Associations between Serum Inflammatory Biomarkers and Colorectal Cancer Incidence in the Singapore Chinese Health Study (SCHS)

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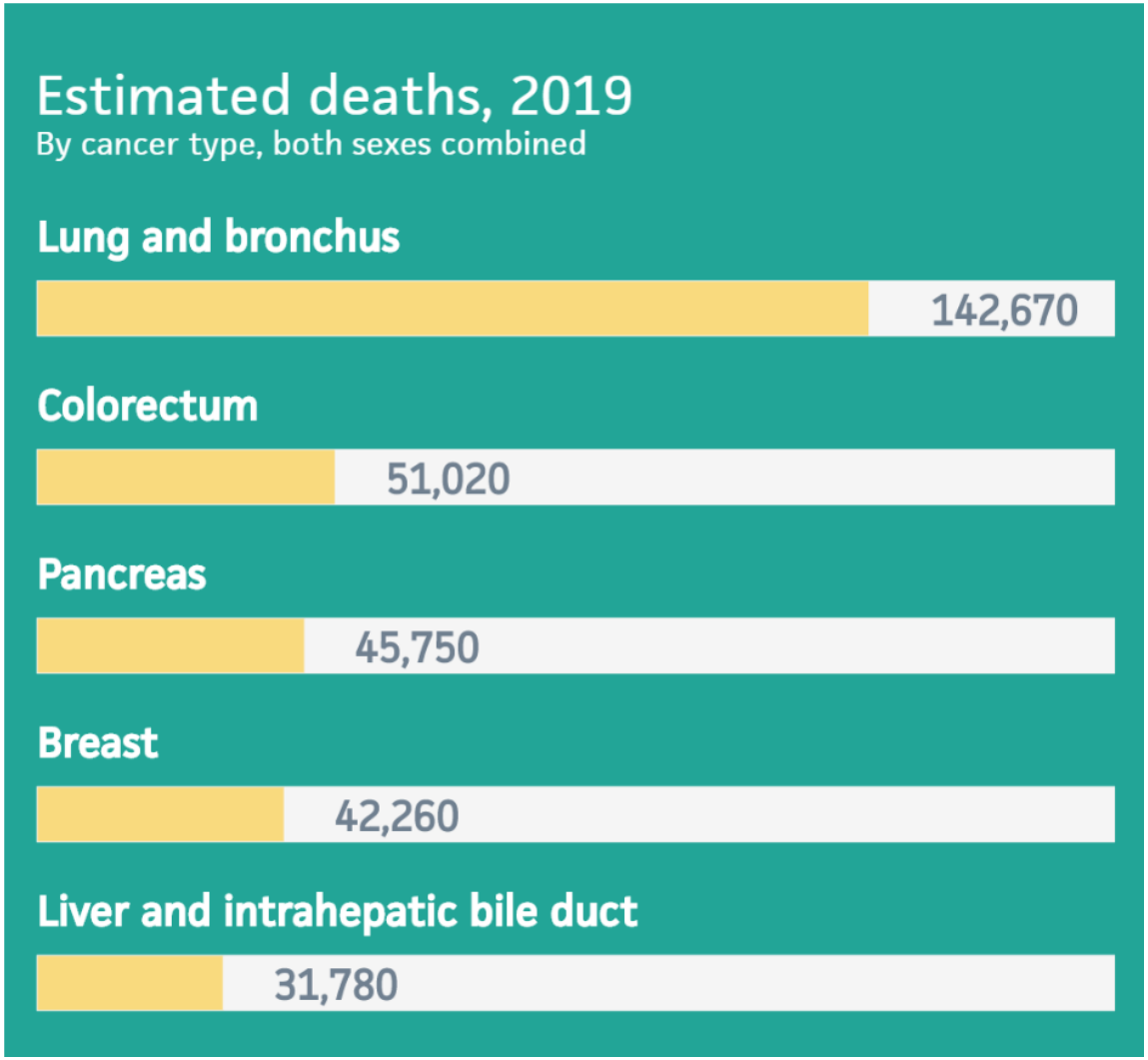
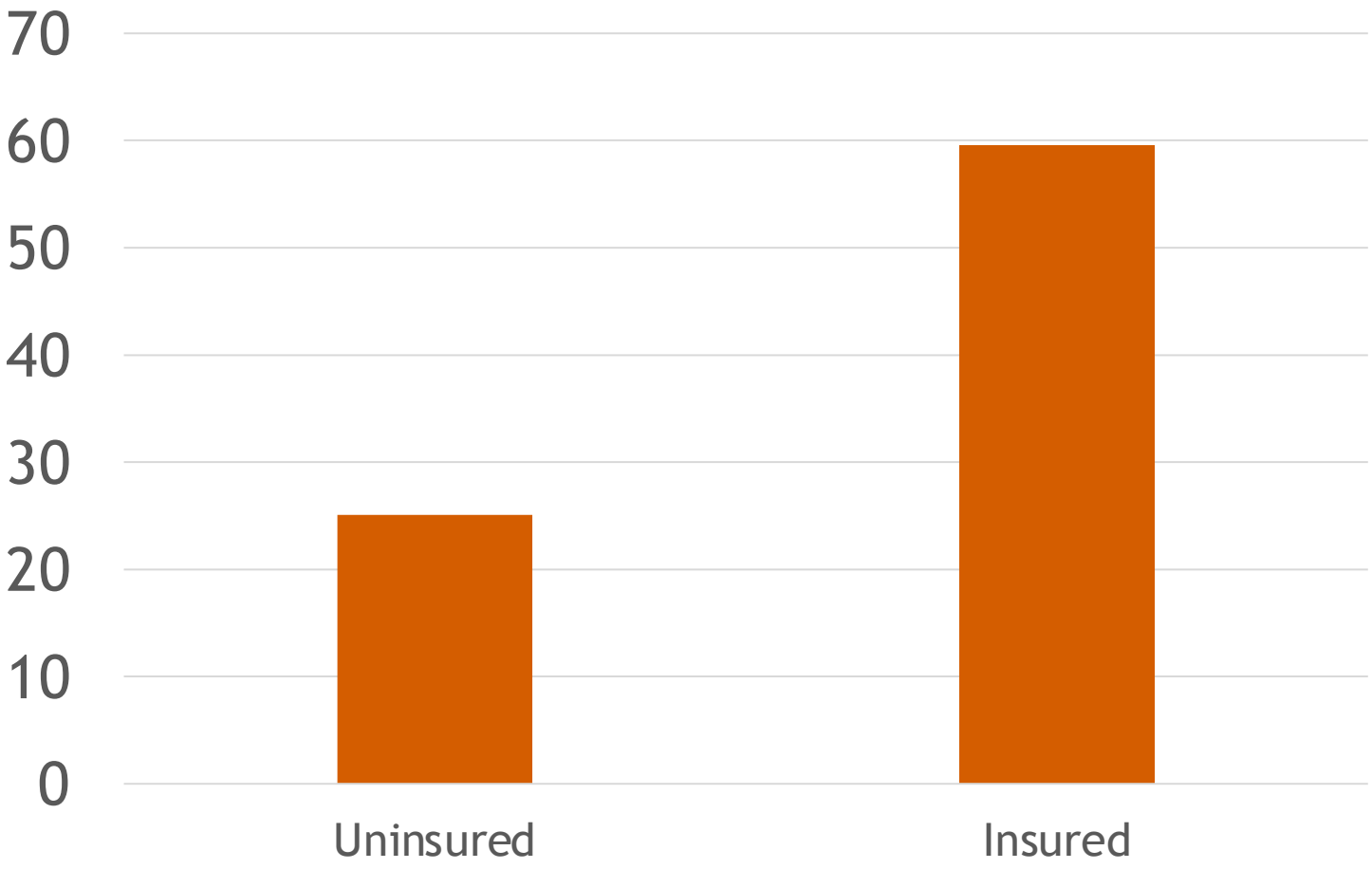
Background



Source: American Cancer Society, 2019

Colorectal Screening (%), Adults 50 Years and Older, US, 2015



Source: Colorectal Cancer Facts and Figures 2017-2019
American Cancer Society, 2019

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Long-term aim:

To derive a score of serum inflammatory biomarker concentrations for early colorectal cancer detection and risk prediction

Aim of this Pilot Study

In a prospective analysis of 140 cases and controls nested within the Singapore Chinese Health Study, to:

1. Identify individual inflammatory biomarkers associated with colorectal cancer
2. Through principal components analysis, evaluate the ability of combined colorectal concentrations to predict colorectal cancer status

Participants: Singapore Chinese Health Study

- Sampled from 63,257 Chinese Singaporean men and women
- 45-74 years of age at baseline (1993-1998)
- Followed for 7.03 years on average
- 71 colorectal cancer cases and 69 controls without cancer at baseline who had serum samples
  - Matched by age, sex, dialect

Olink/Proseek Multiplex Inflammation Assay

- Simultaneous measurement of 92 markers
- 1 µL of serum per participant
- Biomarkers relevant to inflammation research
- Proximity Extension Assay allows highly specific binding and amplification of multiple biomarkers

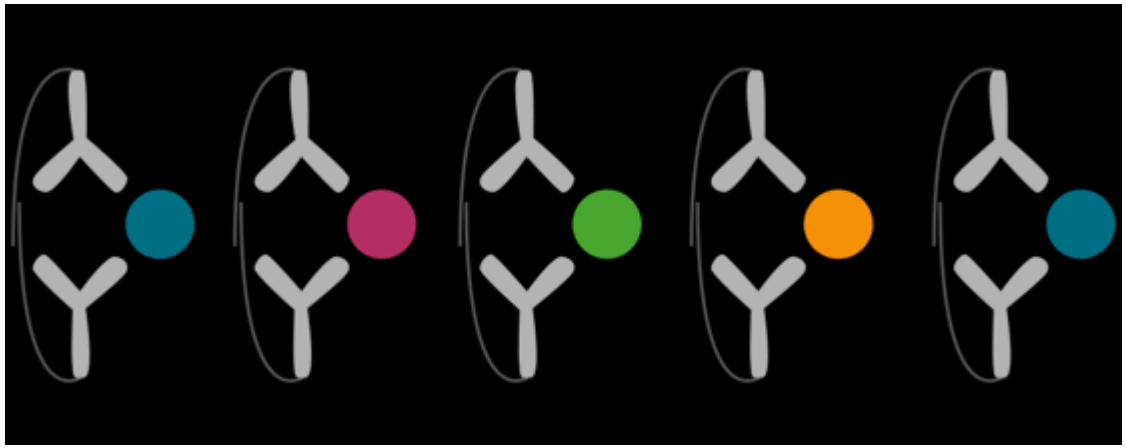


Image Source: Olink Proteomics

Reproducibility of Olink Concentrations

- 92 biomarkers for a randomly selected subset of 15 cases and 15 controls were measured in two laboratories:
  - 90% of biomarkers had intraclass correlation coefficients >0.5
  - 74% of biomarkers had intraclass correlation coefficients > 0.7

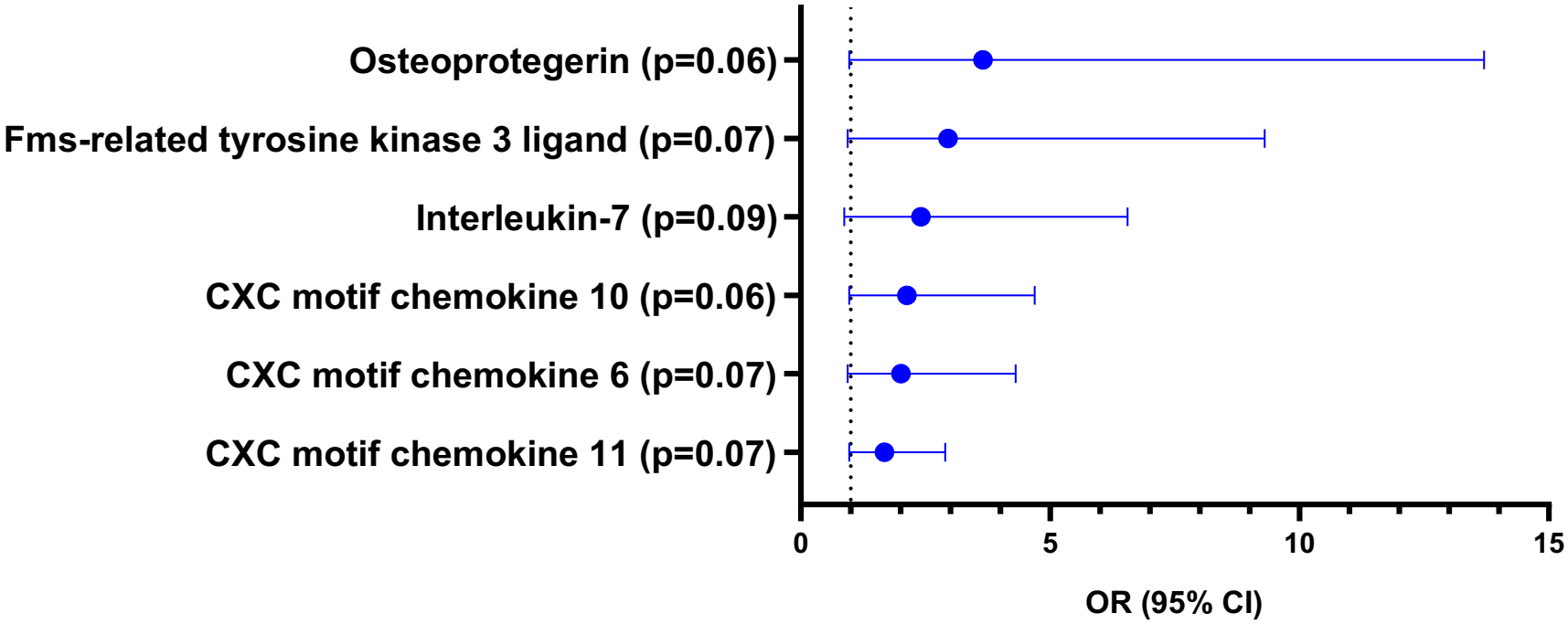
Analysis

- Sample divided into discovery and replication sets with 70 participants each
  - Discovery set: 36 cases, 34 controls
  - Replication set: 35 cases, 35 controls
- Biomarkers were eliminated from all analyses if they were undetectable for at least 10 participants (N=22)
  - 70 biomarkers included in this analysis

Analysis: Discovery Dataset (n=70)

- Associations between each individual biomarker concentration and colorectal cancer case/control status:
  - Multivariable Logistic Regression
    - Adjustment for age at baseline, sex, BMI, date of sample collection

Odds Ratios and 95% Confidence Intervals for Colorectal Cancer by Serum Biomarker, Singapore Chinese Health Study (n=70)



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Principal Component Analysis

- Completed two analyses in the **discovery** dataset:
  - Including 6 proteins associated with colorectal cancer in individual analyses ($p<0.10$)
  - Including all 70 available proteins
  - Biomarker concentrations standardized with mean=0 and SD=1
  - Components with eigenvalues >1 were retained
  - Component scores, weighted sums of biomarker's contribution to each component, were computed.
- Component scores retained from the discovery dataset were applied to the **replication** dataset in multivariable logistic regression

Area Under the Curve (AUC) and 95% Confidence intervals for Multivariable Logistic Regression Models in the Replication Dataset

	AUC (95% CI	Components Included
Principal Components derived from 6 significant biomarkers		
Crude	0.67 (0.54-0.80)	2
Adjusted for age, sex, BMI, education, and date of collection	0.72 (0.60-0.84)	2
Principal Components derived from all 70 available biomarkers		
Crude	0.78 (0.67-0.90)	13
Adjusted for age, sex, BMI, education, and date of collection	0.82 (0.71-0.91)	13

Conclusions and Future Directions

- Though preliminary, our findings are promising
- Primary limitation is low sample size
- Individual biomarkers identified in this study have been associated with colorectal cancer incidence in other studies
- Next step: replicate our finings in a larger cohort

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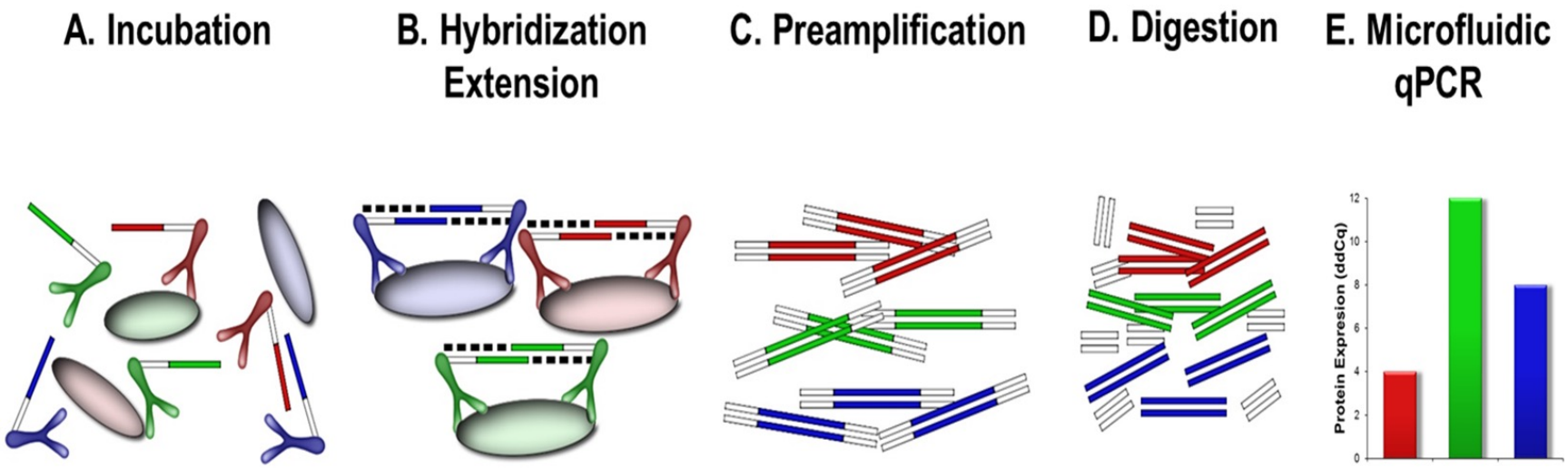
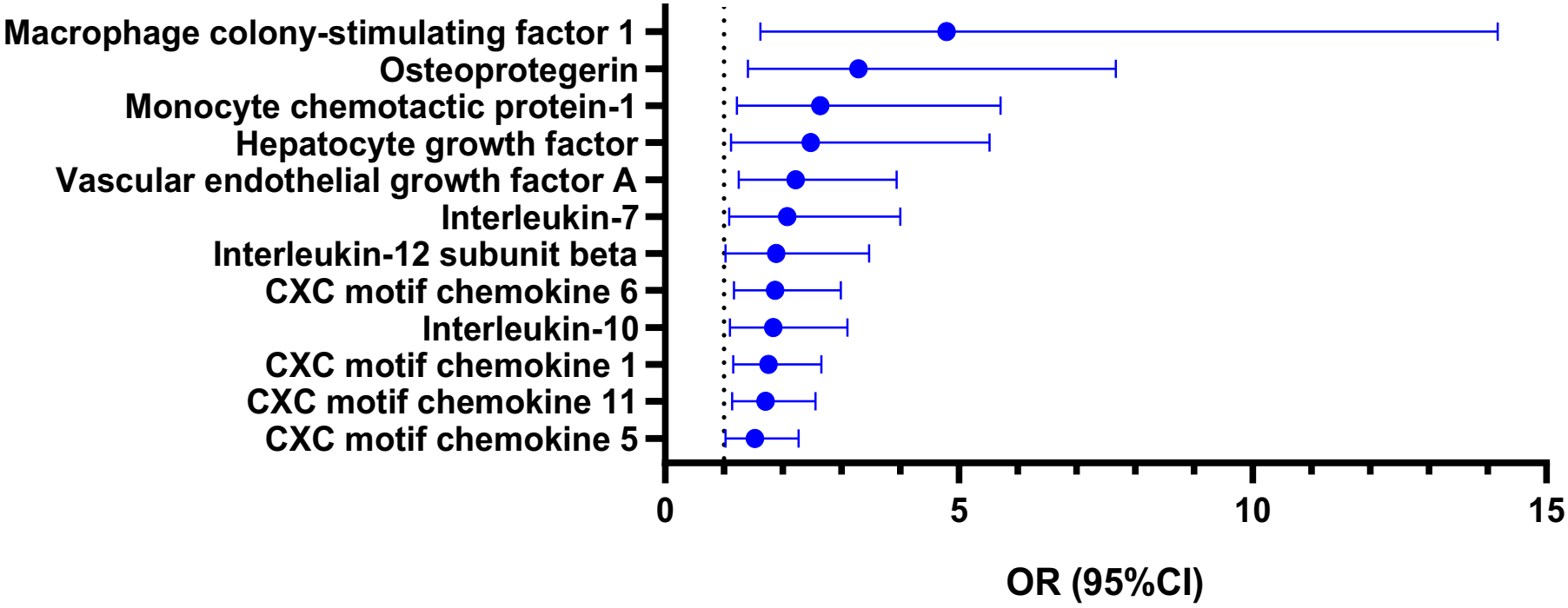
Olink Methodology



Source: Assarson et al 2014

Preliminary Results: Odds Ratios and 95% Confidence Intervals for Colorectal Cancer Incidence by Biomarker Concentratons, Singapore Chinese Health Study (n=140)



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