MULTIPLE-TIERED SCREENING AND ANALYSES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of and priority to U.S. Provisional Patent Application No. 63/304,536 filed January 28, 2022, U.S. Provisional Patent Application No. 63/312,741 filed February 22, 2022, U.S. Application No. 17/898,154 filed August 29, 2022, the entire disclosure of each which is hereby incorporated by reference in its entirety for all purposes.

BACKGROUND

[0002] Diagnostic technologies include simple, point of care (POC) tests applied to large populations to identify relatively common diseases as well as complex, centralized tests applied to select populations. However, although POC tests can be applied to large populations, they are incapable of diagnosing individuals for rare health conditions at a high enough accuracy to be feasible for implementation. Similarly, although complex, centralized testing can be deployed for rare population testing, such testing is often invasive, expensive, and fails when applied for detecting rare health conditions in large patient populations. For example, complex, centralized testing suffers from poor performance (e.g., high number of false positives and/or low positive predictive value) when attempting to diagnose rare health conditions in large patient populations.

SUMMARY

[0002a] In a first aspect, the present invention relates to a tiered, multipart method for detecting one or more early stage cancers in a subject, comprising:

performing an analysis of sequence information of the subject that has been obtained from a biological sample of the subject to identify whether the subject is not at risk of having one or more of the early stage cancers; and then if the patient has not been identified as not at risk:

analyzing sequence information of the subject not identified as not at risk by performing a second analysis to detect the presence of at least one specific cancer in the subject.

[0002b] In a second aspect, the present invention relates to a kit comprising:

a. equipment to draw a sample from a subject;

b. a set of detection reagents that, when combined with the sample, allows detection of biomarkers in the sample; and

c. instructions for accessing computer program instructions stored on a computer storage medium that, when processed by a processor of a computer system, cause the processor to:

perform an analysis of sequence information to identify whether the subject is not at risk of having one or more early stage cancers; and then if the patient has not been identified as not at risk:

analyze sequence information of the subject not identified as not at risk derived from second analysis to detect the presence of the one or more early stage cancers in the subject.

[0003] Disclosed herein are methods involving a multiple tiered analysis for identifying individuals with a health condition. In particular, the methods disclosed herein involving a multiple tiered analysis are useful for identifying individuals from a large population (e.g., millions of individuals) who have a rare health condition. The multiple tiered analysis involves a first screen, which eliminates a large proportion of individuals who are identified as not at risk for a health condition.

[0004] Disclosed herein is a tiered, multipart method for detecting one or more early stage cancers in a subject, comprising: performing an analysis of sequence information of the subject that has been obtained from a biological sample of the subject to identify whether the subject is not at risk of having one or more of the early stage cancers; and then if the patient has not been identified as not at risk: analyzing sequence information of the subject not identified as not at risk by performing a second analysis to detect the presence of at least one specific cancer in the subject.

[0005] Additionally disclosed herein is a tiered, multipart method for detecting a candidate population of subjects having an early stage cancer out of a plurality of subjects, the method comprising: for each of one or more subjects in the plurality of subjects: obtaining sequence information derived from a first assay performed on a sample obtained from the subject; performing an analysis of sequence information of the subject to identify whether the subject is not at risk of having one or more early stage cancers; responsive to not having identified that the subject is not at risk for one or more early stage cancers, obtaining sequence information derived from a second assay performed on the sample or an additional sample obtained from the subject to generate the sequence information derived from the second assay; and performing an analysis of the sequence information derived from the second assay for the subject to determine whether to include the subject in the candidate population. In various embodiments, less than 10% of the plurality of subjects are not identified as not at risk for one or more early stage cancers, wherein performing the analysis of the sequence information derived from the second assay is performed for the less than 10% of plurality of subjects. In various embodiments, less than 5% of the plurality of subjects are not identified as not at risk for one or more early stage cancers, wherein performing the analysis of the sequence information derived from the second assay is performed for the less than 5% of plurality of subjects. In various embodiments, the tiered, multipart method that analyzes the plurality of subjects across two or more tier of testing delivers improved performance as a function of resource consumption in comparison to the single tier method. In various embodiments, the tiered, multipart method that analyzes the plurality of subjects across two or more tier of testing achieves an improved performance metric in comparison to a single tier method. In various embodiments, the tiered, multipart method that analyzes the plurality of subjects across two or more tier of testing achieves a similar or decreased performance metric in comparison to a single tier method.

[0006] In various embodiments, the one or more of the early stage cancers is fifteen or more different cancers. In various embodiments, the one or more of the early stage or preclinical phase cancers is a set of acute lymphoblastic leukemia, acute myeloid leukemia, adrenocortical carcinoma, soft tissue sarcoma, lymphoma, anal cancer, gastrointestinal cancer, brain cancer, skin cancer, bile duct cancer, bladder cancer, bone cancer, breast cancer, lung cancer, cardiac cancer, central nervous system cancer, cervical cancer, chronic lymphocytic leukemia, chronic myelogenous leukemia, chronic myeloproliferative neoplasms, colorectal cancer, uterine cancer, esophageal cancer, head and neck cancer, eye