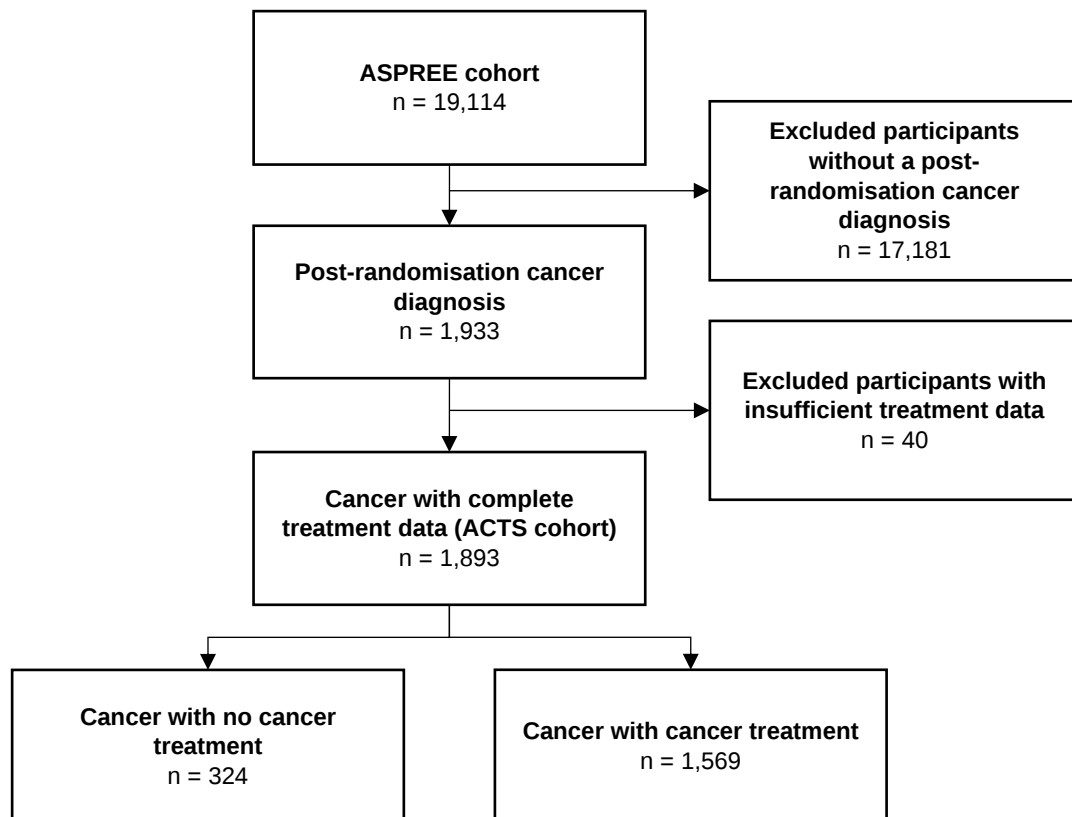


Supplementary Figure S1. Flow diagram of inclusion for the ASPREE Cancer Treatment Substudy (ACTS).



Supplementary Table S1. Coding criteria for cancer treatment data, stratified by treatment modality.

Type of cancer treatment data	Criteria
Systemic therapy - Cytotoxic chemotherapy - Hormonal therapy - Targeted therapy - Immunotherapy	<i>Inclusion</i> - Any systemic therapy including, but not limited to, cytotoxic chemotherapy, hormonal therapy, targeted therapy, and immunotherapy <i>Exclusion</i> - Regional chemotherapy e.g. transarterial chemoembolisation, hypothermic intraperitoneal chemotherapy, intravesical mitomycin c - Regional immunotherapy e.g. intravesical BCG (Bacillus Calmette-Guerin) immunotherapy (early-stage bladder cancer) <i>Miscellaneous</i> - Arsenic trioxide + all-trans retinoic acid for acute promyelocytic leukaemia should be coded as targeted therapy
Radiation therapy	<i>Inclusion</i> - Any radiation therapy procedure used in the treatment of a primary tumour or its metastases <i>Exclusions</i> - None <i>Miscellaneous</i> - Radioactive iodine for thyroid cancer should be coded as radiation therapy
Surgery	<i>Inclusion</i> - Any operation that has been undertaken to remove a tumour e.g. anterior resection for colorectal cancer, mastectomy for breast cancer, wide local excisions of melanoma, endoscopic resection of a known tumour - Any operation that has been undertaken to debulk the tumour - Any operation related to the treatment of the tumour or its associated symptoms e.g. video-assisted thoracoscopic pleurodesis for pleural effusion secondary to lung cancer, transurethral resection of the prostate for prostatomegaly secondary to prostate cancer, bypass surgery for pancreatic surgery <i>Exclusion</i> - Endoscopic procedures without intent for curative resection of a tumour e.g. colonoscopy, cystoscopy, bronchoscopy - Biopsies and other diagnostic procedures e.g. excision biopsies for melanoma or breast cancer - Procedures in which a cancer was incidentally discovered e.g. diagnosis of prostate cancer on transurethral resection of the prostate for benign prostatic hyperplasia
Regional therapy	<i>Inclusion</i>

	• Regional chemotherapy e.g. transarterial chemoembolisation, hypothermic intraperitoneal chemotherapy, intravesical mitomycin c • Regional immunotherapy for confirmed cancers e.g. intravesical BCG (Bacillus Calmette-Guerin) immunotherapy <i>Exclusion</i> • Regional therapy for in-situ cancers e.g. intravesical BCG for bladder carcinomas in-situ
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Supplementary Table S2. Cancer treatment modalities received for other incident post-randomisation cancers during ASPREE, stratified by cancer type and metastatic status, and cause of death and time from diagnosis to death.

		Systemic Therapy						
	Any treatment (n=1,569)	Any systemic therapy (n=869)	Chemotherapy (n=537)	Hormonal therapy (n=351)	Targeted therapy (n=85)	Immunotherapy (n=31)	Radiation therapy (n=544)	Surgery (n=1,029)
Non-metastatic solid tumours								
Bladder (n=59)	48 (81%)	15 (25%)	15 (25%)	-	-	1 (2%)	9 (15%)	32 (54%)
Brain (n=25)	17 (68%)	8 (32%)	8 (32%)	-	-	-	10 (40%)	16 (64%)
Cervical (n=3)	3 (100%)	3 (100%)	3 (100%)	-	-	-	3 (100%)	-
Gallbladder or bile duct (n=11)	6 (55%)	4 (36%)	4 (36%)	-	-	-	2 (18%)	3 (27%)
Kidney (n=25)	24 (96%)	1 (4%)	-	-	1 (4%)	-	1 (4%)	24 (96%)
Liver (n=3)	2 (67%)	2 (67%)	-	-	2 (67%)	1 (33%)	1 (33%)	1 (33%)
Mesothelioma (n=14)	12 (86%)	6 (43%)	6 (43%)	-	-	-	3 (21%)	8 (57%)
Oesophageal (n=14)	13 (93%)	8 (57%)	8 (57%)	-	-	-	11 (79%)	5 (36%)
Ovary or endometrium (n=39)	36 (92%)	12 (31%)	11 (28%)	1 (3%)	-	-	15 (38%)	35 (90%)
Pancreas (n=31)	23 (74%)	14 (45%)	14 (45%)	-	-	-	2 (6%)	18 (58%)
Stomach (n=21)	17 (81%)	8 (38%)	8 (38%)	-	-	-	5 (24%)	16 (76%)
Thyroid (n=10)	10 (100%)	-	-	-	-	-	6 (60%)	9 (90%)
Metastatic solid tumours								
Bladder (n=10)	7 (70%)	4 (40%)	4 (40%)	-	-	-	3 (30%)	2 (20%)
Brain (n=0)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Cervical (n=0)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Gallbladder or bile duct (n=10)	5 (50%)	5 (50%)	5 (50%)	-	-	-	-	1 (10%)
Kidney (n=10)	7 (70%)	3 (30%)	2 (20%)	-	1 (10%)	-	4 (40%)	4 (40%)
Liver (n=4)	3 (75%)	1 (25%)	-	-	1 (25%)	-	1 (25%)	1 (25%)
Mesothelioma (n=1)	1 (100%)	-	-	-	-	-	-	1 (100%)

Oesophageal (n=13)	11 (85%)	9 (69%)	9 (69%)	-	-	-	9 (69%)	-
Ovary or endometrium (n=34)	28 (82%)	24 (71%)	23 (68%)	2 (6%)	3 (9%)	-	2 (6%)	18 (53%)
Pancreas (n=33)	20 (61%)	16 (48%)	16 (48%)	-	-	-	2 (6%)	7 (21%)
Stomach (n=8)	6 (75%)	2 (25%)	2 (25%)	-	-	-	3 (38%)	1 (13%)
Thyroid (n=0)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Percentages represent the proportion of participants who received cancer treatment relative to the first column. For example, 81% of participants with bladder cancers received any cancer treatment.

“-“ indicates that no one (0 participants) in this group received a particular treatment modality.

Supplementary Table S3. Cancer treatment modalities received for common non-sex specific incident post-randomisation cancers during ASPREE, stratified by cancer type and sex (F = female, M = male).

			Systemic Therapy											
	Any treatment (n=1,569)		Any systemic therapy (n=869)		Chemotherapy (n=537)		Targeted therapy (n=85)		Immunotherapy (n=31)		Radiation therapy (n=544)		Surgery (n=1,029)	
	<i>F</i>	<i>M</i>	<i>F</i>	<i>M</i>	<i>F</i>	<i>M</i>	<i>F</i>	<i>M</i>	<i>F</i>	<i>M</i>	<i>F</i>	<i>M</i>	<i>F</i>	<i>M</i>
Non-metastatic solid tumours														
Colorectal (n _F =98; n _M =108)	90 (92%)	101 (94%)	30 (31%)	41 (38%)	30 (31%)	41 (38%)	1 (1%)	3 (3%)	-	-	7 (7%)	13 (12%)	98 (100 %)	98 (91%)
Lung (n _F =31; n _M =44)	29 (94%)	36 (82%)	10 (32%)	10 (23%)	9 (29%)	9 (20%)	-	1 (2%)	2 (6%)	-	14 (45%)	19 (43%)	16 (52%)	22 (50%)
Melanoma (n _F =60; n _M =100)	57 (95%)	94 (94%)	3 (5%)	2 (2%)	-	-	-	-	3 (5%)	2 (2%)	1 (2%)	4 (4%)	55 (92%)	91 (91%)
Metastatic solid tumours														
Colorectal (n _F =26; n _M =30)	23 (88%)	27 (90%)	20 (77%)	22 (73%)	20 (77%)	22 (73%)	12 (46%)	8 (27%)	-	-	4 (15%)	7 (23%)	14 (54%)	21 (70%)
Lung (n _F =26; n _M =51)	20 (77%)	39 (76%)	12 (46%)	27 (53%)	9 (35%)	27 (53%)	3 (12%)	3 (6%)	2 (8%)	4 (8%)	16 (62%)	24 (47%)	5 (19%)	10 (20%)
Melanoma (n _F =10; n _M =18)	8 (80%)	15 (83%)	3 (30%)	12 (67%)	1 (10%)	1 (6%)	1 (10%)	4 (22%)	1 (10%)	10 (56%)	3 (30%)	7 (39%)	5 (50%)	11 (61%)
Haematological malignancy (n _F =97; n _M =88)	64 (66%)	48 (55%)	58 (60%)	44 (50%)	54 (56%)	43 (49%)	10 (10%)	9 (10%)	-	2 (2%)	10 (10%)	6 (7%)	6 (6%)	4 (5%)
Percentages represent the proportion of participants who received cancer treatment relative to the first column. For example, 92% of female participants with non-metastatic colorectal cancers received any cancer treatment. “-“ indicates that no one (0 participants) in this group received a particular treatment modality.														

Supplementary Table S4. Cancer treatment modalities received for common incident post-randomisation cancers during ASPREE, stratified by cancer type and country of residence (Aus = Australia, US = United States).

			Systemic Therapy													
	Any treatment (n=1,569)		Any systemic therapy (n=869)		Chemotherapy (n=537)		Hormonal therapy (n=351)		Targeted therapy (n=85)		Immunotherap y (n=31)		Radiation therapy (n=544)		Surgery (n=1,029)	
	<i>Aus</i>	<i>US</i>	<i>Aus</i>	<i>US</i>	<i>Aus</i>	<i>US</i>	<i>Aus</i>	<i>US</i>	<i>Aus</i>	<i>US</i>	<i>Aus</i>	<i>US</i>	<i>Aus</i>	<i>US</i>	<i>Aus</i>	<i>US</i>
All cancers (n _{AUS} =1,758; n _{US} =175)	1,444 (82%)	125 (71%)	799 (45%)	70 (40%)	501 (28%)	36 (21%)	317 (18%)	34 (19%)	82 (5%)	3 (2%)	27 (2%)	4 (2%)	512 (29%)	32 (18%)	944 (54%)	85 (49%)
Non-metastatic solid tumours																
Breast (n _{AUS} =181; n _{US} =30)	181 (100%)	29 (97%)	150 (83%)	21 (70%)	46 (25%)	3 (10%)	129 (71%)	20 (67%)	13 (7%)	-	-	-	97 (54%)	7 (23%)	179 (99%)	27 (90%)
Colon/rectum (n _{AUS} =198; n _{US} =8)	185 (93%)	6 (75%)	68 (34%)	3 (38%)	68 (34%)	3 (38%)	N/A	N/A	4 (2%)	-	-	-	19 (10%)	1 (13%)	182 (92%)	5 (63%)
Lung (n _{AUS} =68; n _{US} =7)	60 (88%)	5 (71%)	20 (29%)	-	18 (26%)	-	N/A	N/A	1 (1%)	-	2 (3%)	-	33 (49%)	-	33 (49%)	5 (71%)
Melanoma (n _{AUS} =154; n _{US} =6)	149 (97%)	2 (33%)	4 (3%)	1 (17%)	-	-	N/A	N/A	-	-	4 (3%)	1 (17%)	5 (3%)	-	145 (94%)	1 (17%)
Prostate (n _{AUS} =248; n _{US} =18)	182 (73%)	9 (50%)	94 (38%)	4 (22%)	5 (2%)	-	92 (37%)	4 (22%)	-	-	-	-	102 (41%)	4 (22%)	79 (32%)	4 (22%)
Metastatic solid tumours																
Breast (n _{AUS} =27; n _{US} =5)	24 (89%)	4 (80%)	22 (81%)	4 (80%)	8 (30%)	2 (40%)	17 (63%)	3 (60%)	4 (15%)	-	-	-	12 (44%)	3 (60%)	7 (26%)	1 (20%)
Colon/rectum (n _{AUS} =54; n _{US} =2)	49 (91%)	1 (50%)	41 (76%)	1 (50%)	41 (76%)	1 (50%)	N/A	N/A	20 (37%)	-	-	-	11 (20%)	-	35 (65%)	-
Lung (n _{AUS} =68; n _{US} =9)	54 (79%)	5 (56%)	36 (53%)	3 (33%)	33 (49%)	3 (33%)	N/A	N/A	6 (9%)	-	4 (6%)	2 (22%)	36 (53%)	4 (44%)	15 (22%)	-
Melanoma (n _{AUS} =25; n _{US} =3)	21 (84%)	2 (67%)	14 (56%)	1 (33%)	1 (4%)	1 (33%)	N/A	N/A	5 (20%)	-	11 (44%)	-	9 (36%)	1 (33%)	15 (60%)	1 (33%)
Prostate (n _{AUS} =87; n _{US} =11)	80 (92%)	8 (73%)	78 (90%)	8 (73%)	24 (28%)	1 (9%)	76 (87%)	7 (64%)	-	-	-	-	31 (36%)	4 (36%)	16 (18%)	2 (18%)
Haematological malignancy (n _{AUS} =164; n _{US} =21)	103 (63%)	9 (43%)	94 (57%)	8 (38%)	90 (55%)	7 (33%)	N/A	N/A	18 (11%)	1 (5%)	2 (1%)	-	14 (9%)	2 (10%)	10 (6%)	-

NB: Percentages represent the proportion of participants who received cancer treatment relative to the first column. For example, 100% of Australian participants with non-metastatic breast cancers received any cancer treatment.

“-“ indicates that no one (0 participants) in this group received a particular treatment modality.