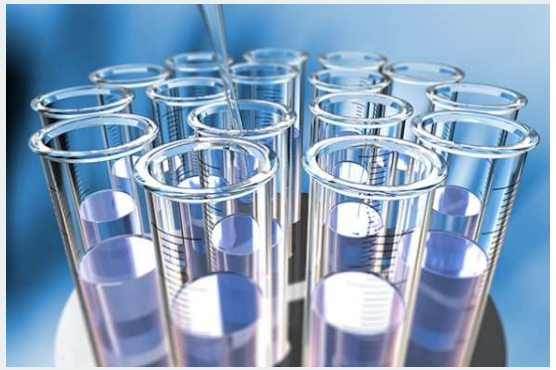

Application Market Sizing

Short summary report

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Presented to

Oxford NANOPORE Technologies

March 10, 2021, summarized
August 2021

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Included Market Segments

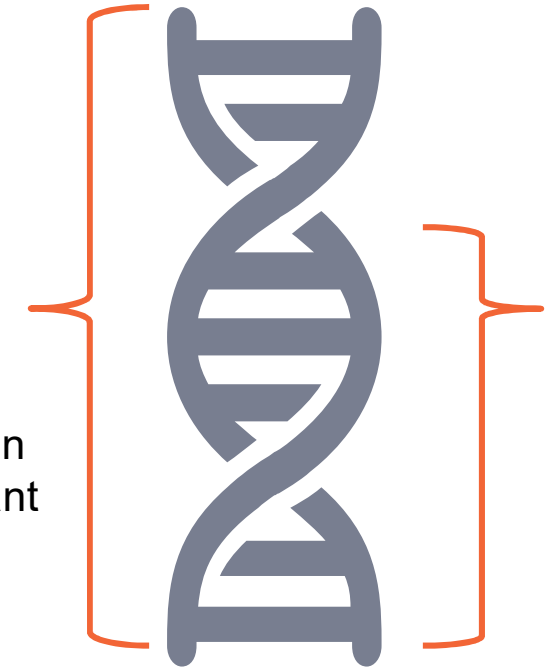
Market Segments	
Clinical Infectious Disease	• All conditions with potential molecular test use segmented by metagenomic and targeted panel sizes
Clinical Immunoprofiling	• Includes HLA typing for transplant, other existing clinical HLA typing applications, and potential applications in immune status profiling (e.g., DNA repertoire profiling, RNA signatures).
Clinical Oncology	• All molecular test areas today and potentially in the future with segmentation by use case (e.g. therapy selection) and sample type (e.g., liquid biopsy)
Microbiome	• Includes biomedical research, select applied, and consumer applications

Definition of PTAM and TAM

Potential Total Available Market (PTAM)

100%

Use of Molecular Methods in **Current and Future** Relevant Use Cases/Groups



Current Total Available Market (TAM)

Actual

Use of Molecular Methods in **Current** Relevant Use Cases/Groups

- Molecular is defined as any molecular method (nucleic acid measurement) rather than what is currently done by a sequencing technology. It is assumed that the cost position and speed of ONT technologies can replace or add to more than just sequencing based approaches.
- Revenues reflect only the sale of ***diagnostic testing products;*** revenue for testing services is not included.

Note: Potential Total Addressable Market = PTAM; Total Addressable Market = TAM; Serviceable Available Market = SAM; Serviceable Obtainable Market = SOM..

PTAM and TAM Definitions: Product versus Service Revenues

The total and potential addressable market output will include product revenues from sale of kits and reagents but not the services associated with performing tests.

Products

Revenues generated from the sale of ***diagnostic testing products***, including:

- Approved Kits and Reagents
- Non-approved reagents and platforms to enable performing LDTs
- Does not include services revenue

To be Included in PTAM and TAM Estimates

Services

Revenues generated from the ***services associated with performing testing***

- Includes basic testing services for non-proprietary tests and specialty testing services for novel, proprietary tests
- Product revenue is embedded in the service revenue along with labor, ancillaries and lab profit

Note: LDT = laboratory developed tests.
Source: Health Advances analysis.

Diagnostic Continuum Definitions

To estimate volume and revenue TAMs, clinical applications of molecular testing will take into consideration all types of tests.

	Risk Assessment	Screening	Diagnosis	Staging and Prognosis	Therapy Selection	Monitoring
Description	• Assessment of a healthy person's risk of developing a particular condition	• Proactive testing of asymptomatic patients to detect disease early in disease progression	• Rule-out and/or confirmation of presence of a disease in symptomatic patients or patients testing positive on a screening test	• Assessment of disease severity/risk of progression • Likelihood of positive/negative outcome	• Predict efficacy or safety response to specific treatments • Determine if patient is likely to be a responder or a non-responder	• Assessment of recurrence risk • Detection of a recurrence • Monitoring for treatment efficacy or safety

Source: Health Advances analysis.

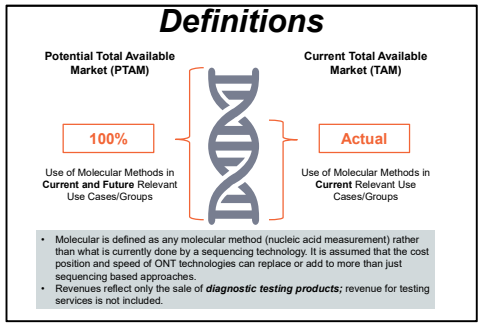
Summary of TAM and PTAM Opportunities

Oxford Nanopore has the potential to unlock significant revenue opportunities across a broad array of clinical and non-clinical markets.

Timeline to Market Disruption

Longer-Term

Nearer-Term



Clinical Infectious Disease

PTAM ~$65B

TAM ~$6B

- Accessible hypothesis-free testing unlocks infectious disease market

Immunoprofiling

PTAM ~$76B

TAM ~$0.3B

- Immune response profiling represents visionary application with broad applicability

Microbiome Testing

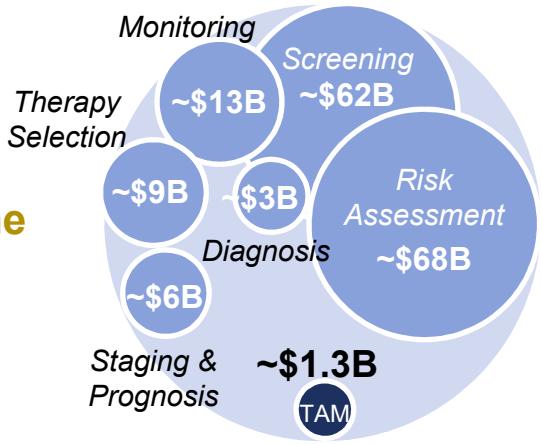
PTAM ~$26B

<$0.1B TAM

- While academia drives current market, strongest potential growth lies in applied markets, such as dairy and fermentation

Clinical Oncology

PTAM ~$158B



- Current molecular market driven by therapy selection
- Significant revenue opportunity in risk assessment and screening

Note: Clinical infectious disease includes targeted molecular diagnostics and metagenomics testing. Immunoprofiling includes HLA typing for transplant, HLA typing for non-transplants applications, and immune response profiling. Microbiome testing includes human-associated microbiome test in biomedical research and direct-to-consumer testing as well as applied markets such as soil, dairy, and fermentation. Clinical oncology includes testing across the diagnostic continuum, from risk assessment to therapy selection and monitoring across all solid tumor and hematological indications, including liquid biopsy and solid tissue sample types. Microbiome reflects global market.

Source: Health Advances model and analysis.

Details Market Definitions

Metagenomics: PTAM Use Cases

The metagenomics PTAM includes all infectious disease applications that have any theoretical need for multiple pathogen identification or resistance profiling.

Included in Metagenomics PTAM

Regardless of the current application of hypothesis-free testing, all infectious disease indications with any potential need for differential pathogen identification or resistance profiling are considered candidates for metagenomics

- Urinary Tract Infections
- Lower RTIs
- Asymptomatic STI screening
- Upper RTIs

- Gastrointestinal infections
- Wound infections
- Onychomycosis
- Symptomatic STIs

- Vaginitis
- Sepsis
- Fever of Unknown Origin
- Transplant patient monitoring

- Tick-borne diseases
- Prosthetic joint infections
- CNS Infections
- Endocarditis
- Osteomyelitis

Notes: STI = sexually transmitted infection, RTI = respiratory tract infection, CNS = central nervous system.
Source: Health Advances previous work and analysis, AACC, GenomeWeb, Messacar 2017 J Clin Microbiol, Dekker 2018 J Clin Microbiol.

Targeted MDx PTAM Use Cases

In order to ensure a clinical infectious disease testing market that is MECE, the targeted MDx PTAM includes only the remaining applications of molecular testing.

Included in Targeted Molecular Testing PTAM

For the metagenomics and targeted molecular testing markets to be **mutually exclusive and collectively exhaustive**, the targeted MDx PTAM includes ***only*** applications for which metagenomics would never be applicable (one pathogen at a time)

- Human papilloma virus (HPV) screening and typing
- Viral load monitoring for patients receiving antiviral therapy for HIV, HBV, and HCV
- MRSA screening for ICU patients
- Mycobacteria/Tuberculosis diagnosis
- HIV drug resistance testing

Note: Targeted test list not fully comprehensive but will focus on most significant markets with scale up factors for more esoteric testing. HBV = hepatitis B virus, HCV= hepatitis C virus, MRSA = methicillin-resistant staphylococcus aureus.
Source: Health Advances analysis, Kalorama, LabTestsOnline, competitor test menus, Arney 2010 Laboratory Medicine, Choi 2007 J Epidemiol Community Health, ASCCP guidelines.

Immunoprofiling Market Definition

Immunoprofiling includes HLA typing for transplant and non-transplant applications, as well as more visionary applications in immune response profiling.

Immunoprofiling

HLA Typing

1 HLA for Transplant

- Sequencing of HLA alleles to establish cross-matches between donors and transplant patients
- Performed for both solid organ transplantation (SOT) and hematopoietic stem cell transplantation (HSCT) to prevent post-transplant complications such as graft-versus-host disease

2 HLA for Non-Transplant Applications

- HLA typing applied to screening, diagnosis, prognosis, and treatment selection for disease
- Current applications primarily for confirmatory diagnosis of autoimmune disorders
- Potential applications in autoimmune screening, infectious disease prognosis, and therapy selection

3 Immune Response Profiling

- Sequencing of immune and immune-response markers (T- and B-cell receptor repertoire or diversity, clonotyping, immune system transcriptome profile) to generate a response profile that informs disease risk, diagnosis, prognosis, and treatment selection
- Includes measurement of nucleic acid-based markers (RNA/mRNA, DNA)
- Most current use is in the research setting; research applications are not included
- Potential futures applications for the PTAM assumed to include in host response for infection detection and identification, oncology, inflammatory, and autoimmune disorders

Source: Health Advances analysis.

HLA for Non-Transplant Applications: Overview

Clinical Immuno-Profiling

HLA typing can be used across the diagnostic continuum to determine risk of developing a disease, confirm diagnosis, and predict severity or treatment response.

	Risk Assessment	Screening	Diagnosis	Staging and Prognosis	Therapy Selection	Monitoring
Use Today (TAM)						
Future Potential (PTAM)						
Application of HLA Typing	• The presence of specific HLA alleles can suggest that an individual is likely to be pre-disposed to developing a particular condition	• Limited use	• Although HLA typing alone has not been shown to be sufficient for diagnosis, it can provide confirmation when conducted with other tests	• HLA typing can indicate disease severity and risk of progression to a negative outcome	• The presence of specific HLA alleles can help identify responders, non-responders, or those that may be hypersensitive to a treatment	• Limited use

Source: Health Advances analysis.

HLA for Non-Transplant TAM and PTAM Applications

Clinical Immuno-Profiling

Current applications of HLA typing in disease association are included in the TAM estimate. Future applications with existing clinical evidence are factored into the PTAM.

	Screening	Diagnosis	Staging and Prognosis	Therapy Selection
Autoimmune	• **Celiac disease** • Scleroderma	• **Ankylosing spondylitis** • **RA/Juvenile RA** • **Acute anterior uveitis** • **Birdshot chorio-retinopathy** • **Bechet's disease** • Lupus • Psoriasis • Narcolepsy	• Psoriatic arthritis	
Oncology				
Infectious Disease			• Severity of HBV/HCV • Severity of Malaria and Dengue infection • Severity of HIV/AIDS infection	• **Abacavir hypersensitivity screening (HIV/AIDS)**
Other				• **Carbamazepine hypersensitivity screening (epilepsy)** • **Allopurinol hypersensitivity screening (gout)**

PTAM Only | **PTAM and TAM**

Source: Health Advances interviews and analysis, Quest Diagnostics, LabCorp, Gough 2019 Curr Genomics, Cruz-Tapias 2013, Fiorillo 2017 Front in Imm, Orenbach 2020, Promocell, Kaneko 2011 BMC Cancer, McGranahan 2017 Cell, Park 2019 JPTM, Chaudhari 2000 PNAS, Fung 2015 Can Control, Cardoza 2014 Blackwell 2009 Clin Micro Rev.

Immune Response Profiling: Overview

Analyses of immune cell diversity and clonality, and immune cell function, are the primary future use cases for molecular methods within immune response profiling.

	Immunophenotyping			Immunosequencing
	Assess Immune Cell Function/ Response	**Measure Number of Immune Cells**	**Measure Immune Cell Protein Secretion**	**Analyze Immune Cell Diversity**
Description	• Assessment of population or single T cell for the ability to produce/secrete cytokines, proliferate, or activate/suppress/ kill another cell with or without an external stimuli	• Measurement of the number of T or B cells using surface markers to assess disease onset/risk in a healthy patient or to determine disease severity in a diseased patient	• Analysis of systemic protein secretion (chemokine/cytokine/etc.) by immune cells to infer patient status	• Analysis of T or B cell/cell-receptor repertoire by genomic or transcriptomic sequencing • Measurement and tracking of immune cell diversity and clonality • Measures RNA/mRNA/DNA
Relevant Technologies	• ELISA, Multiplex Protein Assay, Flow Cytometry, Mass Cytometry, EliSPOT, RNASeq	Flow Cytometry, Mass Cytometry, IHC	ELISA, Multiplex Protein Assay, WB, IHF/IHC,	NGS, RNAseq, Single-Cell RNASeq
Current Clinical Use				
Current Use of Molecular Methods				

Source: Health Advances past work and analysis, Robins 2013 Curr Opi in Immu, Watkins 2021, Wolf 2016 Trends in Immu, Emerson 2015 BioRx.

Immune Response Profiling: PTAM Applications

Clinical Immuno-Profiling

The PTAM includes all potential applications of immune cell diversity and function analysis that inform diagnosis, prognosis, therapy selection, and monitoring.

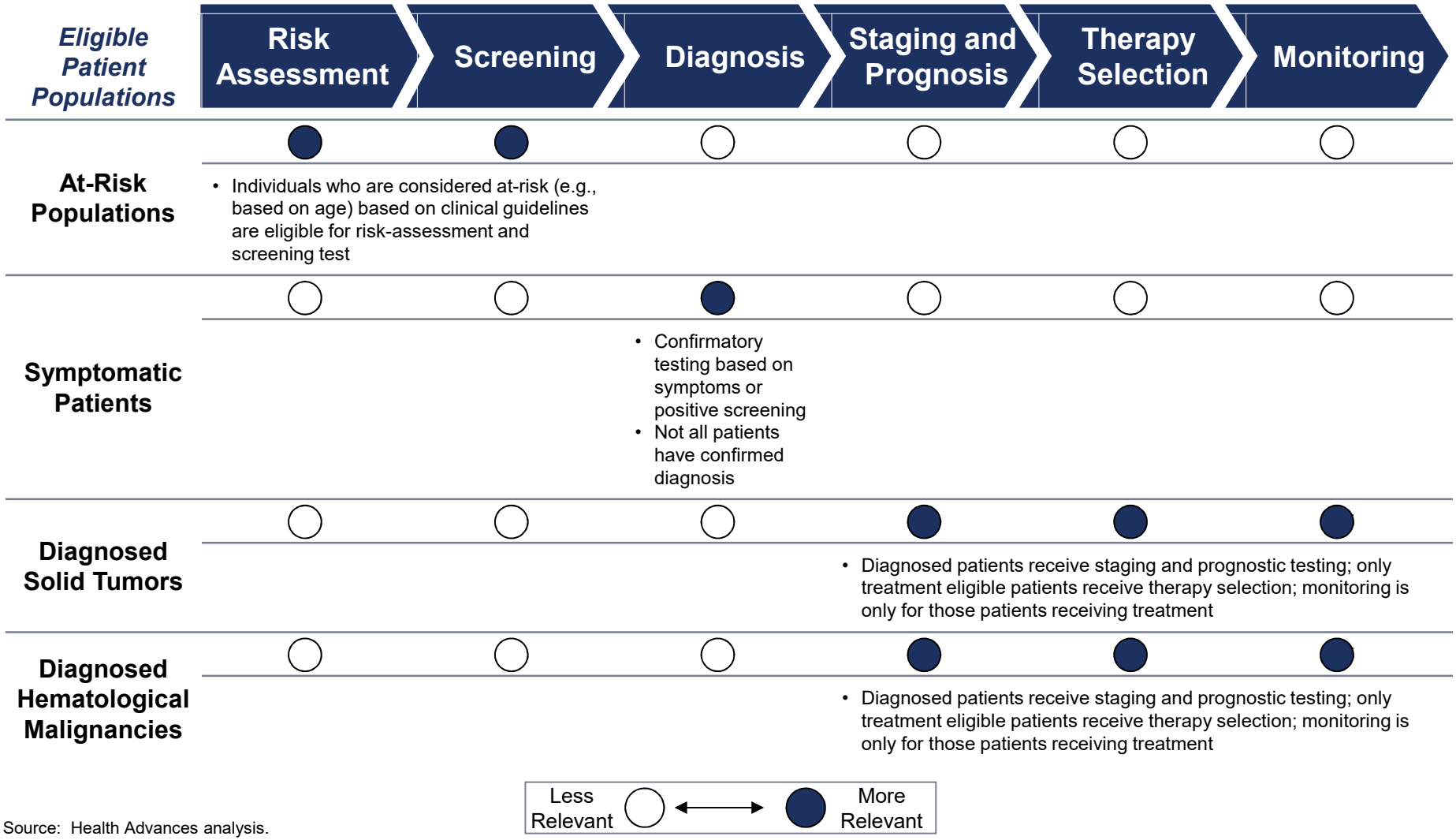
	Diagnosis	Staging and Prognosis	Therapy Selection	Monitoring
Infectious Disease	• Host Response – Acute infection (Sepsis) – Bacterial vs. viral vs. no infection – Lyme disease	• Prediction of infection severity		
Oncology			• Prediction of immunotherapy response	• MRD monitoring in solid and hematological cancers • Durability of immunotherapy response
Autoimmune Disease	• Rheumatoid arthritis • Psoriasis • SLE • Multiple sclerosis		• TNF-a therapy response	• TNF-a therapy response monitoring
Post-Transplant Monitoring				• Post-transplant infection monitoring

Source: Health Advances analysis, company websites, Pruessmann 2020 Nat Cancer, Demaree 2020 JNCCN, Harden 2015 F1000Res, Allez 2019 Gut, Kelkka 2020 JCI, Liu 2019 Ann of Rheum Diseases, Loussius 2016 Ann Clin Trans Neuro, Jacobsen 2017 Curr Diab Rep, Strand 2020 Front in Imm.

Clinical oncology: Eligible Patient Populations

Clinical Oncology

A wide array of patient populations are or could be eligible for cancer-related molecular testing across the continuum of clinical applications.

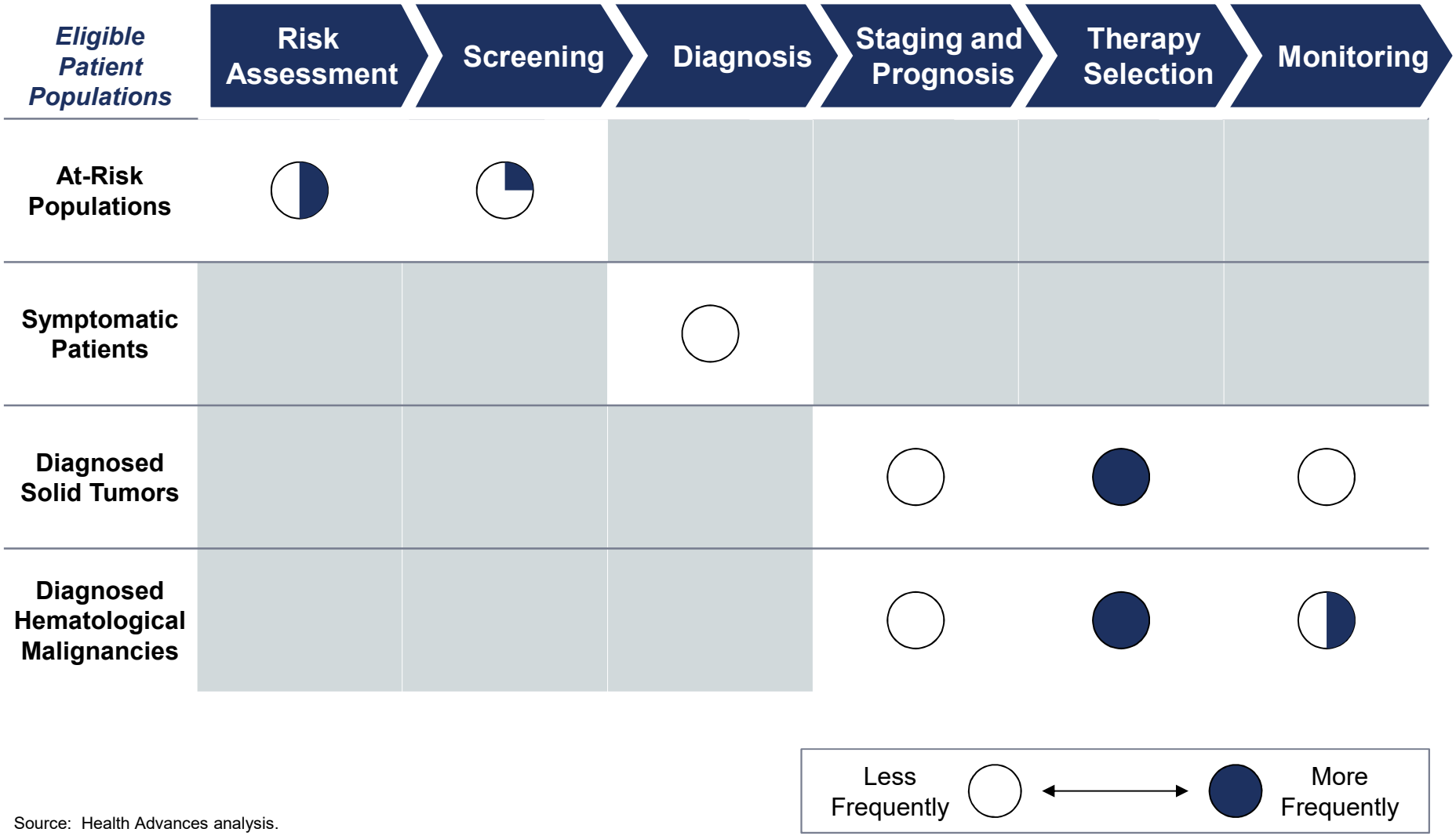


Source: Health Advances analysis.

Clinical oncology: Relative Use of Molecular Testing Today

Clinical Oncology

Molecular-based methods are used frequently today across a wide array of test purposes and patient populations. The TAM captures the total volume for each clinical application.



Source: Health Advances analysis.

Microbiome Testing Definition

Microbiome

Analyze genomes of existing organisms in the sample

Bacteria, fungi, protozoa, viruses, etc.

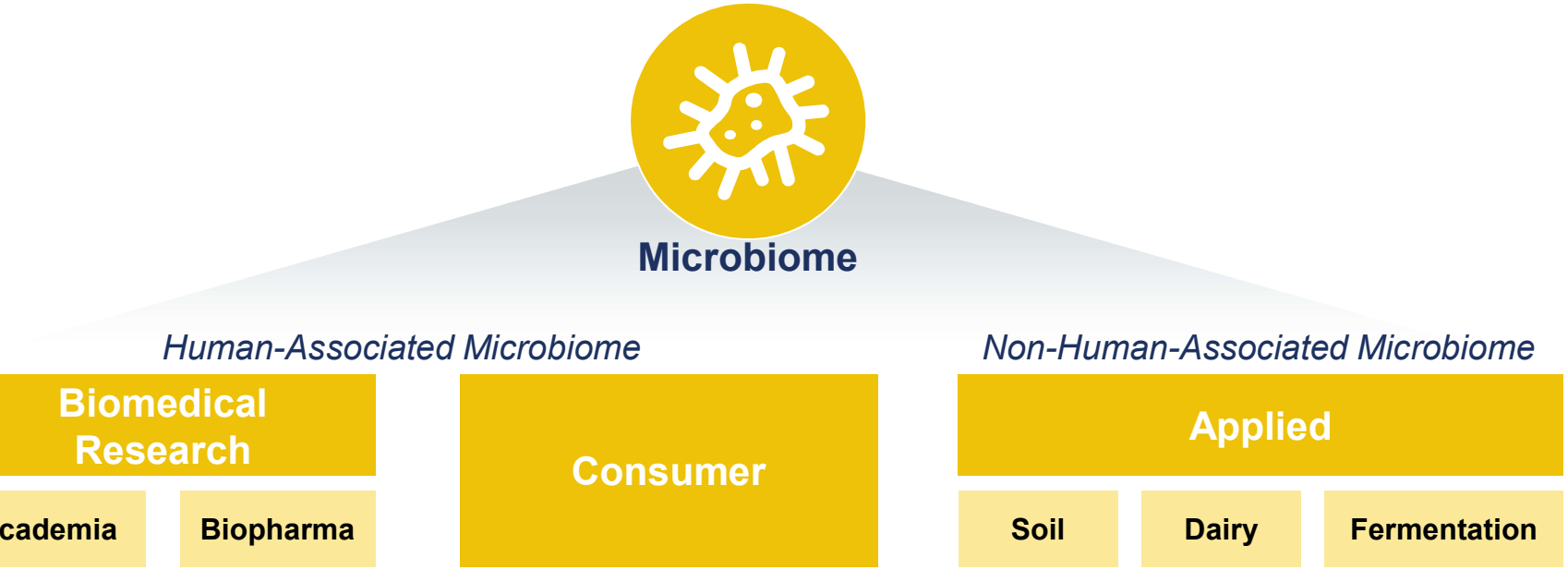
Testing to ***explore the ecosystem*** of ***organisms*** and ***shift in populations*** based on external factors at a given point in time.

Overall organism population analysis that excludes testing for presence or absence of individual microbes

Source: Health Advances analysis.

Microbiome Market Definition

The microbiome market is segmented into three distinct areas, each with different end users and potential applications of microbiome testing.



- Research to detect, identify, and characterize microorganisms and their function as well as to develop microbiome-based biomarkers and diagnostic and therapeutic interventions
- Health and wellness direct-to-consumer testing to provide recommendations regarding nutritional and dietary health, personalized skin care, and other wellness categories
- Identification of shifts in microbiome for improved farming, dairy production, and beer and wine fermentation process improvement

Source: Health Advances analysis.

Example Methodologies and Assumptions

PTAM Methodology: infectious disease (Metagenomics)

Clinical Infectious Disease

The metagenomics PTAM utilized a bottoms-up approach based on epidemiology, incorporating testing frequency and per test pricing, across the US, EU, and China.

Methodology	Description	Sources
Incidence/Prevalence of Relevant Infectious Diseases	• Number of diagnosed patients or size of screening populations by indication determined by epidemiological data	• Clinical literature • Epidemiology databases • National/government organizations (e.g., CDC)
✖ Frequency of Testing by Indication	• Number of tests per patient • Varies by clinical purpose (e.g., monitoring vs. diagnosis)	• Clinical testing guidelines by indication
✖ Testing Negativity Rate by Indication	• Scale up, where relevant, from diagnosed patients to total patients with suspected infection or receiving testing	• Clinical literature • Past Health Advances analysis
= **PTAM (Test Volume)**		
✖ Price per Test	• Assumes a premium on current reimbursement of PCR, constrained by current per test revenue of syndromic panels metagenomics	• Clinical lab fee schedules • Competitor investor presentations, SEC filings, analyst reports
= **PTAM (Revenue)**		

Note: EU refers to 27EU and UK.
Source: Health Advances analysis.

Key PTAM Assumptions: Infectious disease (Metagenomics)

Clinical Infectious Disease

The metagenomics PTAM was built from specific key assumptions across 17 different indications, each with varying approaches unique to the use case.

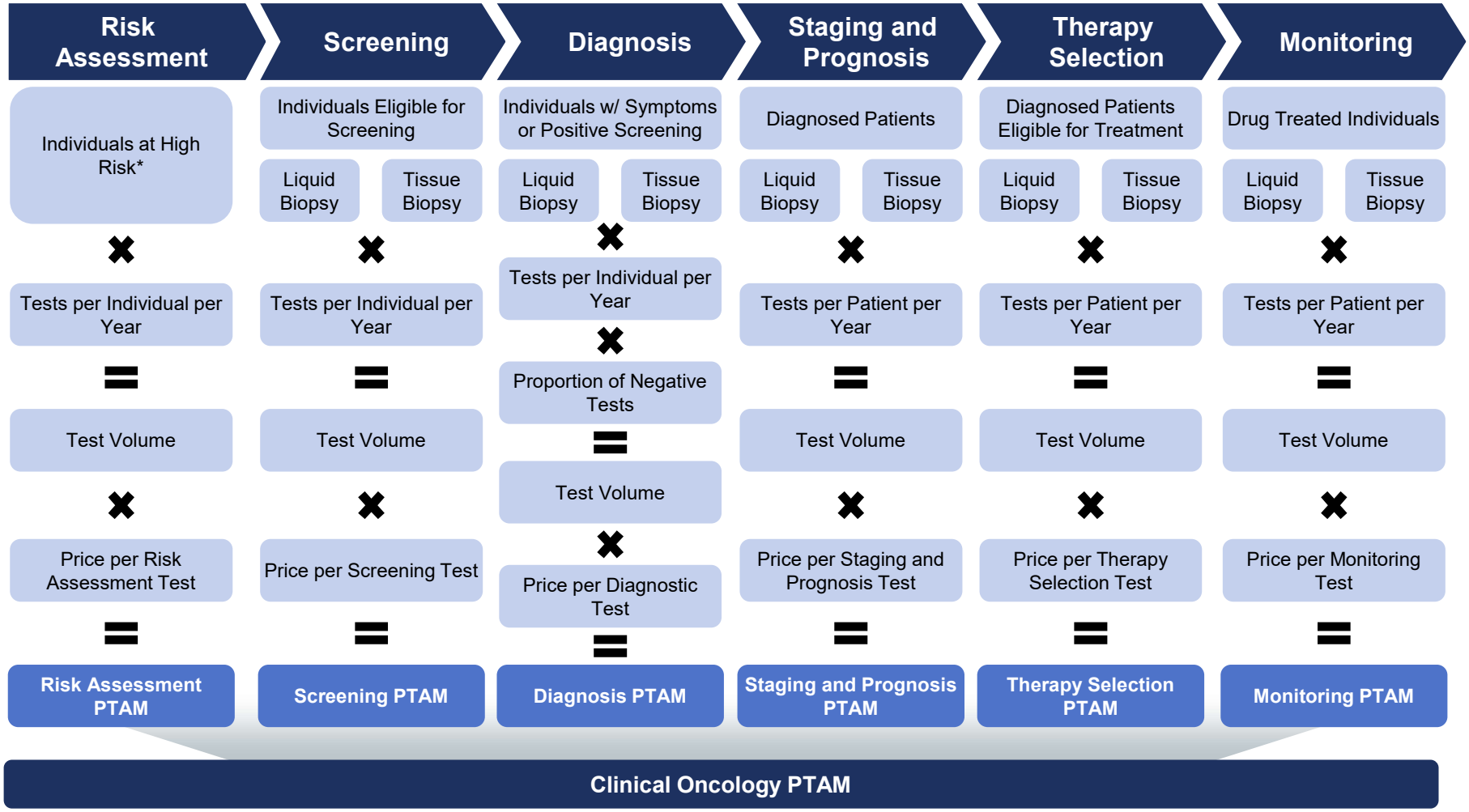
Methodology	Key Assumptions
Incidence/Prevalence of Relevant Infectious Diseases	• Primary method: Reported incidence values of diagnosed disease • Incidence rates scaled to geographic populations of: US (330MM), EU(515MM), and China (1.4B)
✖	
Frequency of Testing by Indication	• Diagnostic/pathogen ID = one test per suspected infection • Screening = multiple tests per patient based on guidelines
✖	
Testing Negativity Rate by Indication	• Applies only to diagnostic applications, not used for screening • Diagnostic negativity rates vary widely by indication and sample type (e.g., bone biopsies = 5%, stool = 75%) • Alternative method compared CPT code volumes to diagnosed incidence
=	
PTAM (Test Volume)	
✖	
Price per Test	• Two pricing options are provided to illustrate the dynamic market opportunity between increasing utilization and capturing the value the test holds US: $65 / $115 Europe: $35 / $65 China: $35 / $65
=	
PTAM (Revenue)	

Note: Europe refers to 27EU+UK.
Source: Health Advances analysis.

PTAM Methodology: clinical oncology

Clinical Oncology

The PTAM reflects a bottom-up epidemiology-based approach to estimate total test volumes multiplied by expected test price per application.



Note: Pricing for each application will vary based on anticipated volume and frequency of test, as well as if it is paired with liquid or solid tissue biopsy.
Source: Health Advances analysis.

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