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Supplementary information

Hematopoietic mosaic chromosomal alterations increase the risk for diverse types of infection

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Supplementary Information:

Hematopoietic mosaic chromosomal alterations increase the risk for diverse types of infection

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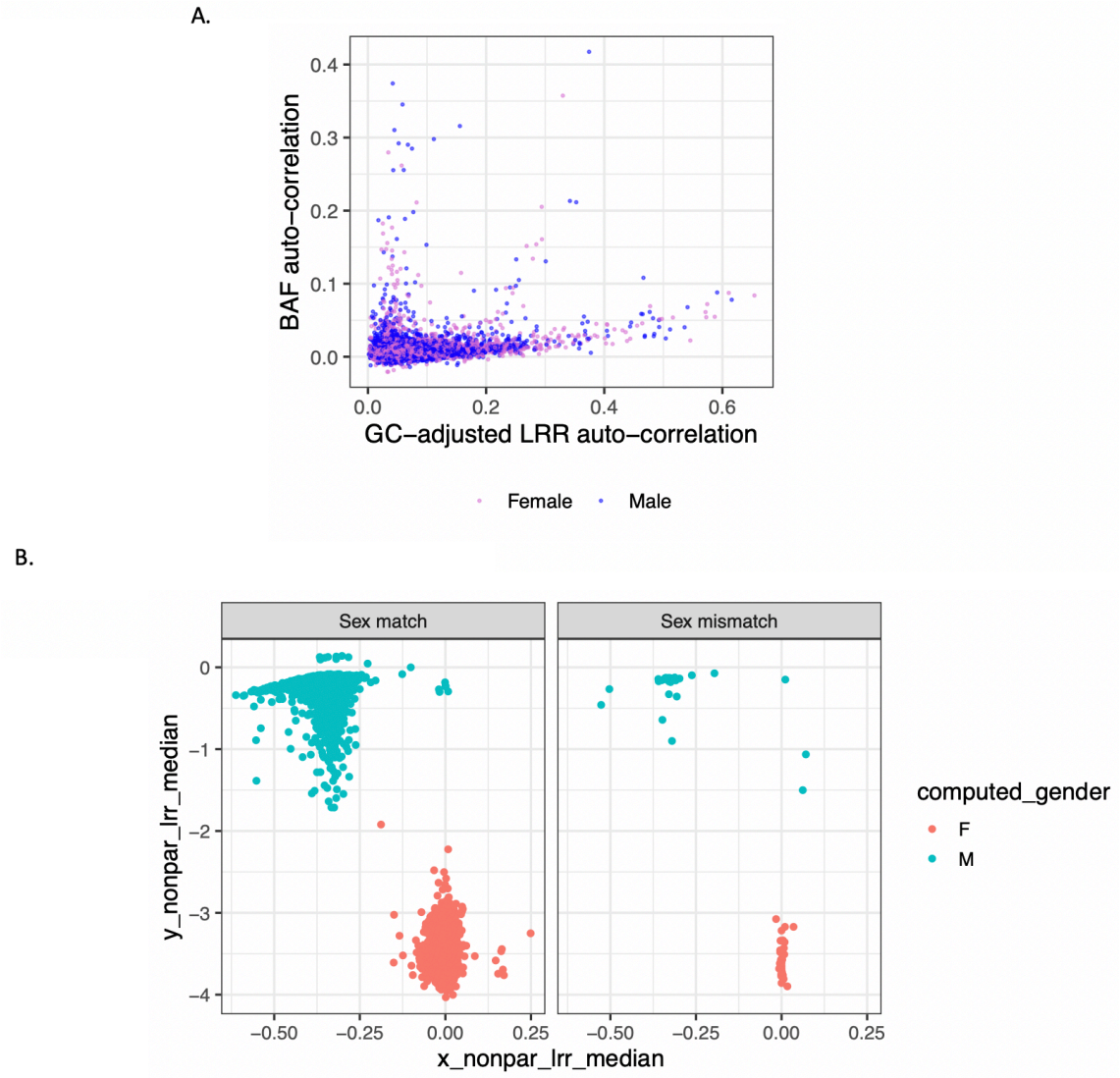
* These authors equally contributed to this work.

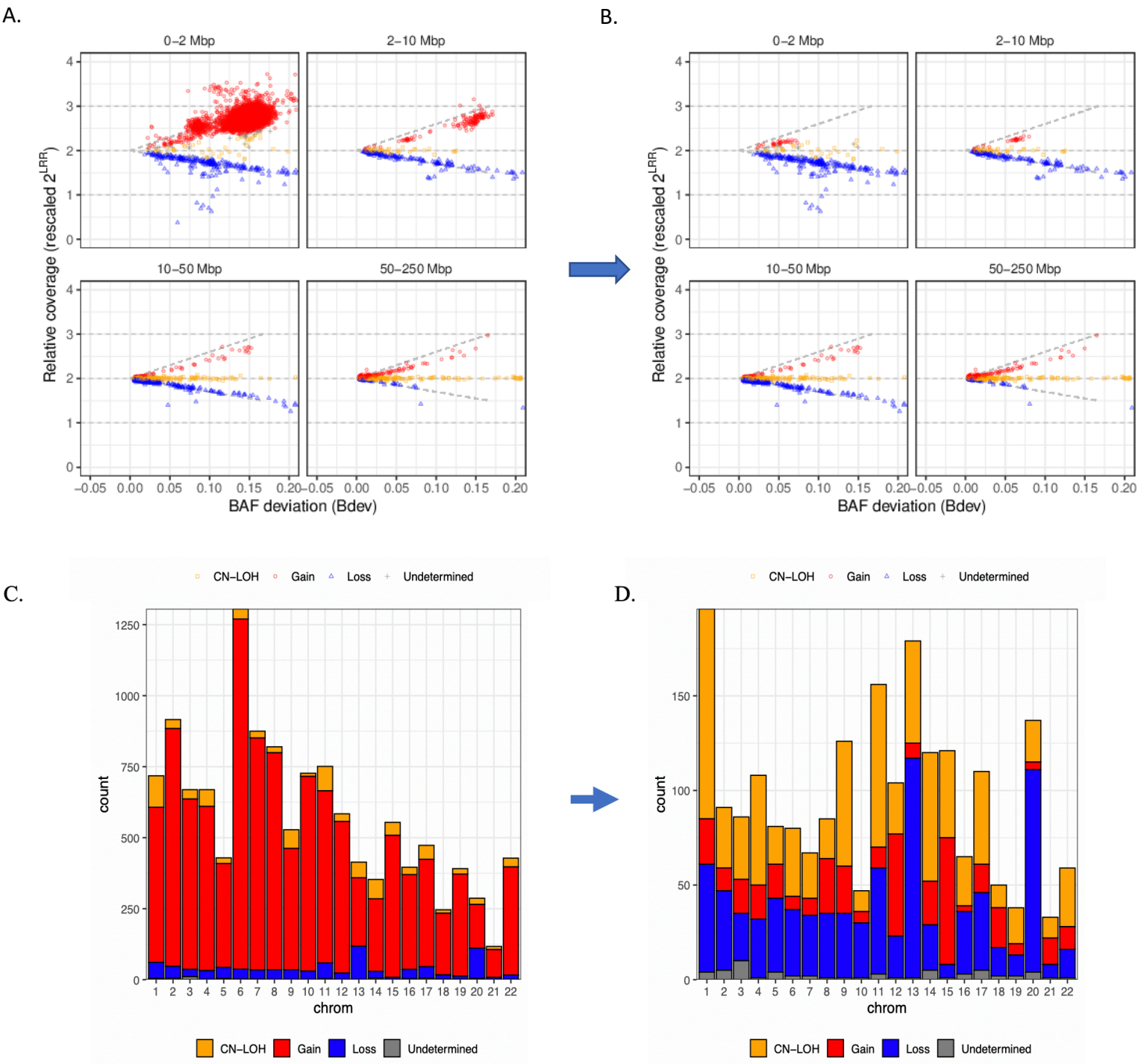
\# These authors equally supervised this work.

Table of Contents

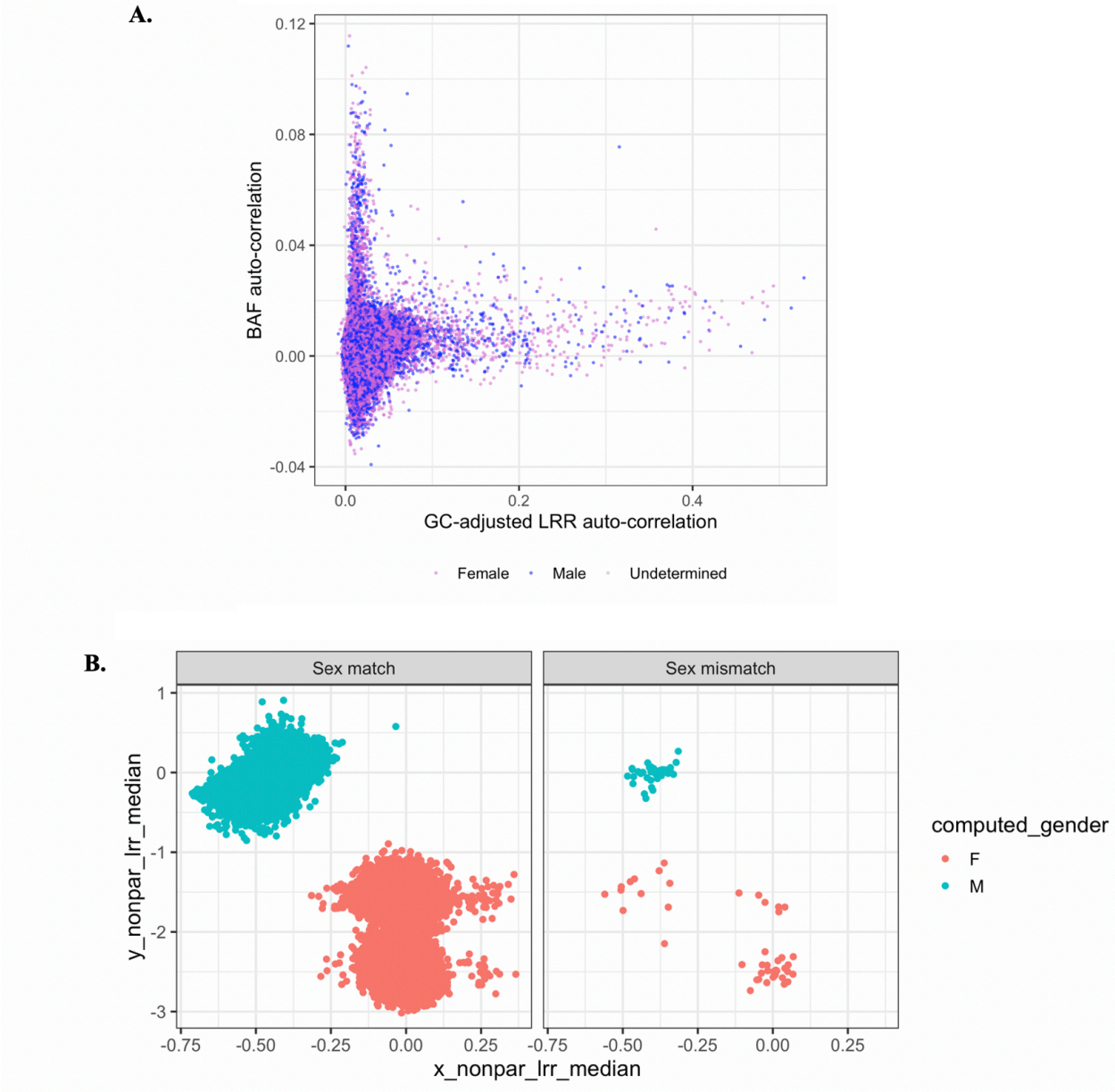
Supplementary Figures:



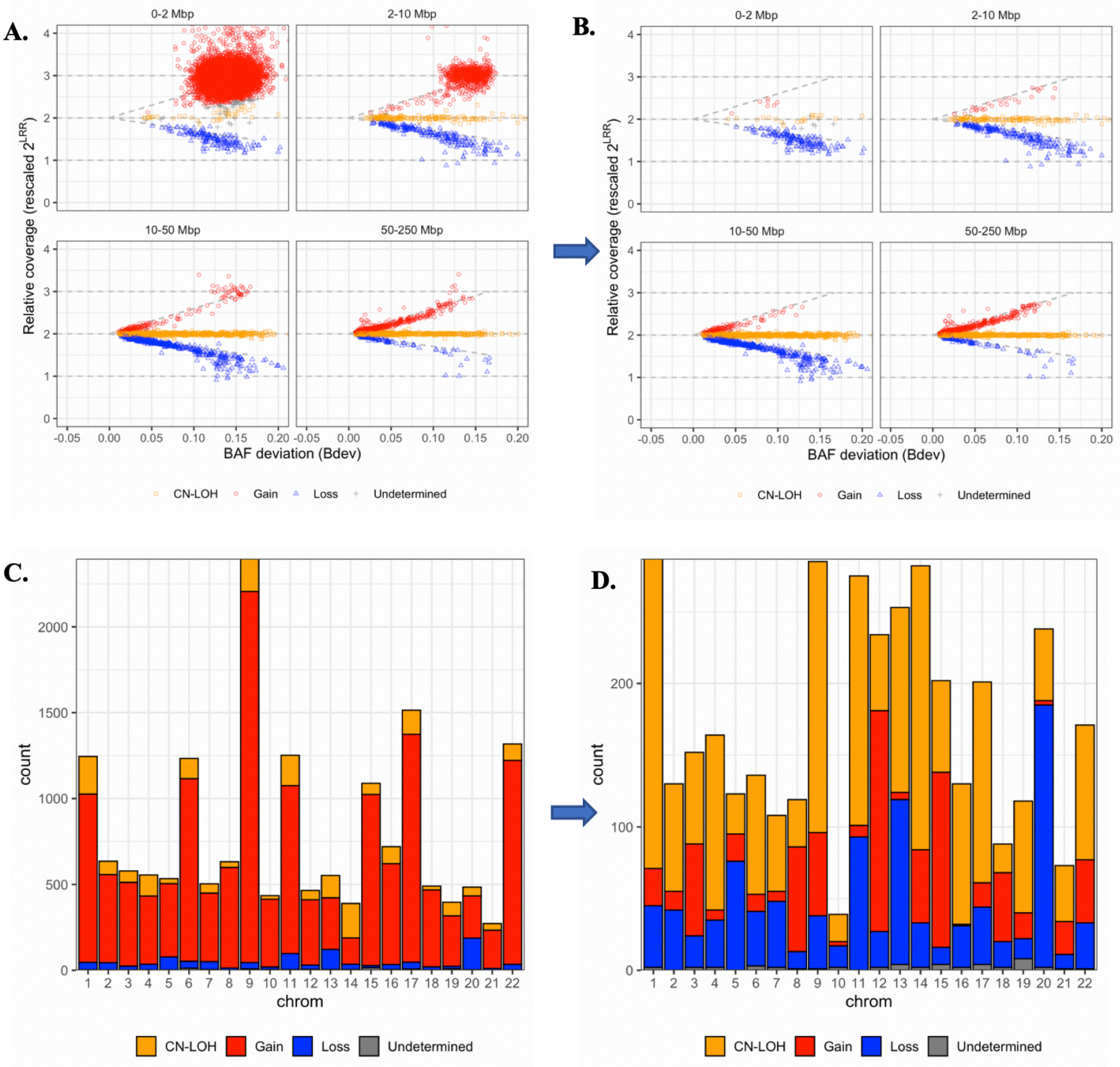
Supplementary Figure 1: MGB Biobank mCA sample quality control analyses. A. plotting sample-level phased B allele frequency (BAF) auto-correlation across consecutive phased heterozygous sites versus Log R Ratio (LRR) of intensities using local GC content. B. Showing sex mismatches between MoChA-derived sex computed using the chrX nonPAR region versus reported sex. LRR=Log R Ratio, MoChA = mosaic chromosomal alterations caller, BAF=B allele frequency, nonPAR = Non-pseudoautosomal region



Supplementary Figure 2: MGB Biobank mCA variant quality control analyses. Plots A. and C. represent mCAs carried among the quality-control filtered sample set, and after removal of likely germline variants (LOD_BAF_PHASE <20 for autosomal or mCAs annotated as known germline copy number polymorphisms). Plots B. and D. reflect additional variant quality control filters to remove constitutional duplications (0-2Mbp mCAs with relative coverage >2.25 and 2-10Mbp mCAs with relative coverage >2.4) and remove constitutional deletions (mCAs with relative coverage <0.5). CN-LOH = copy-neutral loss of heterozygosity, LOD_BAF_PHASE = log odds score for mCA model based on BAF and genotype phase, mCA = mosaic chromosomal alteration

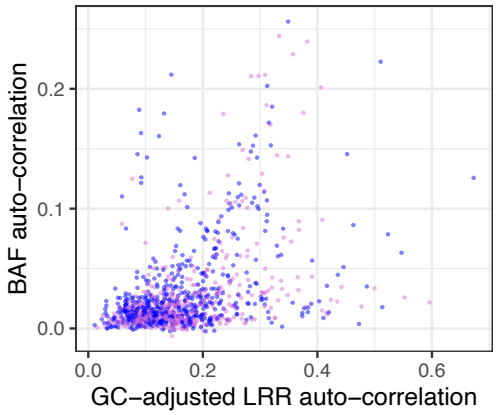


Supplementary Figure 3: FinnGen mCA sample quality control analyses. A. plotting sample-level phased B allele frequency (BAF) auto-correlation across consecutive phased heterozygous sites versus Log R Ratio (LRR) of intensities using local GC content. B. Showing sex mismatches between MoChA-derived sex computed using the chrX nonPAR region versus reported sex. LRR=Log R Ratio, MoChA = mosaic chromosomal alterations caller, BAF=B allele frequency, nonPAR = Non-pseudoautosomal region

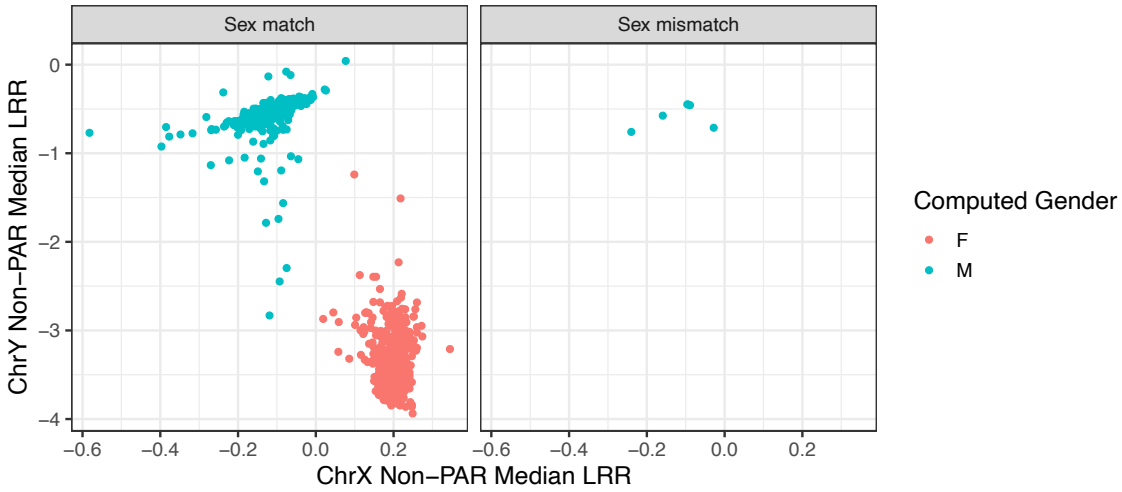


Supplementary Figure 4: FinnGen mCA variant quality control analyses. Plots A. and C. represent mCAs after removal of likely germline variants (LOD_BAF_PHASE <20 for autosomal variants or mCAs annotated as known germline copy number polymorphisms). Plots B. and D. reflect additional sample quality control filters including removal of samples with call rate <0.97 and BAF_AUTO >0.03, and removal of calls with LOD_BAF_PHASE <10 unless they are larger than 5Mbp (or 10 Mbp if they span the centromere) and calls that are likely constitutional duplications (0.5-5Mbp mCAs with relative coverage >2.5 and Bdev<0.1 and 5-10Mbp mCAs with relative coverage >2.75) and constitutional deletions (mCAs with relative coverage <0.5). CN-LOH = copy-neutral loss of heterozygosity, LOD_BAF_PHASE = log odds score for mCA model based on BAF and genotype phase, mCA = mosaic chromosomal alteration

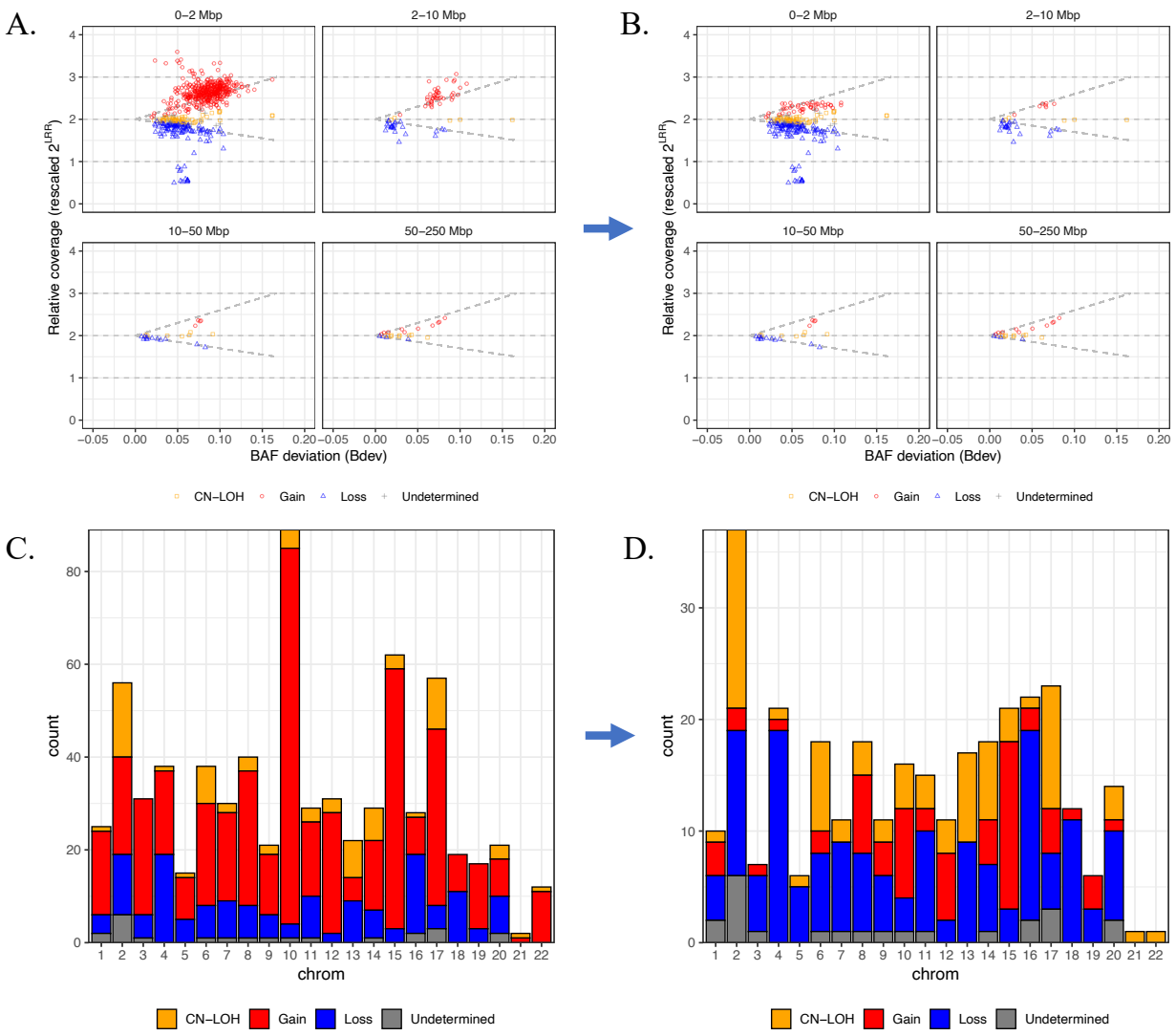
A.



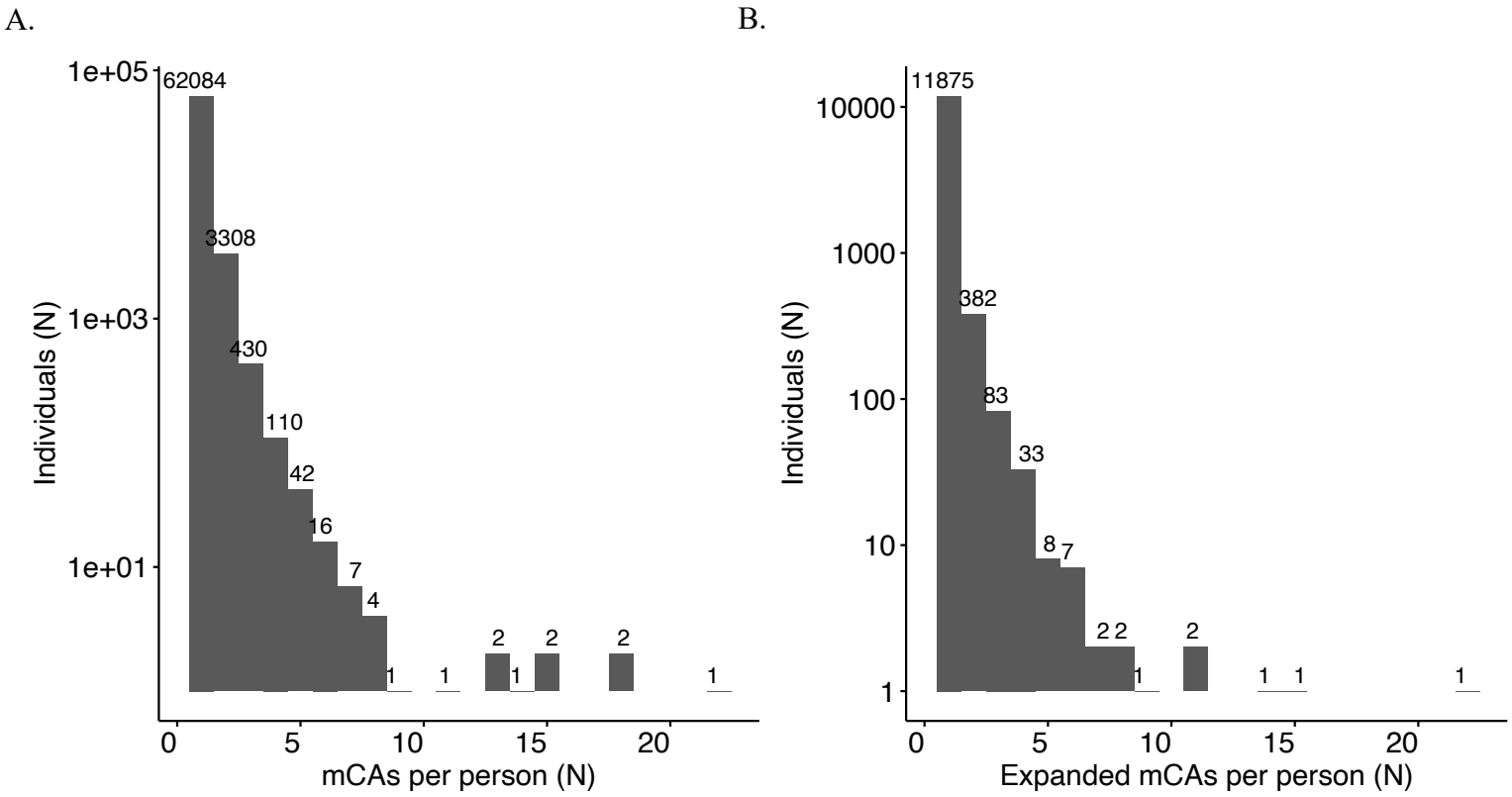
B.



Supplementary Figure 5: CUB COVID-19 mCA sample quality control analyses. A. plotting sample-level phased B allele frequency (BAF) auto-correlation across consecutive phased heterozygous sites versus Log R Ratio (LRR) of intensities using local GC content. B. Showing sex mismatches between MoChA-derived sex computed using the chrX nonPAR region versus reported sex. LRR=Log R Ratio, MoChA = mosaic chromosomal alterations caller, BAF=B allele frequency, nonPAR = Non-pseudoautosomal region

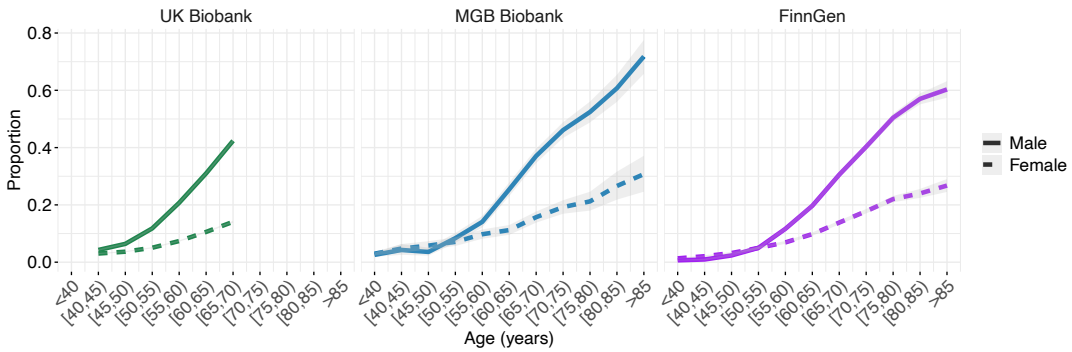


Supplementary Figure 6: CUB COVID-19 mCA variant quality control analyses. Plots A. and C. represent mCAs carried among the quality-control filtered sample set, and after removal of likely germline variants (LOD_BAF_PHASE <20 for autosomal or mCAs annotated as known germline copy number polymorphisms). Plots B. and D. reflect additional variant quality control filters to remove constitutional duplications (0-10Mbp mCAs with relative coverage >2.4) and remove constitutional deletions (mCAs with relative coverage <0.5). CN-LOH = copy-neutral loss of heterozygosity, LOD_BAF_PHASE = log odds score for mCA model based on BAF and genotype phase, mCA = mosaic chromosomal alteration

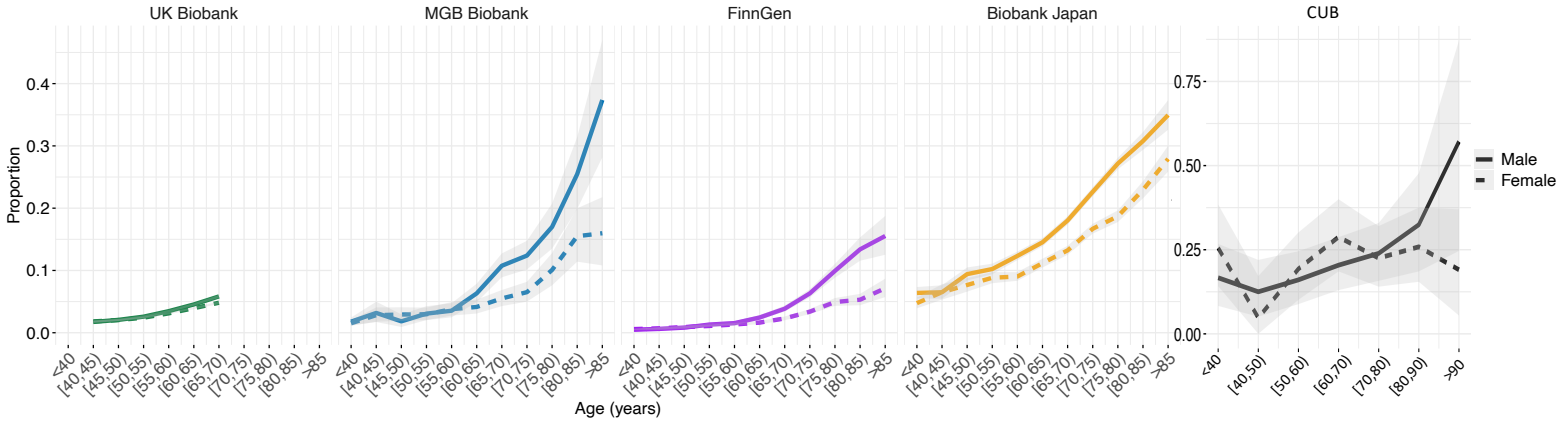


Supplementary Figure 7: Total number of mCAs (A) and expanded mCAs (B) per individual in the UK Biobank for mCA carriers. mCAs = mosaic chromosomal alterations

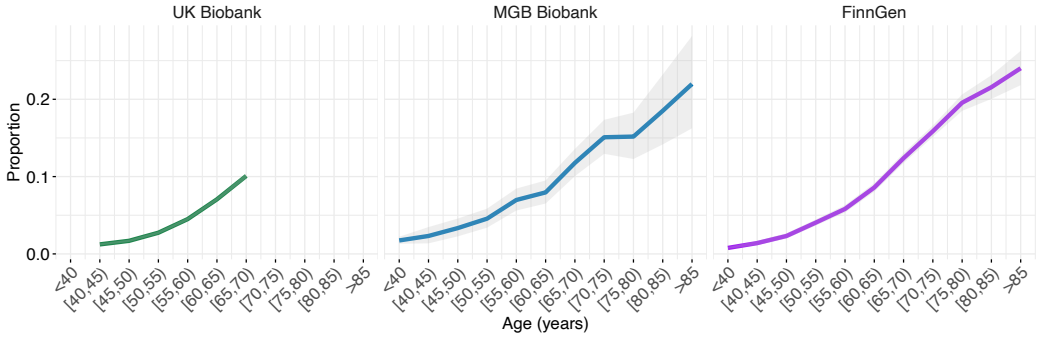
A. Any mCA:



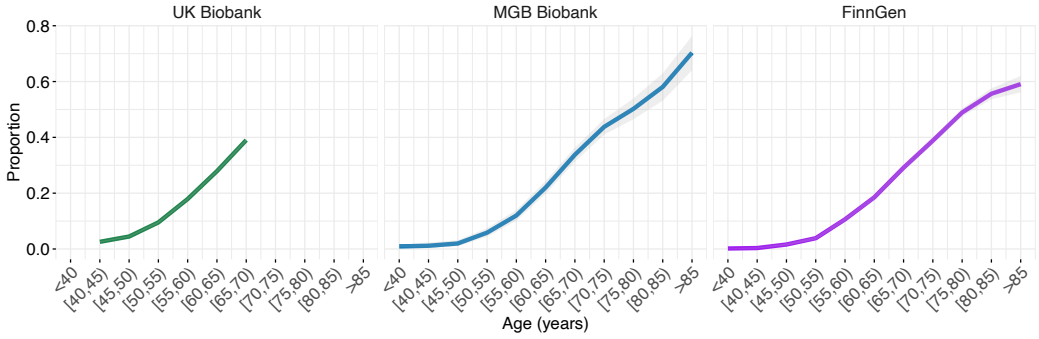
B. Autosomal mCA:



C. ChrX:

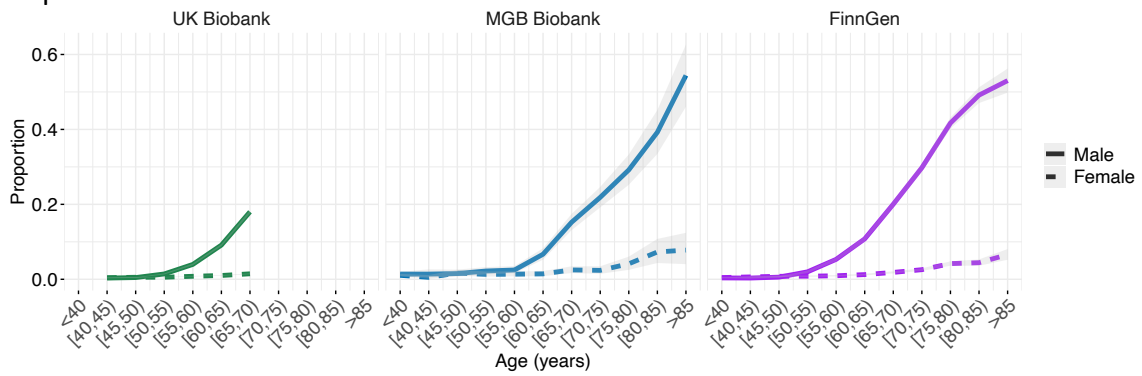


D. ChrY:

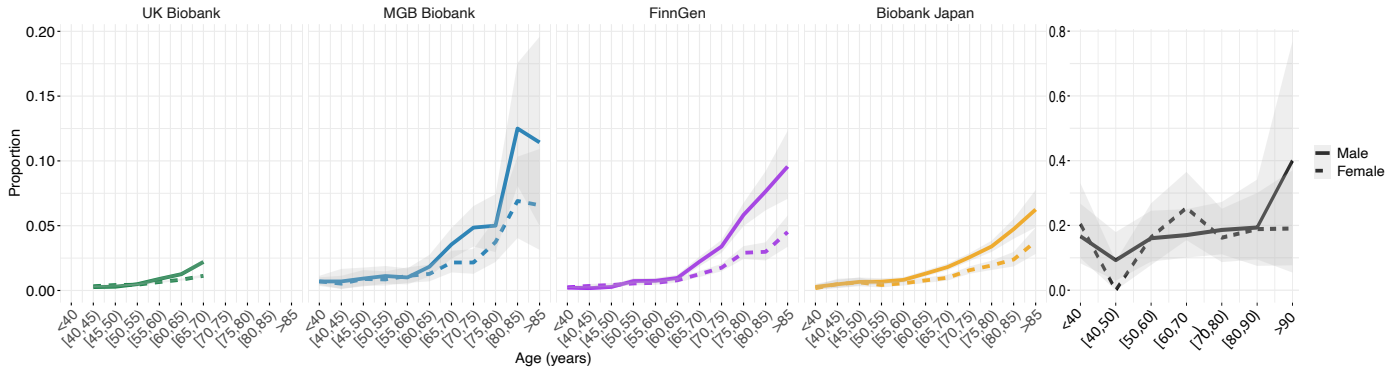


Supplementary Figure 8: Prevalence of mCA categories by age bin across cohorts. Error bands were derived from binomial proportion 95% confidence intervals. mCA = mosaic chromosomal alterations.

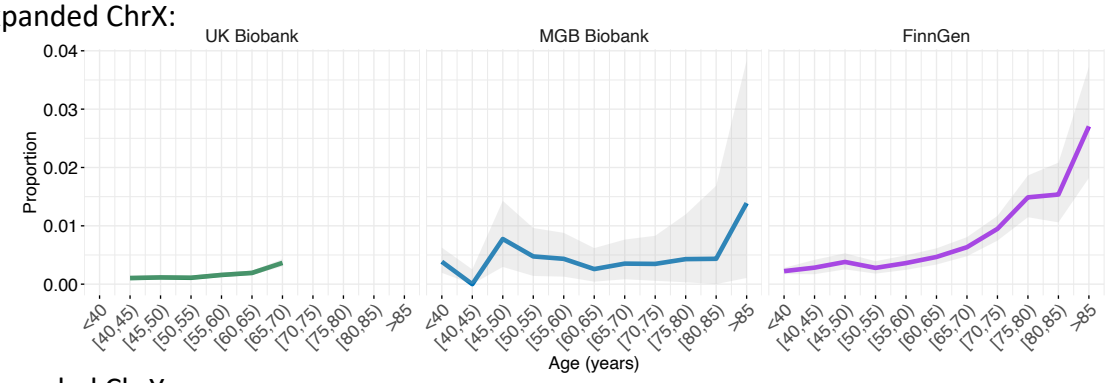
A. Any expanded mCA:



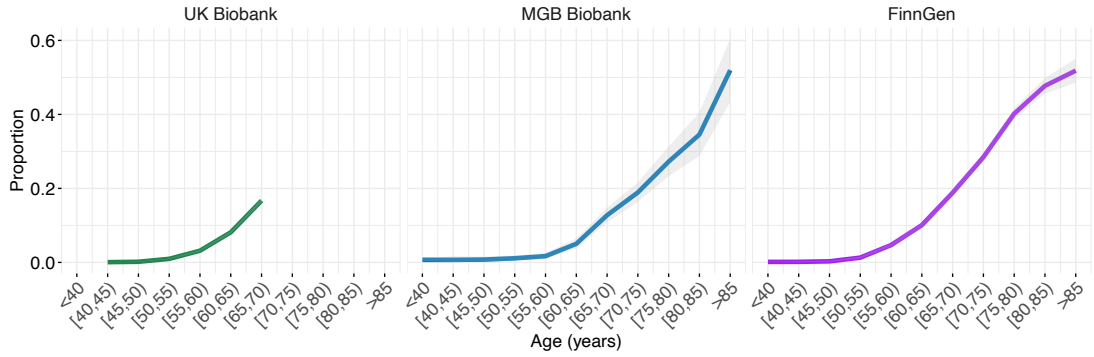
B. Expanded Autosomal mCA:



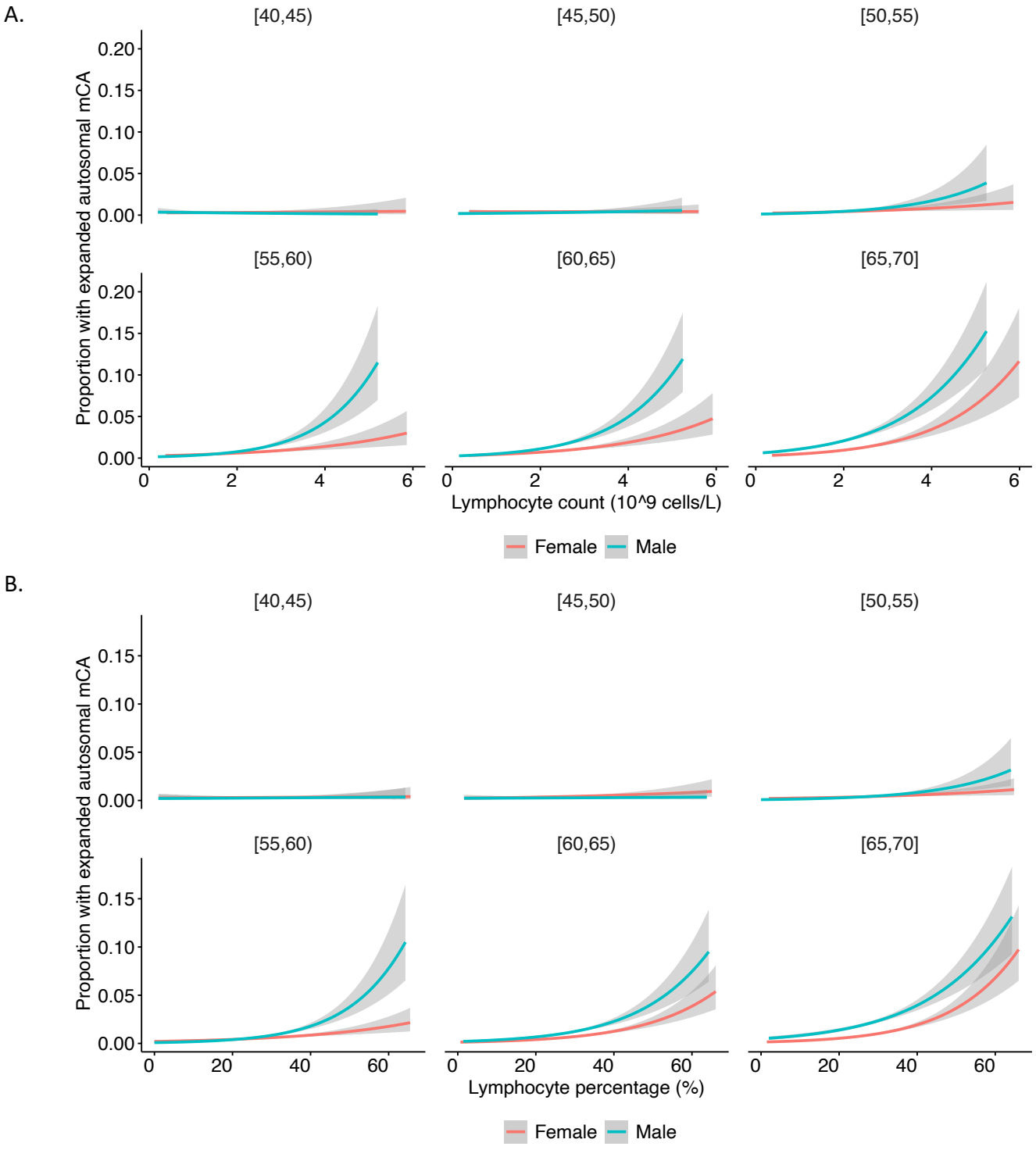
C. Expanded ChrX:



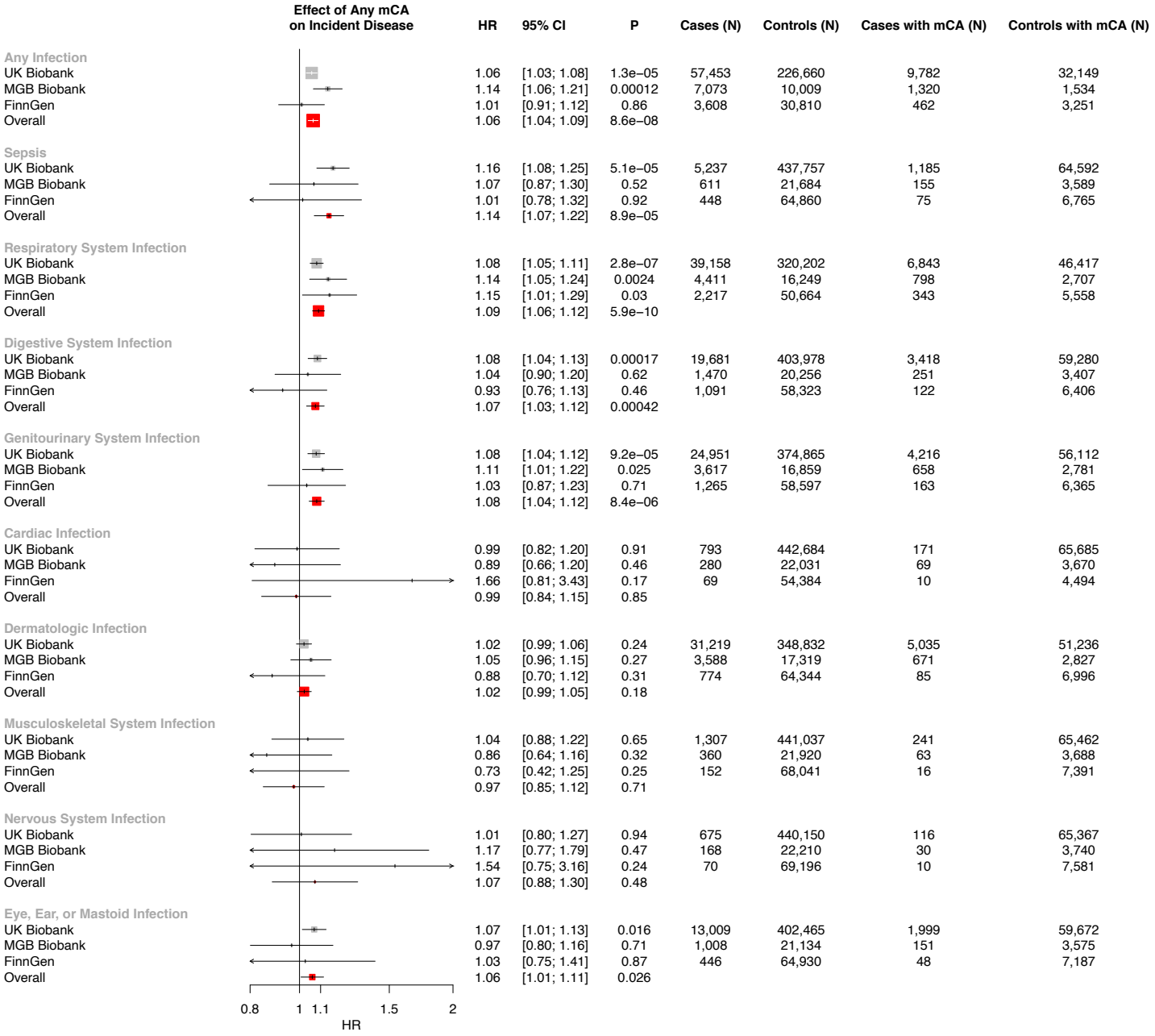
D. Expanded ChrY:



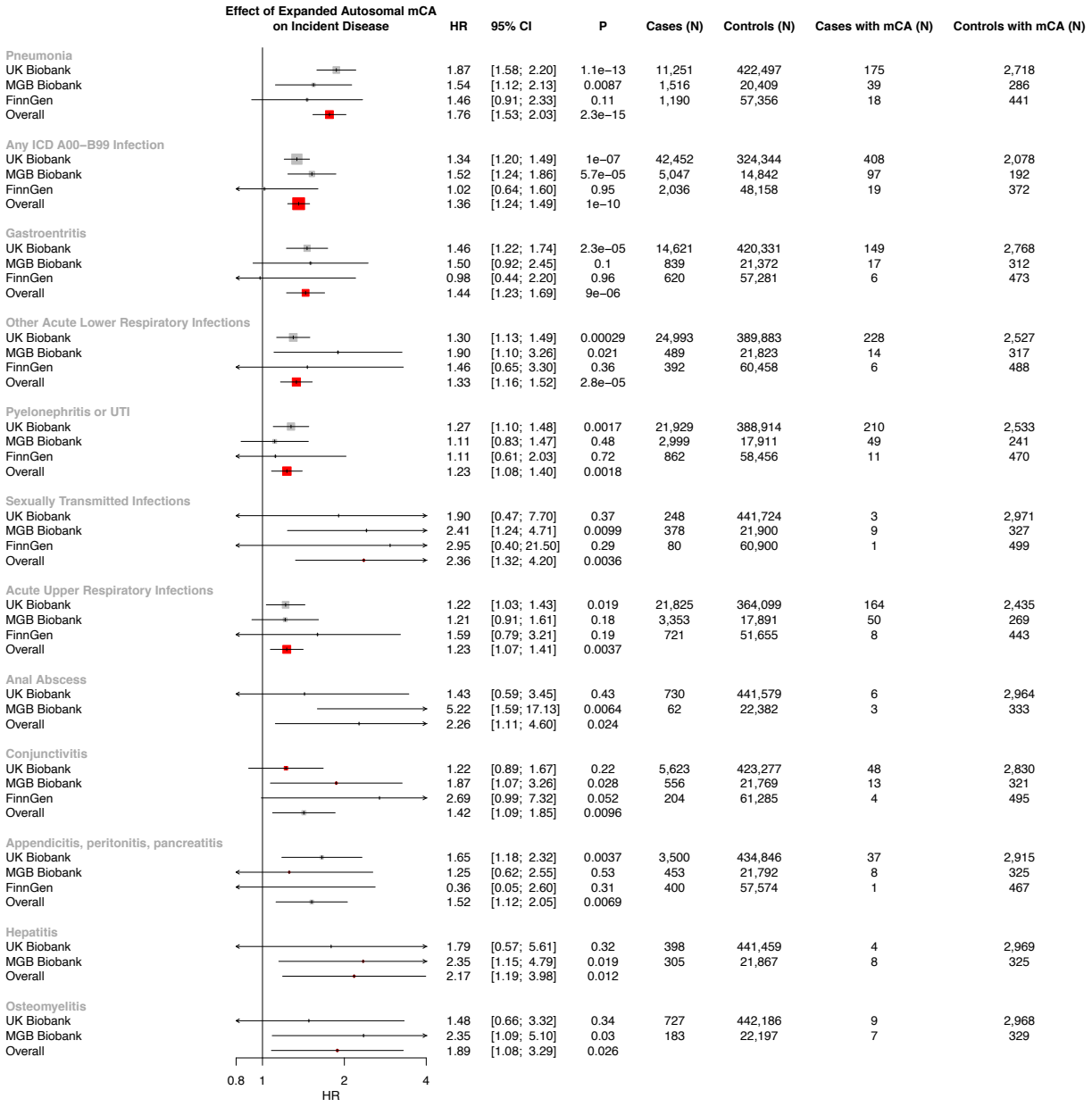
Supplementary Figure 9: Prevalence of expanded mCA categories by age bin across cohorts. Error bands were derived from binomial proportion 95% confidence intervals. mCA = mosaic chromosomal alterations.



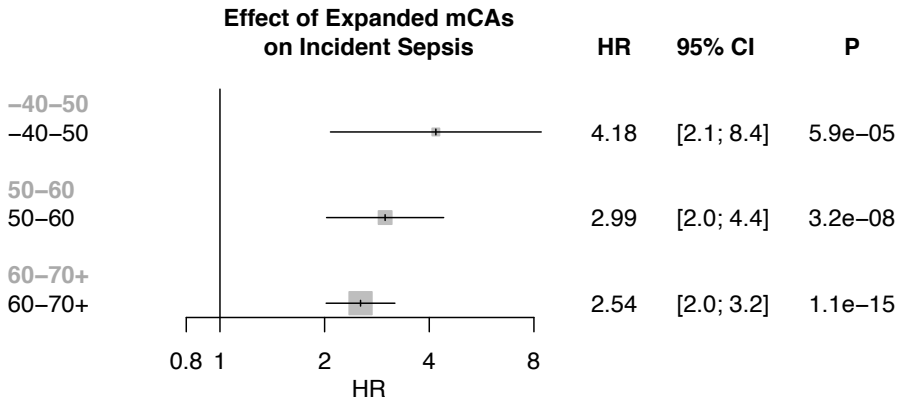
Supplementary Figure 10: Proportion of expanded autosomal mCAs carriers across lymphocyte count and percentage by age bin and sex. Association of expanded autosomal mCA prevalence with A. Lymphocyte count and B. Lymphocyte percentage across bins of age and sex. Error bands were derived from binomial proportion 95% confidence intervals. mCA = mosaic chromosomal alterations.



Supplementary Figure 11: Associations of any mCA with incident infections by Cox proportional-hazards models with the underlying time scale of time-on-study. Analyses are adjusted for age, age^2, sex, smoking status, and principal components 1-10 of ancestry. Bonferroni correction was used to determine the level of statistical significance. Overall estimates across studies are generated via fixed effect meta-analysis. Error bars show 95% confidence intervals. mCA = mosaic chromosomal alterations.

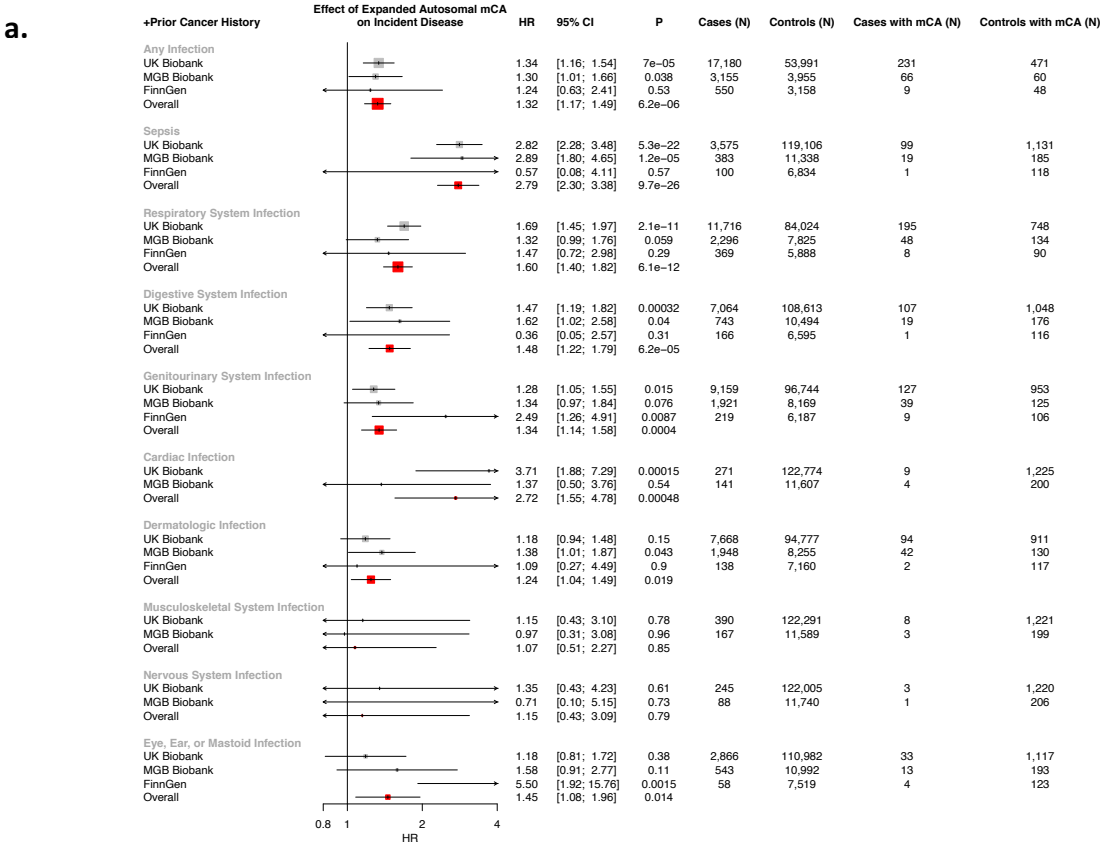


Supplementary Figure 12: Suggestive associations (P<0.05) of expanded autosomal mCAs with incident infection categories by Cox proportional-hazards models with the underlying time scale of time-on-study. Analyses are adjusted for age, age^2, sex, smoking status, and principal components 1-10 of ancestry. Bonferroni correction was used to determine the level of statistical significance. Overall estimates across studies are generated via fixed effect meta-analysis. Error bars show 95% confidence intervals. mCA = mosaic chromosomal alterations.

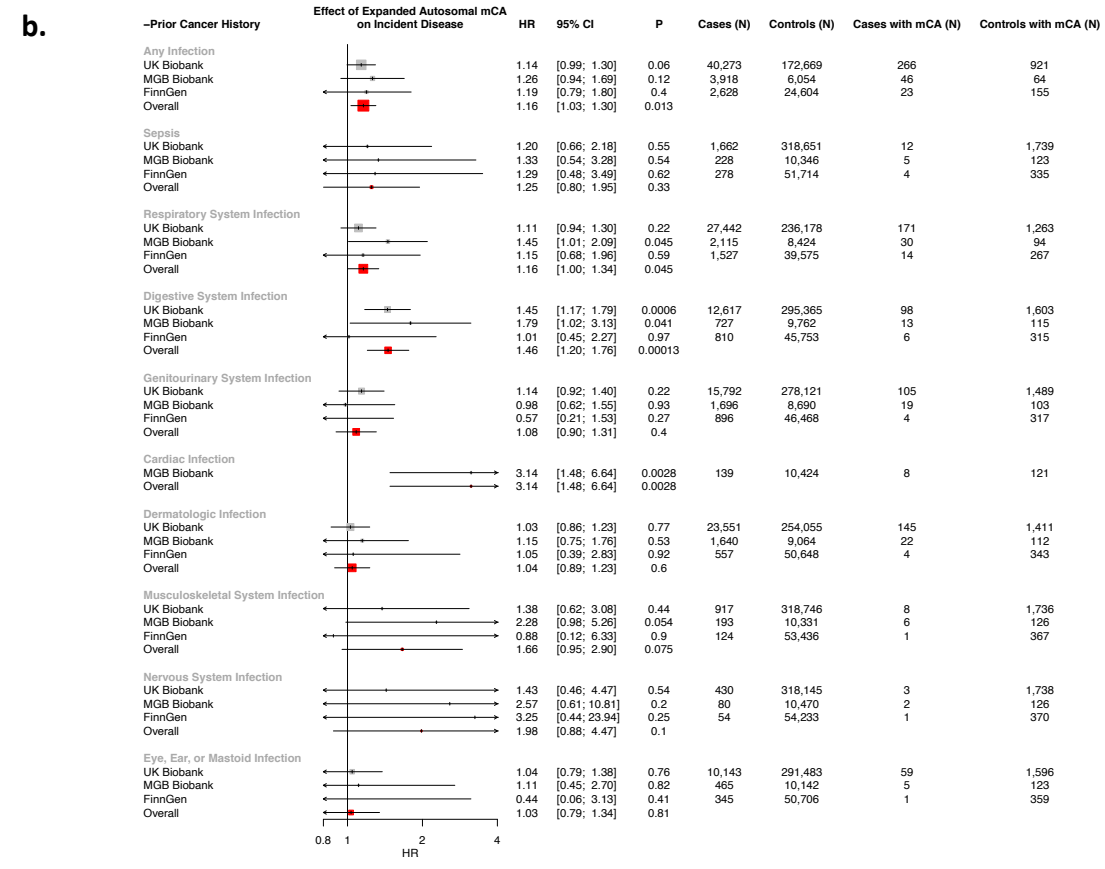


Supplementary Figure 13: Associations of expanded autosomal mCAs with incident sepsis and among different age strata in the UK Biobank by Cox proportional-hazards models with the underlying time scale of time-on-study. Analyses are adjusted for age, age^2, sex, smoking status, and principal components 1-10 of ancestry. Bonferroni correction was used to determine the level of statistical significance. Error bars show 95% confidence intervals. Individuals with prevalent hematologic cancer were excluded from analyses. Associations were adjusted for sex, ever smoking status, and principal components 1-10 of ancestry. mCA = mosaic chromosomal alterations.

a.

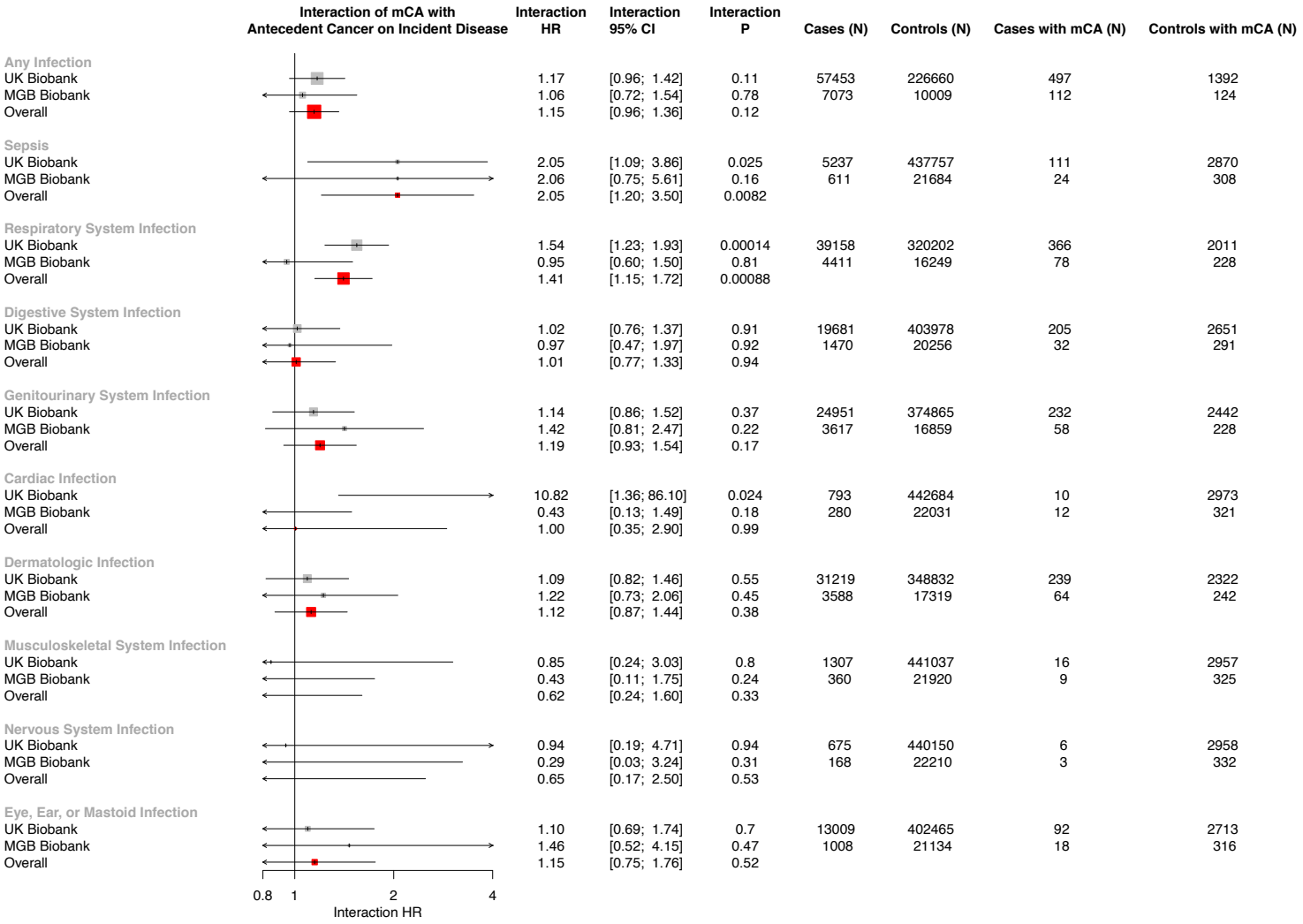


b.

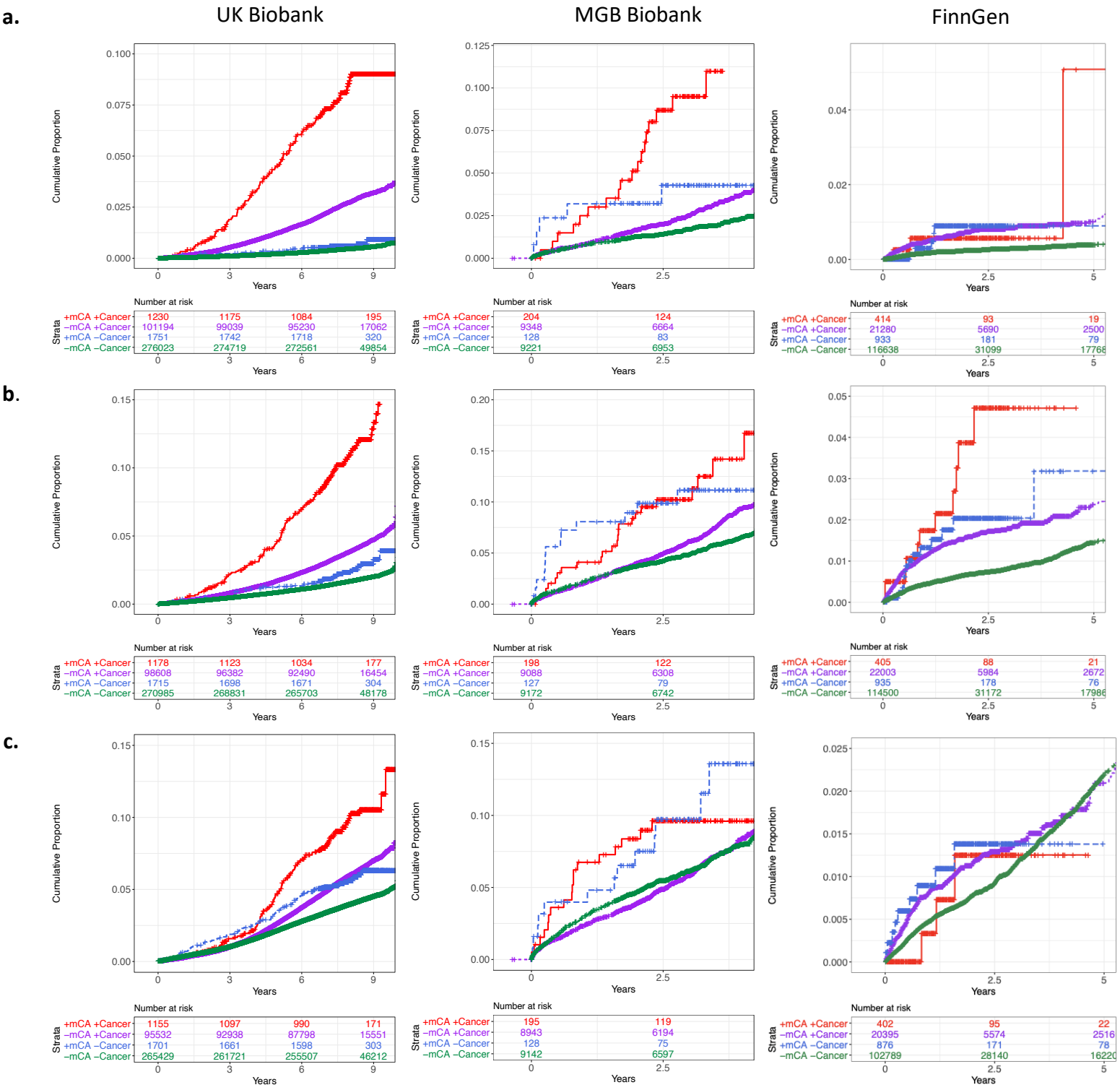


Supplementary Figure 14: Associations of expanded autosomal mCAs with incident infections among A) those with antecedent cancer (ie: cancer prior to their infection) B) those without

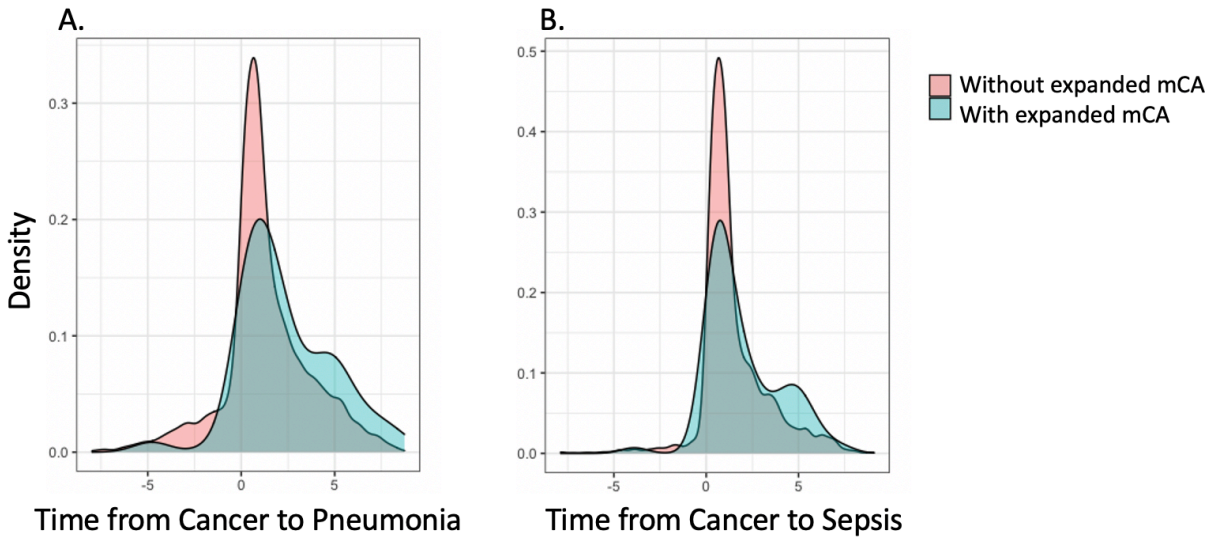
antecedent cancer. Cox proportional-hazards models with the underlying time scale of time-on-study are employed to access the associations. Analyses are adjusted for age, age^2, sex, smoking status, and principal components 1-10 of ancestry. Bonferroni correction was used to determine the level of statistical significance. Overall estimates across studies are generated via fixed effect meta-analysis. Error bars show 95% confidence intervals. mCA = mosaic chromosomal alterations.



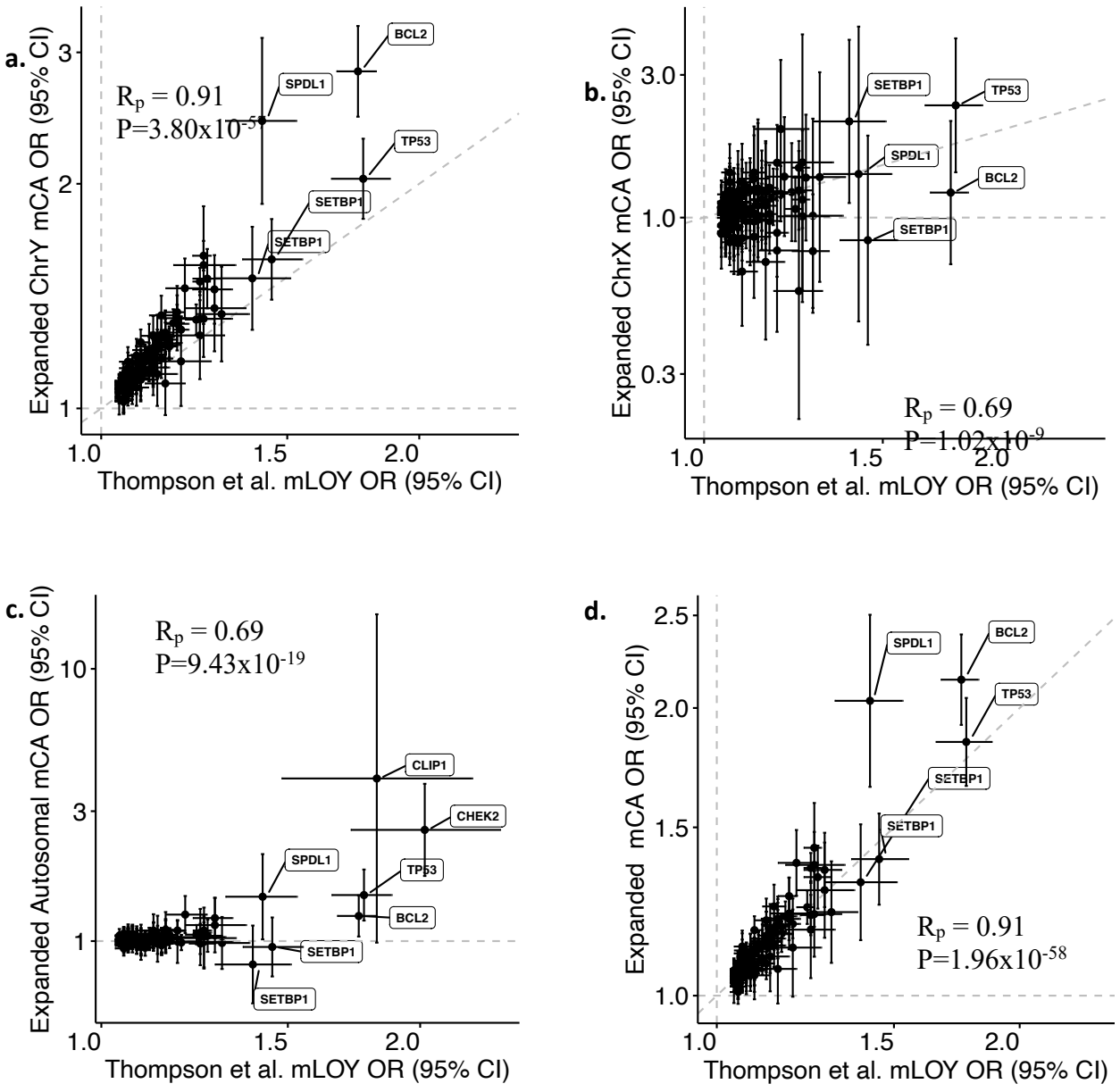
Supplementary Figure 15: Interaction of expanded autosomal mCAs with antecedent cancer prior to infection in the UK Biobank and MGB Biobank evaluated by Cox proportional-hazards models with the underlying time scale of time-on-study. Analyses are adjusted for age, age^2, sex, smoking status, and principal components 1-10 of ancestry. Bonferroni correction was used to determine the level of statistical significance. Overall estimates across studies are generated via fixed effect meta-analysis. Error bars show 95% confidence intervals. mCA = mosaic chromosomal alterations.



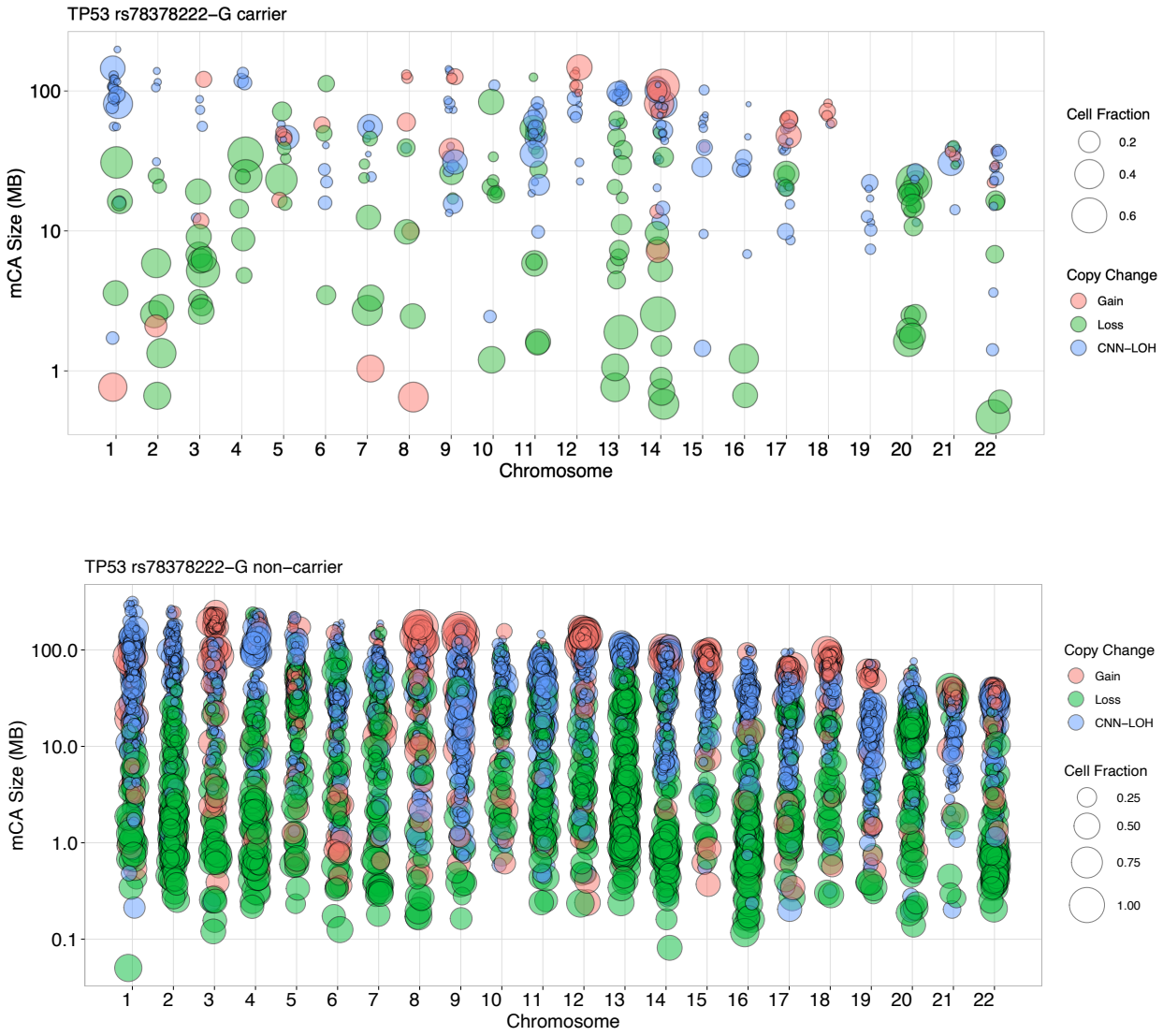
Supplementary Figure 16: Cumulative incidence curves visualizing the association of expanded autosomal mCAs with incident infections stratified by prior cancer status. **a.** sepsis, **b.** pneumonia, and **c.** digestive system infection across carrier status for expanded autosomal mCAs and any cancer diagnosis prior to the incident infection date. Individuals with known hematologic cancer at time of or prior to blood draw for genotyping were excluded. mCA = mosaic chromosomal alterations.



Supplementary Figure 17: Time difference between cancer diagnosis and A) pneumonia B) sepsis. mCA = mosaic chromosomal alterations



Supplementary Figure 18: Association of a mLOY PRS consisting of 156 previously identified[1] independent genome-wide significant variants associated with mLOY from Thompson et al (Nature 2019), with a) expanded ChrY mCA, b) expanded ChrX mCA, c) expanded Autosomal mCA, and d) all expanded mCAs in UKB. Logistic regression models are adjusted for age, age^2, sex, smoking status, and principal components 1-10 of ancestry. Bonferroni correction was used to determine the level of statistical significance. mCA = mosaic chromosomal alterations, mLOY = mosaic Loss-of-chromosome Y, PRS = polygenic risk score.



Supplementary Figure 19: Autosomal mCAs carried by UKB individuals with TP53 rs78378222-G are diverse in size, copy-change, and location in the genome.

	UK Biobank	MGB Biobank	FinnGen*	Biobank Japan	CUB
N	444,199	22,461	175,690	125,541	871
Age of DNA collection (mean (SD))	56.5 (8)	55.0 (16.8)	53.4 (18.4)	64.6 (12.4)	62.3 (17.9)
Sex (Male (%))	204,579 (46.1%)	10,306 (45.9%)	71,000 (40.4)	72,186 (57.5%)	480 (55.1%)
Prior or Current Smoker (%)	188,875 (45.0%)	9,094 (40.5%)	30,554 (42.7)	66,913 (53.3%)	NA
Race	White: 417,828 (94.1%) Asian: 10,277 (2.3%) Black: 7,173 (1.6%) Mixed: 2,634 (0.6%) Other: 4,160 (0.9%) Unknown 187 (0.04%)	White: 18,933 (84.3%) Asian: 569 (2.5%) Black: 1,056 (4.7%) Other: 744 (3.3%) Unknown: 1,159 (5.2%)	White: 175,690 (100%)	Asian: 125,541 (100%)	Hispanic: 450 (51.7%) Black: 125 (14.4%) White: 97 (11.1%) Asian: 5 (0.6%) Other: 3 (0.3%) Unknown: 191 (22.0%)
BMI (mean (SD))	27.4 (4.8)	28.5 (6.2)	NA	23.4 (3.7)	NA
Prevalent Solid Cancer	66,551 (15.0%)	6,080 (27.1%)	31,855 (18.1%)	25,987 (20.7%)	221 (25.4%)
Prevalent Type 2 Diabetes Mellitus	10,835 (2.4%)	1,782 (7.9%)	22,326 (13.2%)	31,636 (25.2%)	310 (35.6%)
Prevalent Coronary Artery Disease	25,287 (5.7%)	3,908 (17.4%)	19,474 (11.1%)	23,099 (18.4%)	176 (20.2%)
Prevalent Hypertension	129,888 (29.2%)	11,010 (49.0%)	NA	37,913 (30.2%)	468 (53.7%)
Prevalent Hypercholesterolemia	66,483 (15.0%)	9,881 (44.0%)	8,583 (5.2%)	35,026 (27.9%)	NA

Supplementary Table 1: Baseline summary statistics across the UK Biobank, MGB Biobank, FinnGen, Biobank Japan, and Columbia University Biobank (CUB) among individuals analyzed.
* of note, 104,175 individuals from FinnGen had missing smoking status; BMI and hypertension were not available
BMI = body mass index; MGB = Mass General Brigham; SD = standard deviation.

	UK Biobank	*MGB Biobank*	*FinnGen*	*Biobank Japan*	*CUB*
N	444,199	22,461	175,690	125,541	871
Any mCA(%)	66,011 (14.9)	3,784 (16.8)	22,040 (12.5)	NA	258 (29.6)
Autosomal mCA (%)	15,350 (3.5)	1,025 (5.2)	3,164 (2.0)	20,440 (16.3)	168 (19.3)
ChrX (%)	12,265 (5.1)	820 (7.0)	7,058 (6.8)	NA	65 (7.5)
ChrY (%)	41,284 (20.1)	2,201 (22.0)	12,599 (18.0)	NA	67 (7.7)
Any expanded mCA (%)	12,398 (3.2)	1,026 (5.2)	9,558 (5.9)	NA	177 (20.3)
Expanded autosomal mCA (%)	2,985 (0.8)	337 (1.8)	1,620 (1.0)	1,676 (1.3%)	128 (14.7)
Expanded ChrX (%)	397 (0.2)	44 (0.2)	479 (0.5)	NA	8 (0.9)
Expanded ChrY (%)	9168 (4.5)	669 (3.4)	7663 (11.8)	NA	54 (6.2)

Supplementary Table 2: mCA counts by cohort.
Chr = chromosome; CUB = Columbia University Biobank, mCA = mosaic chromosomal alteration; MGB = Mass General Brigham; N = number.

	OR	*Lower 95% CI*	*Upper 95% CI*	*P*
Age	0.92	0.86	1.005	0.068
Age^2	1.0013	1.0006	1.002	2.84E-05
Sex (Male)	1.44	1.33	1.56	1.33E-19
Prior or Current Smoking	1.09	1.01	1.18	0.03
Prevalent Solid Cancer	0.95	0.82	1.09	0.44
Prevalent Type 2 Diabetes Mellitus	1.05	0.84	1.32	0.66

Supplementary Table 3: Association of potential risk factors with expanded autosomal mCAs in the UK Biobank. Logistic regression models are adjusted for variables listed in the table. Bonferroni correction was used to determine the level of statistical significance.
CI = confidence interval; OR = odds ratio

Phenotype	*Exposure*	*Sex*	*HR*	*P*	*Controls (N)*	*Incident Cases (N)*	*Incident Cases with mCA (N)*	*Controls with mCA (N)*
Nervous System Infection	Autosomal mCA	Male	3.71	0.0085	39,978	17	8	6,298
Meningitis or Encephalitis		Male	3.71	0.0085	39,978	17	8	6,298
Pneumonia		All	1.16	0.023	72,317	1,299	334	10,485
Nervous System Infection		All	2.81	0.025	72,317	21	8	10,485
Meningitis or Encephalitis		All	2.81	0.025	72,317	21	8	10,485
Respiratory System Infection		All	1.15	0.028	72,317	1,353	346	10,485
Any Infection		All	1.12	0.037	72,317	1,998	476	10,485
Pneumonia		Male	1.17	0.039	39,978	928	259	6,298
Endocarditis or Myocarditis		Female	2.46	0.043	32,339	25	8	4,187
Respiratory System Infection		Male	1.16	0.050	39,978	971	269	6,298
Sepsis	Expanded	All	2.04	0.050	72,317	276	8	753
Sepsis	Autosomal mCA	All	2.04	0.050	72,317	276	8	753

Supplementary Table 6: Association of mCAs with mortality from incident infection in Biobank Japan by Cox proportional-hazards models with the underlying time scale of time-on-study. Analyses are adjusted for age, age^2, sex, smoking status, and principal components 1-10 of ancestry. Bonferroni correction was used to determine the level of statistical significance. Suggestive associations (P<0.05) are presented among individuals without antecedent cancer prior to the infection phenotype.
HR = hazard ratio; mCA = mosaic chromosomal alteration; N = number

Incident Sepsis Multivariate Model Component	*HR*	*P*	*Lower 95% CI*	*Upper 95% CI*
Expanded Autosomal mCA	2.00	2.64E-08	1.56	2.54
Antecedent Cancer Prior to Incident Sepsis	5.49	<1E-300	5.09	5.93
Age	1.02	0.64	0.95	1.09
Age^2	1.00	0.41	1.00	1.00
Sex (Male)	1.27	9.56E-11	1.18	1.37
current cigar pipe smoker, former cigarette smoker	1.90	0.011	1.16	3.12
current cigar pipe smoker, not former cigarette smoker	1.81	0.077	0.94	3.49
current cigarette smoker, 10 to <20/day	1.83	1.79E-10	1.52	2.20
current cigarette smoker, 20 to <40/day	2.06	8.23E-14	1.70	2.49
current cigarette smoker, <10/day	1.39	0.047	1.00	1.92
current cigarette smoker, ≥40/day	3.33	3.65E-05	1.88	5.89
current occasional smoker, smoked cigarettes daily in past, <20/day	1.37	0.19	0.86	2.18
current occasional smoker, smoked cigarettes daily in past, ≥20/day	1.83	0.01	1.13	2.96
current occasional smoker, smoked cigars or pipes daily in past	0.51	0.50	0.07	3.60
current occasional smoker, smoked ≥100 cigarettes in lifetime	0.99	0.94	0.70	1.39
former cigarette smoker, <20/day, quit 1-5 year ago	1.14	0.48	0.80	1.63
former cigarette smoker, <20/day, quit 10-20 year ago	1.15	0.27	0.90	1.46
former cigarette smoker, <20/day, quit 5-10 year ago	1.29	0.11	0.94	1.78
former cigarette smoker, <20/day, quit <1 year ago	1.90	0.06	0.98	3.65
former cigarette smoker, <20/day, quit ≥20 year ago	1.08	0.34	0.92	1.26
former cigarette smoker, ≥20/day, quit 1-5 year ago	2.25	1.07E-13	1.82	2.79
former cigarette smoker, ≥20/day, quit 10-20 year ago	1.54	7.00E-07	1.30	1.82
former cigarette smoker, ≥20/day, quit 5-10 year ago	1.64	1.11E-05	1.31	2.04
former cigarette smoker, ≥20/day, quit <1 year ago	2.08	0.0064	1.23	3.53
former cigarette smoker, ≥20/day, quit ≥20 year ago	1.25	0.00080	1.10	1.42
former daily cigar pipe smoker	1.23	0.19	0.91	1.66
former occasional cigarette smoker, lifetime cigarette smoking unknown	1.07	0.76	0.70	1.63
former occasional cigarette smoker, smoked <100 cigarettes in lifetime	1.27	0.085	0.97	1.66
former occasional cigarette smoker, smoked ≥100 cigarettes in lifetime	1.02	0.72	0.90	1.17
Missing smoking	1.55	0.0085	1.12	2.15
BMI (SD)	1.21	7.08E-31	1.17	1.25
Prevalent Type 2 Diabetes Mellitus	1.84	1.75E-16	1.59	2.12
Leukocyte count (SD)	1.31	1.38E-07	1.19	1.45
Lymphocyte count (SD)	0.71	4.57E-07	0.63	0.81
Lymphocyte percentage (SD)	1.12	0.054	1.00	1.27
PC1	0.98	0.18	0.96	1.01
PC2	0.99	0.42	0.97	1.01
PC3	0.99	0.59	0.97	1.02
PC4	0.99	0.37	0.98	1.01
PC5	1.01	0.07	1.00	1.01
PC6	1.01	0.46	0.99	1.03
PC7	0.99	0.23	0.97	1.01
PC8	1.01	0.58	0.99	1.03
PC9	1.00	0.58	0.99	1.01
PC10	1.00	0.61	0.99	1.02

Supplementary Table 7: Sensitivity analysis of incident sepsis association in the UK Biobank with the addition of a 25-factor smoking covariate, leukocyte count, lymphocyte count and percentage, BMI, and prevalent type 2 diabetes mellitus. Cox proportional-hazards models are adjusted for variables listed in the table. Bonferroni correction was used to determine the level of statistical significance.
BMI = body mass index; CI = confidence interval; HR = hazard ratio; PC = principal component; SD = standard deviation

Outcome	*Population of people with cancer prior to infection*	*HR*	*P*	*Lower 95% CI*	*Upper 95% CI*	*Cases (N)*	*Controls (N)*	*Cases with mCA (N)*	*Controls with mCA (N)*
Sepsis	Prevalent Solid Cancer	1.86	0.0097	1.16	2.96	1258	64921	20	521
	Incident Solid Cancer Prior to Infection	0.76	0.44	0.38	1.53	1619	51867	10	361
	Incident Hematologic Cancer Prior to Infection	0.98	0.88	0.77	1.25	833	2864	83	312
	Incident Hematologic Cancer and Prevalent Solid Cancer Prior to Infection	0.94	0.85	0.52	1.72	144	546	15	63
	Any Cancer Prior to Infection	2.82	5.28E-22	2.28	3.48	3575	119106	99	1131
Pneumonia	Prevalent Solid Cancer	1.68	0.0057	1.16	2.43	2382	62325	40	480
	Incident Solid Cancer Prior to Infection	1.33	0.18	0.87	2.03	2369	49466	24	323
	Incident Hematologic Cancer Prior to Infection	1.19	0.18	0.92	1.54	655	2886	80	300
	Incident Hematologic Cancer and Prevalent Solid Cancer Prior to Infection	1.73	0.076	0.94	3.18	119	528	16	55
	Any Cancer Prior to Infection	2.26	5.08E-17	1.86	2.73	5295	114149	130	1048

Supplementary Table 8: Sensitivity analysis of incident sepsis and pneumonia association in the UK Biobank among populations of individuals with different types of cancer prior to incident infection, where solid cancer is defined as any non-hematologic cancer. Cox proportional-hazards models with the underlying time scale of time-on-study are adjusted for age, age^2, sex, smoking status, and PC1-10 of ancestry as well as variables listed in the table. Bonferroni correction was used to determine the level of statistical significance.
CI = confidence interval; HR = hazard ratio; mCA = mosaic chromosomal alteration; N = number

Outcome	*Adjustment*	*HR*	*P*	*Lower 95% CI*	*Upper 95% CI*
Sepsis	Chemotherapy	2.39	6.80E-16	1.93	2.65
	Neutropenia	1.72	5.79E-07	1.39	1.91
	Aplastic anemia	2.39	8.06E-16	1.94	2.66
	Decreased white blood cell count	1.72	5.79E-07	1.39	1.91
	Bone marrow or stem cell transplant	2.59	8.64E-19	2.10	2.88
	Effects radiation NOS	2.63	2.65E-19	2.13	2.92
Pneumonia	Chemotherapy	1.94	1.00E-11	1.60	2.13
	Neutropenia	1.82	8.26E-10	1.50	2.00
	Aplastic anemia	1.91	3.21E-11	1.58	2.10
	Decreased white blood cell count	1.82	8.26E-10	1.50	2.00
	Bone marrow or stem cell transplant	2.00	9.82E-13	1.65	2.20
	Effects radiation NOS	2.04	2.52E-13	1.68	2.24

Supplementary Table 9: Sensitivity analysis of expanded autosomal mCA with incident sepsis and with pneumonia association in the UK Biobank among those with cancer prior to incident infection, separately adjusting for chemotherapy, neutropenia, aplastic anemia, decreased white blood cell count, bone marrow or stem cell transplant, and radiation effects prior to infection (as defined using the Vanderbilt ICD-10 and ICD-9 phecode groupings[10]) in Cox proportional hazards models. Other covariates in the model included age, age^2, sex, smoking status, PC1-10 of ancestry, and several common cancer subtypes (malignant neoplasm, nervous system cancer, bladder cancer, breast cancer, prostate cancer, cervical_cancer, colorectal cancer, lung cancer, and skin cancer) to adjust for potential differences in the adjustment parameter across different neoplasms. The summary stats (HR, P-value, 95% CI) reflect those for the expanded autosomal mCA term in each model. Bonferroni correction was used to determine the level of statistical significance.
CI = confidence interval; HR = hazard ratio; mCA = mosaic chromosomal alteration; N = number; NOS = not otherwise specified

Disease	Time since cancer diagnoses	Case with expanded mCA	Incidence Rate Ratio [95% CI]	P
Pneumonia	>0	90	2.25 [1.99, 2.55]	$< 2.2 \times 10^{-16}$
Pneumonia	0-3	59	1.06 [0.91, 1.22]	0.46
Pneumonia	>3	31	2.38 [1.85, 3.07]	2.99×10^{-12}
Sepsis	>0	79	1.57 [1.33, 1.84]	4.26×10^{-8}
Sepsis	0-3	58	0.87 [0.73, 1.05]	0.14
Sepsis	>3	21	2.02 [1.42, 2.87]	6.08×10^{-5}

Supplementary Table 10: Differences in incidence rate of post-cancer diagnosis infections by mCA status. Estimates of confidence interval were calculated by following Ederer and Mantel, 1974[2]. Bonferroni correction was used to determine the level of statistical significance. mCA = mosaic chromosomal alterations

Predictor	*OR*	*SE*	*Lower 95% CI*	*Upper 95% CI*	*P*
Expanded Autosomal mCAs	1.52	0.19	1.04	2.21	3.09E-02
Sex: Male	1.36	0.15	1.02	1.83	3.92E-02
Age (per year)	1.02	0.00	1.01	1.03	1.78E-07
Population: African	1.00	0.30	0.56	1.79	9.96E-01
Population: Hispanic	0.94	0.25	0.57	1.52	7.89E-01
Population: Other/Unknown	1.04	0.27	0.61	1.79	8.72E-01

Supplementary Table 11: Columbia University Biobank COVID-19 cohort ordinal regression analysis for expanded autosomal mCAs. The COVID-19 outcome phenotypes are classified into three ordinal categories: mild (non-hospitalized; WHO stage 1-3), moderate (requiring hospitalization; WHO stage 4-6), and severe (death or intubation; WHO stage 7-10) cases. The model is adjusted for age, sex, and self-reported ancestry. Bonferroni correction was used to determine the level of statistical significance.
OR = Odds Ratio, SE = Standard Error, CI = Confidence Interval.

Models	*N*	*Severe*	*Moderate*	*Mild*	*OR*	*SE*	*Lower 95% CI*	*Upper 95% CI*	*P*
Original model	871	379	440	52	1.52	0.19	1.04	2.21	3.09E-02
Cancer adjustment	871	379	440	52	1.51	0.19	1.04	2.21	3.15E-02
Cancer interaction	871	379	440	52	1.51	0.23	0.97	2.35	7.12E-02
Cancer exclusion	650	277	335	38	1.50	0.23	0.96	2.35	7.40E-02

Supplementary Table 12: Sensitivity analysis of cancers and COVID-19 association in the Columbia University Biobank COVID-19 cohort. The COVID-19 outcome phenotypes are classified into three ordinal categories: mild (non-hospitalized; WHO stage 1-3), moderate (requiring hospitalization; WHO stage 4-6), and severe (death or intubation; WHO stage 7-10) cases. The original model is ordinal logistic regression analysis for expanded autosomal mCAs with adjustment for age, sex, and self-reported ancestry. In addition to the original model, the cancer adjustment model incorporates cancer status as a covariate and the cancer interaction model is further adjusted for interaction between cancer status and mCA. The cancer exclusion model is the original model performed on a subset of individuals excluding 221 patients with any cancers. Bonferroni correction was used to determine the level of statistical significance. OR = Odds Ratio, SE = Standard Error, CI = Confidence Interval.

y	*OR*	*P*	*Lower 95% CI*	*Upper 95% CI*	*TP53 rs78378222_G Carriers (N)*	*TP53 rs78378222_G WT (N)*	*mCA cases with TP53 variant (N)*	*mCA controls with TP53 variant (N)*
Any mCA	1.53	7.17E-50	1.45	1.62	9421	432822	1985	7436
Expanded mCA	1.85	4.23E-28	1.66	2.06	7867	381035	431	7436
Autosomal mCA	1.17	0.0033	1.05	1.31	9421	432822	393	9028
Expanded Autosomal mCA	1.51	0.00031	1.21	1.88	7526	372014	90	7436
ChrX mCA	1.31	5.08E-06	1.17	1.48	4995	233601	349	4646
Expanded ChrX mCA	2.26	0.0038	1.30	3.92	4501	215356	22	4479
ChrY mCA	1.79	8.81E-56	1.66	1.92	4426	199221	1348	3078
Expanded ChrY mCA	2.03	1.33E-27	1.79	2.31	3284	162944	327	2957
Thompson et al. mLOY	1.77	1.40E-70	1.65	1.88				

Supplementary Table 14: Association of TP53 rs78378222_G with mCAs across the genome. Logistic regression model was used among unrelated individuals adjusting for age, age2, sex, PC1-10 of genetic ancestry, and genotyping array. Bonferroni correction was used to determine the level of statistical significance.

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References:

1. Thompson, D.J.*, et al.* Genetic predisposition to mosaic Y chromosome loss in blood. *Nature* **575**, 652-657 (2019).
2. Ederer, F. & Mantel, N. Confidence limits on the ratio of two Poisson variables. *Am J Epidemiol* **100**, 165-167 (1974).