Balancing High NPV and Insufficient PPV: Results of a Pilot Cancer Screening Study Using the CA-62 biomarker, with Applicability to its Commercial Use.

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Background: Cancer remained the world's second leading cause of death in 2024, claiming an estimated 9.9 million lives (IARC). Among adults over 50, the annual incidence of cancer now exceeds 1.1 %, although the point-prevalence of any single epithelial malignancy in asymptomatic cohorts is only 0.05–0.2 %. Such low baseline rates erode the positive predictive value (PPV) even for high-specificity molecular assays. Extending high-resolution imaging (LDCT, MRI, or PET) to every at-risk adult is financially prohibitive and organisationally unworkable. Additionally, when imaging studies are performed, most stage I–II lesions are not detected. Organ-specific serum markers likewise contribute little when patients are asymptomatic.

Many benign or subclinical conditions—adenomatous polyps of the intestine, atypical endometrial hyperplasia, chronic ulcerative GI disease—are now recognised as precancerous states. A blood-based early-stage cancer screening biomarker that flags these shared low-differentiation phenotypes may therefore provide significant preventive value, by prompting for earlier colonoscopic or gynecologic (and other) clinical intervention before malignant transformation occurs.

Method: We used a competitive chemiluminescent immunoassay (CLIA-CA-62) in this study. The assay targets N-glycan branches on surface glycoproteins that appear on poorly differentiated cells — a phenotype shared by hematopoietic and immune stem cells and by most cancer cells, particularly at early stages and during metastatic spread [1-6]. Frozen serum samples were collected at three independent sites, shipped on dry ice, and analyzed in a single authorized reference laboratory. The study included 1,005 asymptomatic employees undergoing routine occupational health screening; all had documented occupational cancer-risk exposure and were older than 45 years at the time of sampling.

Description of the CA-62 Measurement Method: A fixed tracer concentration (CA-62-acridinium) competes with endogenous CA-62 for monoclonal antibodies immobilized in 96-well plates. After a one-step 2-hour incubation and three washes, flash chemiluminescence is measured on a dedicated flash CL reader; signal decreases logarithmically with antigen concentration (log-inverse relationship). Precision: CV < 10 % across 1,250–10,000 U/mL. The clinical cut-off of 5,000 U/mL was established at 95 % specificity in healthy controls.

Results: Retrospective analysis of early-stage (I–II) cases for five high-mortality epithelial cancers (lung, breast, prostate, colorectal, renal) yielded sensitivities of 88–94 % at the predefined 95 % specificity, with AUC-ROC values of 0.95–0.98. These figures confirm CA-62's suitability for first-line screening where a high negative predictive value is required while retaining manageable follow-up loads.

Of the 1,005 employees screened, 63 individuals (6.2 %) exceeded the 5,000 U/mL clinical cut-off. Ten were already known to harbor histologically confirmed but as-yet-untreated malignancies at various stages — B-cell lymphoma, sigmoid carcinoma, choroidal melanoma, acute leukemia, renal cell carcinoma, two breast cancers, two prostate cancers, and one endometrial carcinoma. CA-62 correctly flagged every one of these baseline cancers**.**

Three employees were undergoing investigation for suspected malignancy (two breast, one prostate). All three tested below the cut-off, and subsequent work-ups did not identify any traces of cancer in these patients. A further fifteen participants with either long-term cancer remission (n = 12; 2–20 years disease-free) or benign prostatic hyperplasia (n = 3) also remained CA-62-negative.

During the 12-month surveillance window, one woman whose baseline CA-62 approached 8,000 U/mL was diagnosed with stage I endometrial carcinoma. This brought the total cancer yield to eleven, corresponding to a positive predictive value of 17.5 %.

Approximately one-third of the CA-62 positive employees declined further clinical evaluation. Among the 31 subjects who completed follow-up, clinicians documented:

- nine adenomatous polyps (eight colorectal, one uterine),
- a single prostate adenoma,
- five acute gastrointestinal disorders (including peptic ulcers),
- four hepatobiliary conditions (gallstones or steatosis),
- three immune-mediated lung diseases (two sarcoidosis, one asthma),
- one renal cyst under observation. See Fig. 1

No malignancies emerged in the **942 CA-62-negative subjects, maintaining a negative predictive value expected of 100%.** Retrospective review of 182 historical charts indicated that these comorbid conditions elevate CA-62 only during acute phases; levels of CA-62 normalize once the flare subsides, supporting a transient "flare" rather than a chronic background rise.

Chart review of subjects with CA-62 ≥ 5,000 U/mL showed that pronounced marker "flares" were largely confined to a limited set of conditions. During exacerbations of autoimmune lung disease (asthma, sarcoidosis) and chronic dermatoses (psoriasis), the probability of an elevated CA-62 signal was ≈ 50 %, whereas no more than 5% of patients with simple gastrointestinal disorders had elevated CA-62 levels. Two cancer cases carried additional serious comorbidities—active gastroduodenitis with multiple advanced adenomas (B-cell lymphoma, C85) and progressive sarcoidosis (prostate cancer)—yet any direct effect of these conditions on CA-62 levels remains uncertain. Overall, longitudinal CA-62 monitoring not only uncovers occult malignancies but also flags active inflammatory-proliferative events in systemic diseases, broadening the assay's utility in both annual population screening and routine occupational health check-ups.

Simplified Distribution of CA-62 Findings. Table 1:

Diagnostic category	n (CA-62 ≥ 5 000)	n (CA-62 < 5 000)
Malignancy (active or interval)	11	0
Cancer in long-term remission	0	12
Adenomatous polyps (colon + uterine)	9	0
Benign prostate disorders	1	14
GI ulcer / erosive diseases	8	54
Hepatobiliary & pancreatic	5	29
Immune-mediated lung (asthma/sarcoidosis)	5	12
Other chronic conditions (Thyroid, arthritis, renal cysts, skin disorders, etc.)	9	63
No diagnosis in history and with other diagnoses (Hypertension, etc.)	15	780

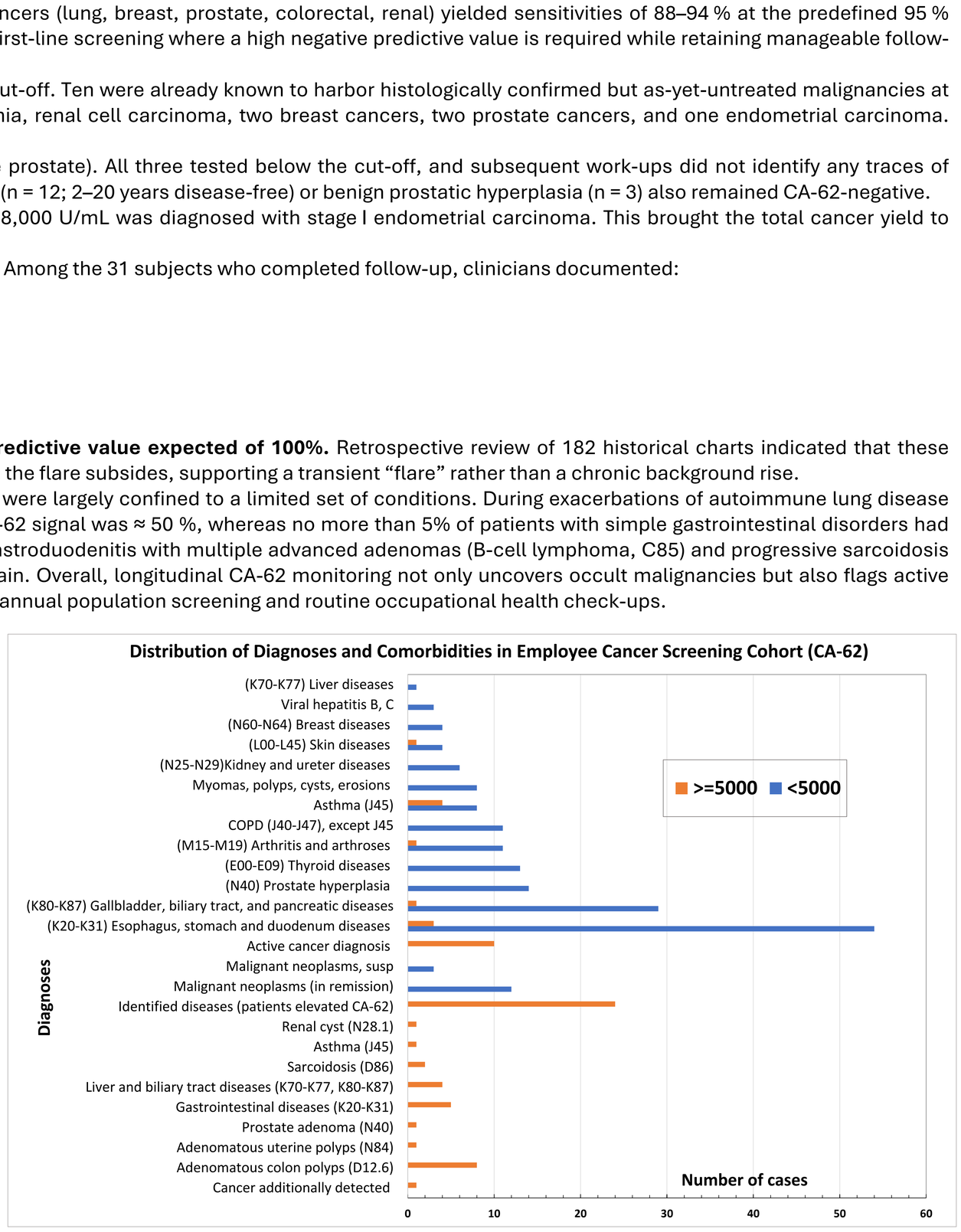


Figure 1. Distribution of diagnoses and comorbidities in the employee cancer screening cohort after CA-62 testing.

Conclusions:

- **Occupational screening.** The CLIA-CA-62 assay is now technically validated and logistically simple for large-scale, routine health examinations. Consequently, the test is readily deployable within annual—or more frequent—corporate medical check-ups.
- **Dual value for employers and shareholders.** In addition to detecting all cancer cases in our 1,005-employee study, CA-62 reliably highlighted acute inflammatory-proliferative states, most notably in the lungs (asthma, sarcoidosis) and gastrointestinal tract (adenomatous colon polyps, active gastroduodenitis). Early detection of these high-impact conditions enables timely intervention, reduced sick leave, and healthier, more productive staff.
- **Actionable follow-up algorithm.** A simple "screen-and-retest" loop—repeat CA-62 after 6–8 weeks for initial positives—filters out transient flares, focusing diagnostic resources on persistent elevations that merit targeted imaging or specialty referral. This pragmatic pathway keeps employer-funded programs cost-efficient while maximizing clinical benefit for employees.
- **A single low-cost annual CA-62 run** yields actionable oncologic and systemic findings, transforming routine occupational screening into a **strategic health-management tool.**

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