Supplementary Online Content

Moore SC, Lee I-M, Weiderpass E, et al. Association between leisure-time physical activity and risk of 26 types of cancer. *JAMA Intern Med*. Published online May 16, 2016. doi:10.1001/jamainternmed.2016.1548

eFigure 3. Summary multivariable hazard ratios (HR) and 95% confidence intervals (CI) for a high (90th percentile) versus low (10th percentile) level of leisure-time physical activity, by cancer type, with adjustment for BMI

eFigure 4. Summary multivariable hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by geographic region, United States or Europe.

eFigure 5. Summary multivariable hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by history of hormone replacement therapy, never users or ever users.

eFigure 6. Summary multivariable hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by gender.

eFigure 7. Summary multivariable hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by race/ethnicity.

eFigure 8. Summary multivariable hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by period of follow-up.

eFigure 9. Multivariable hazard ratios (HRs) and 95% confidence intervals (CIs) in the NIH-AARP Diet and Health Study for breast cancer subtypes (Panel A), for prostate cancer subtypes (Panel B), and for malignant melanoma, stratified by ground level solar ultraviolet radiation† (Panel C).

eAcknowledgments

eMethods. Physical activity questionnaire validation and NIH-AARP Diet and Health Study analyses

Physical activity questionnaire validation

Of the 12 physical activity assessments used in our pooled analysis, 10 of these assessments—or assessments worded nearly identically to these 10—have been previously validated. Several cohorts, for example, have adapted the following question from the College Health Alumni Study:

> "At least once a week, do you engage in any regular activity similar to brisk walking, jogging, bicycling, etc., long enough to work up a sweat? If yes, how many times per week?"

In the Breast Cancer Detection and Demonstration Project (BCDDP), participants were asked:

> "At least once a week, do you engage in any regular activity similar to brisk walking, bicycling, etc., long enough to work up a sweat? (If yes) Number of times per week?

In the Physician's Health Study (PHS), participants were asked:

> "Do you engage in a regular program of exercise vigorous enough to work up a sweat? If yes, how many days per week?"

The College Health Alumni survey question, and alternate versions performed similarly in validation studies[1-3], as reviewed in 2011 by Milton et al[4].

The table below shows, for each cohort, a study or studies examining the validity of the physical activity assessment used, or a nearly identical instrument. Reference measures in these studies included seven day physical activity records, accelerometry, and doubly labeled-based assessments of physical activity.

Cohort	Validation study	Reference measure	Primary findings
AARP	Milton et al. 2011[4] Milton et al. 2013[5]	Accelerometry	r=0.46 between self-reported days of 30+ minutes of MVPA vs. accelerometry-measured days of 30+ minutes of MVPA
BCDDP	Milton et al. 2011[4] Milton et al. 2013[5]	Accelerometry	r=0.46 between self-reported days of 30+ minutes of MVPA vs. accelerometry-measured days of 30+ minutes of MVPA
COSM	Orsini et al.[6]	7-day physical activity record	r=0.42 between past year leisure-time activity and 7-day record leisure-time physical activity
CPSII	Bonnefoy et al.[7]	Doubly labeled water*	r=0.61 between participation in leisure time activities and physical activity level ratio
EPIC	Besson et al.[8]	Doubly labeled water*	r=0.44 between recreational physical activity and PAEE**
IWHS	Marshall et al.[9]	Accelerometry	71% agreement between self-report and accelerometry in number of days meeting physical activity recommendations (kappa=0.4)
PHS	Milton et al. 2011[4] Milton et al. 2013[5]	Accelerometry	r=0.46 between self-reported days of 30+ minutes of MVPA vs. accelerometry-measured days of 30+ minutes of MVPA

SMC	Orsini et al.[6]	7-day physical activity record	r=0.42 between past year leisure-time activity and 7-day record leisure-time physical activity
USRT	Orsini et al.[6]	7-day physical activity record	r=0.42 between past year leisure-time activity and 7-day record leisure-time physical activity
WLH	None		
WHS	Bonnefoy et al.[7]	Doubly labeled water*	r=0.61 between participation in leisure time activities and physical activity level ratio
PLCO	None		

NIH-AARP Diet and Health Study analyses

We conducted three additional analyses solely within the NIH-AARP Diet and Health Study to take advantage of data items not otherwise available to the consortium. Specifically, we evaluated 1) associations between physical activity and risk of non-advanced, advanced, and fatal prostate cancers; 2) associations between physical activity and risk of estrogen receptor positive (ER+) and estrogen receptor negative (ER-) breast cancers; and; 3) the association between physical activity and risk of malignant melanoma, stratified by ground-level solar ultraviolet radiation exposure.

The NIH-AARP analyses included a total of 507,826 participants, including 308,073 men and 199,753 women, from 11 different states who were followed for cancer incidence from 1995 through 2006. Incident first primary cancer cases were identified through probabilistic linkage with cancer registry databases for the state of residence for study participants. The cancer registries are certified by the North American Association of Central Cancer Registries as being ≥90% complete within two years of cancer occurrence and we have previously validated that cancer case ascertainment through these registries is approximately 90% complete within our cohort[10]. Incident cancer cases were invasive and comprised only the first malignancy diagnosed during the follow-up period if multiple cancers were diagnosed in the same participant.

Analyses of non-advanced, advanced, and fatal prostate cancers

Information on prostate cancer stage was obtained from the state cancer registry databases. Advanced prostate cancer cases were defined as cases with clinical or pathologic tumor classifications, according to the American Joint Committee on Cancer 1998 tumor-lymph node-metastasis classification system[11], of T3 or T4, N1 status, or M1 status, or incident cases who subsequently died of prostate cancer (through 2011). Any incident cases that subsequently died from prostate cancer (through 2011) were also classified as fatal cases. Censoring of follow-up occurred on the date of the incident case, regardless of later mortality.

Analyses of estrogen receptor positive (ER+) and estrogen receptor negative (ER-) breast cancers

Hormone receptor status was available from 7 (California, Louisiana, Georgia, North Carolina, New Jersey, Arizona, and Nevada) of the 11 reporting states, with a positive hormone receptor status recorded at a threshold of at least 10 fmol receptor/mg total protein. Although hormone receptor data were unavailable for cases from Florida, Pennsylvania, Michigan, and Texas, the distribution of risk factors considered in our study was similar for women from states with and without hormone receptor information.

Analyses stratified by solar ultraviolet radiation for malignant melanoma

Solar ultraviolet radiation (erythemal dose) was assessed from the Total Ozone Mapping Spectrometer (TOMS) dataset of the National Aeronautics and Space Administration. The NASA TOMS database (http://toms.gsfc.nasa.gov) provided ground-level noon-time erythemal estimates on a 1° latitude by 1.25° longitude grid within the United States. Erythemal exposure was assigned by deterministic linkage of the census tract centroid of participant residence to the closest point on the TOMS grid using ArcView 9.3 (Esri,Redlands, CA). The census tract for each subject was assigned by geocoding the longitude and latitude coordinates of residential address. The erythemal exposure was averaged across the month of July because summer is when surface UVR is strongest, noise factors such as clouds and aerosols are less influential[12], and because it is when the TOMS UVR data are in their best agreement with ground-based data[13]. Erythemal exposure was expressed in terms of biological damage per square meter[14].

We analyzed associations between physical activity and melanoma according to low and high solar ultraviolet radiation exposure levels, defined as the bottom tertile and the top two tertiles of erythemal exposure. Multiplicative interaction was determined by modeling with and without the cross-products of physical activity and erythemal exposure group, and conducting likelihood ratio tests.

eMethods references

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eTable 1. Case numbers in the current study as compared with those in most recent meta-analyses examining leisure time physical activity and cancer risk in prospective studies

Cancer	Reference	Current study	Literature meta-analysis	Ratio†
Esophageal adenocarcinoma	1	899	454	2.0
Gallbladder	2	382	123	3.1
Liver*	2	1,384	628	2.2
Lung	3	19,133	12,966	1.5
Kidney	4	4,548	2,435	1.9
Small intestine*	5	503	237	2.1
Gastric cardia adenocarcinoma	1	790	436	1.8
Endometrial	6	5,346	4,525	1.2
Esophageal squamous cell carcinoma	1	442	149	3.0
Myeloid leukemia	7	1,692	338	5.0
Myeloma	8	2,161	1,355	1.6
Colon	9	14,160	15,537	0.9
Head and neck*	10	3,985	1,249	3.2
Rectum	11	5,531	2,617	2.1
Bladder	12	9,073	3,418	2.7
Breast	13	35,178	37,568	0.9
Non-Hodgkin Lymphoma	8	6,953	3,897	1.8
Thyroid	14	1,829	818	2.2
Gastric non-cardia adenocarcinoma	1	1,428	781	1.8
Soft Tissue	--	851	0	∞
Pancreas	15	4,186	5,720	0.7
Lymphocytic leukemia	--	2,160	0	∞
Ovary	16	2,880	2,467	1.2
Brain*	17	2,110	257	8.2
Prostate	18	46,890	31,106	1.5
Malignant melanoma	--	12,438	0	∞

* Case numbers are based on the largest prospective cohort study as no meta-analyses or reviews have been published

† Ratio compares the number of cases in the present study with those in the cited literature

eTable 1 references

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eTable 2. Median and interquartile range (IQR) of physical activity levels in the seven cohorts in which MET-hours/week could be estimated

Study	Median (IQR) MET-hours/week
Cohort of Swedish Men	8 (4-16)
Cancer Prevention Study II	8 (4-18)
Prostate, Lung, Colorectal, and Ovarian Cancer Trial	8 (2-12)
Swedish Mammography Cohort	8 (4-8)
U.S. Radiologist Technologist Study	8 (2-22)
Women's Health Study	8 (2-17)
Women's Lifestyle and Health Study	11 (3-23)

eTable 3. *International Classification of Diseases for Oncology, 3rd Ed. Codes* by cancer site

Cancer site	ICD-O-3 codes and, if applicable, ICD-O-3 histology
Esophageal adenocarcinoma	C150-159; histologies 8140,8142,8144,8261,8310,8480,8481,8570
Gallbladder	C239
Liver*	C220 and C221
Lung	C340-C349; excluding 9050-9055, 9140, 9590-9992
Kidney	C649 and C659
Small intestine	C170-179
Gastric cardia	C160
Endometrial	C540-C549 and C559
Esophageal squamous	C150-159; histologies 8041,8070,8071,8072,8074
Myeloid leukemia	Any histology of 9840, 9861, 9865-9867, 9869, 9871-9874, 9895-9897, 9898, 9910-9911, 9920, 9891, 9863, 9875-9876, 9945-9946, 9860, 9930
Myeloma	Histology 9731-9732, 9734
Colon	C180-C189, C260
Head and neck	C000-C009, C019-C119, C129-C140, C142-C148, C300-C301, C310-C329, C339-C349, C381-C384, C388, C390, C398, and C399
Rectum	C199, C209; excluding histologies 9050-9055, 9140, 9590-9992
Bladder	C670-C679
Breast	C500-C509
Non-Hodgkin's Lymphoma	C024, C098, C099, C111, C142, C379, C422, C770-C779 & histologies of: 9590-9597, 9670-9671, 9673, 9675, 9678-9680, 9684, 9687-9691, 9695, 9698-9702, 9705, 9708-9709, 9712, 9714-9719, 9724-9729, 9735, 9737-9738, 9811-9818, 9823, 9827, 9837 All sites except C024, C098-C099, C111, C142, C379, C422, C770-C779 & histologies of: 9590-9597, 9670-9671, 9673, 9675, 9678-9680, 9684, 9687, 9688, 9689-9691, 9695, 9698-9702, 9705, 9708-9709, 9712, 9714-9719, 9724-9729, 9735, 9737, 9738 All sites except C024, C098-C099, C111, C142, C379, C420-C422, C424, C770-C779 & histologies of: 9811-9818, 9823, 9827, 9837
Thyroid	C739
Gastric non-cardia	C161-169
Soft tissue	C380, C470-C479, C490-C499; excluding histologies 9050-9055, 9140, 9590-9992
Pancreas	C250-C259; excluding histologies 9050-9055, 9140, 9590-9992
Lymphocytic leukemia	Any histology of 9826, 9835-9836, 9820, 9832-9834, 9940. C420, C421, C424; histologies of 9811-9818, 9837, 9823
Ovary	C569
Brain	C710-C719
Prostate‡	C619
Malignant melanoma	C440-C449; histologies 8720-8790

* A small proportion (17%) of the liver cancer classification consists of intrahepatic bile duct cancer cases

† A small proportion (9%) of the kidney cancer classification consists of renal pelvis cancer cases

‡ Advanced prostate cancer cases were defined as cases with clinical or pathologic tumor classifications of T3 or T4, N1 status, or M1 status, or as cases first identified by stage cancer registry and who subsequently died of prostate cancer between 1995 and December 31, 2006.

eTable 4. Number of cohorts and cases excluded due to insufficient case numbers in cohort, by cancer type

Cancer	N of excluded cohorts	N of excluded cases
Esophageal adenocarcinoma	7	16
Gallbladder	6	42
Liver	2	11
Lung	0	0
Kidney	1	4
Small intestine	5	37
Gastric cardia	6	9
Endometrial	1	10
Esophageal squamous	6	16
Myeloid leukemia	2	23
Myeloma	3	27
Colon	0	0
Head and neck	1	8
Rectum	0	0
Bladder	0	0
Breast	0	0
Non−Hodgkin lymphoma	1	13
Thyroid	1	8
Gastric non−cardia	5	7
Soft tissue	2	11
Pancreas	2	20
Lymphocytic leukemia	2	18
Ovary	1	4
Brain	2	3
Prostate	0	0
Malignant melanoma	0	0

eTable 5. Prevalence of demographic and lifestyle characteristics by leisure time physical activity quintile

Characteristics by gender	Category	Participants	0-19.9%	20-39.9%	40-59.9%	60-79.9%	80%+
Males (n)		619,956	77,568	155,080	106,162	149,891	131,255
Age	<60	286,282	41%	56%	43%	44%	44%
	60-69.9	290,403	52%	38%	50%	50%	49%
	70+	43,271	8%	6%	7%	6%	8%
Smoking	Never	199,102	27%	31%	32%	34%	34%
	Former	310,706	51%	45%	52%	53%	52%
	Current	95,954	19%	23%	13%	11%	11%
Alcohol intake	0	102,336	23%	14%	17%	15%	17%
	>0	507,767	75%	84%	82%	83%	82%
Education	< High School	100,437	18%	26%	14%	10%	12%
	High School Grad / GED	89,175	20%	13%	15%	13%	14%
	Post High School	70,590	9%	14%	9%	11%	12%
	Some College	88,371	18%	10%	17%	15%	14%
	College Graduate	133,920	16%	20%	23%	24%	24%
	Graduate School	123,168	18%	14%	20%	25%	22%
BMI	<25.0	201,979	28%	29%	30%	35%	39%
	25-29.9	297,110	44%	49%	49%	49%	47%
	30+	110,717	26%	21%	19%	15%	12%
Race	White	587,993	92%	96%	95%	94%	95%
	Black	11,117	3%	1%	2%	2%	2%
	Other	8,975	2%	1%	1%	2%	2%

Characteristics by gender	Category	Participants	0-19.9%	20-39.9%	40-59.9%	60-79.9%	80%+
Females (n)		816,668	92,721	257,792	117,383	197,183	151,589
Age	<60	487,604	48%	64%	56%	61%	60%
	60-69.9	284,760	46%	30%	40%	34%	35%
	70+	44,304	6%	6%	4%	5%	5%
Smoking status	Never	438,174	46%	57%	53%	54%	53%
	Former	240,473	32%	24%	32%	31%	32%
	Current	122,962	20%	17%	13%	13%	13%
Alcohol	0	216,764	36%	28%	28%	21%	23%
	>0	587,331	62%	70%	70%	78%	75%
Education	< High School	149,634	16%	28%	10%	15%	14%
	High School Grad / GED	188,090	25%	23%	23%	23%	22%
	Post High School	135,493	16%	16%	17%	17%	17%
	Some College	97,875	17%	9%	17%	11%	12%
	College Graduate	155,110	13%	17%	18%	23%	23%
	Graduate School	62,164	9%	5%	11%	8%	8%
BMI	<25.0	417,763	38%	46%	49%	58%	62%
	25-29.9	248,405	31%	33%	32%	29%	27%
	30+	135,803	29%	20%	17%	12%	10%
Race	White	782,257	92%	97%	94%	96%	96%
	Black	17,703	4%	1%	3%	2%	2%
	Other	8,343	1%	1%	1%	1%	1%

eTable 6. Leisure time physical activity and hazard ratios* of cancer: impact of omitting each cohort in turn from the analysis

	Omitted study†						
Cancer	**None omitted**	**AARP**	**BCDDP**	**COSM**	**CPSII**	**EPIC**	**IWHS**
Esophageal adenocarcinoma	0.58 (0.37−0.89)	0.48 (0.24-0.95)	N/A	0.73 (0.60-0.89)	0.49 (0.26-0.93)	0.52 (0.29-0.92)	N/A
Gallbladder	0.72 (0.51−1.01)	0.84 (0.58-1.21)	N/A	N/A	0.71 (0.46-1.09)	0.70 (0.46-1.06)	0.64 (0.46-0.88)
Liver	0.73 (0.55−0.98)	0.80 (0.58-1.10)	0.70 (0.52-0.93)	0.78 (0.57-1.06)	0.67 (0.51-0.90)	0.79 (0.56-1.11)	0.70 (0.52-0.94)
Lung	0.74 (0.71−0.77)	0.74 (0.70-0.79)	0.74 (0.71-0.78)	0.74 (0.71-0.78)	0.73 (0.70-0.77)	0.75 (0.72-0.78)	0.74 (0.71-0.78)
Kidney	0.77 (0.70−0.85)	0.78 (0.68-0.89)	0.77 (0.70-0.84)	0.76 (0.69-0.83)	0.77 (0.69-0.87)	0.76 (0.68-0.85)	0.77 (0.69-0.86)
Small intestine	0.78 (0.60−1.00)	0.93 (0.65-1.33)	N/A	0.76 (0.58-0.98)	0.75 (0.57-0.99)	0.76 (0.58-1.01)	0.77 (0.59-1.00)
Gastric cardia	0.78 (0.64−0.95)	0.83 (0.61-1.13)	N/A	0.78 (0.63-0.96)	0.75 (0.61-0.94)	0.77 (0.62-0.97)	0.78 (0.64-0.96)
Endometrial	0.79 (0.68−0.92)	0.85 (0.76-0.95)	0.78 (0.66-0.92)	N/A	0.79 (0.66-0.94)	0.74 (0.66-0.84)	0.79 (0.66-0.95)
Esophageal squamous	0.80 (0.61−1.06)	0.77 (0.52-1.13)	N/A	0.83 (0.63-1.10)	0.79 (0.58-1.06)	0.84 (0.61-1.17)	0.79 (0.60-1.05)
Myeloid leukemia	0.80 (0.70−0.92)	0.80 (0.66-0.96)	0.81 (0.70-0.93)	0.79 (0.69-0.91)	0.80 (0.68-0.93)	0.80 (0.69-0.93)	0.80 (0.70-0.93)
Myeloma	0.83 (0.72−0.95)	0.76 (0.64-0.89)	N/A	0.81 (0.69-0.95)	0.80 (0.67-0.96)	0.83 (0.70-0.98)	0.83 (0.72-0.97)
Colon	0.84 (0.77−0.91)	0.86 (0.79-0.93)	0.82 (0.76-0.90)	0.84 (0.77-0.93)	0.84 (0.76-0.92)	0.85 (0.77-0.94)	0.85 (0.78-0.94)
Head and neck	0.85 (0.78−0.93)	0.94 (0.82-1.07)	0.86 (0.78-0.95)	0.87 (0.78-0.97)	0.83 (0.75-0.92)	0.88 (0.78-0.99)	0.87 (0.78-0.97)
Rectum	0.87 (0.80−0.95)	0.89 (0.79-1.00)	0.87 (0.79-0.96)	0.87 (0.79-0.96)	0.87 (0.78-0.96)	0.89 (0.79-0.99)	0.88 (0.80-0.97)
Bladder	0.87 (0.82−0.92)	0.87 (0.80-0.95)	0.87 (0.82-0.92)	0.86 (0.81-0.92)	0.87 (0.82-0.93)	0.88 (0.83-0.94)	0.87 (0.82-0.93)
Breast	0.90 (0.87−0.93)	0.90 (0.86-0.94)	0.90 (0.87-0.93)	N/A	0.90 (0.86-0.94)	0.88 (0.85-0.92)	0.90 (0.87-0.94)
Non−Hodgkin lymphoma	0.91 (0.83−1.00)	0.90 (0.80-1.02)	0.90 (0.84-0.97)	0.90 (0.83-0.98)	0.92 (0.81-1.03)	0.92 (0.83-1.03)	0.92 (0.83-1.02)
Thyroid	0.92 (0.81−1.06)	0.88 (0.75-1.05)	0.93 (0.81-1.07)	0.93 (0.80-1.07)	0.94 (0.81-1.09)	0.94 (0.79-1.11)	0.90 (0.78-1.03)
Gastric non−cardia	0.93 (0.73−1.19)	1.01 (0.73-1.39)	N/A	0.91 (0.70-1.18)	0.82 (0.67-0.99)	1.02 (0.76-1.36)	0.94 (0.72-1.23)
Soft tissue	0.94 (0.67−1.31)	0.92 (0.60-1.40)	N/A	0.91 (0.63-1.31)	0.89 (0.61-1.30)	0.93 (0.62-1.38)	0.99 (0.70-1.39)
Pancreas	0.95 (0.83−1.08)	0.97 (0.82-1.15)	0.92 (0.82-1.04)	0.92 (0.82-1.02)	0.94 (0.81-1.10)	0.97 (0.83-1.13)	0.94 (0.82-1.09)
Lymphocytic leukemia	0.98 (0.87−1.11)	0.99 (0.84-1.16)	N/A	0.99 (0.87-1.12)	0.96 (0.84-1.11)	0.98 (0.86-1.12)	0.98 (0.86-1.11)
Ovary	1.01 (0.91−1.13)	1.03 (0.91-1.17)	1.01 (0.90-1.13)	N/A	1.00 (0.89-1.13)	1.03 (0.91-1.17)	1.00 (0.89-1.12)
Brain	1.06 (0.93−1.20)	1.11 (0.95-1.31)	N/A	1.07 (0.94-1.21)	1.02 (0.89-1.17)	1.08 (0.92-1.28)	1.05 (0.91-1.21)
Prostate	1.05 (1.03−1.08)	1.04 (1.00-1.08)	N/A	1.06 (1.03-1.09)	1.06 (1.02-1.09)	1.06 (1.03-1.09)	N/A
Malignant melanoma	1.27 (1.16−1.40)	1.28 (1.14-1.44)	1.27 (1.14-1.40)	1.25 (1.14-1.37)	1.27 (1.13-1.42)	1.24 (1.13-1.36)	1.29 (1.16-1.42)

	Omitted study†						
Cancer	**None omitted**	**PHS**	**PLCO**	**SMC**	**USRT**	**WHS**	**WLH**
Esophageal adenocarcinoma	0.58 (0.37−0.89)	N/A	0.56 (0.34-0.94)	N/A	N/A	N/A	N/A
Gallbladder	0.72 (0.51−1.01)	N/A	0.75 (0.55-1.02)	0.71 (0.47-1.07)	N/A	N/A	N/A
Liver	0.73 (0.55−0.98)	0.74 (0.54-1.01)	0.76 (0.55-1.05)	0.69 (0.53-0.90)	N/A	0.74 (0.55-1.01)	N/A
Lung	0.74 (0.71−0.77)	0.74 (0.71-0.78)	0.74 (0.71-0.78)	0.74 (0.71-0.77)	0.74 (0.71-0.78)	0.74 (0.71-0.77)	0.74 (0.71-0.78)
Kidney	0.77 (0.70−0.85)	0.77 (0.69-0.86)	0.78 (0.70-0.86)	0.78 (0.70-0.86)	0.78 (0.71-0.85)	0.77 (0.70-0.86)	N/A
Small intestine	0.78 (0.60−1.00)	0.78 (0.60-1.01)	0.76 (0.58-0.98)	N/A	N/A	N/A	N/A
Gastric cardia	0.78 (0.64−0.95)	N/A	0.77 (0.63-0.95)	N/A	N/A	N/A	N/A
Endometrial	0.79 (0.68−0.92)	N/A	0.80 (0.68-0.95)	0.79 (0.67-0.94)	0.79 (0.67-0.94)	0.78 (0.66-0.93)	N/A
Esophageal squamous	0.80 (0.61−1.06)	N/A	0.80 (0.60-1.06)	N/A	N/A	N/A	N/A
Myeloid leukemia	0.80 (0.70−0.92)	0.80 (0.70-0.92)	0.82 (0.71-0.94)	0.80 (0.69-0.92)	N/A	0.79 (0.69-0.91)	N/A
Myeloma	0.83 (0.72−0.95)	N/A	0.88 (0.77-1.00)	0.81 (0.70-0.95)	0.82 (0.70-0.96)	0.83 (0.71-0.96)	N/A
Colon	0.84 (0.77−0.91)	0.85 (0.78-0.93)	0.82 (0.75-0.89)	0.83 (0.76-0.90)	0.84 (0.77-0.92)	0.84 (0.76-0.92)	0.83 (0.76-0.90)
Head and neck	0.85 (0.78−0.93)	0.86 (0.77-0.95)	0.86 (0.77-0.95)	0.86 (0.78-0.96)	0.84 (0.77-0.92)	0.85 (0.77-0.93)	N/A
Rectum	0.87 (0.80−0.95)	0.85 (0.79-0.92)	0.87 (0.79-0.96)	0.87 (0.79-0.96)	0.86 (0.79-0.93)	0.87 (0.80-0.96)	0.86 (0.79-0.93)
Bladder	0.87 (0.82−0.92)	0.87 (0.82-0.92)	0.87 (0.82-0.93)	0.87 (0.82-0.92)	0.87 (0.82-0.93)	0.87 (0.82-0.92)	0.87 (0.82-0.92)
Breast	0.90 (0.87−0.93)	N/A	0.91 (0.88-0.94)	0.90 (0.87-0.94)	0.90 (0.86-0.94)	0.90 (0.87-0.94)	0.90 (0.86-0.93)
Non−Hodgkin lymphoma	0.91 (0.83−1.00)	0.91 (0.82-1.01)	0.90 (0.81-1.00)	0.91 (0.82-1.01)	0.91 (0.83-1.01)	0.93 (0.85-1.01)	N/A
Thyroid	0.92 (0.81−1.06)	0.94 (0.82-1.08)	0.91 (0.79-1.05)	0.93 (0.80-1.07)	0.92 (0.79-1.07)	0.93 (0.80-1.08)	N/A
Gastric non−cardia	0.93 (0.73−1.19)	N/A	0.97 (0.73-1.27)	0.88 (0.70-1.11)	N/A	N/A	N/A
Soft tissue	0.94 (0.67−1.31)	0.91 (0.63-1.31)	0.96 (0.67-1.37)	0.98 (0.70-1.38)	0.88 (0.67-1.16)	1.02 (0.77-1.34)	N/A
Pancreas	0.95 (0.83−1.08)	0.96 (0.85-1.09)	0.96 (0.83-1.11)	0.93 (0.82-1.05)	N/A	0.96 (0.84-1.10)	N/A
Lymphocytic leukemia	0.98 (0.87−1.11)	0.98 (0.86-1.10)	0.97 (0.85-1.10)	0.98 (0.87-1.11)	0.98 (0.87-1.11)	0.98 (0.87-1.11)	N/A
Ovary	1.01 (0.91−1.13)	N/A	1.01 (0.90-1.13)	1.01 (0.90-1.13)	1.01 (0.91-1.13)	1.03 (0.92-1.15)	N/A
Brain	1.06 (0.93−1.20)	1.03 (0.90-1.17)	1.04 (0.91-1.20)	1.06 (0.94-1.21)	N/A	1.07 (0.93-1.23)	1.05 (0.92-1.19)
Prostate	1.05 (1.03−1.08)	1.06 (1.03-1.09)	1.05 (1.02-1.08)	N/A	1.05 (1.03-1.08)	N/A	N/A
Malignant melanoma	1.27 (1.16−1.40)	1.28 (1.15-1.42)	1.30 (1.18-1.43)	1.27 (1.15-1.40)	1.30 (1.18-1.43)	1.25 (1.14-1.38)	1.28 (1.17-1.41)

* Multivariable models were adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other). Models for endometrial, breast, and ovarian cancers are additionally adjusted for hormone replacement therapy use (ever, never), oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children)

† Abbreviations. AARP: NIH-AARP Diet and Health Study, BCDDP: Breast Cancer Detection and Demonstration Project, COSM: Cohort of Swedish Men, CPS II: Cancer Prevention Study II, EPIC: European Prospective Investigation into Cancer and Nutrition, IWHS: Iowa Women's Health Study, PHS: Physician's Health Study I and II, PLCO: Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, SMC: Swedish Mammography Cohort, USRT: U.S. Radiologic Technologists Cohort, WHS: Women's Health Study, WLH: Women's Lifestyle and Health Study

eTable 7. Comparison of summary hazard ratios (HRs)[*] and 95% confidence intervals (CIs) in all studies and in only studies with a validated questionnaire (qx)

Cancer[†]	HR (95% CI) all studies	HR (95% CI) validated qx	Percent difference in HR
Esophageal adenocarcinoma	0.58 (0.37−0.89)	0.56 (0.34-0.94)	-3.4
Gallbladder	0.72 (0.51−1.01)	0.75 (0.55-1.02)	4.2
Liver	0.73 (0.55−0.98)	0.76 (0.55-1.05)	4.1
Lung	0.74 (0.71−0.77)	0.74 (0.70-0.78)	0.0
Kidney	0.77 (0.70−0.85)	0.78 (0.70-0.86)	1.3
Small intestine	0.78 (0.60−1.00)	0.76 (0.58-0.98)	-2.6
Gastric cardia	0.78 (0.64−0.95)	0.77 (0.63-0.95)	-1.3
Endometrial	0.79 (0.68−0.92)	0.80 (0.68-0.95)	1.3
Esophageal squamous	0.80 (0.61−1.06)	0.80 (0.60-1.06)	0.0
Myeloid leukemia	0.80 (0.70−0.92)	0.82 (0.71-0.94)	2.5
Myeloma	0.83 (0.72−0.95)	0.88 (0.77-1.00)	6.0
Colon	0.84 (0.77−0.91)	0.81 (0.75-0.88)	-3.6
Head and neck	0.85 (0.78−0.93)	0.86 (0.77-0.95)	1.2
Rectum	0.87 (0.80−0.95)	0.86 (0.79-0.93)	-1.1
Bladder	0.87 (0.82−0.92)	0.87 (0.82-0.93)	0.0
Breast	0.90 (0.87−0.93)	0.90 (0.87-0.94)	0.0
Non−Hodgkin lymphoma	0.91 (0.83−1.00)	0.90 (0.81-1.00)	-1.1
Thyroid	0.92 (0.81−1.06)	0.91 (0.79-1.05)	-1.1
Gastric non−cardia	0.93 (0.73−1.19)	0.97 (0.73-1.27)	4.3
Soft tissue	0.94 (0.67−1.31)	0.96 (0.67-1.37)	2.1
Pancreas	0.95 (0.83−1.08)	0.96 (0.83-1.11)	1.1
Lymphocytic leukemia	0.98 (0.87−1.11)	0.97 (0.85-1.10)	-1.0
Ovary	1.01 (0.91−1.13)	1.01 (0.90-1.13)	0.0
Brain	1.06 (0.93−1.20)	1.04 (0.91-1.19)	-1.9
Prostate	1.05 (1.03−1.08)	1.05 (1.02-1.08)	0.0
Malignant melanoma	1.27 (1.16−1.40)	1.31 (1.19-1.44)	3.1

[*] All models were adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other). Models for endometrial, breast, and ovarian cancers are additionally adjusted for postmenopausal hormone therapy use (ever, never), oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children)

[†] The Surveillance Epidemiology and End Results site recode and the *International Classification of Diseases for Oncology, Third Edition* code corresponding to each cancer type are shown in **eTable 3**

eTable 8. Comparison of hazard ratios (HRs) and 95% confidence intervals (CIs) in the NIH-AARP Diet and Health Study in models adjusted for standard risk factors and models additionally adjusted for diet

Cancer[*]	HR (95% CI) standard adjusted[†]	HR (95% CI) diet adjusted[‡]	Percent difference in HR
Esophageal adenocarcinoma	0.74 (0.58-0.94)	0.79 (0.62-1.01)	7.1
Gallbladder	0.52 (0.31-0.85)	0.51 (0.30-0.85)	-1.8
Liver	0.52 (0.42-0.65)	0.55 (0.43-0.69)	5.0
Lung	0.74 (0.70-0.78)	0.77 (0.73-0.82)	4.8
Kidney	0.76 (0.67-0.85)	0.79 (0.70-0.89)	4.2
Small intestine	0.65 (0.45-0.93)	0.66 (0.46-0.95)	2.2
Gastric cardia	0.74 (0.57-0.97)	0.76 (0.57-0.99)	2.0
Endometrial	0.60 (0.52-0.69)	0.61 (0.53-0.71)	3.1
Esophageal squamous	0.85 (0.57-1.27)	0.95 (0.63-1.43)	12.2
Myeloid leukemia	0.81 (0.65-1.00)	0.80 (0.64-0.99)	-1.3
Myeloma	0.98 (0.81-1.18)	0.98 (0.81-1.18)	0.1
Colon	0.73 (0.68-0.78)	0.76 (0.70-0.82)	4.2
Head and neck	0.78 (0.69-0.88)	0.81 (0.71-0.91)	3.2
Rectum	0.84 (0.75-0.95)	0.89 (0.78-1.00)	5.4
Bladder	0.87 (0.80-0.95)	0.89 (0.82-0.97)	2.3
Breast	0.89 (0.84-0.94)	0.91 (0.86-0.97)	2.2
Non−Hodgkin lymphoma	0.95 (0.86-1.05)	0.96 (0.86-1.07)	1.2
Thyroid	1.00 (0.80-1.27)	0.97 (0.77-1.23)	-3.3
Gastric non−cardia	0.78 (0.61-0.99)	0.77 (0.60-0.99)	-0.8
Soft tissue	0.94 (0.69-1.30)	0.95 (0.68-1.30)	0.1
Pancreas	0.89 (0.78-1.02)	0.90 (0.79-1.03)	1.1
Lymphocytic leukemia	0.97 (0.80-1.17)	1.00 (0.82-1.21)	3.3
Ovary	0.98 (0.79-1.20)	0.99 (0.81-1.23)	2.0
Brain	0.96 (0.79-1.18)	0.91 (0.74-1.12)	-5.9
Prostate	1.07 (1.03-1.11)	1.07 (1.03-1.11)	0.2
Malignant melanoma	1.23 (1.13-1.33)	1.23 (1.13-1.33)	0.0

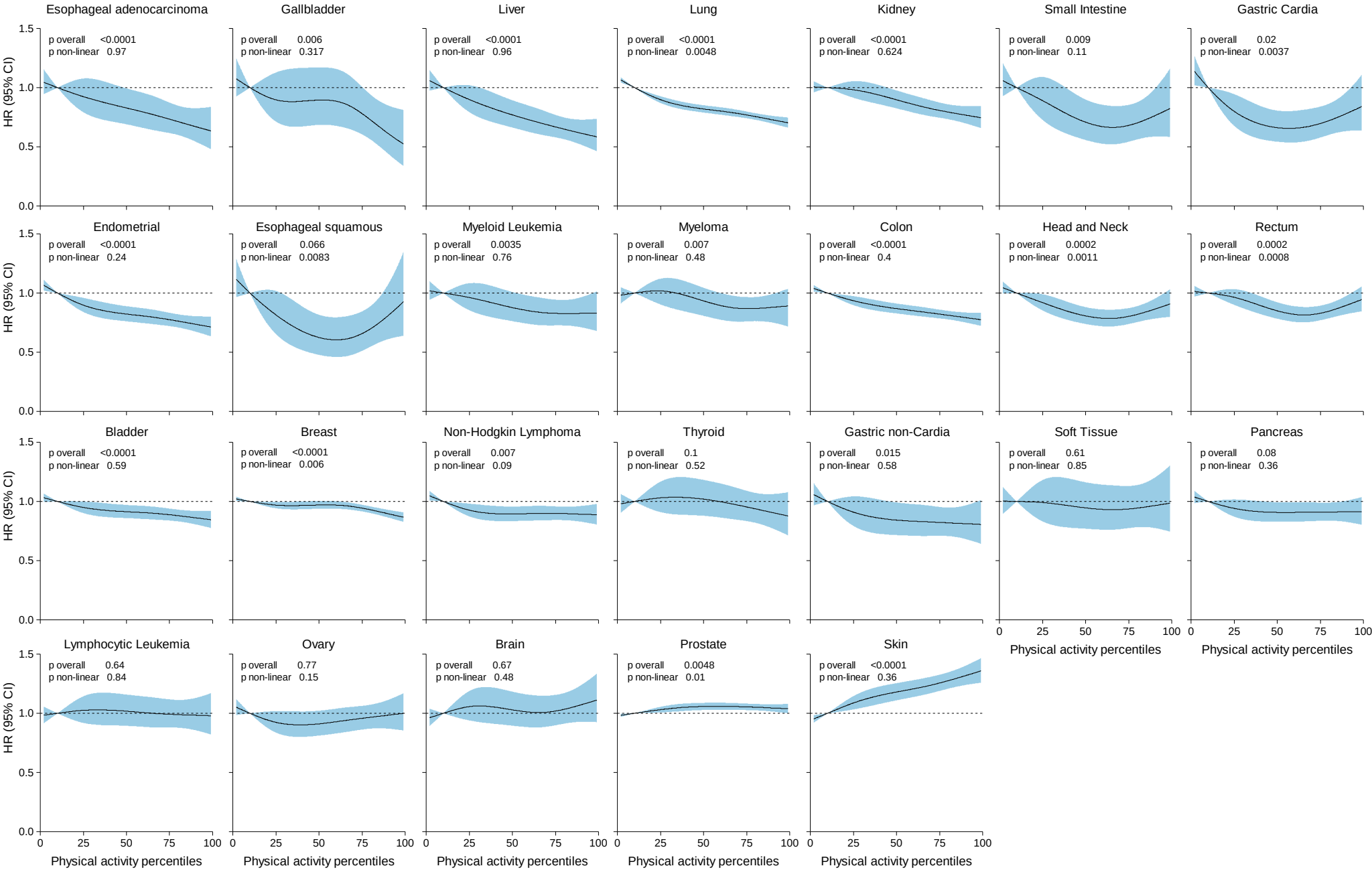
[*] The Surveillance Epidemiology and End Results site recode and the *International Classification of Diseases for Oncology, Third Edition* code corresponding to each cancer type are shown in **eTable 3**

[†] All models were adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other). Models for endometrial, breast, and ovarian cancers are additionally adjusted for postmenopausal hormone therapy use (ever, never), oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children)

[‡] Models adjusted for the covariates above and also for kilocalories consumed per day (continuous), multivitamin use during the past 12 months (yes, no), use of zinc, iron, selenium or folic acid (yes, no), use of Vitamin A, Beta-

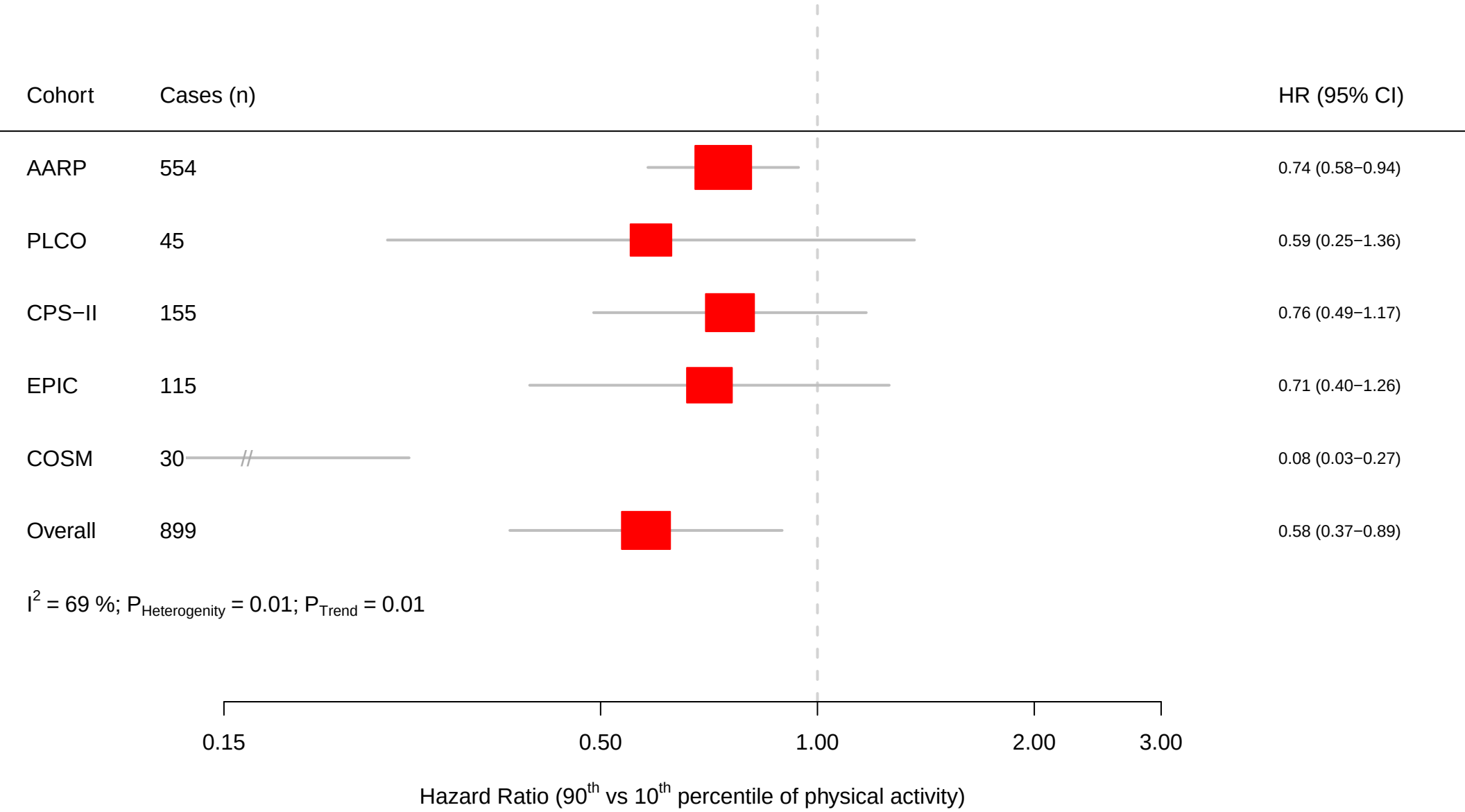
carotene, vitamin C, vitamin E, or calcium (yes, no), and consumption of fruits (continuous My Pyramid servings per day), vegetables (continuous My Pyramid servings per day), and red meat (continuous My Pyramid servings per day).

eFigure 1. Association between leisure-time physical activity and cancer type, allowing for non-linear effects, with 95% confidence intervals

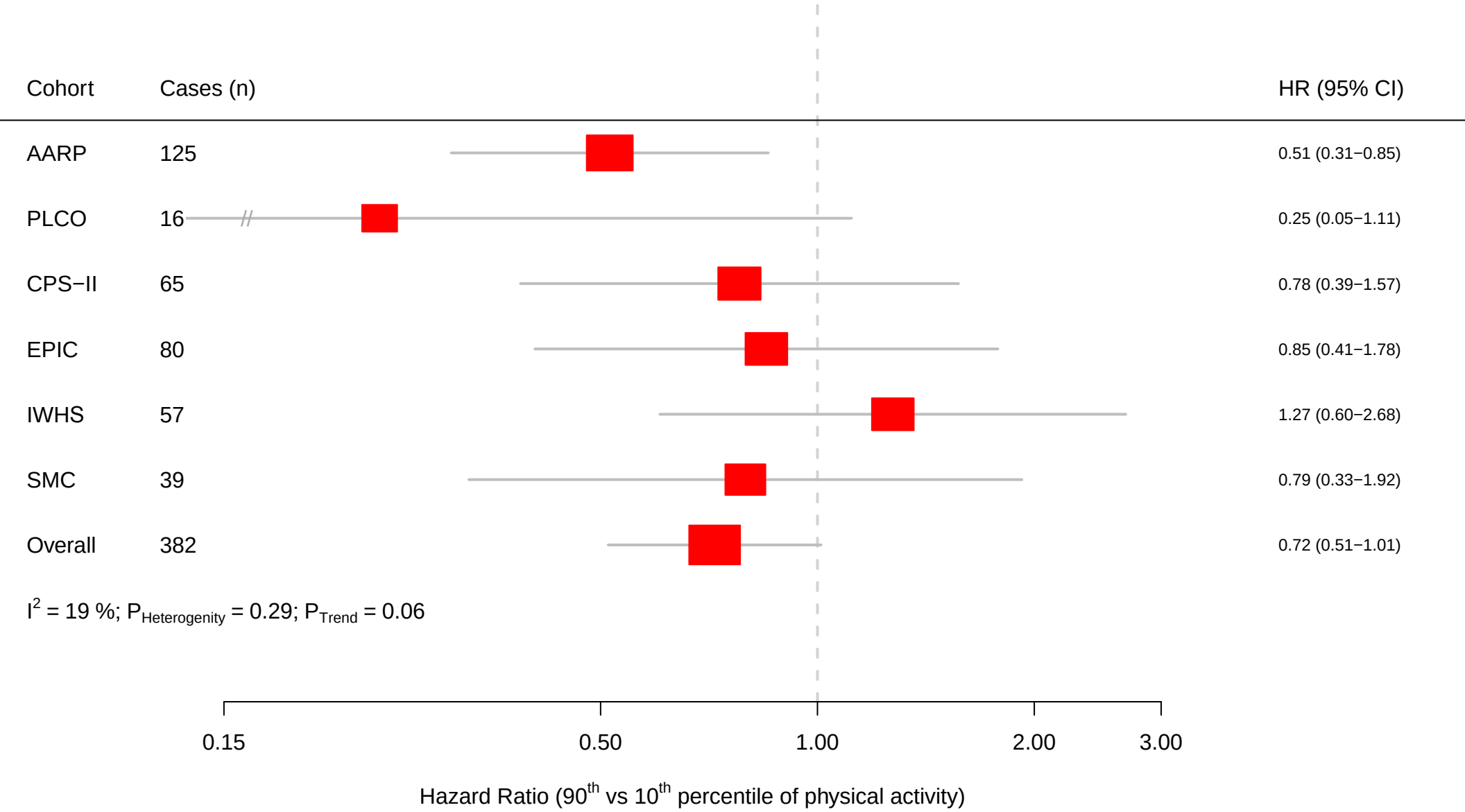


The reference level of leisure-time physical activity for these plots was the 10th percentile, with the HR fixed at 1.0 at this percentile. Separate models were fit for each cancer type using cubic restricted splines, stratified by cohort, and adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9, and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other). Models for endometrial, breast, and ovarian cancers are additionally adjusted for hormone replacement therapy (ever, never), oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children).

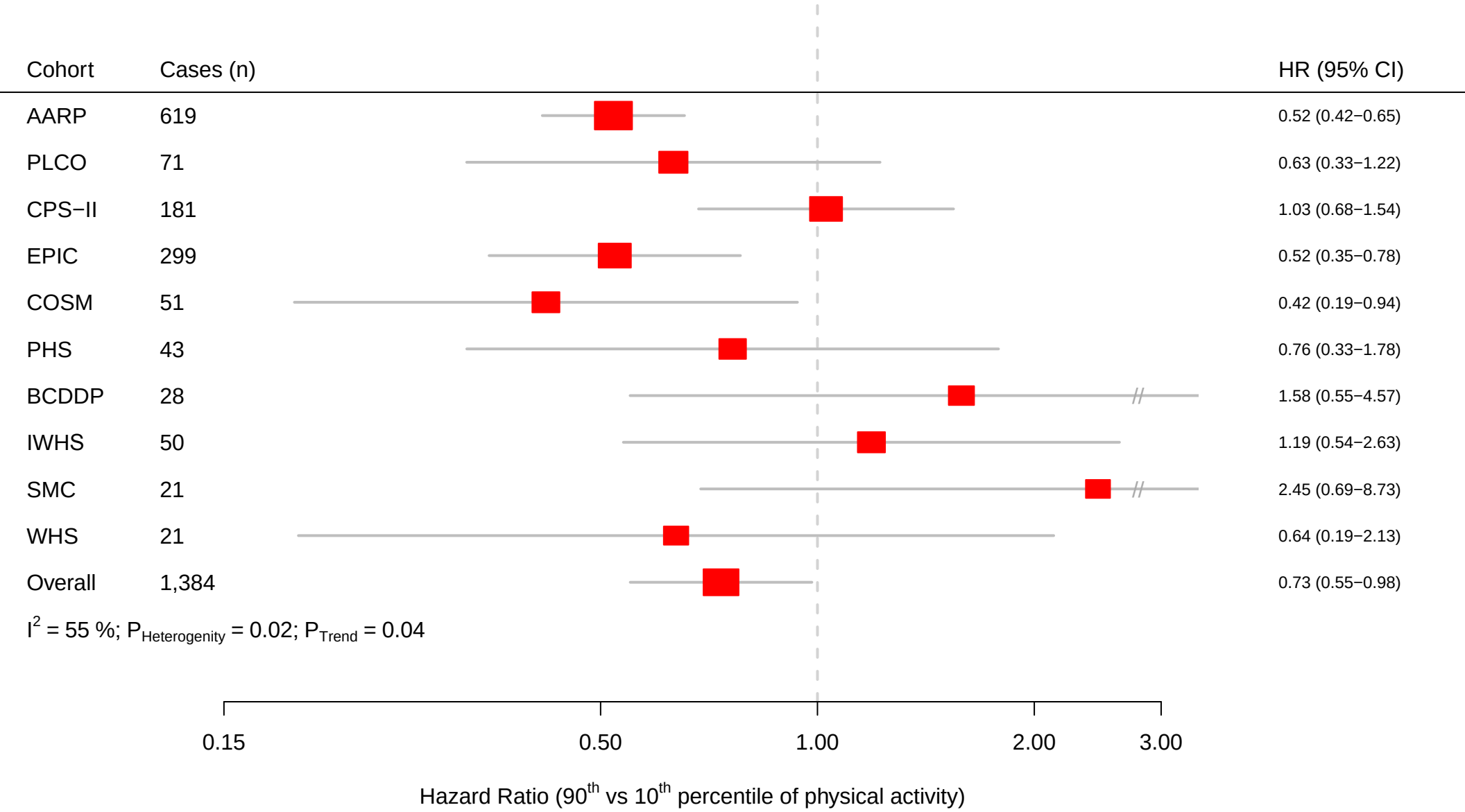
eFigure 2a. Physical activity and risk of esophageal adenocarcinoma



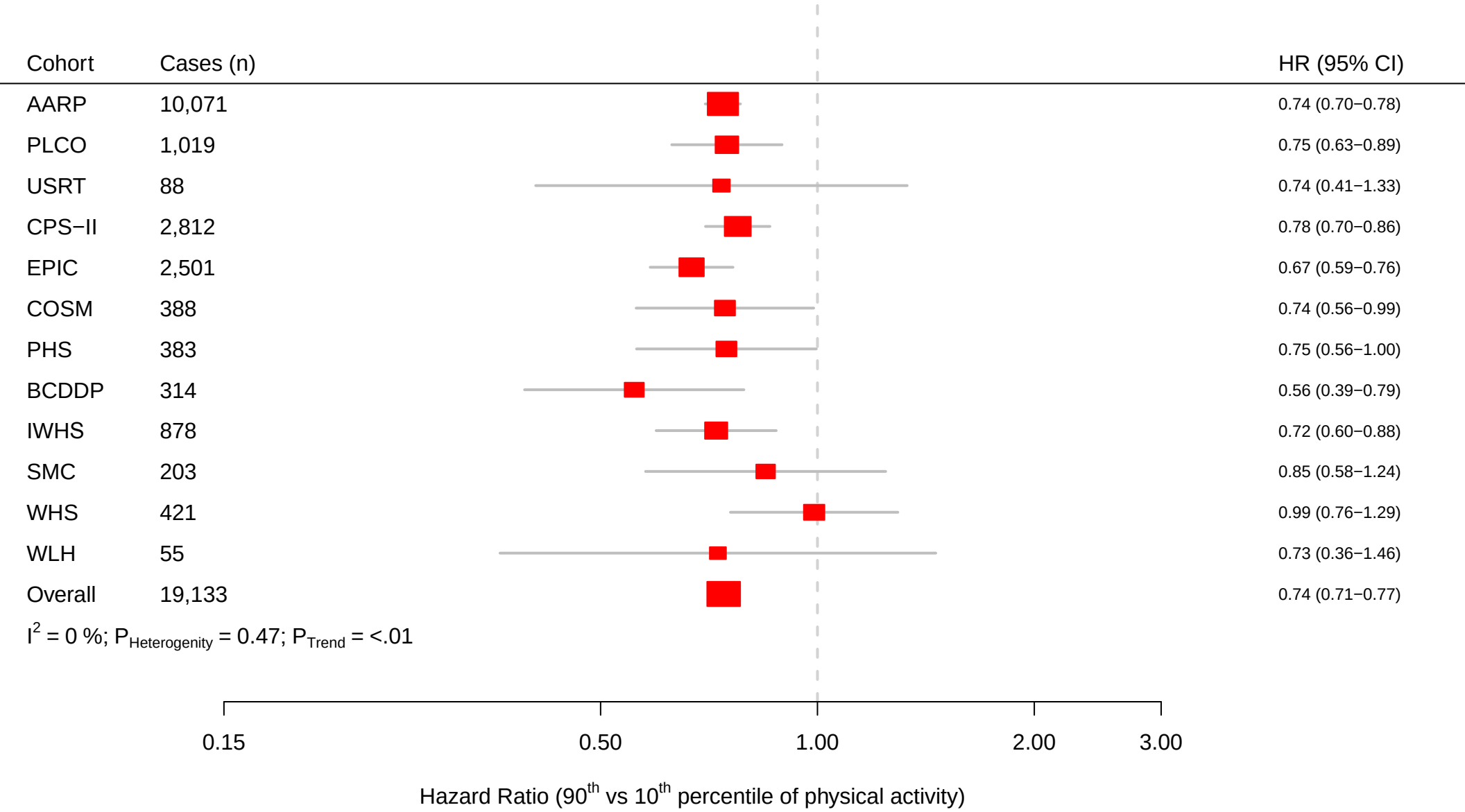
eFigure 2b. Physical activity and risk of gallbladder cancer



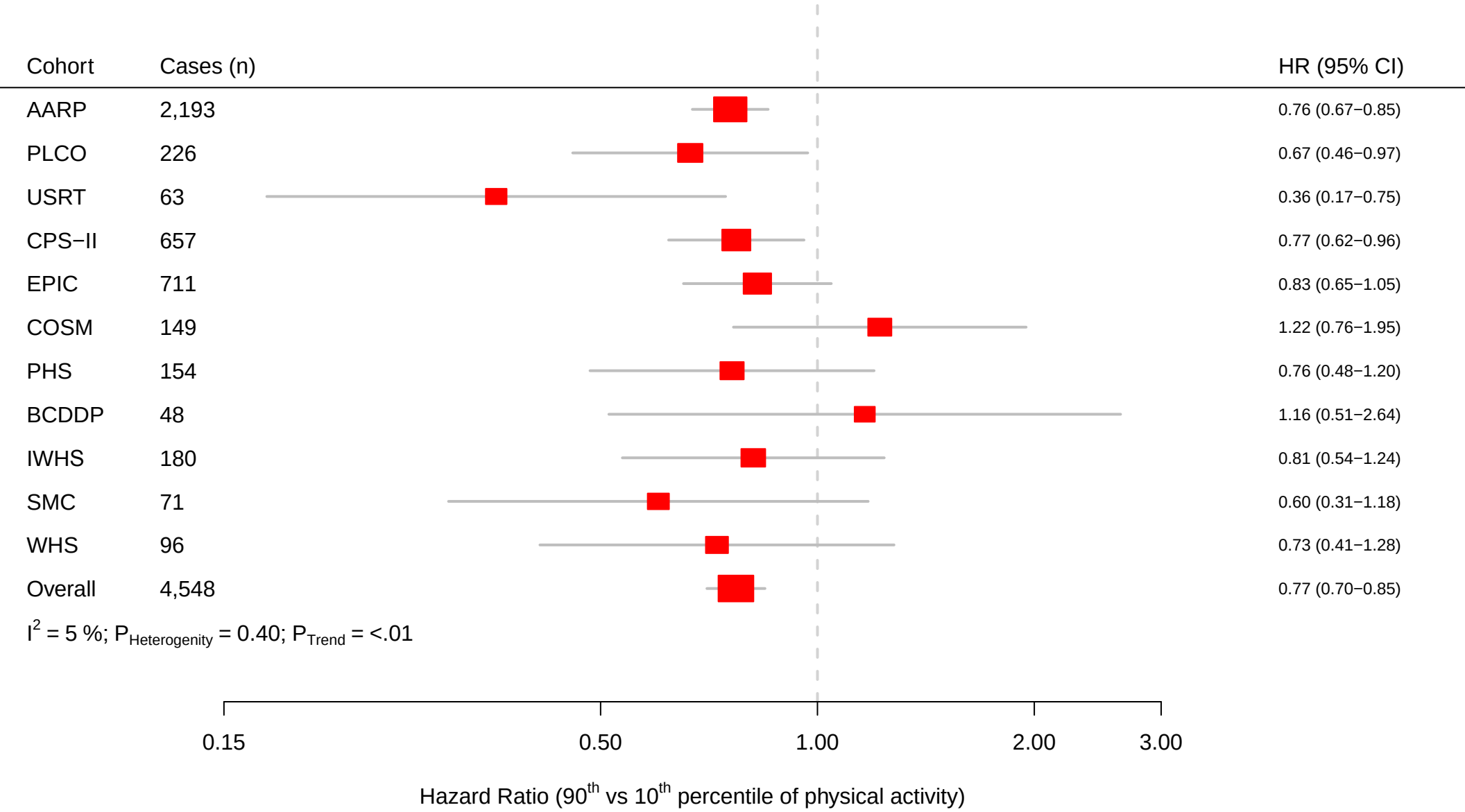
eFigure 2c. Physical activity and risk of liver cancer



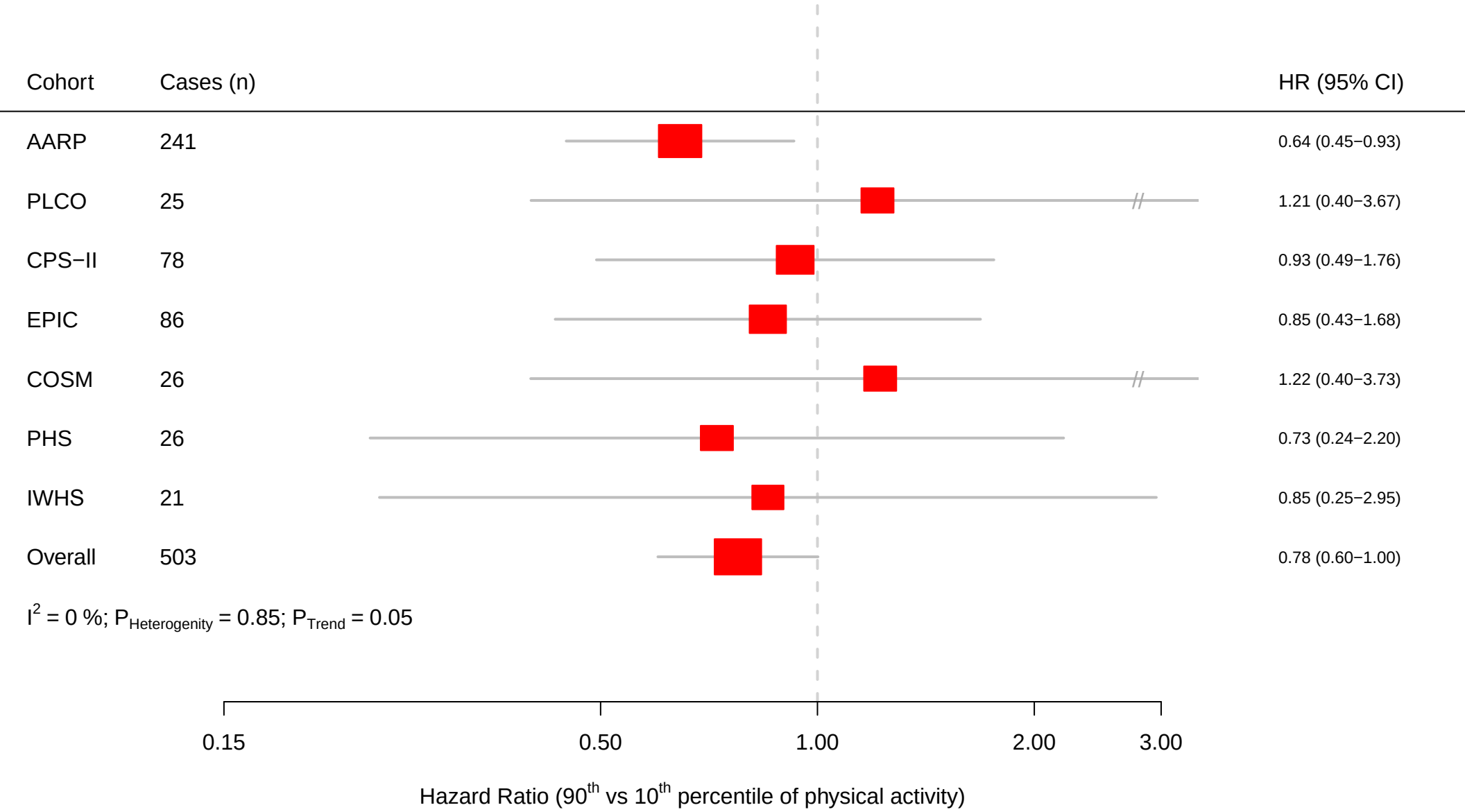
eFigure 2d. Physical activity and risk of lung cancer



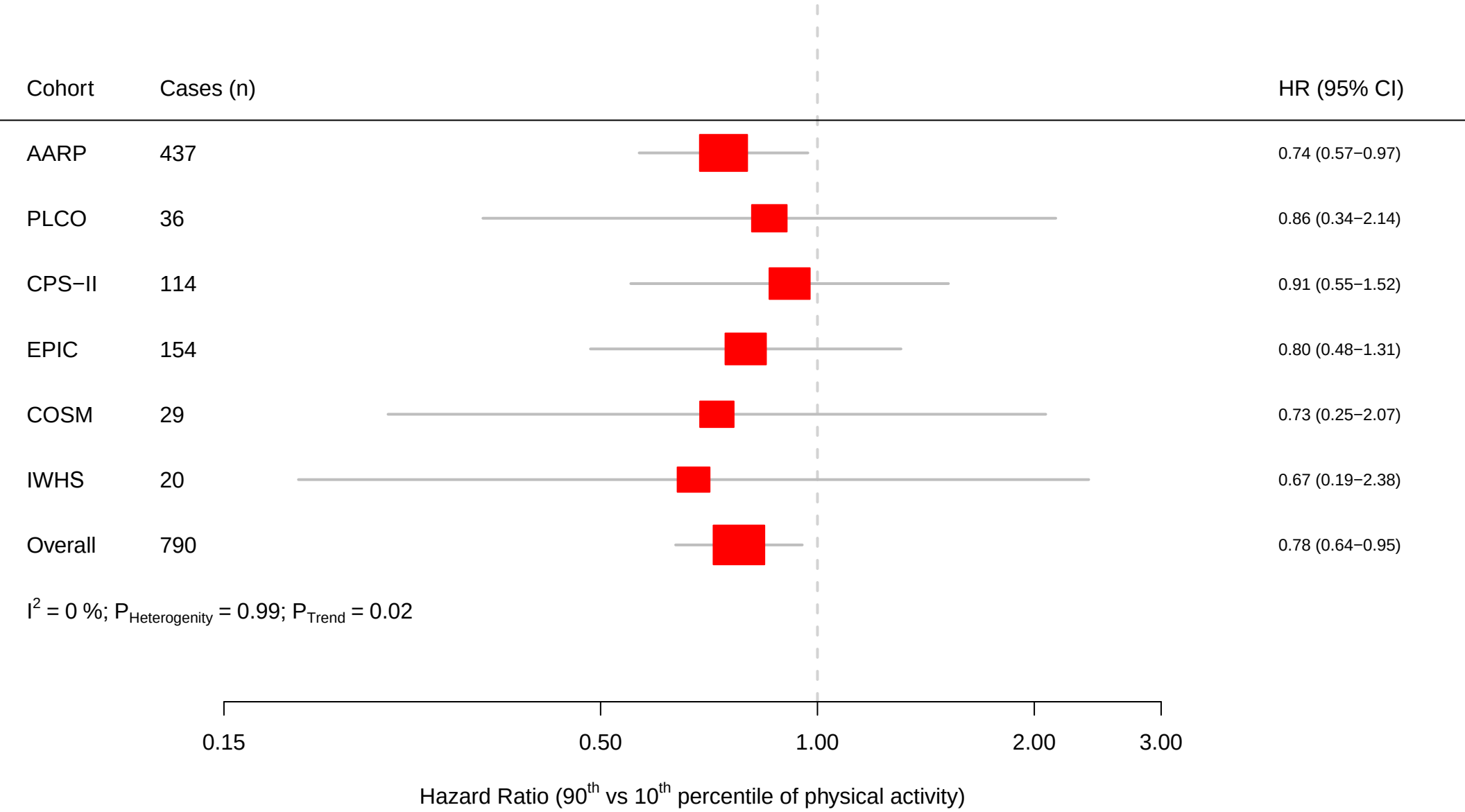
eFigure 2e. Physical activity and risk of kidney cancer



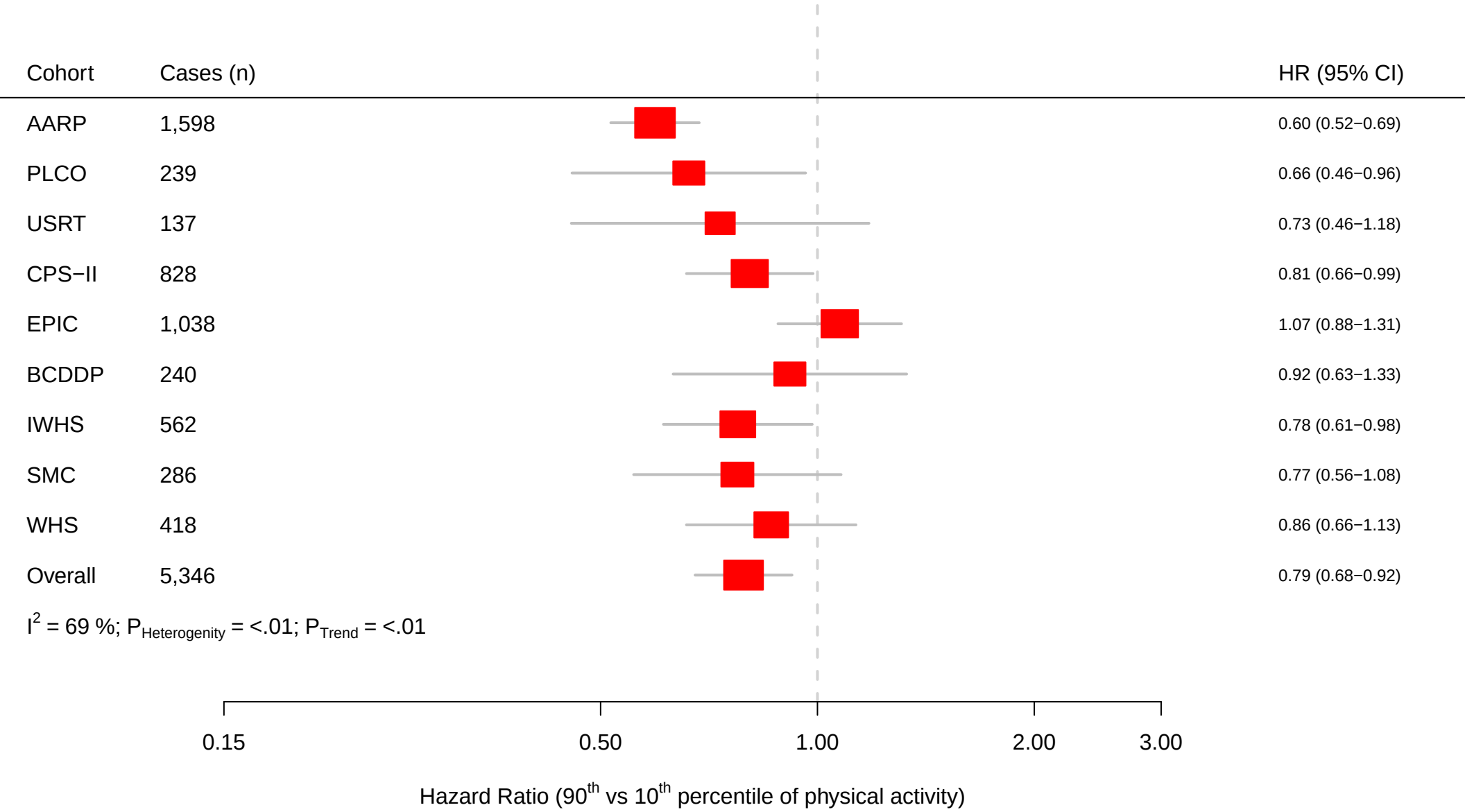
eFigure 2f. Physical activity and risk of small intestine cancer



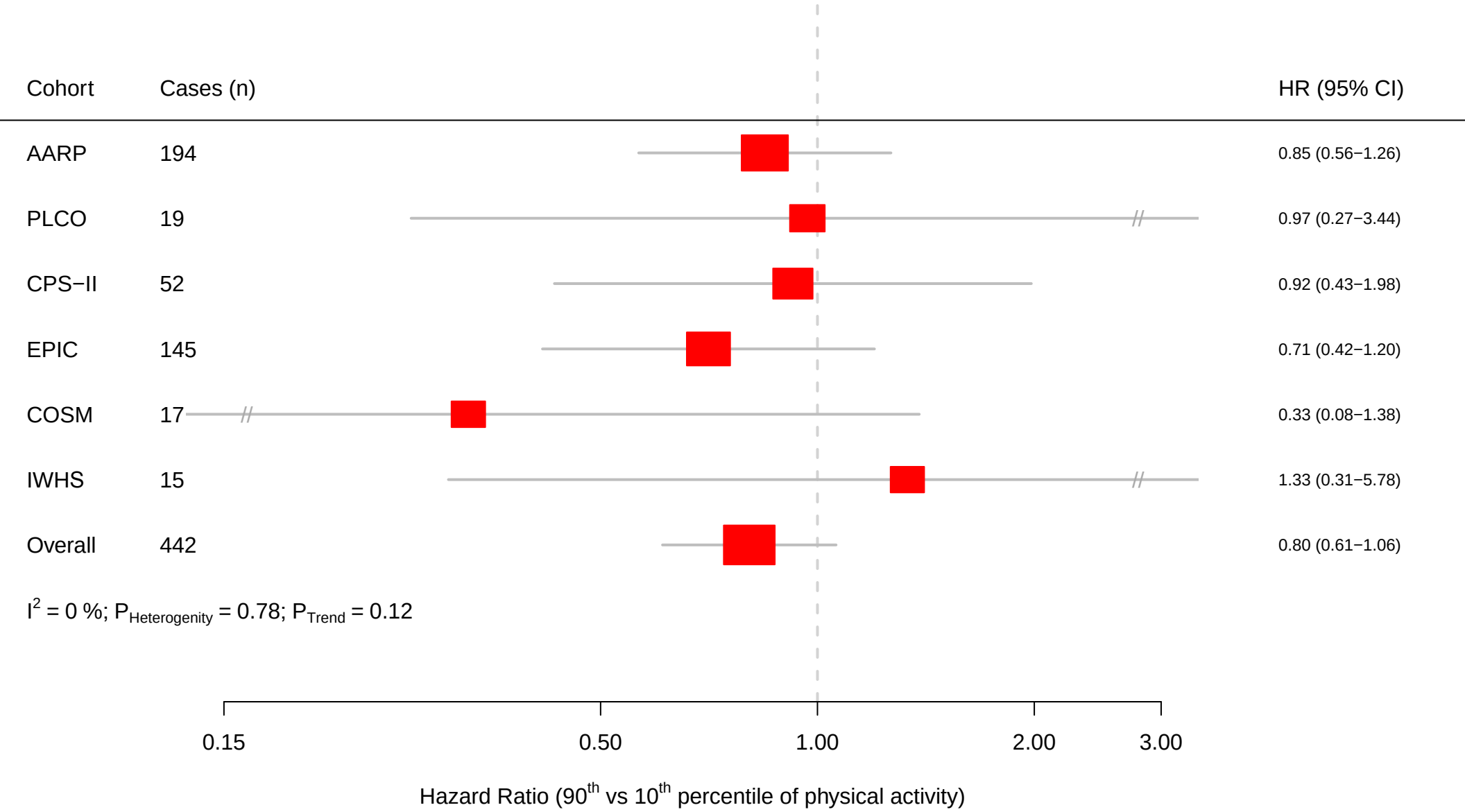
eFigure 2g. Physical activity and risk of gastric cardia cancer



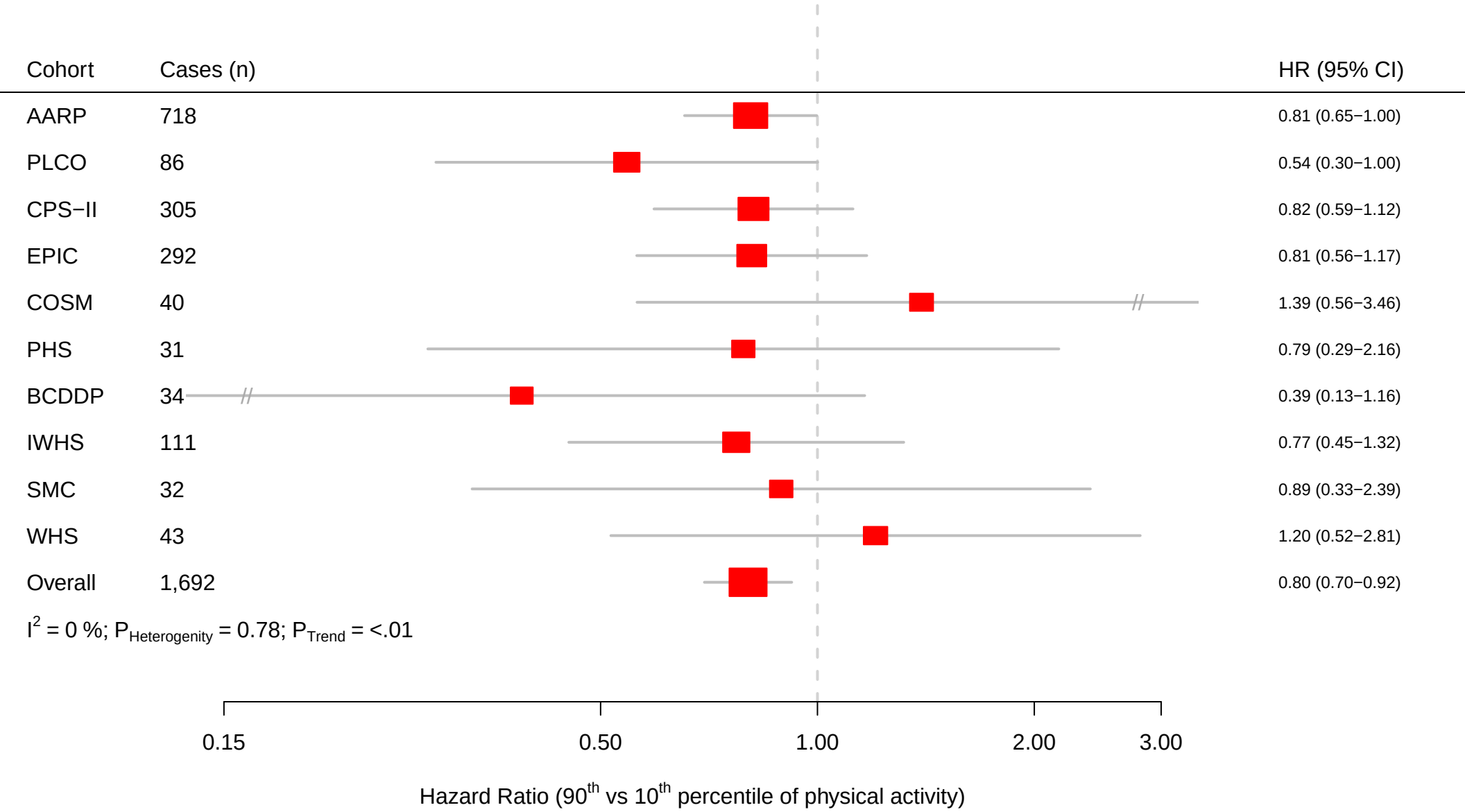
eFigure 2h. Physical activity and risk of endometrial cancer



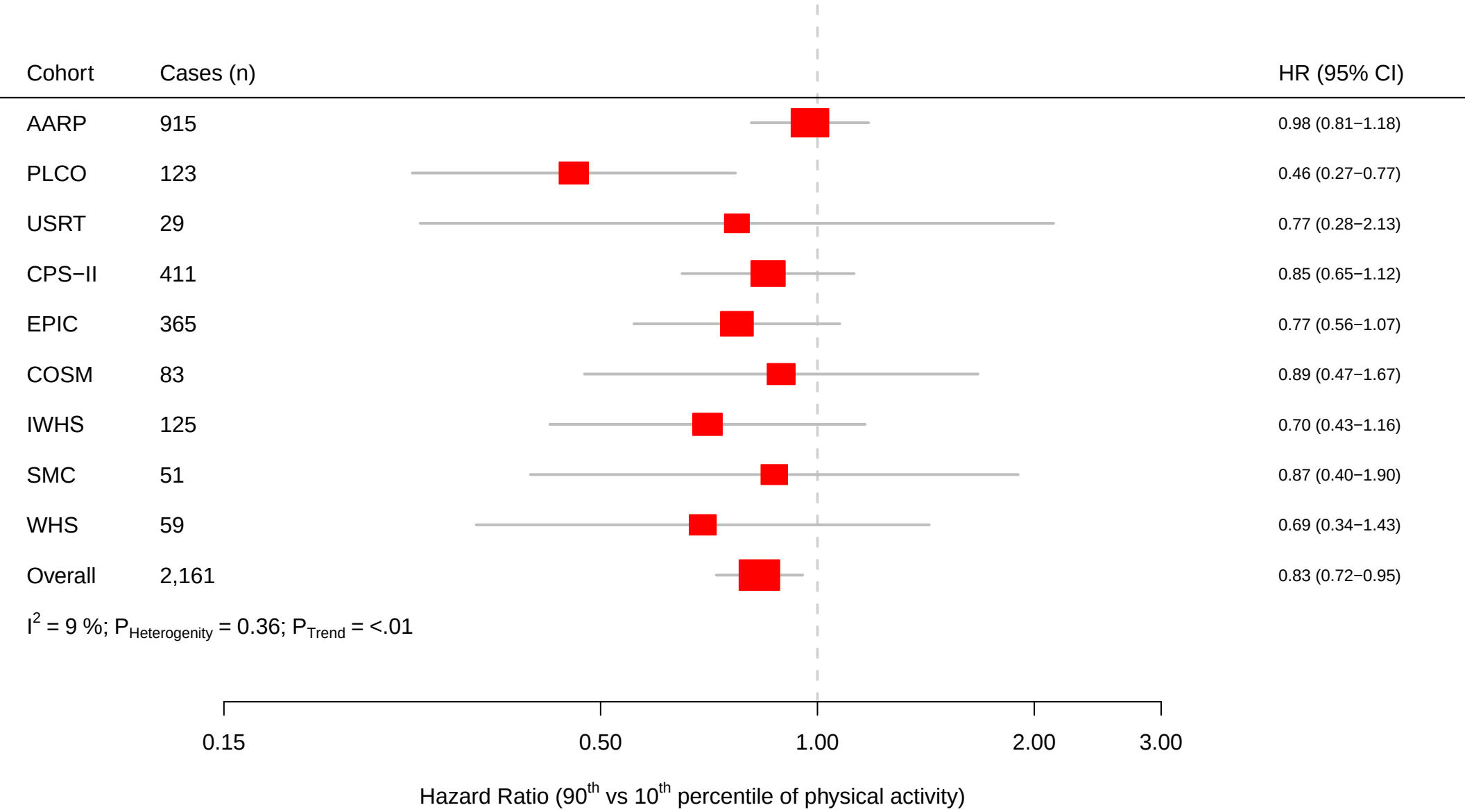
eFigure 2i. Physical activity and risk of esophageal squamous cancer



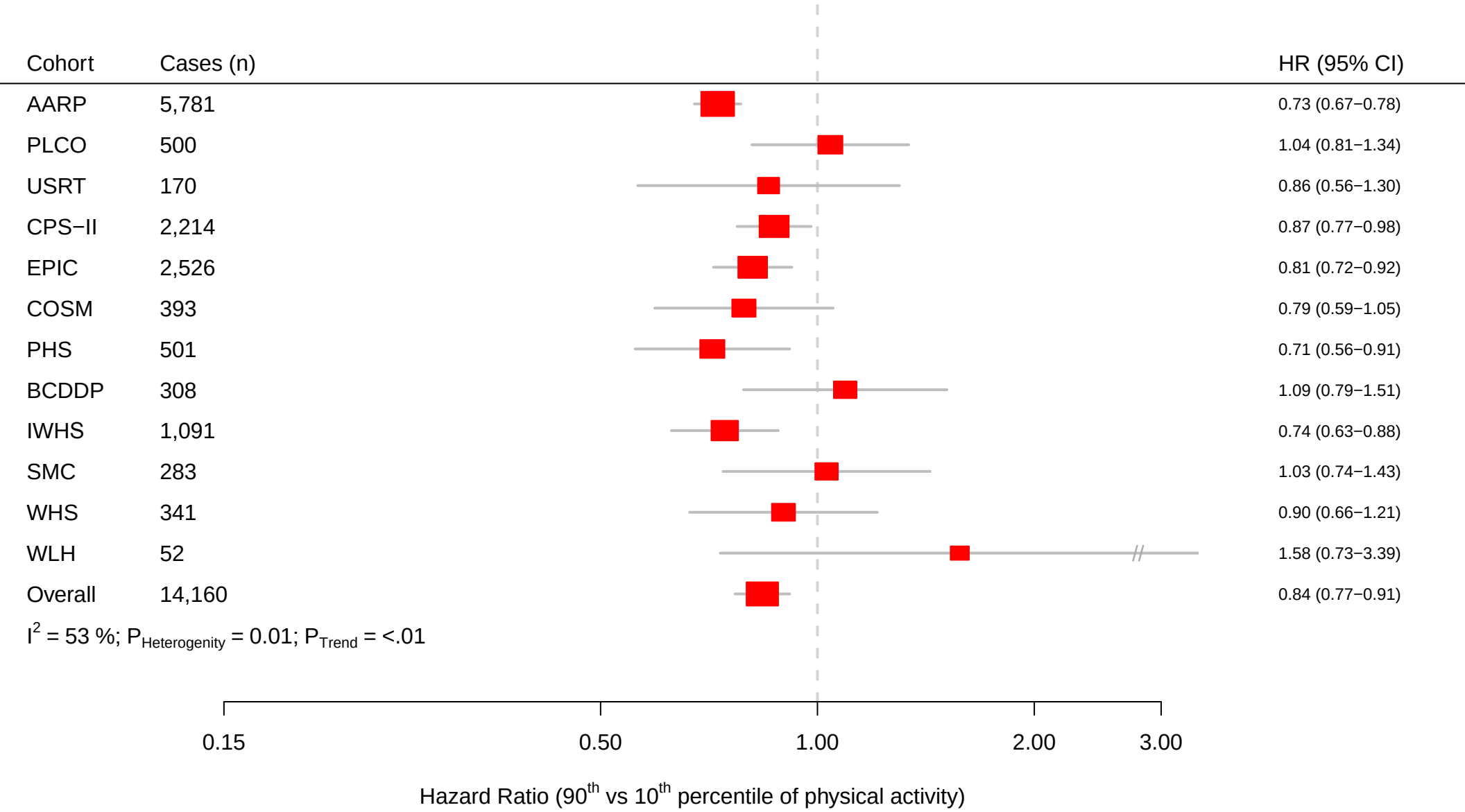
eFigure 2j. Physical activity and risk of myeloid leukemia



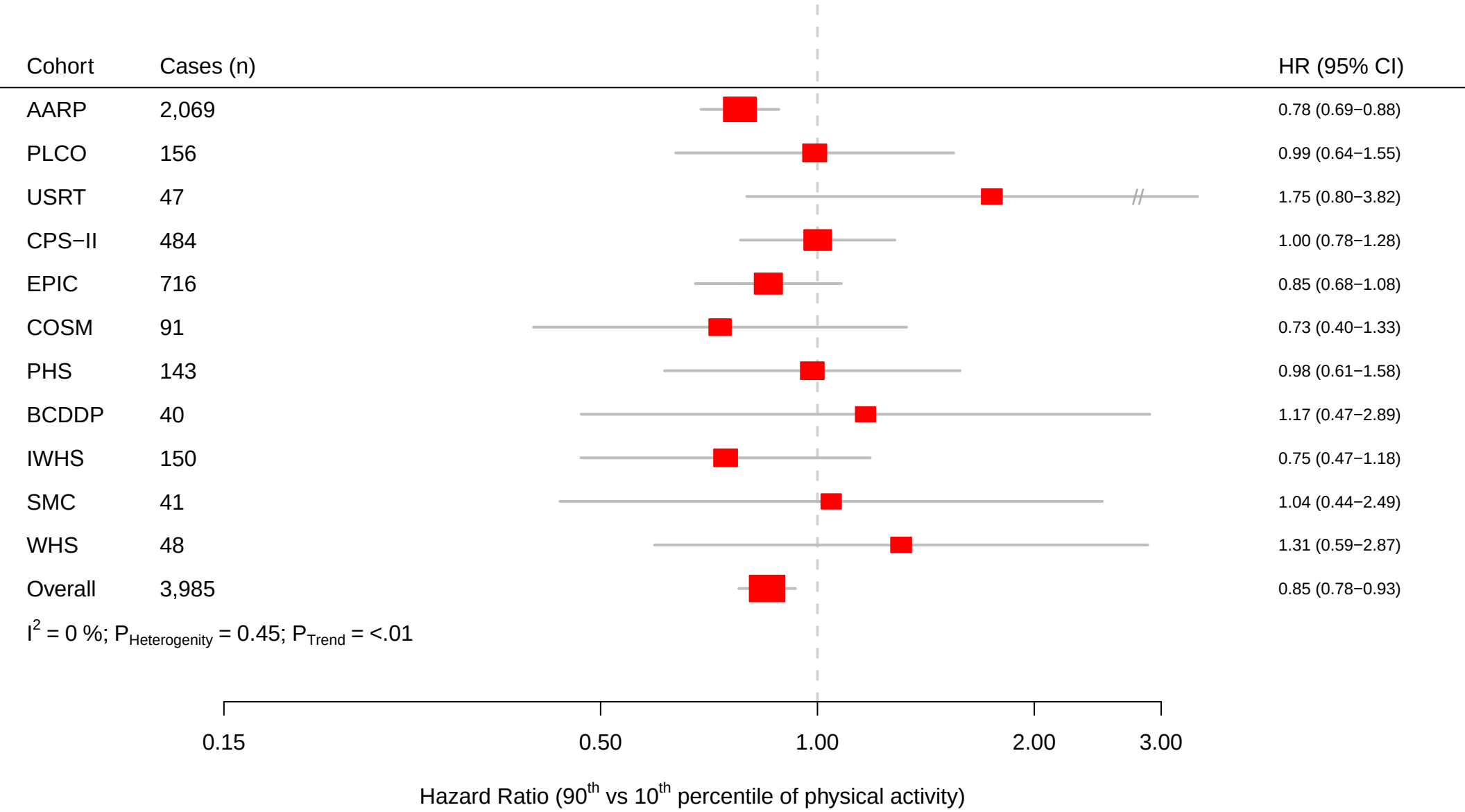
eFigure 2k. Physical activity and risk of myeloma



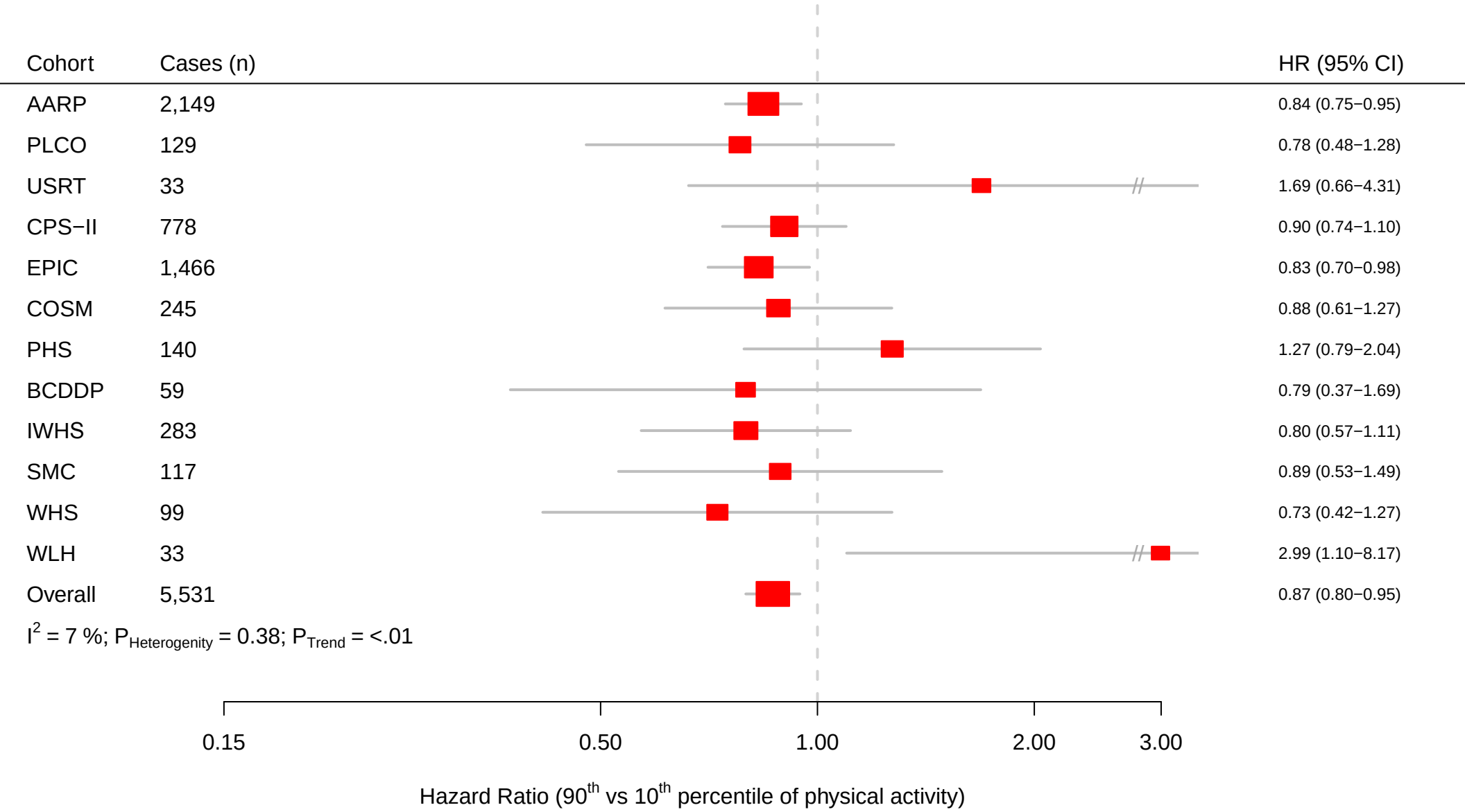
eFigure 2l. Physical activity and risk of colon cancer



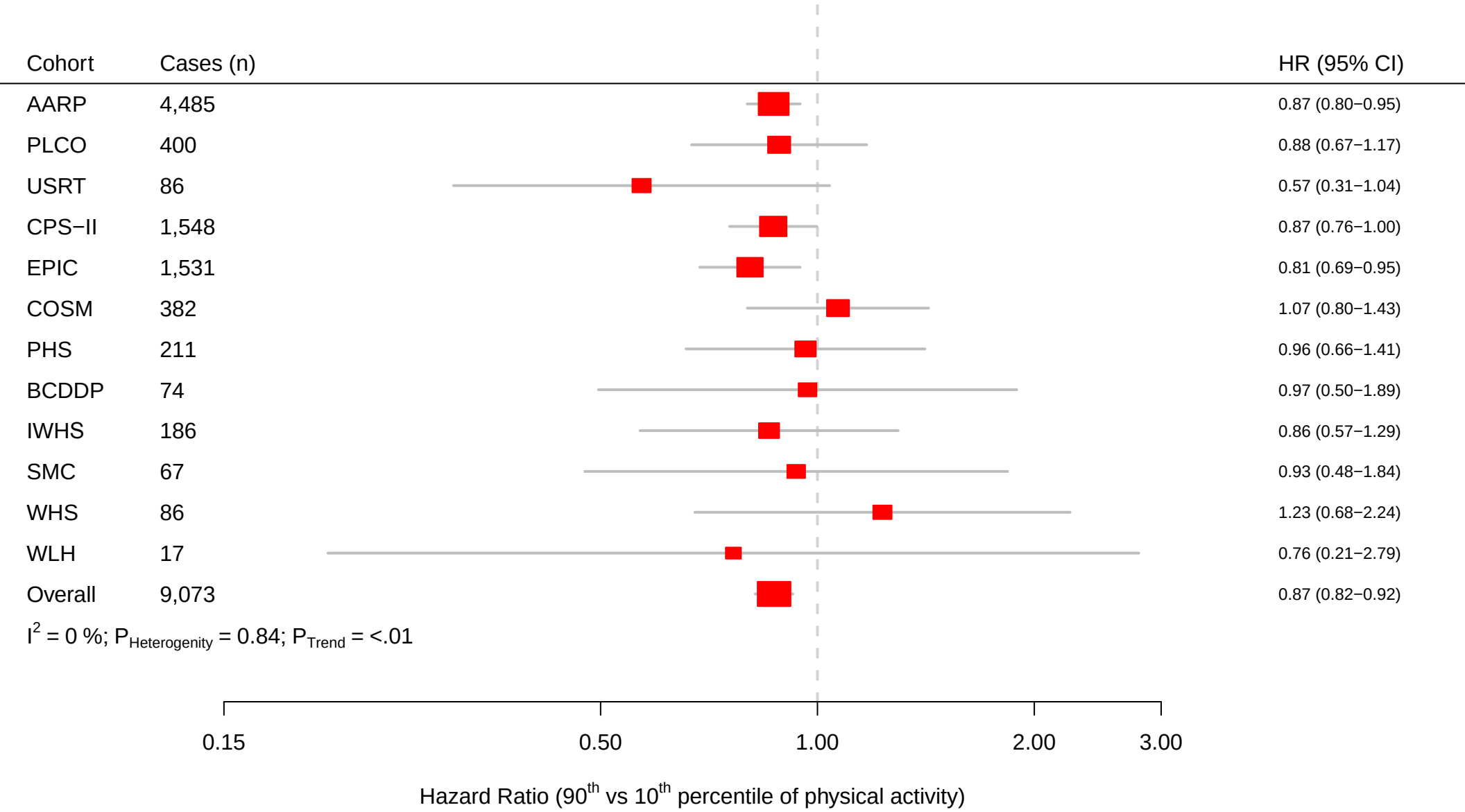
eFigure 2m. Physical activity and risk of head and neck cancer



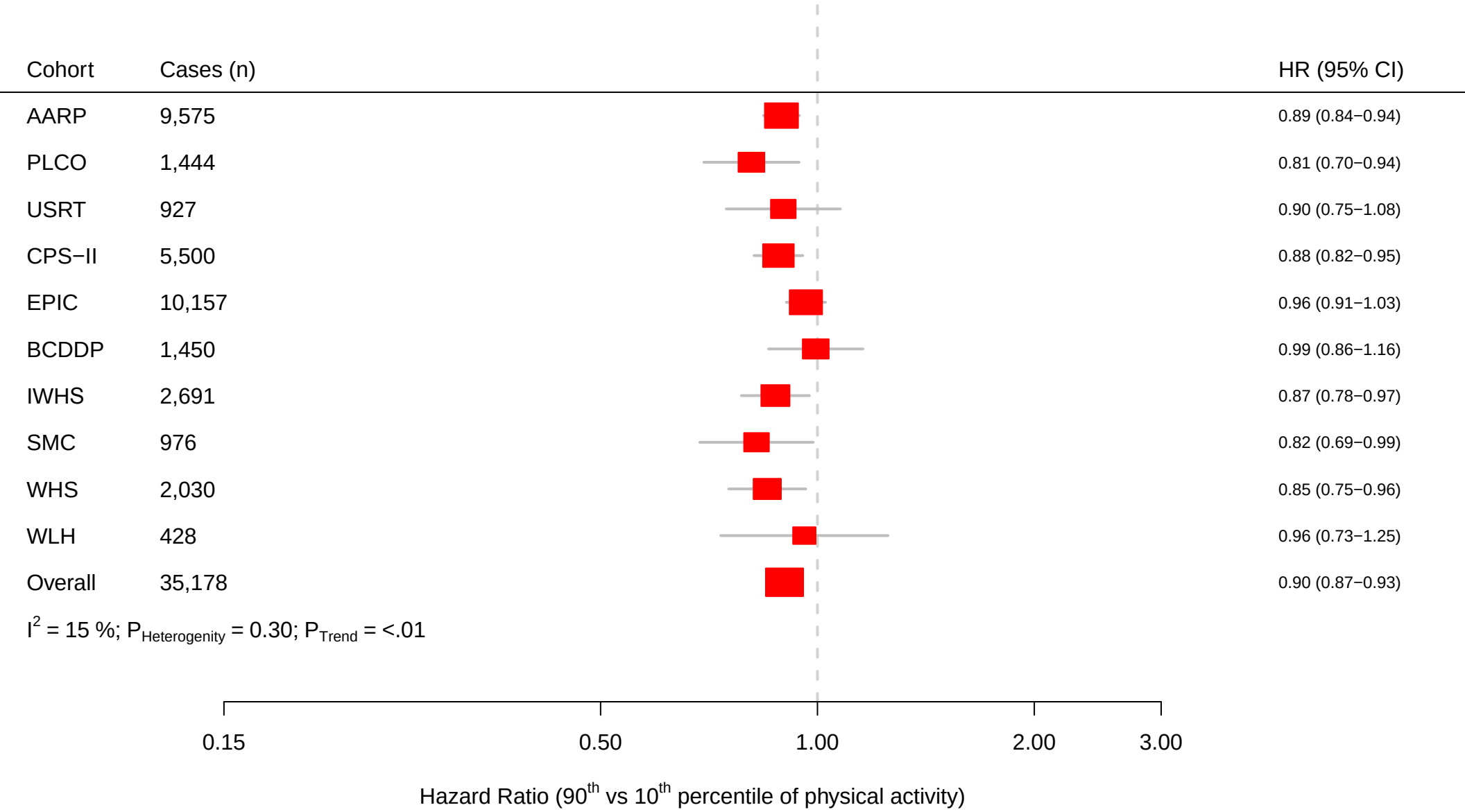
eFigure 2n. Physical activity and risk of rectum cancer



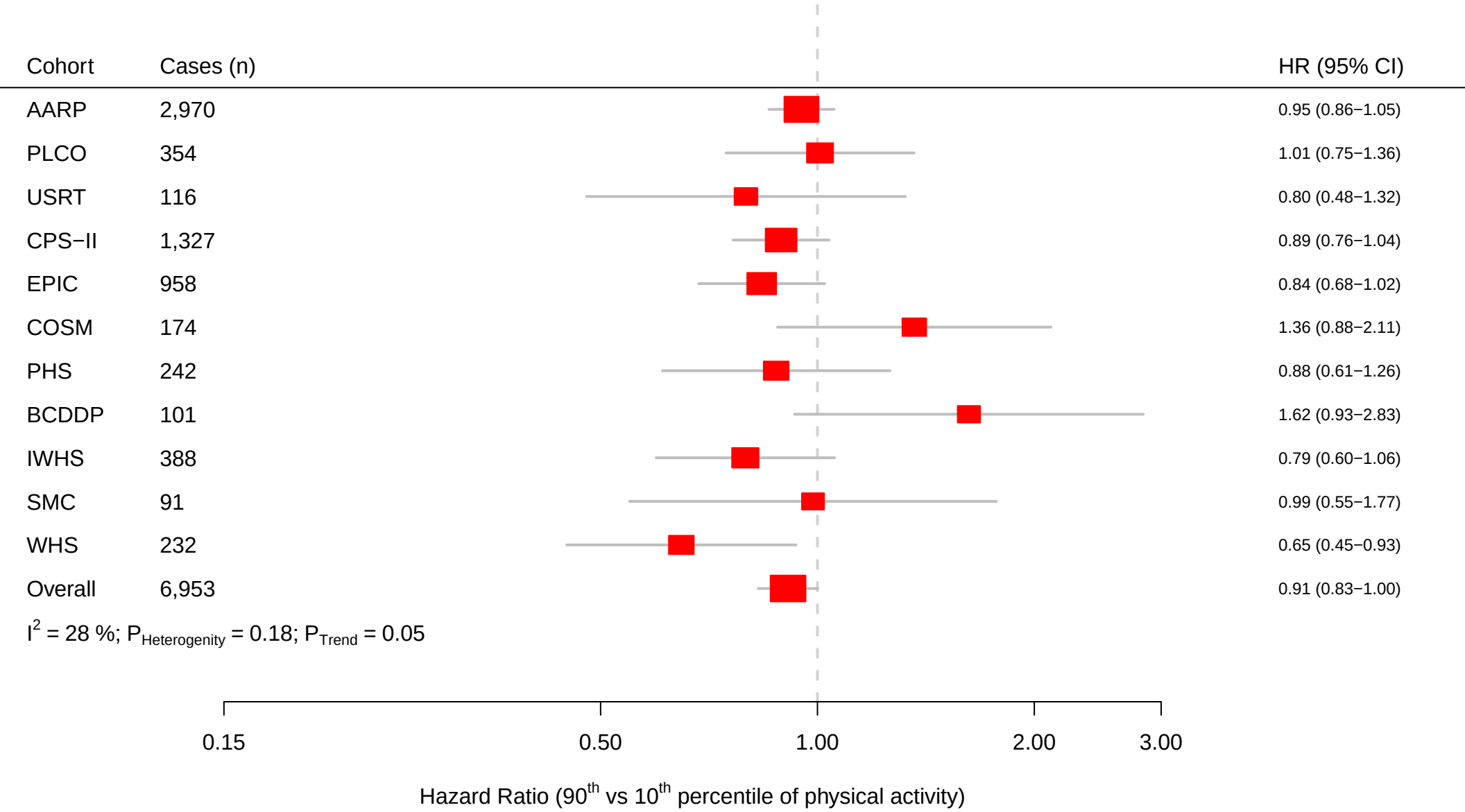
eFigure 2o. Physical activity and risk of bladder cancer



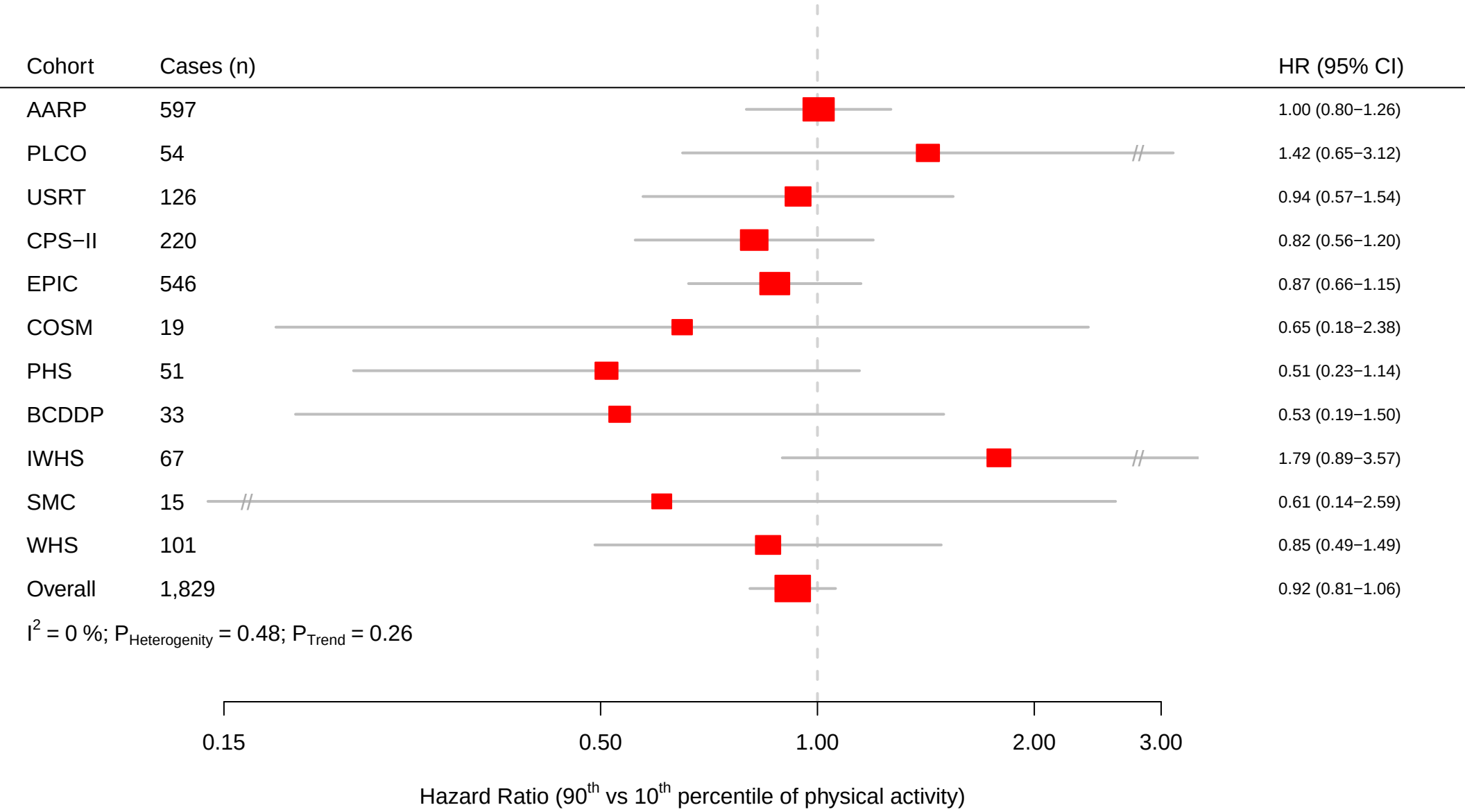
eFigure 2p. Physical activity and risk of breast cancer



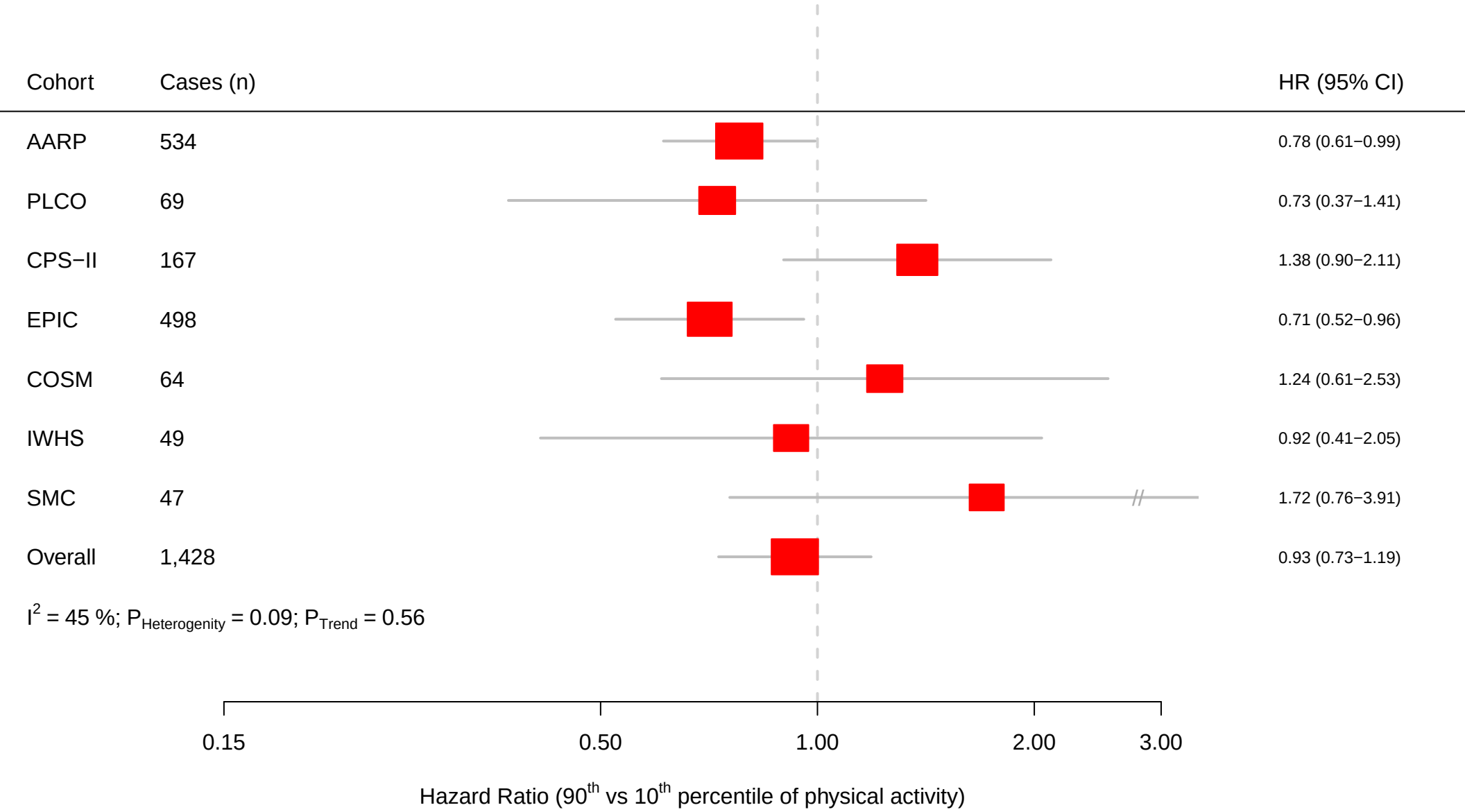
eFigure 2q. Physical activity and risk of non−hodgkin lymphoma



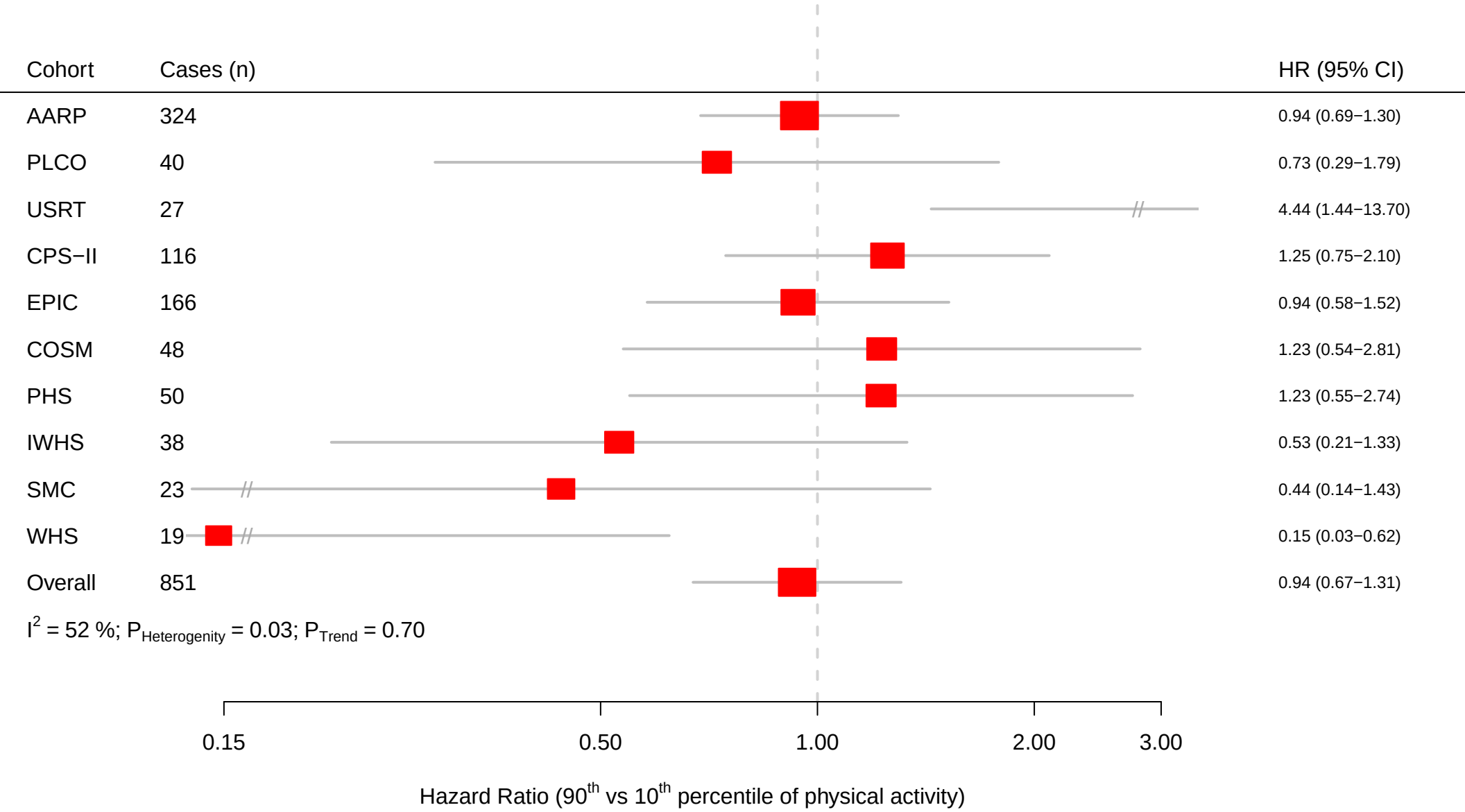
eFigure 2r. Physical activity and risk of thyroid cancer



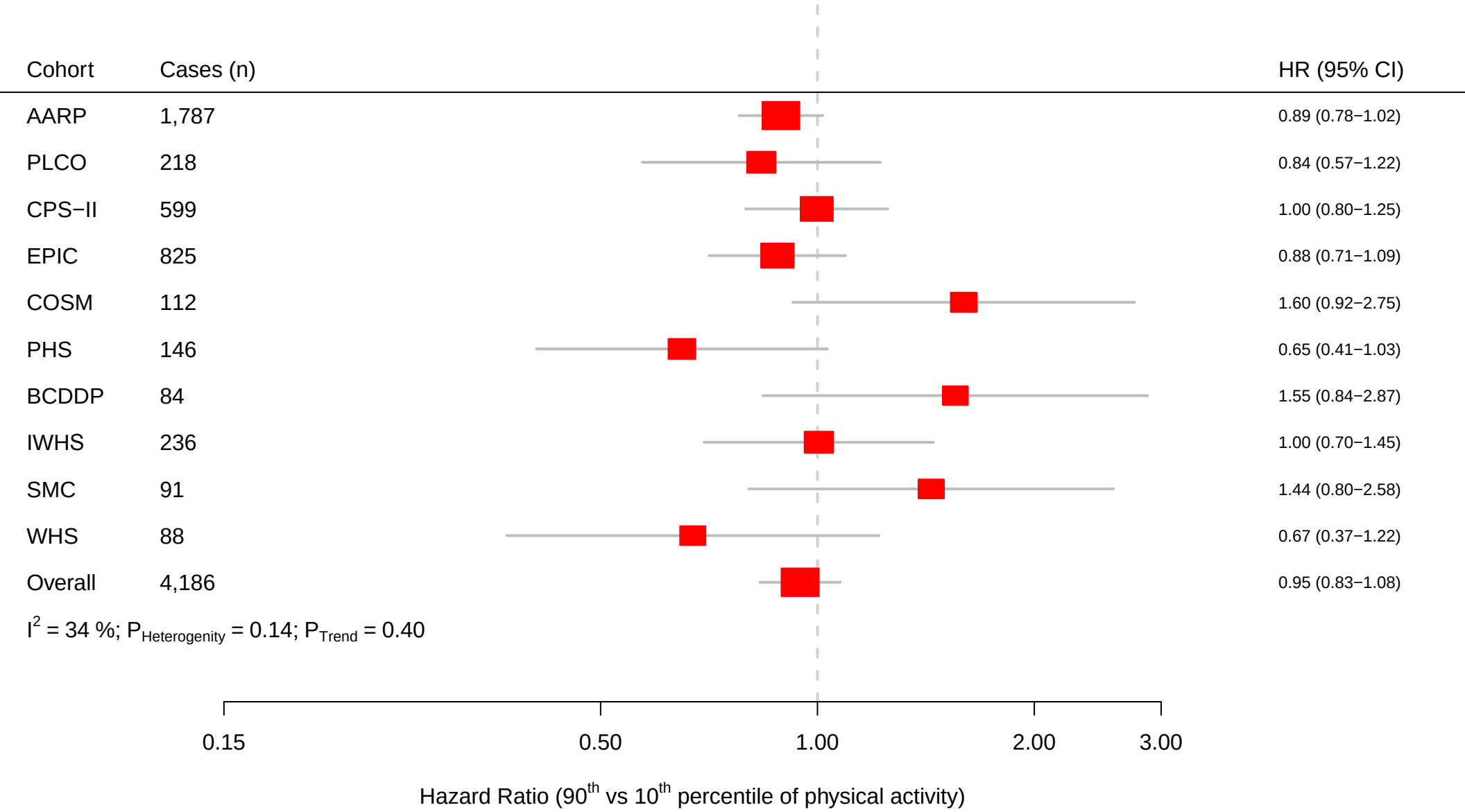
eFigure 2s. Physical activity and risk of gastric non−cardia cancer



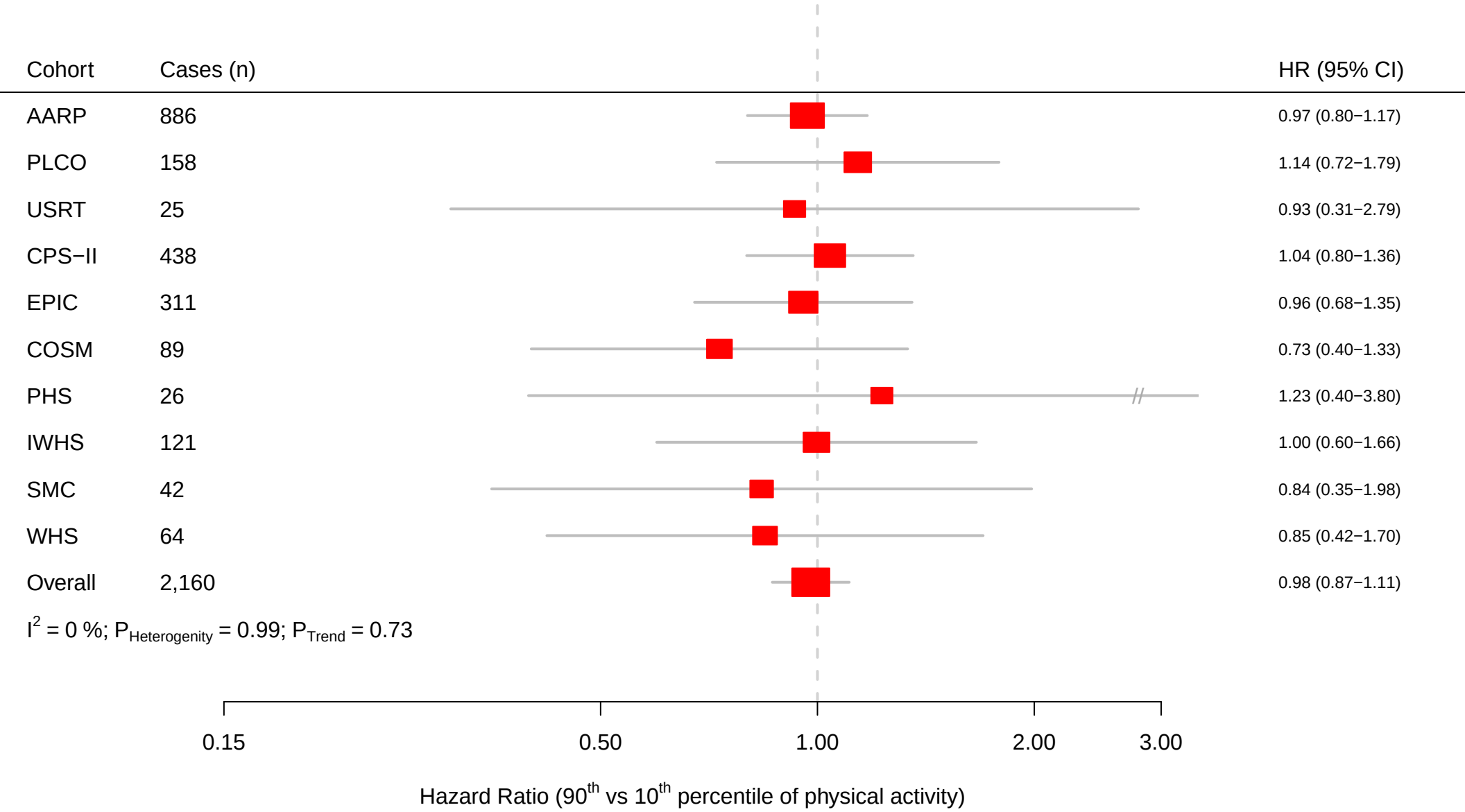
eFigure 2t. Physical activity and risk of soft tissue cancer



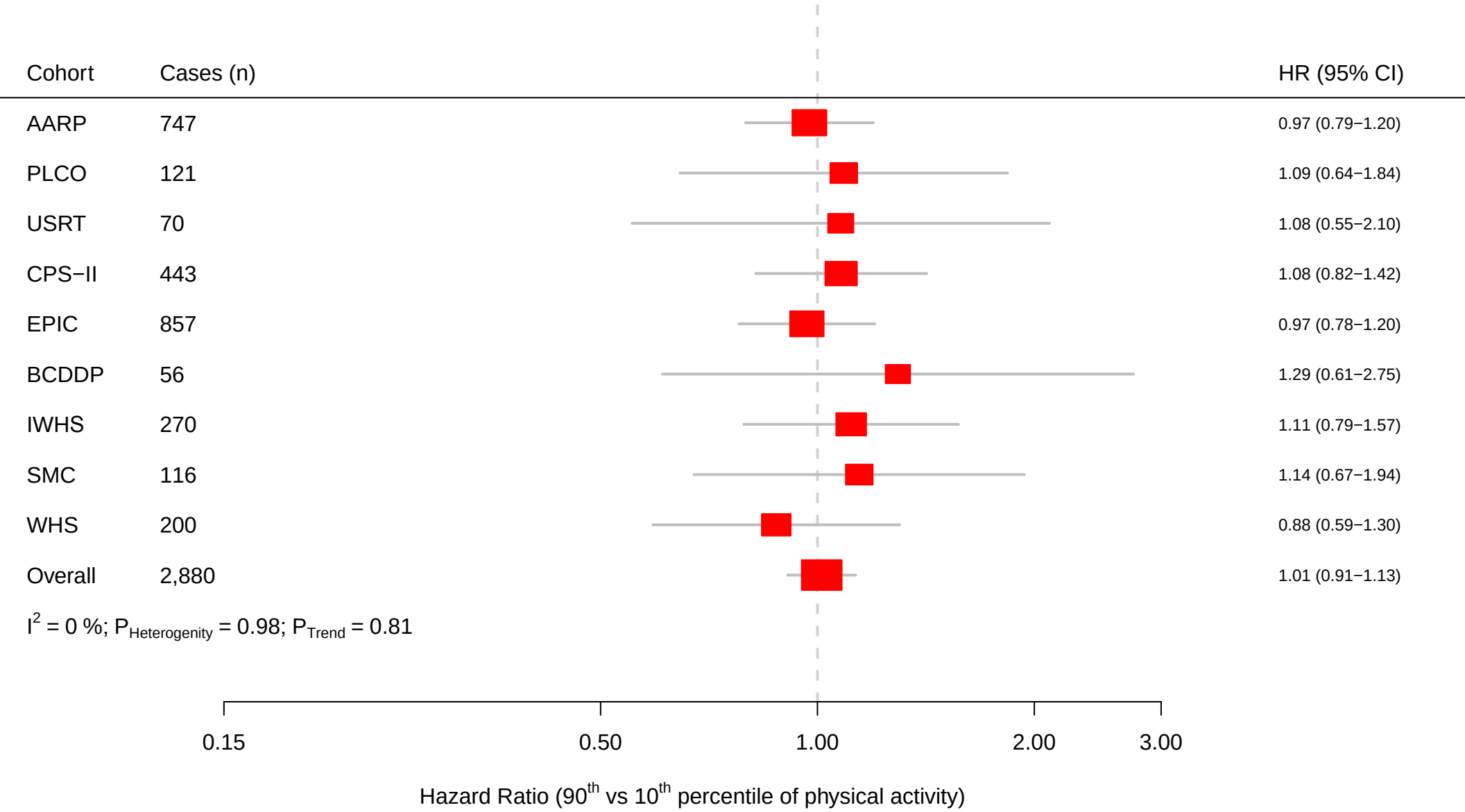
eFigure 2u. Physical activity and risk of pancreas cancer



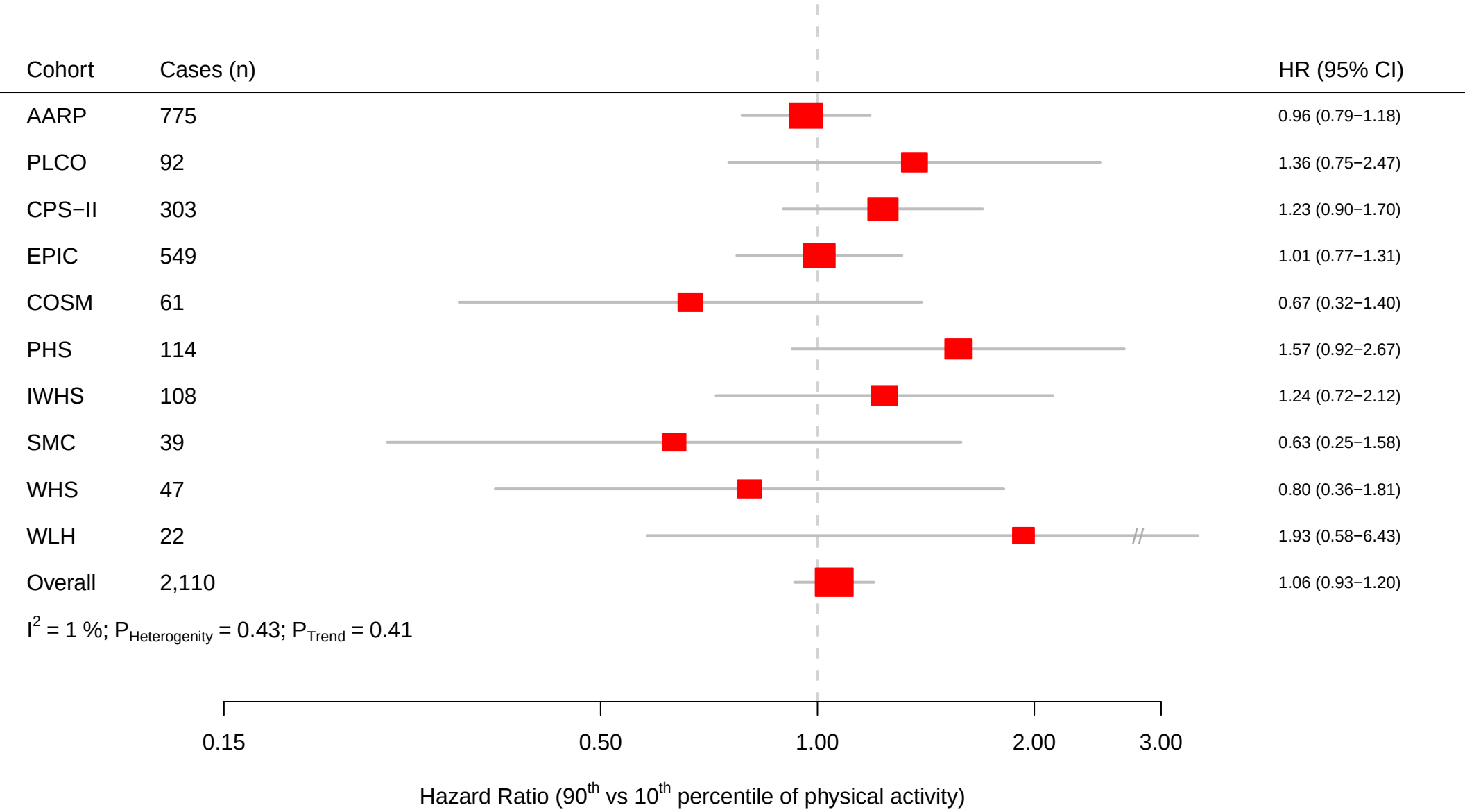
eFigure 2v. Physical activity and risk of lymphocytic leukemia



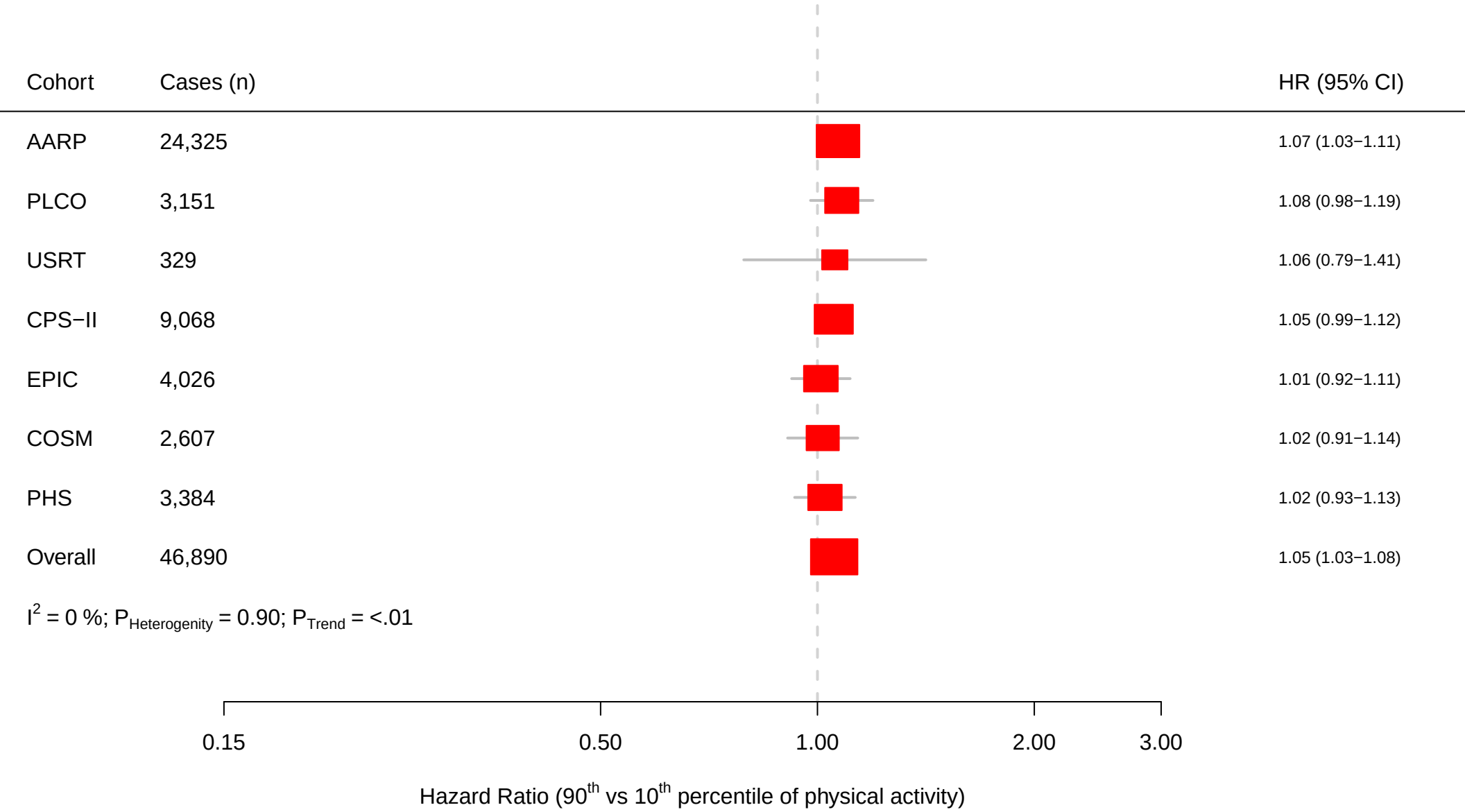
eFigure 2w. Physical activity and risk of ovary cancer



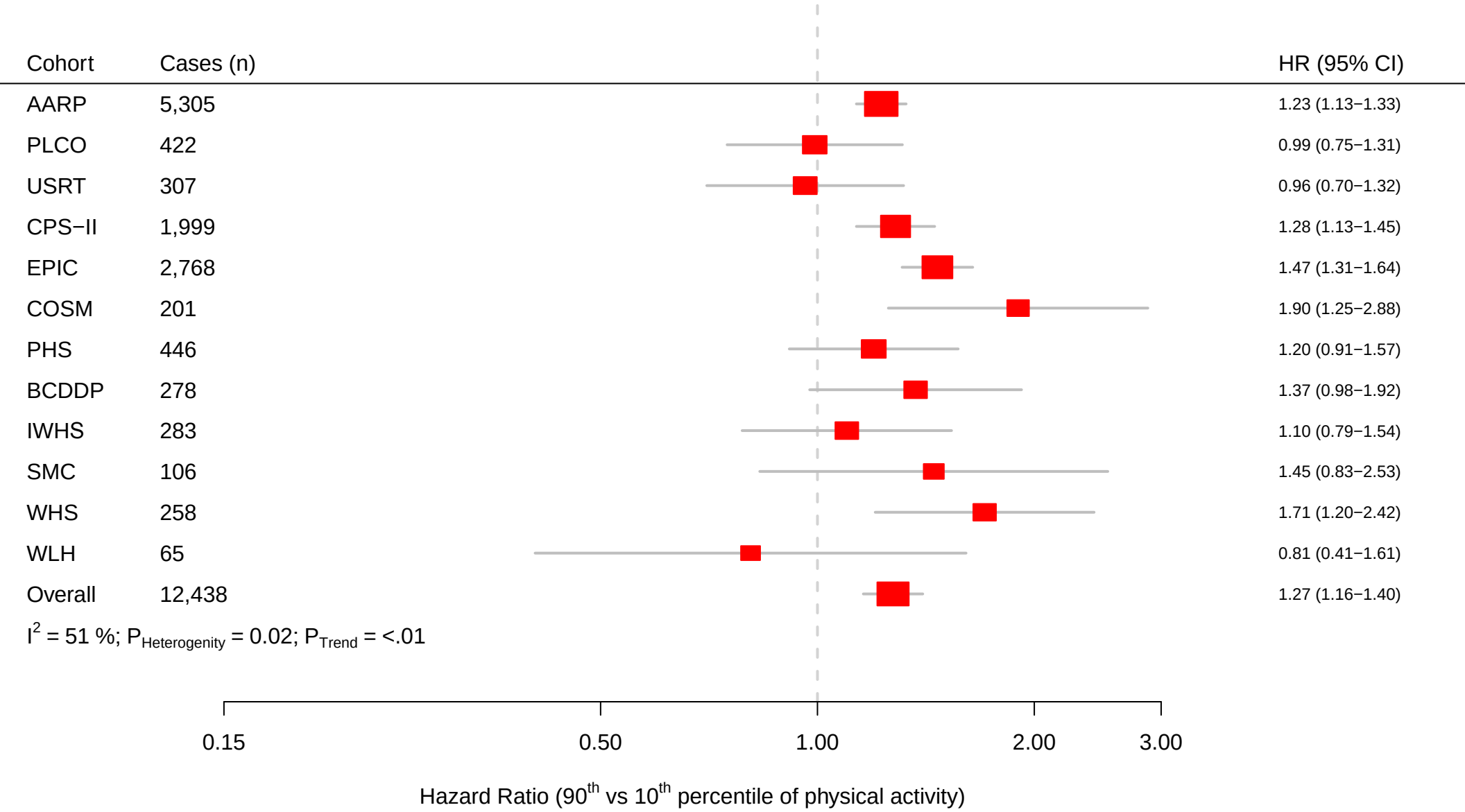
eFigure 2x. Physical activity and risk of brain cancer



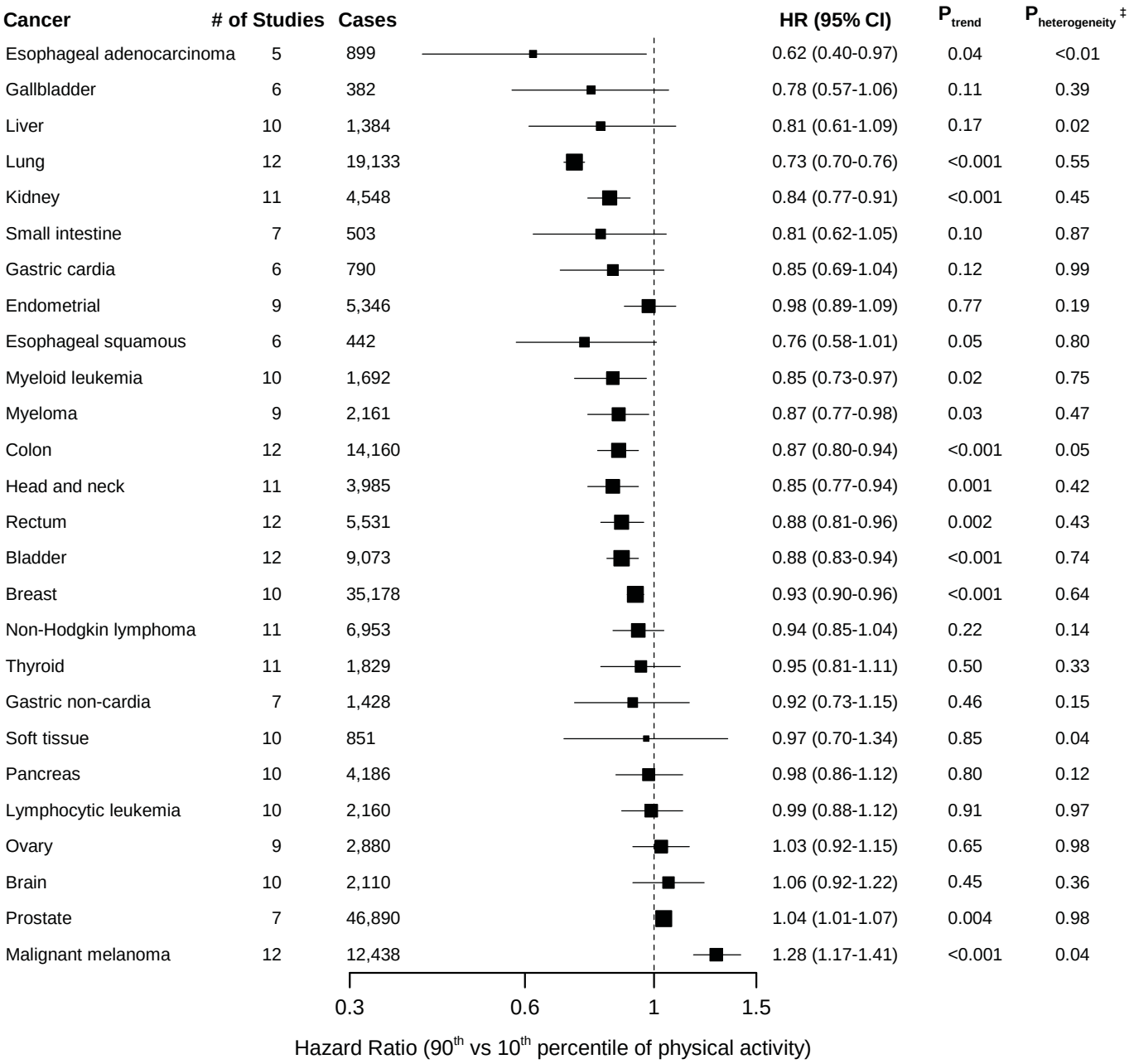
eFigure 2y. Physical activity and risk of prostate cancer



eFigure 2z. Physical activity and risk of melanoma



eFigure 3. Summary multivariable* hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type†, with adjustment for BMI

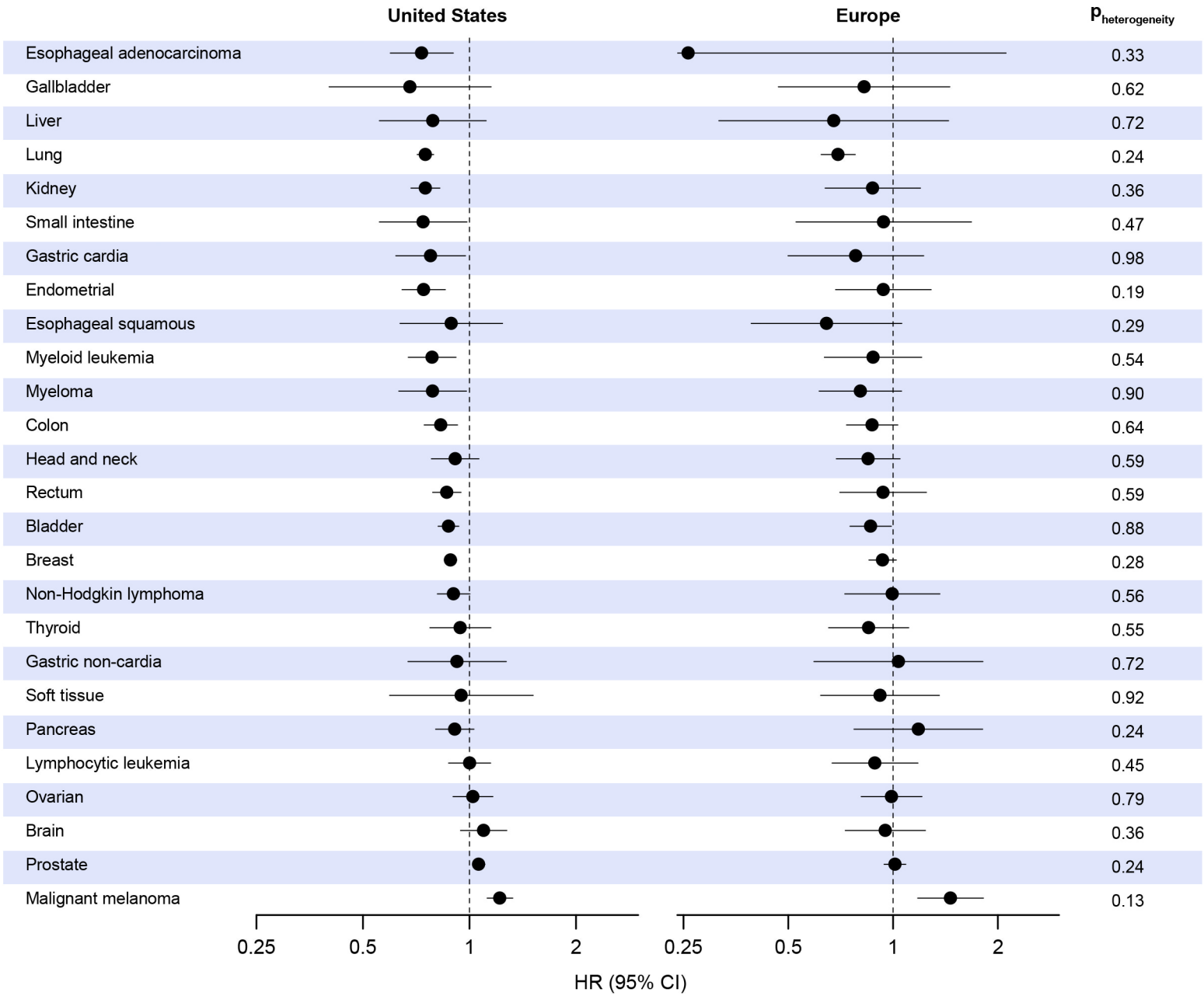


* Multivariable models were adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other), and body mass index (<18.5, 18.5-24.9, 25.0-29.9, 30-34.9, 35.0-39.9, 40+ kg/m^2). Models for endometrial, breast, and ovarian cancers are additionally adjusted for hormone replacement therapy use (ever, never), oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children).

† The Surveillance Epidemiology and End Results site recode and the International Classification of Diseases for Oncology, Third Edition code corresponding to each cancer type are shown in Supplementary Table 1.

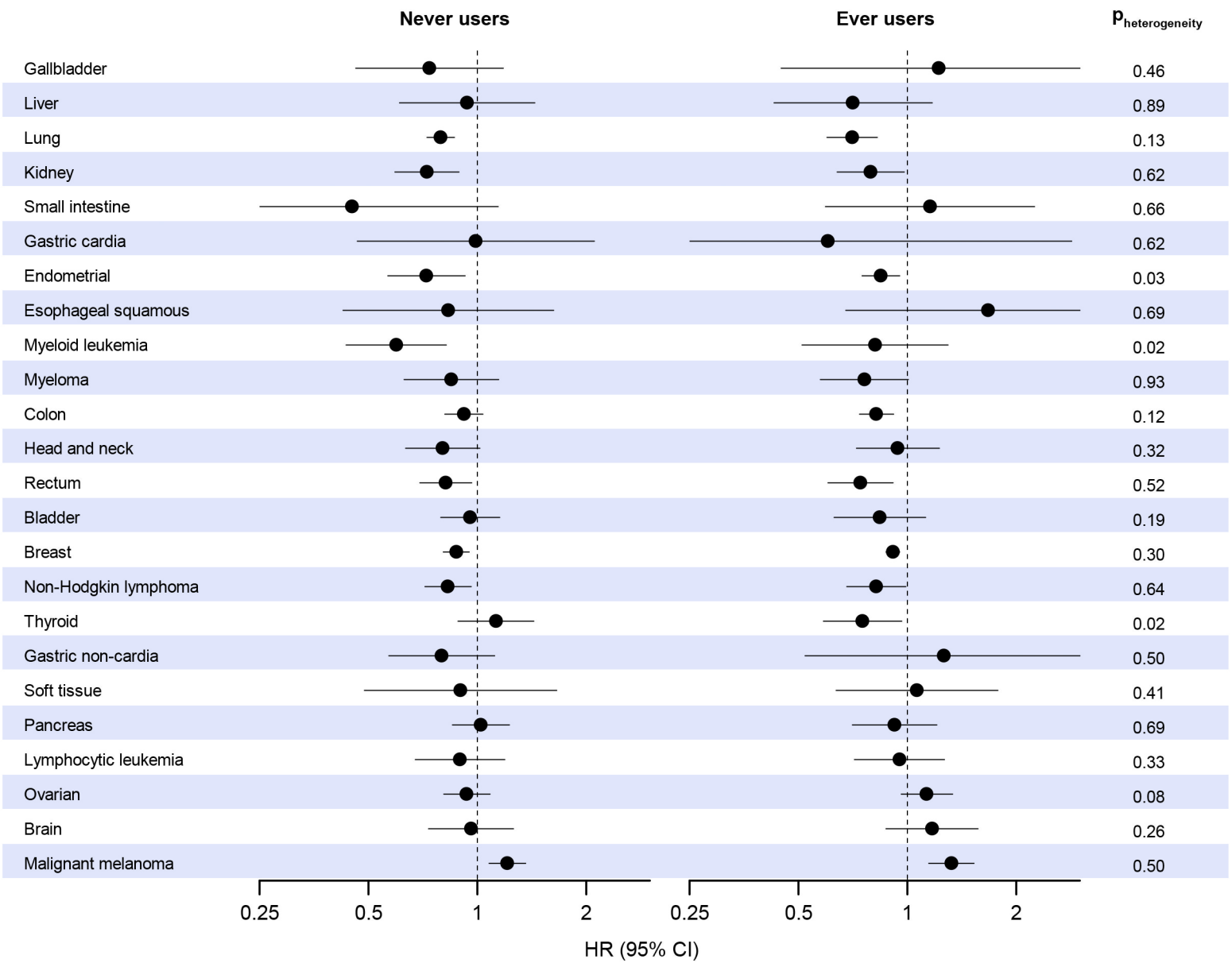
‡ $P_{heterogeneity}$ indicates the P-value for heterogeneity of hazard ratios across participating studies.

eFigure 4. Summary multivariable* hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by geographic region, United States or Europe.



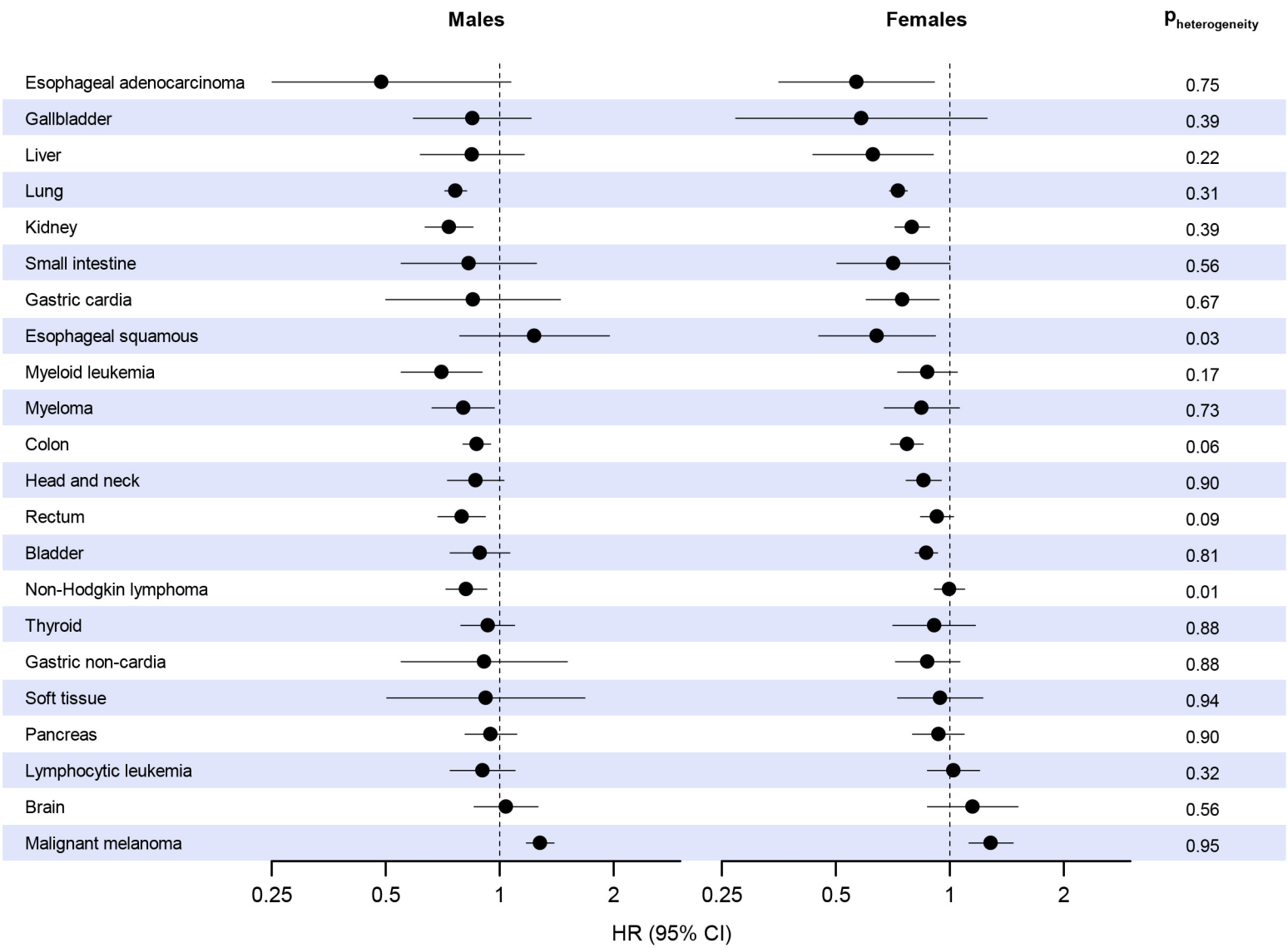
* All models were adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other). Models for endometrial, breast, and ovarian cancers are additionally adjusted for oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children).

eFigure 5. Summary multivariable* hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by history of hormone replacement therapy, never users or ever users.



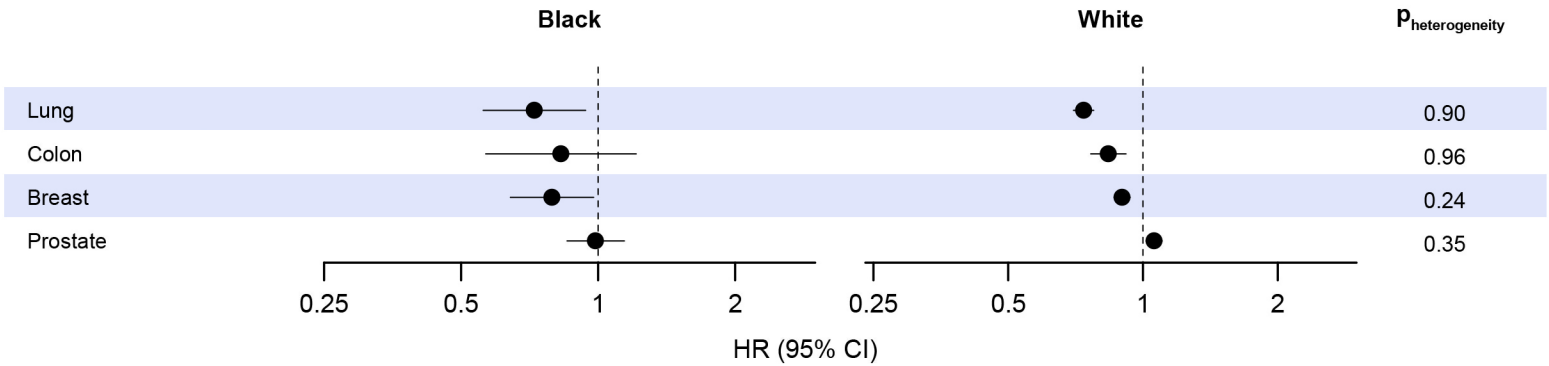
* All models were adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other). Models for endometrial, breast, and ovarian cancers are additionally adjusted for oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children).

eFigure 6. Summary multivariable* hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by gender.



* All models were adjusted for age, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other).

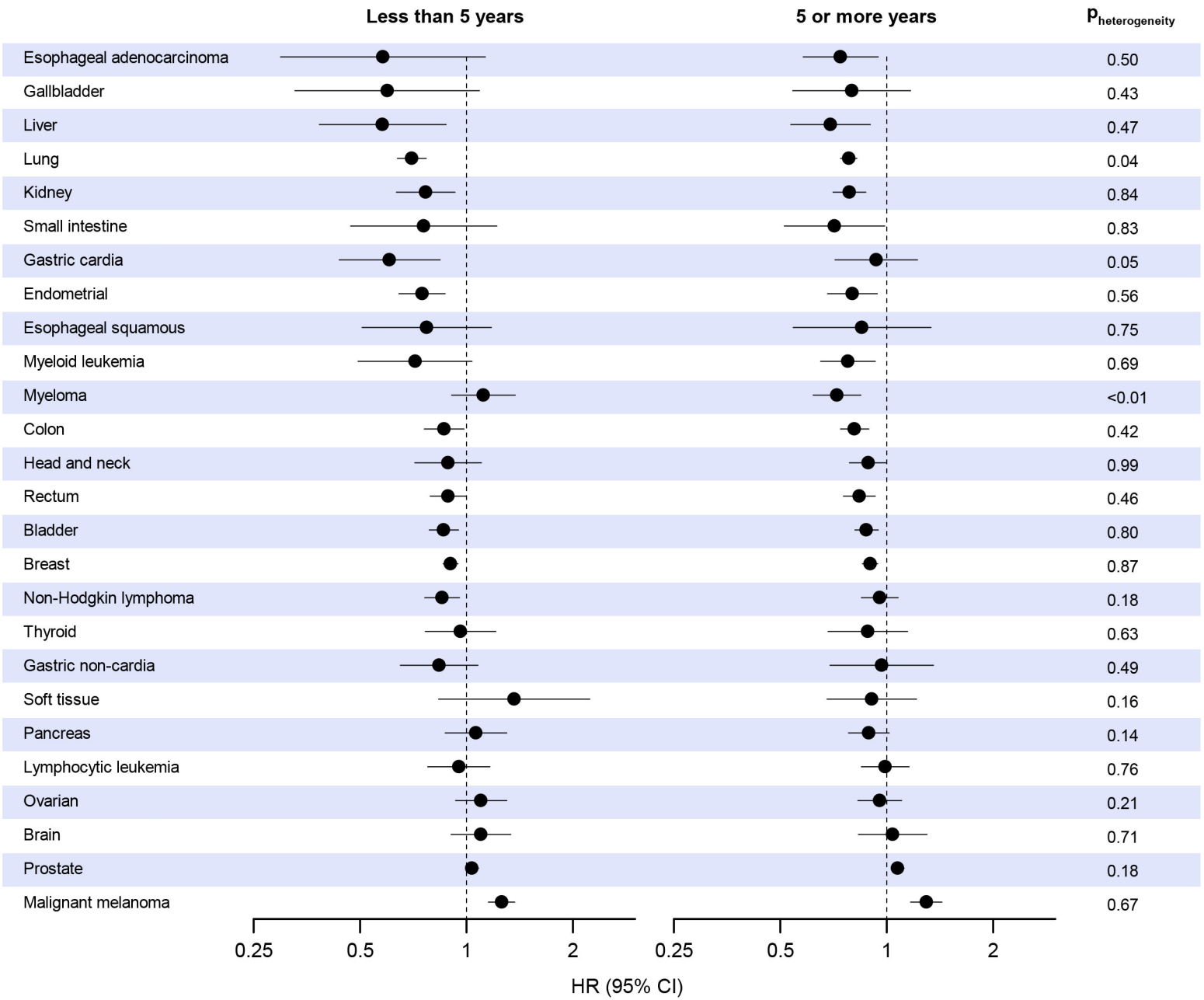
eFigure 7. Summary multivariable* hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by race/ethnicity†.



* All models were adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other). Models for endometrial, breast, and ovarian cancers are additionally adjusted for hormone replacement therapy use (ever, never), oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children).

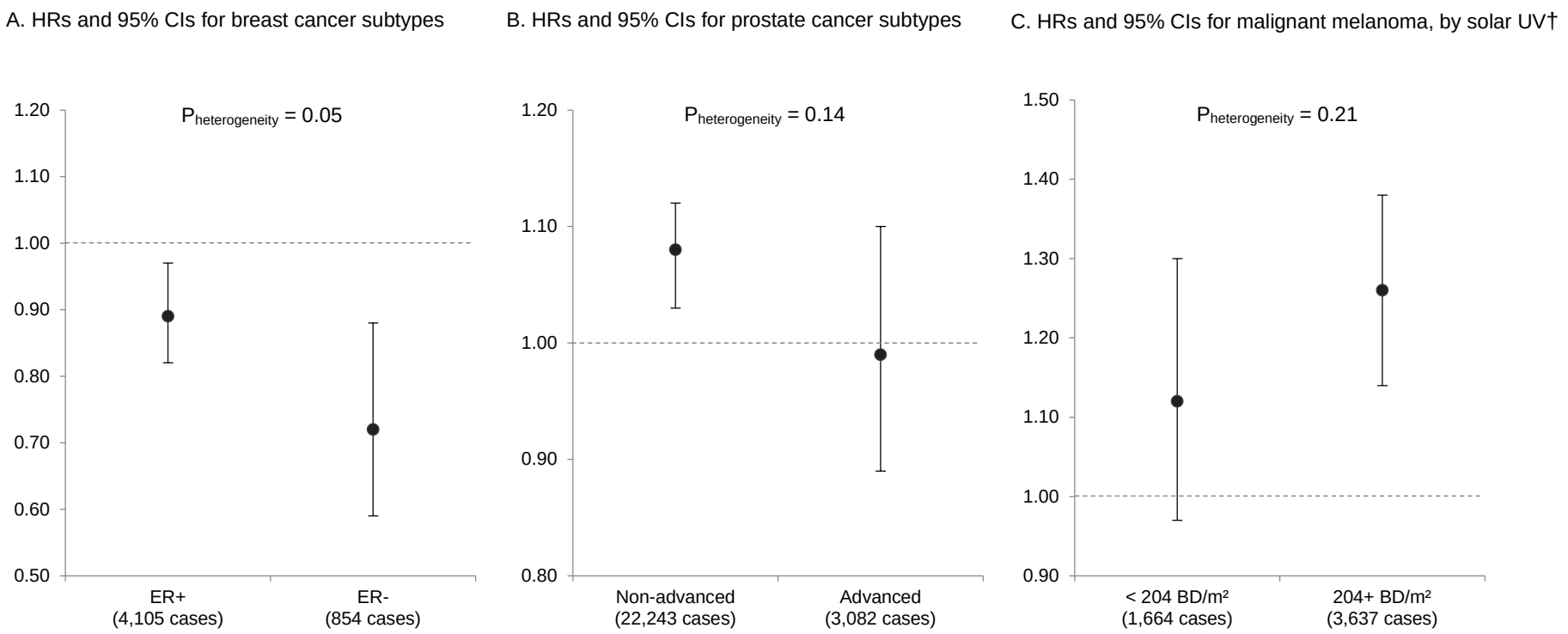
† Black and white participants only; case numbers for other race/ethnicity groups too small for analysis. Restricted to cancer types with at least 100 cases total among Blacks.

eFigure 8. Summary multivariable* hazard ratios (HR) and 95% confidence intervals (CI) for a higher (90th percentile) versus lower (10th percentile) level of leisure-time physical activity, by cancer type, stratified by period of follow-up.



* All models were adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other). Models for endometrial, breast, and ovarian cancers are additionally adjusted for hormone replacement therapy use (ever, never), oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children).

eFigure 9. Multivariable* hazard ratios (HRs) and 95% confidence intervals (CIs) in the NIH-AARP Diet and Health Study for breast cancer subtypes (Panel A), for prostate cancer subtypes (Panel B), and for malignant melanoma, stratified by ground level solar ultraviolet radiation† (Panel C).



* Multivariable models were adjusted for age, gender, smoking status (never, former, current), alcohol consumption (0, 0.1-14.9, 15.0-29.9 and 30.0+ g/day), education (did not complete high school, completed high school, post high-school training, some college, completed college), and race/ethnicity (white, black, other). Models for breast cancer are additionally adjusted for postmenopausal hormone therapy use (ever, never), oral contraceptive use (ever, never), age at menarche (<10 years, 10-11 years, 12-13 years, 14+ years), age at menopause (premenopausal, 40-44 years, 45-49 years, 50-54 years, 55+ years), and parity (0 children, 1 child, 2 children, 3+ children)

† Ground-level solar ultraviolet radiation (erythemal dose) was assessed by linking census tract of participant residence to the Total Ozone Mapping Spectrometer (TOMS) dataset of the National Aeronautics and Space Administration. The erythemal dose is based on average noon-time exposure during the month of July and is defined specifically in terms of biological damage per square meter (BD/m^2).

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