Cancer before, during and after pregnancy

National Cancer Registration and Analysis Service

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Executive summary

The occurrence of cancer during pregnancy is uncommon with an incidence rate of approximately 1 in 1,000 pregnancies. The rate of pregnancy-associated cancer is increasing and this is partly caused by a trend in delaying child bearing to an older age.

This report summarises data on cancers that are diagnosed in women during pregnancy in England. The key findings.

Between 2012 and 2014, 3,272 women in England aged between 15 and 44 were identified as being diagnosed with malignant cancer before, during or after their pregnancy. This is out of 2,503,174 women who were pregnant. The associated age-standardised incidence rate (ASIR) of cancer in women before, during and after pregnancy was 173 per 100,000 pregnancies (95% CI 164 -182), 48% higher than the equivalent ASIR of cancer in the female population aged 15-44 nationally (117 per 100,000 female population, 95% CI 115 -118).

The most common cancers in women before, during and after pregnancy were breast (784 cases), melanoma of skin (504), cervical (498), haematological (286), ovarian (240), and colorectal and anus (188), accounting for 76% of all the observed cases. Comparing the ASIR of cancer in women before, during and after pregnancy with the ASIR of cancer in the female population, by site, rates were over 30% higher for breast cancer (55 vs 41 per 100,000 respectively) and around double those for melanoma (26 vs 13 per 100,000).

When compared with the general female population, incidence of all cancers in women before, during and after pregnancy was:

- higher in most regions
- higher in most age-groups
- two-thirds higher for those living in the most deprived quintile nationally (ASIR 189 vs 115 per 100,000)
- statistically significantly higher in most stage of disease groups

When compared with the general female population, incidence of breast cancer in women before, during and after pregnancy was:

- almost 50% higher in those aged 35 to 39 (ASIR 93 vs 63 per 100,000)
- not statistically significantly different in all quintiles of deprivation

- twice as high in stage group 4 (ASIR 4.3 vs 1.9 per 100,000), (Stage 4 means cancer has spread to other parts of the body)

When compared with the general female population, incidence of melanoma of the skin in women before, during and after pregnancy was:

- around double in those aged 30-34, 35-39, and 40-44 in pregnancy (27, 40 and 59 per 100,000 respectively) than in the female population (14, 18 and 23 per 100,000)
- more than twice as high in the least deprived quintile (ASIR 35 vs 16 per 100,000)
- statistically significantly higher in stage group 1 (ASIR 20 vs 9 per 100,000) (Stage 1 means cancer is relatively small and contained within the organ it started in)

When compared with the general female population, incidence of cervical cancer in women before, during and after pregnancy was:

- almost 50% higher in those aged 25 to 29 (ASIR 31 vs 21 per 100,000)
- almost twice as high in the most deprived quintile (ASIR 27 vs 15 per 100,000)
- statistically significantly higher in stage group 1 (ASIR 8.9 vs 5.8 per 100,000)

The higher rates of pregnancy-associated cancers compared to the general female population may be due to frequent obstetric examinations which increases the chances of cancer detection.

Further work using a more robust maternity dataset would be required to ascertain timing of cancer diagnosis in relation to delivery.

Chapter 1: Introduction

The occurrence of cancer during pregnancy is uncommon with an incidence rate of approximately 1 in 1,000 pregnancies.[1] The rate of pregnancy-associated cancer is increasing and this is partly caused by a trend in delaying child bearing to an older age.[2]

Pregnancy-associated cancer is generally defined as a diagnosis during pregnancy or up to one year after delivery.[2,3] Some studies also include cancers diagnosed prior to pregnancy.[4] The incidence of different cancers in pregnant women varies between studies, and appears to be dependent on the underlying incidence of cancer within the population and age distribution of mothers. Breast, malignant melanoma, cervix, lymphoma, thyroid, haematological, ovarian, colon and central nervous system cancers are the most common cancers associated with pregnancy.[2,5,6,7]

There is a lack of national data in the UK concerning the number of women who are diagnosed with cancer during pregnancy.[3] In view of this, this report summarises data on cancers that are diagnosed in women during pregnancy in England.

Cancer registry data was linked to Hospital Episode Statistics Admitted Patient Care (HES APC) inpatient data to establish pregnancy-associated cancers. Incidence of pregnancy-associated cancers was then investigated for different age groups, by income deprivation, region of residence (Government Office Region, GOR), and stage at diagnosis.

Chapter 2: Methods

2.1 Data sources

All malignant cancers (excluding non-melanoma skin cancer), (ICD10 C00-C97 excl C44), diagnosed between 2012 and 2014 in residents of England were extracted from the Cancer Analysis System (CAS) held by the National Cancer Registration and Analysis Service (NCRAS) within Public Health England (PHE). These records were linked at patient level to the NHS admitted patient care (APC) Hospital Episode Statistics (HES) data for all patients diagnosed with cancer. NCRAS holds a cancer-related HES APC dataset which is linked to the cancer register. However, this dataset does not include information on conception dates or gestation, and as a result the cohort could not be defined using pregnancy dates, so instead is defined on dates of cancer diagnosis.

Population estimates used in the calculation for age-standardised rates in general female population were provided by Office for National Statistics (ONS) for England and Wales. Conceptions (pregnancies) data for the period 2012 to 2014 were provided by ONS.[8]

2.2 Study population

The study population included females aged 15 to 44 years diagnosed with malignant cancer from 2012 to 2014 who had a pregnancy or delivery code recorded in the HES inpatient dataset. Women who were diagnosed with cancer and had pregnancy or delivery related care one year before, during, or up to one year after a cancer diagnosis, were included. Where a patient had more than one tumour, the earliest diagnosed in the period was analysed, and all subsequent tumours were excluded. In this study, women who had a cancer diagnosed one year before, during, or up to one year after pregnancy are referred to as 'pregnant women'.[4]

The International Classification of Diseases, 10th revision[9] was used to classify the following sites; malignant neoplasms (C00-C97), pregnancy, childbirth and the puerperium (O00-O99) and persons encountering health services in circumstances related to reproduction (Z30-Z39). The full list of ICD10 codes used is included in the appendix.

2.3 Study factors

Sociodemographic information analysed included age at cancer diagnosis, Government Office Region (GOR) of residence, based on postcode at time of diagnosis, and socio-economic deprivation (as recorded by the income domain of the Indices of Multiple Deprivation (IMD) 2015).[10] The Indices of Deprivation 2015 provide a relative measure of deprivation in small areas (Lower-layer Super Output Areas, (LSOAs)) across England. The areas were grouped into quintiles according to their deprivation score and were numbered from the least deprived (1) to the most deprived (5).

All cancers were staged using the TNM[11] classification including mapping from FIGO stage for gynaecological cancers. Staging is a way of describing where the cancer is located, the size of cancer and how far it has grown. Stage 1 means cancer is relatively small and contained within the organ it started in. Stage 2 and 3 means cancer is larger or has spread into nearby tissues or lymph nodes. Stage 4 means cancer has spread to another organ of the body.

2.4 Statistical analysis

Age-specific rates were calculated in five-year age groups ranging from 15 -19 through to 40 - 44 for pregnant women and the general female population. Age-standardised rates together with 95% confidence intervals were calculated using the 2013 European Standard Population[12] by GOR of residence, stage group and deprivation quintile for pregnant women and the general female population.

Statistical significance was determined by assessing whether the confidence intervals overlap the benchmark value[13] (general female population rate). Non-overlapping confidence intervals are considered as statistically significantly different.

Deprivation in pregnant women was calculated by assigning weights to the population with each quintile representing 20% of the total pregnancies.[14]

Due to low counts of pregnancy-associated cancers, detailed analyses are presented only for cancers with total counts of around 500 cases or more over the study period. These cancers are: breast (ICD10 C50), malignant melanoma of skin (ICD10 C43) and cervical cancer (ICD10 C53).

Chapter 3: Results

3.1 Overall and by site

Between 2012 and 2014, a total of 3,272 pregnancy-associated cancers were identified in 2,503,174 pregnancies. The associated age-standardised incidence rate in pregnant women was 173 per 100,000 pregnancies. 24 women had 2 diagnoses of cancer over the study period. Of the 24 women with multiple diagnoses, 16 were diagnosed with the same type of cancer and 8 women had different cancer diagnoses. Under the assumption that each individual had only one primary diagnosis, the second cancer was excluded.

The most common cancers were breast (784 cases, 55 per 100,000), melanoma of skin (504 cases, 26 per 100,000), cervical (498 cases, 19 per 100,000), haematological (286 cases, 15 per 100,000), ovarian (240 cases, 11 per 100,000), colorectal and anus (188 cases, 9 per 100,000), (Table 1). These cancers accounted for 76% of all cancers diagnosed in pregnancy.

Table 1: Cancer incidence in pregnant women and general female population by site, England, 15-44 years, 2012-2014 combined.

Site	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
All cancers	3,272	173 (164 - 182)	36,169	117 (116 - 118)
Female breast	784	55 (50 - 60)	12,537	41 (41 - 42)
Melanoma of skin	504	26 (23 - 30)	4,128	13 (13 - 13)
Cervix uteri	498	19 (17 - 22)	3,883	13 (12 - 13)
Haematological	286	15 (12 - 17)	3,147	9.9 (9.6 - 10.3)
Ovary	240	11 (9 -13)	2,217	7.1 (6.8 - 7.4)
Colorectal and anus	188	8.5 (6.8 - 10.5)	1,971	6.3 (5.9 - 6.8)
CNS	99	4.5 (3.2 -6.0)	1,044	3.4 (3.2 - 3.6)
Other gynaecological	52	3.0 (1.9 - 4.4)	1,003	3.2 (2.8 - 3.5)
Urological	48	2.5 (1.6 - 3.7)	607	2.0 (1.8 - 2.1)
Lung	40	2.5 (1.5 -3.8)	567	1.8 (1.7 - 2.0)
Other malignant neoplasm	533	26 (23 - 30)	5,065	16 (16 - 17)

Rate is age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

Breast cancer was the most commonly diagnosed cancer amongst both the general female population as well as pregnant women (Figure 1). Breast cancer, malignant melanoma of skin, cervical, haematological, ovarian and colorectal cancer incidence rates were statistically significantly higher in pregnant women when compared to the general female population.

Melanoma incidence rates in pregnant women were around double those in the general female population.

Figure 1: Age-standardised incidence rates and 95% confidence intervals for cancers in pregnant women and general female population by site, England, 15-44 years, 2012-2014.
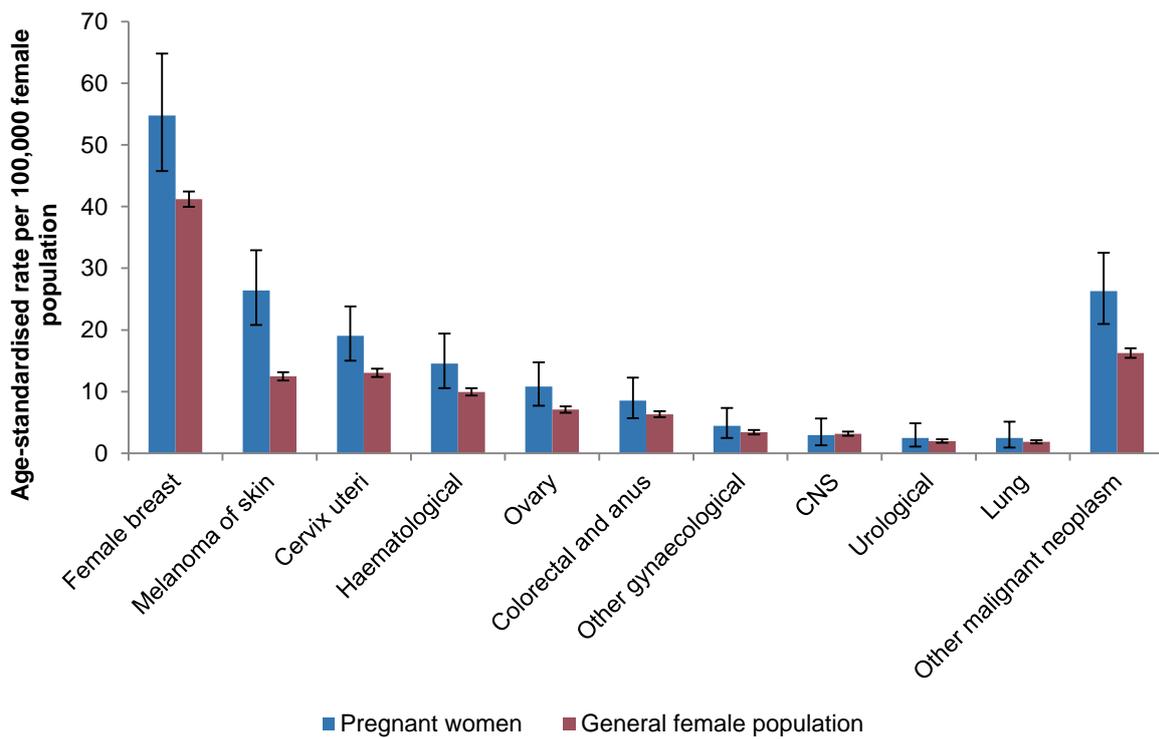
3.2 By Government Office Region (GOR)

Figure 2: Age-standardised incidence rates and 95% confidence intervals for all cancers (ICD10 C00-C97 excl C44) in pregnant women and general female population by Government Office Region (GOR), 15-44 years, 2012-2014.
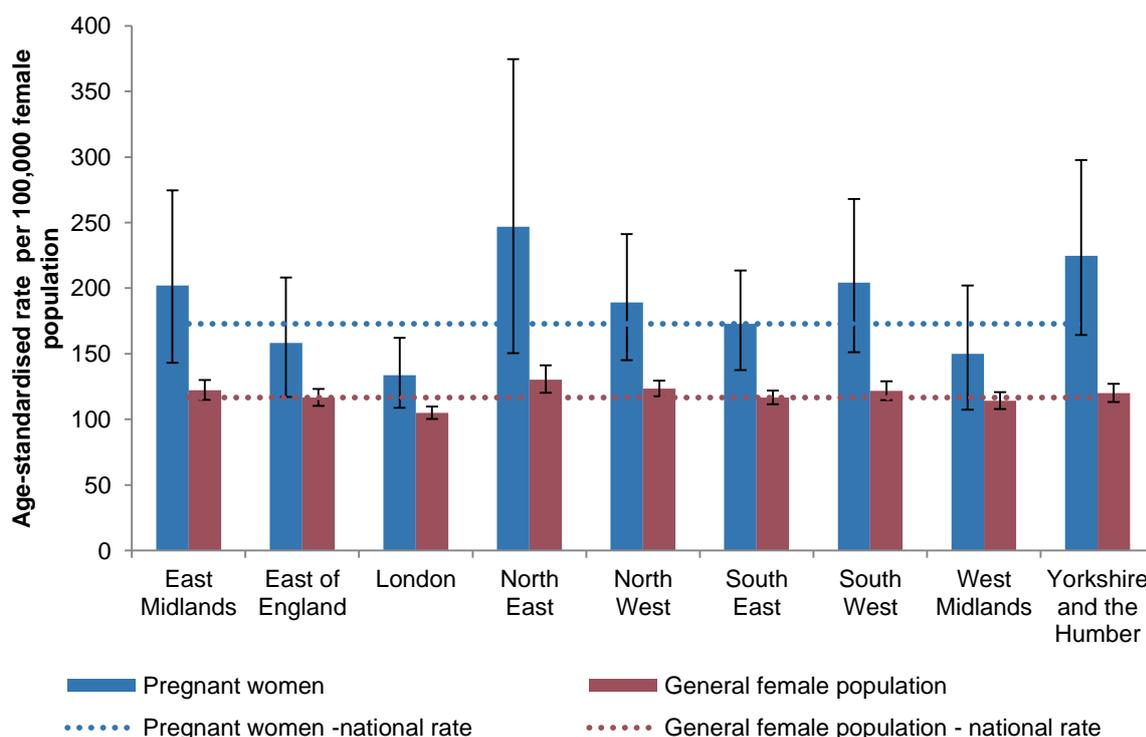
Table 2: Annual age-standardised incidence rates and cases for all cancers (ICD10 C00-C97 excl C44) in pregnant women and general female population by Government Office Region (GOR), 15-44 years, 2012-2014.

	Pregnant women		General female population	
GOR	Cases	Rate (95 % CI)	Cases	Rate (95 % CI)
East Midlands	90	202 (143 - 275)	1,034	122 (115 - 130)
East of England	112	158 (117 - 208)	1,299	117 (110 - 123)
London	186	134 (109 - 162)	2,012	105 (100 - 110)
North East	55	247 (151 - 375)	613	130 (120 - 141)
North West	156	189 (145 - 241)	1,637	124 (118 - 130)
South East	168	173 (138 - 214)	1,934	117 (112 -122)
South West	110	204 (151 - 268)	1,141	122 (115 - 129)
West Midlands	99	150 (107 - 202)	1,202	114 (108 - 121)
Yorkshire and the Humber	114	225 (164 - 298)	1,185	120 (113 - 127)
England	1,091	173 (158 - 189)	12,056	117 (115 - 119)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

Age-standardised rates were significantly higher in pregnant women compared to the general female population in all the regions except for East of England and West Midlands (Figure 2 and Table 2).

3.3 By age

Figure 3: Age-specific incidence rates and 95% confidence intervals for all cancers (ICD10 C00-C97 excl C44) in pregnant women and general female population by 5 year age group, 15-44 years, 2012-2014.
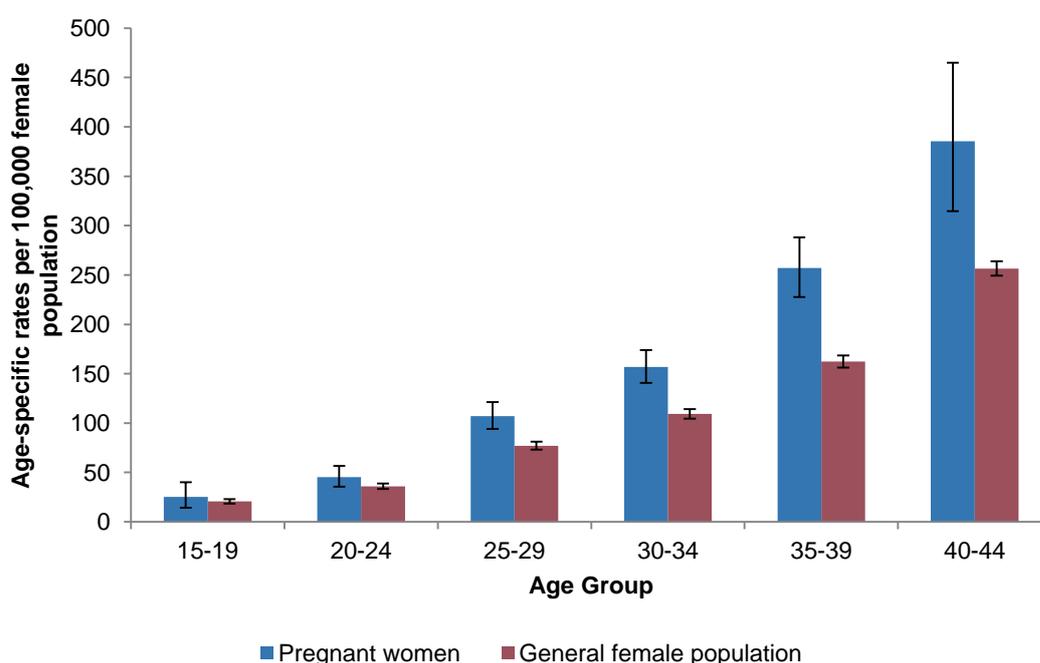
Table 3: Annual age-specific incidence rates and cases for all cancers (ICD10 C00-C97 excl C44) in pregnant women and general female population by 5 year age group, 15-44 years, 2012-2014.

Age group	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
15 - 19	16	25 (14 - 40)	329	21 (19 - 23)
20 - 24	78	45 (36 - 57)	638	36 (33 - 39)
25 - 29	251	107 (94 - 121)	1,424	77 (73 - 81)
30 - 34	354	157 (141 - 174)	2,011	109 (105 - 114)
35 - 39	285	257 (228 - 288)	2,760	162 (156 - 168)
40 - 44	106	386 (315 - 465)	4,894	257 (249 - 264)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

In each of the 25 to 29, 30 to 34, 35 to 39 and 40 to 44 age groups, all cancers combined (excluding non-melanoma skin) incidence rates were statistically significantly higher in pregnant women (107, 95% CI 94 -121; 157, 95% CI 141-174; 257, 95% CI 228-288 and 386, 95% CI 315-465) when compared to the general female population (77, 95% CI 73-81; 109, 95% CI 105-114; 162, 95% CI 156-168 and 257 95% CI 249-264), (Figure 3, Table 3).

Figure 4: Age-specific incidence rates and 95% confidence intervals for breast cancer in pregnant women and general female population by 5 year age group, 15-44 years, 2012-2014.
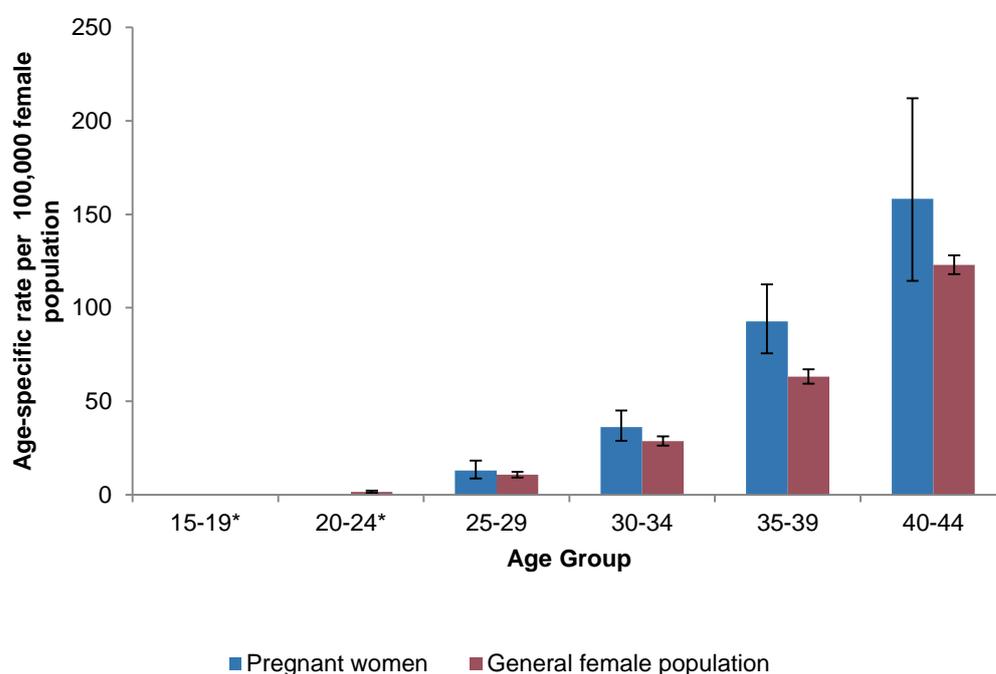
* Insufficient cases to calculate rates for pregnant women and/or and general female population.

Table 4: Annual age-specific incidence rates and cases for breast cancer in pregnant women and general female population by 5 year age group, 15-44 years, 2012-2014.

Age group	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
15 - 19	*	*	*	*
20 - 24	*	*	27	1.5 (1.0 - 2.2)
25 - 29	30	13 (9 - 18)	198	11 (9 - 12)
30 - 34	82	36 (29 - 45)	530	29 (26 - 31)
35 - 39	103	93 (76 - 113)	1,076	63 (60 - 67)
40 - 44	44	158 (114 - 212)	2,346	123 (118 - 128)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

* Insufficient cases to calculate rates for pregnant women and/or general female population.

Age-specific breast cancer incidence rates were highest in the older age groups for both pregnant women and the general female population (Figure 4). In the 35 to 39 age group, breast cancer incidence rates were almost 50% higher in pregnant women (93, 95% CI 76-113) compared to the general female population (63, 95% CI 60-67).

Figure 5: Age-specific incidence rates and 95% confidence intervals for melanoma skin cancer in pregnant women and general female population by 5 year age group, 15-44 years, 2012-2014.
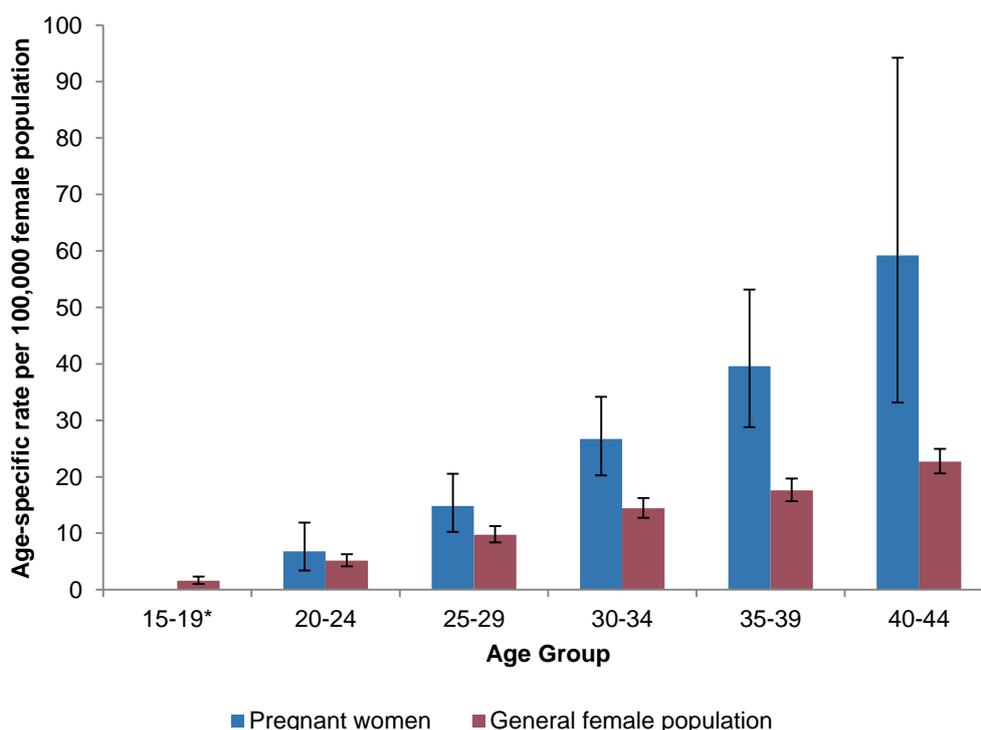
Table 5: Annual age-specific incidence rates and cases for melanoma skin cancer in pregnant women and general female population by 5 year age group, 15-44 years, 2012-2014.

Age group	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
15 - 19	*	*	25	1.6 (1.0 - 2.3)
20 - 24	12	6.8 (3.4 - 11.9)	91	5.1 (4.1 - 6.3)
25 - 29	35	15 (10 - 21)	180	9.7 (8.4 - 11.3)
30 - 34	60	27 (20 - 34)	265	14 (13 - 16)
35 - 39	44	40 (29 - 53)	300	18 (16 - 20)
40 - 44	16	59 (33 - 94)	433	23 (21 - 25)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

* Insufficient cases to calculate rates for pregnant women.

In each of the 30 to 34, 35 to 39 and 40 to 44 age groups, melanoma incidence rates were around double those in pregnant women (27, 95% CI 20-34; 40, 95% CI 29-53 and 59, 95% CI 33-94 respectively) when compared to the general female population (14, 95% CI 13-16; 18, 95% CI 16-20 and 23, 95% CI 21-25), (Figure 5 and Table 5).

Figure 6: Age-specific incidence rates and 95% confidence intervals for cervical cancer in pregnant women and general female population by 5 year age group, 15-44 years, 2012-2014.
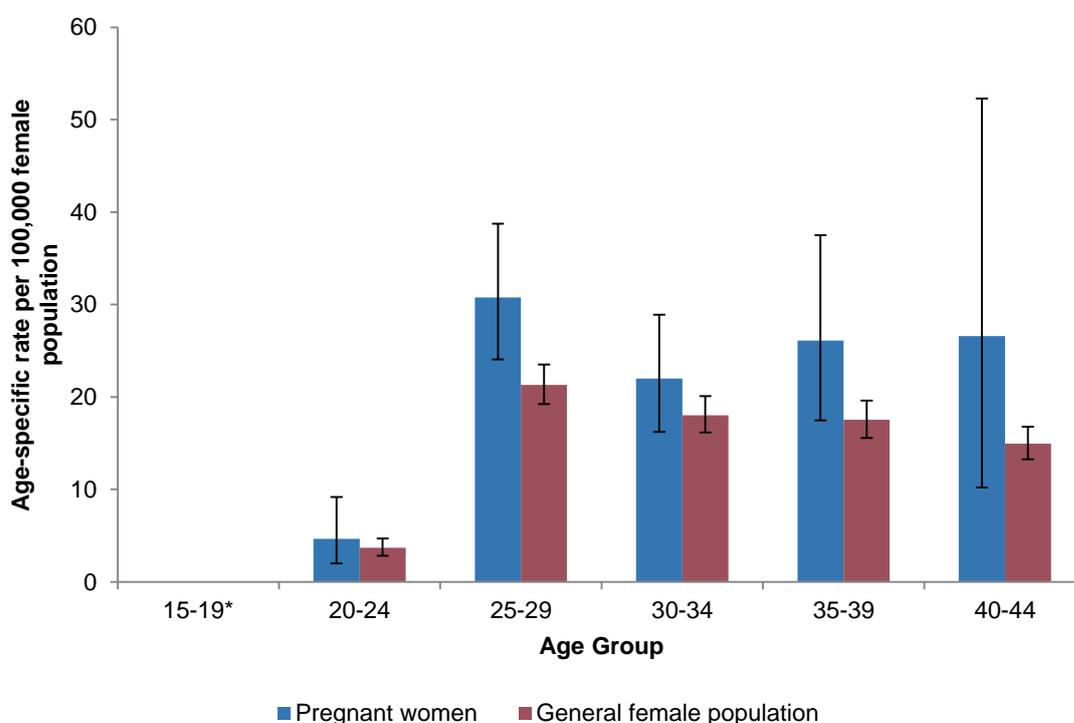
* Insufficient cases to calculate rate for pregnant women and females in general population.

Table 6: Annual age-specific incidence rates and cases for cervical cancer in pregnant women and general female population by five year age group, 15-44 years, 2012-2014.

Age group	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
15 - 19	*	*	*	*
20 - 24	8	4.7 (2.0 - 9.2)	66	3.7 (2.9 - 4.7)
25 - 29	72	31 (24 - 39)	393	21 (19 - 24)
30 - 34	50	22 (16 - 29)	332	18 (16 - 20)
35 - 39	29	26 (18 - 38)	298	18 (16 - 20)
40 - 44	7	27 (10 - 52)	285	15 (13 - 17)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

* Insufficient cases to calculate rate for pregnant women and females in general population.

In the 25 to 29 age group, cervical cancer incidence rates were almost 50% higher in pregnant women (31, 95% CI 24-39) when compared to the general female population (21, 95% CI 19 -24), (Figure 6 and Table 6).

3.4 By deprivation quintile

Figure 7: Age-standardised incidence rates and 95% confidence intervals for all cancers (ICD10 C00-C97 excl C44) in pregnant women and general female population by deprivation quintile, 15-44 years, 2012-2014.
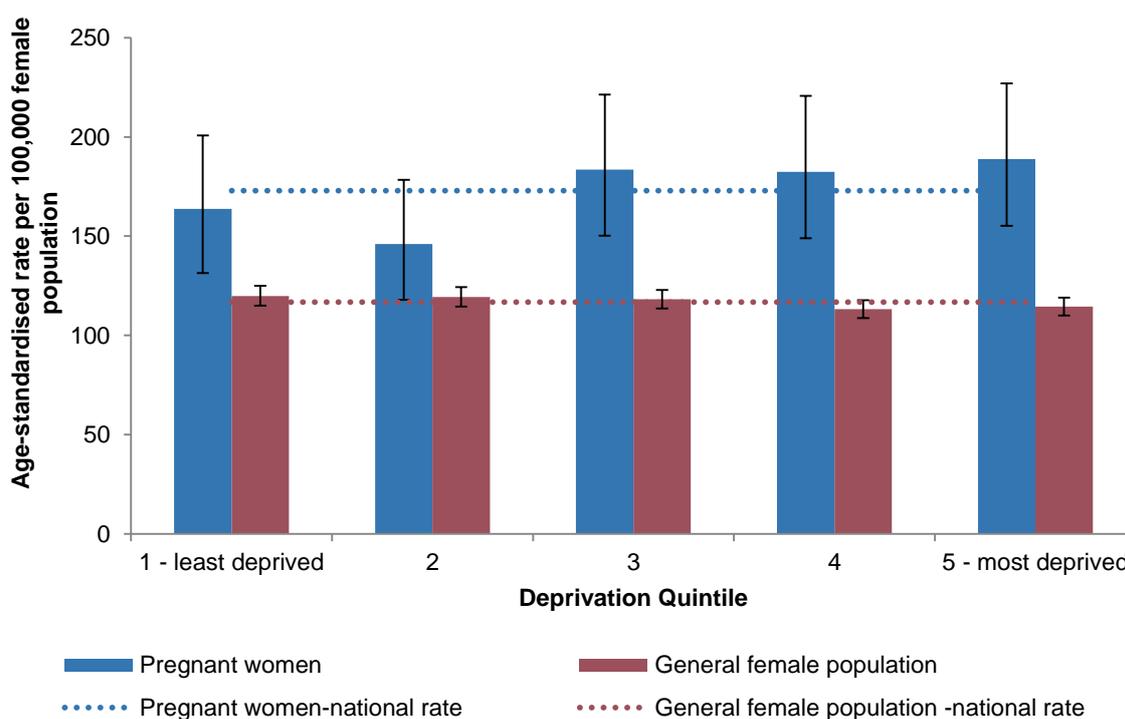
Table 7: Annual age-standardised incidence rates and cases for all cancers (ICD10 C00-C97 excl C44) in pregnant women and general female population by deprivation quintile, 15-44 years, 2012-2014.

Deprivation quintile	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
1 - least deprived	185	163 (131 - 201)	2,248	120 (115 - 125)
2	193	146 (118 - 178)	2,335	119 (115 - 124)
3	233	184 (150 - 221)	2,445	118 (114 - 123)
4	227	183 (149 - 221)	2,467	113 (109 - 118)
5 - most deprived	252	189 (155 - 227)	2,560	115 (110 - 119)
National	1,091	173 (158 -189)	12,056	117 (115 - 119)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

In the most deprived (fifth quintile) areas, age-standardised incidence rates for all cancers combined (excluding non-melanoma skin) were two-thirds higher in pregnant women when compared to the general female population (Figure 7 and Table 7).

Figure 8: Age-standardised incidence rates and 95% confidence intervals for breast cancer in pregnant women and general female population by deprivation quintile, 15-44 years, 2012-2014.
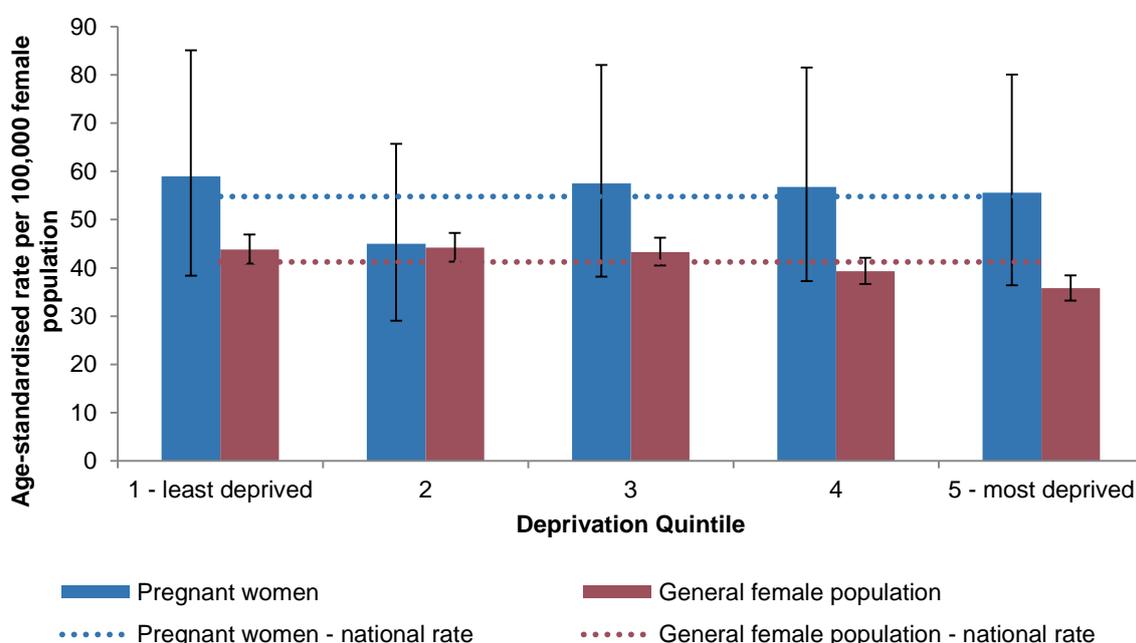
Table 8: Annual age-standardised incidence rates and cases for breast cancer in pregnant women and general female population by deprivation quintile, 15-44 years, 2012-2014.

Deprivation quintile	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
1 - least deprived	49	59 (38 - 85)	847	44 (41 - 47)
2	48	45 (29 - 66)	876	44 (41 - 47)
3	57	58 (38 - 82)	881	43 (41 - 46)
4	54	57 (37 - 82)	823	39 (37 - 42)
5 - most deprived	53	56 (36 - 80)	752	36 (33 - 38)
National	261	55 (46 - 65)	4,179	41 (40 - 43)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

Incidence rates of breast cancer were not statistically significantly different in pregnant women and the general female population in any deprivation quintile (Figure 8 and Table 8).

Figure 9: Age-standardised incidence rates and 95% confidence intervals for melanoma skin cancer in pregnant women and general female population by deprivation quintile, 15-44 years, 2012-2014.

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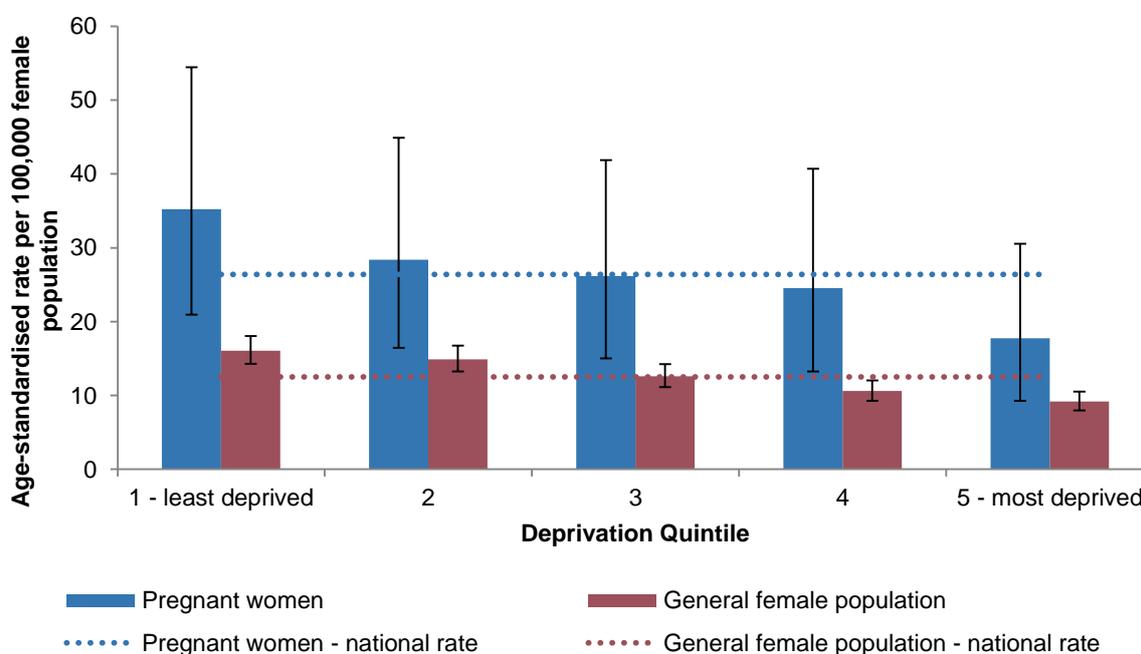
Table 9: Annual age-standardised incidence rates and cases for melanoma skin cancer in pregnant women and general female population by deprivation quintile, 15-44 years, 2012-2014.

Deprivation quintile	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
1 - least deprived	38	35 (21 - 54)	295	16 (14 - 18)
2	35	28 (16 - 45)	289	15 (13 - 17)
3	37	26 (15 - 42)	262	13 (11 - 14)
4	32	25 (13 - 41)	236	11 (9 - 12)
5 - most deprived	26	18 (9 - 31)	212	9.2 (8.0 - 10.5)
National	168	26 (21 - 33)	1,294	13 (12 - 13)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

In the least deprived (quintile 1) areas, melanoma skin cancer incidence rates were double in pregnant women (35, 95% CI 21-54) when compared to the general female population (16, 95% CI 14-18).

Figure 10: Age-standardised incidence rates and 95% confidence intervals for cervical cancer in pregnant women and general female population by deprivation quintile, 15-44 years, 2012-2014.
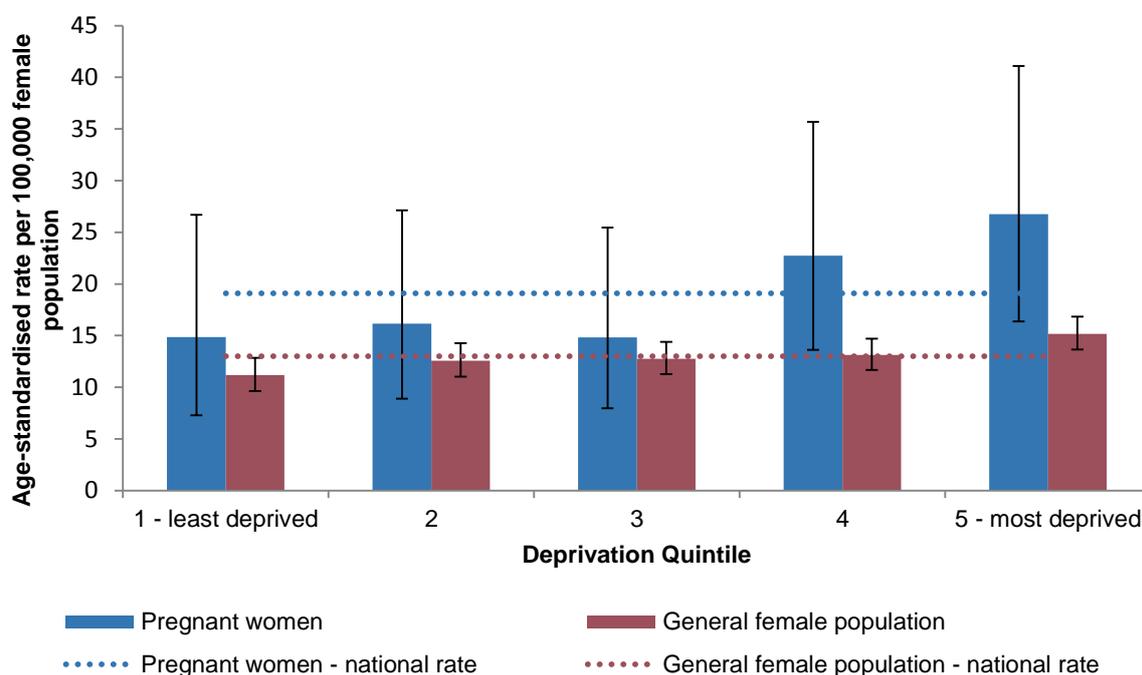
Table 10: Annual age-standardised incidence rates and cases for cervical cancer in pregnant women and general female population by deprivation quintile, 15-44 years, 2012-2014.

Deprivation quintile	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
1 - least deprived	22	15 (7 - 27)	195	11 (10 - 13)
2	29	16 (9 - 27)	240	13 (11 - 14)
3	29	15 (8 - 26)	272	13 (11 - 14)
4	40	23 (14 - 36)	302	13 (12 - 15)
5 - most deprived	47	27 (16 - 41)	367	15 (14 - 17)
National	166	19 (15 - 24)	1,376	13 (12 - 14)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

In the most deprived (quintile 5) areas, cervical cancer incidence rates were almost double in pregnant women (27, 95% CI 16-41) when compared to the general female population (15, 95% CI 14-17).

3.5 By stage of disease

Figure 11: Age-standardised incidence rates and 95% confidence intervals for all cancers (ICD10 C00-C97 excl C44) in pregnant women and general female population by stage, 15-44 years, 2012-2014.
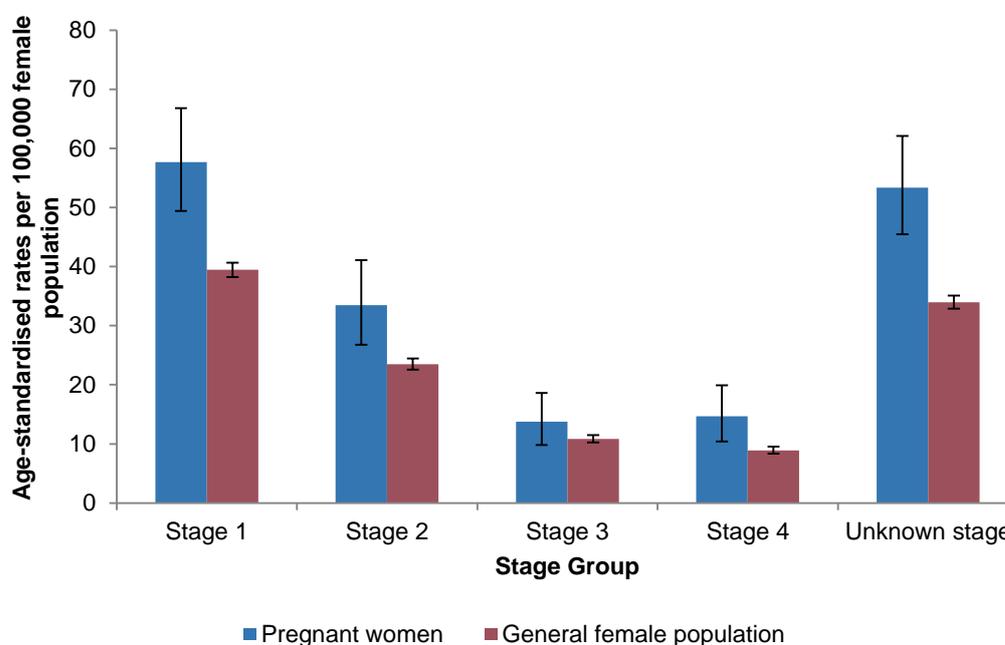
Table 11: Annual age-standardised incidence rates and cases for all cancers (ICD10 C00-C97 excl C44) in pregnant women and general female population by stage, 15-44 years, 2012-2014.

Stage	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
Stage 1	385	58 (49 - 67)	4,085	40 (38 - 41)
Stage 2	185	34 (27 - 41)	2,405	24 (23 - 24)
Stage 3	84	14 (10 - 19)	1,111	11 (10 - 12)
Stage 4	82	15 (10 - 20)	920	8.9 (8.4 - 9.5)
Unknown stage	355	53 (46 - 62)	3,536	34 (33 - 35)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

Incidence rates for all cancers were statistically significantly different in pregnant women and the general female population across all stage groups except for patients diagnosed with stage 3 disease (Figure 11 and Table 11).

Figure 12: Age-standardised incidence rates and 95% confidence intervals for breast cancer in pregnant women and general female population by stage, 15-44 years, 2012-2014.
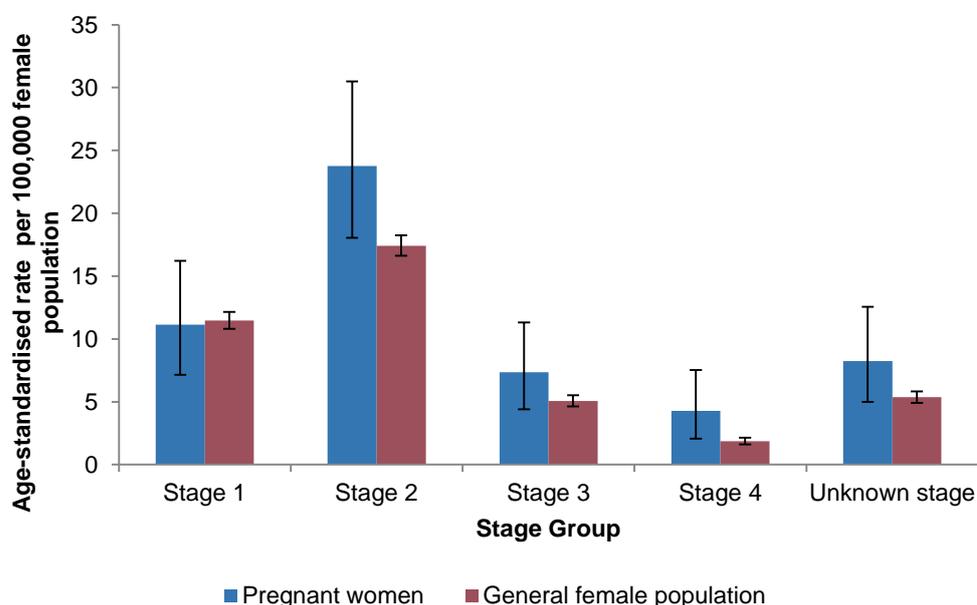
Table 12: Annual age-standardised incidence rates and cases for breast cancer in pregnant women and general female population by stage, 15-44 years, 2012-2014.

Stage	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
Stage 1	47	11 (7 - 16)	1,164	12 (11 - 12)
Stage 2	117	24 (18 - 31)	1,768	17 (17- 18)
Stage 3	38	7.4 (4.4 - 11.3)	515	5.1 (4.6 - 5.5)
Stage 4	21	4.3 (2.1 - 7.5)	189	1.9 (1.6 - 2.1)
Unknown stage	38	8.2 (5.0 - 12.6)	544	5.4 (4.9 - 5.8)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

Incidence rates of breast cancer were double in pregnant women (4.3, 95% CI 2.1 - 7.5) diagnosed with stage 4 disease when compared to the general female population (1.9, 95% CI 1.6 - 2.1), (Figure 12 and Table 12).

Figure 13: Age-standardised incidence rates and 95% confidence intervals for melanoma skin cancers in pregnant women and general female population by stage, 15-44 years, 2012-2014.
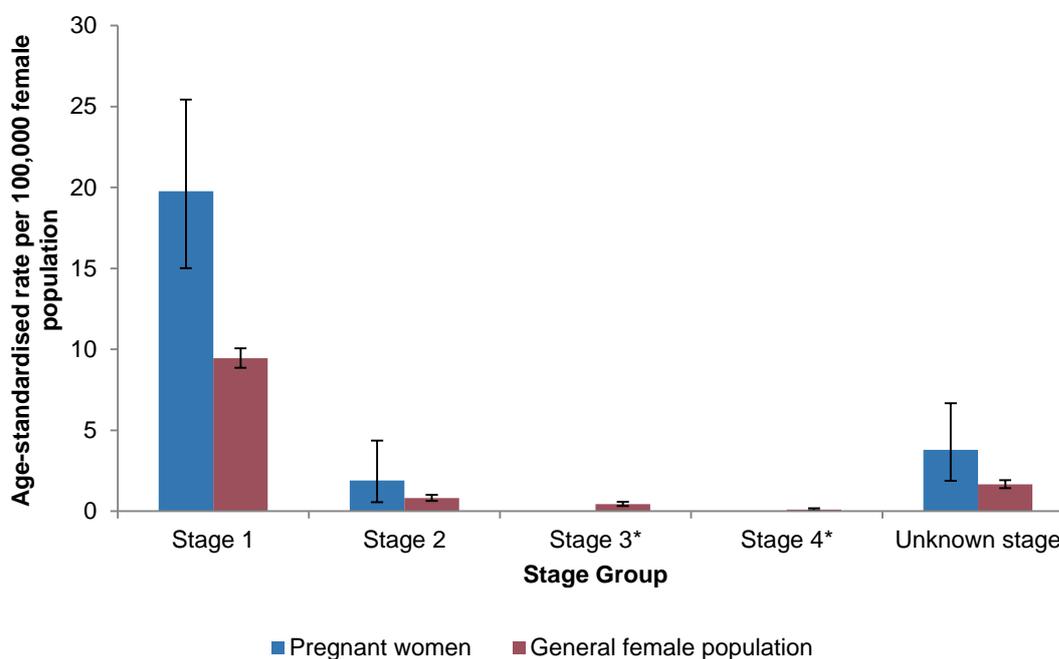
* Insufficient cases to calculate rate for pregnant women.

Table 13: Annual age-standardised incidence rates and 95% confidence intervals for melanoma skin cancers in pregnant women and general female population by stage, 15-44 years, 2012-2014.

Stage	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
Stage 1	128	20 (15 - 25)	981	9.4 (8.9 - 10.1)
Stage 2	11	1.9 (0.6 - 4.4)	85	0.8 (0.6 - 1.0)
Stage 3	*	*	46	0.4 (0.3 - 0.6)
Stage 4	*	*	11	0.1 (0.1 - 0.2)
Unkown stage	22	3.8 (1.9 - 6.7)	172	1.7 (1.4 - 1.9)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

* Insufficient cases to calculate rate for pregnant women.

Incidence rates for melanoma of skin were around double in pregnant women (20, 95% CI 15-25) when compared to the general female population (9, 95% CI 9-10) diagnosed with stage 1 disease (Figure 13 and Table 13).

Figure 14: Age-standardised incidence rates and 95% confidence intervals for cervical cancer in pregnant women and general female population by stage, 15-44 years, 2012-2014.
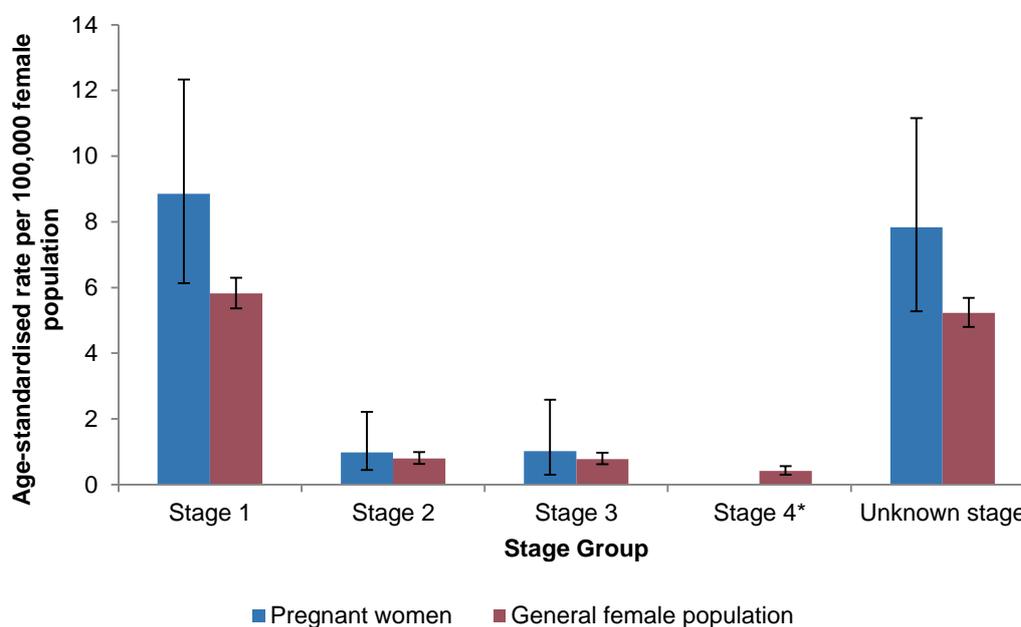
* Insufficient cases to calculate rate for pregnant women.

Table 14: Annual age-standardised incidence rates and cases for cervical cancer in pregnant women and general female population by stage, 15-44 years, 2012-2014.

Stage	Pregnant women		General female population	
	Cases	Rate (95% CI)	Cases	Rate (95% CI)
Stage 1	76	8.9 (6.1 - 12.3)	617	5.8 (5.4 - 6.3)
Stage 2	10	1.0 (0.5 - 2.2)	83	0.8 (0.6 - 1.0)
Stage 3	9	1.0 (0.3 - 2.6)	81	0.8 (0.6 - 1.0)
Stage 4	*	*	42	0.4 (0.3 - 0.6)
Unknown stage	68	7.8 (5.3 - 11.2)	553	5.2 (4.8- 5.7)

Rate is average annual age-standardised rate per 100,000 female population; 95% CI is 95% confidence interval.

* Insufficient cases to calculate rate for pregnant women.

Incidence rates of cervical cancers were statistically significantly different in pregnant women (8.9, 95% CI 6.1 -12.3) and the general female population (5.8, 95% CI 5.4 -6.3) diagnosed with stage 1 disease (Figure 14 and Table 14).

Chapter 4: Discussion

Breast, malignant melanoma, cervical, haematological, ovarian and colorectal cancers were the most common diagnosed in pregnant women. These results are consistent with findings from other studies.[2,4,5,6]

The age-standardised incidence rate of cancer in pregnant women was 173 per 100,000 pregnancies. The overall crude rate was 131 per 100,000 pregnancies which is higher than the generally reported rate of 100 per 100,000.[1,4] Other studies[2,15] have reported overall crude rates of 137 and 173 per 100,000. Differences in incidence rates can be largely explained by variations in the definitions of study populations. Some studies include diagnoses of malignant cancers 9 months before and 12 months after delivery[2,4] and others up to 6 months after delivery.[16] This study included patients who had a delivery, pregnancy or delivery related event 12 months before or after cancer diagnosis.

Another reason for the wide range in incidences may be different data sources. Some studies use hospital records,[15] others use linked cancer registry, birth and hospital records,[2] and some use linked maternal/neonatal hospital discharge records, birth and death certificate records and case files in cancer registry.[4] In this study, linked cancer registration data and hospital admitted patient care records were used.

As seen in a similar study,[2] the results presented here showed that cancer rates in pregnant women were higher than in the general female population of the same age. Pregnancy increases most women's interaction with health services, increasing the likelihood of cancer diagnosis.[2] Another reason for the increase in rates in pregnant women may be due to physiological changes during pregnancy which stimulate cancer progression, resulting in earlier detection.[4] One study attributed higher rates of pregnancy-associated melanoma to endocrine and growth changes of pregnancy.[17]

When compared with the general female population, incidence of melanoma of the skin in pregnant women was more than twice in the least deprived quintile. For breast cancers, incidence rates in pregnant women were not significantly different when compared to the general female population, across all deprivation quintiles. In general, higher incidence rates are associated with lower levels of deprivation for cancers of the breast and malignant melanoma of skin.[14,18] Incidence rates of cervical cancer in the general population for all ages are known to be higher in the most deprived areas.[14]

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Incidence rates of breast cancer were double in pregnant women who were diagnosed with stage 4 disease when compared to the general female population (Figure 12). Some studies[19,20] have shown that pregnant women with breast cancer presented with more advanced disease and larger tumours. This was attributed to difficulties of diagnosing pregnancy-associated breast cancer among other reasons.[20]

Melanoma skin cancer incidence rates were around double in pregnant women when compared to the general female population diagnosed at stage 1 (Figure 13). Similarly, incidence rates of cervical cancers were significantly higher in pregnant women when compared to the general female population diagnosed with stage 1 disease. Diagnosis of melanoma skin cancer[21] and cervical cancer[22] is more frequent in pregnant women due to obstetric examinations.

Results of this analysis should be interpreted with caution due to a number of limitations. The main limitation of our approach is that the HES data used in this study contained hospital records of patients who were admitted for pregnancy or delivery care. This data may be considered crude as HES does not include deliveries that take place at home.

The Maternity Services Data Set[23] (MSDS) contains complete events of pregnancy, including information on routine booking appointments, labour and delivery, and maternal or neonatal death. Use of MSDS may in future allow us to extract data on pregnant women and then establish whether they had a cancer diagnosis. It was not possible to use the MSDS in this analysis as it was recently set up and has data completeness and quality issues[24] (which are improving).

Availability of delivery date in MSDS would allow for analysis on timing of cancer diagnosis to delivery ie prenatal, at delivery or postpartum. One study[4] has shown that timing of diagnosis is affected by cancer type with the majority of breast, cervical, and thyroid being diagnosed in the postpartum year, while ovarian, Hodgkin's disease, and leukemia were diagnosed just before delivery. Another study[2] showed that timing of cancer diagnosis had an effect on pregnancy outcomes such as thromboembolic events, sepsis and severe morbidity. Availability of maternal death data would allow for analyses on survival by cancer type. Survival could be compared for women with cancer diagnosis before delivery, at delivery and at postpartum.

Another limitation is that we selected the first tumour per patient diagnosed within the study period. Choosing one tumour per pregnant women means the rate definitions in the numerator and the denominator for all cancers is

the same, but differs when broken down by cancer type. However, as only 24 women had 2 diagnoses of cancer (same or different type) any effect is likely to be negligible. Finally, the calculated pregnancy rates could be slightly over-estimated as the numerator included miscarriages, abortions, pregnancy and delivery related admissions etc and the denominator included pregnancy resulting in live/still births or legal abortions but did not include miscarriages.

4.1 Conclusions

Breast, malignant melanoma, cervical, haematological, ovarian and colorectal were the most common cancers diagnosed in pregnant women accounting for 76% of the total observed cases between 2012 and 2014. The higher rates of pregnancy-associated cancers compared to the general female population may be due to frequent obstetric examinations which increases the chance of cancer diagnosis. Our results must be interpreted with the limitations of the databases used. Overall however, the results of this study contribute to the understanding of cancer in pregnant women in England.

MSDS should be considered as a source of data for future pregnancy-associated cancer analyses. A future study on timing of diagnosis of cancer in relation to delivery would potentially help to demonstrate when and what type of cancers are diagnosed during pregnancy and the postpartum. Another future study, comparing survival of women with a cancer diagnosis before delivery, at delivery and at postpartum would ascertain survival at different pregnancy stages.

References

1. Pavlidis AN, Coexistence of pregnancy and malignancy. The Oncologist 2002;7:279-287. Available from:
theoncologist.alphamedpress.org/content/7/4/279.long
[Accessed: 16 August 2017].

2. Lee Y, Roberts C, Dobbins T, Stavrou E, Black K, Morris J, Young J. Incidence and outcomes of pregnancy-associated cancer in Australia, 1994-2008: a population-based linkage study. BJOG, 2012; 119:1572-1582. Available from:
www.ncbi.nlm.nih.gov/pmc/articles/PMC3533794
[Accessed: 3 March 2016].

3. Kehoe S, Jauniaux E, Martin-Hirsch P, Savage P. editors. Cancer and reproductive health. Cambridge University Press; 2008. Available from:
books.google.co.uk/books?id=I8ZkAwAAQBAJ&pg=PT5&lpg=PT5&dq=Cancer+and
+reproductive+health,+Cambridge+University+Press&source=bl&ots=rvpxCgL_Mm&
sig=70Ni718lqQiE59JvqW4AwsJHlQ8&hl=en&sa=X&ved=0ahUKEwio2tu0_tzQAhU
MM8AKHWAxDuwQ6AEIJjAD#v=onepage&q=Cancer%20and%20reproductive%20
health%2C%20Cambridge%20University%20Press&f=false
[Accessed: 13 July 2016].

4. Smith H, Danielsen B, Allen E, Cress R. Cancer associated with obstetric delivery: results of linkage with the California cancer registry. American Journal of Obstetrics and Gynaecology 2003;189:1128-35. Available from:
www.sciencedirect.com/science/article/pii/S0002937803005374?via%3Dihub
[Accessed: 24 August 2017].

5. Weisz B, Schiff E, Lishner M. Cancer in pregnancy: maternal and fetal implications. Hum Reprod Update, 2001; 7(4):384-393. Available from:
humupd.oxfordjournals.org/content/7/4/384.long [Accessed: 20 June 2016].

6. Lishner M. Cancer in pregnancy. Annals of Oncology14 (Supplement 3):iii31-iii36, 2003. Available from:
academic.oup.com/annonc/article/14/suppl_3/iii31/167409/Cancer-in-pregnancy
[Accessed: 23 August 2017].

7. Koren G, Lishner M and Farine D editors Cancer in Pregnancy: Maternal and Fetal Risks Cambridge University Press 1996. Available from:
books.google.co.uk/books?id=wYhVvpV5_MQC&pg=PR7&lpg=PR7&dq=Cancer+in
+pregnancy:+identification+of+unanswered+questions+on+maternal+and+fetal+risks
&source=bl&ots=XxlVaW5aRn&sig=AX-
XBqbEreDMHAUexfr5Ws8c5c0&hl=en&sa=X&ved=0ahUKEwiK25KB4tjRAhUKKcA
KHao0C5AQ6AEILTAE#v=onepage&q=Cancer%20in%20pregnancy%3A%20identifi
cation%20of%20unanswered%20questions%20on%20maternal%20and%20fetal%2
0risks&f=false [Accessed : 23 January 2017].

8. Office for National Statistics, Conception Statistics, England and Wales, 2017. Available from: www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/conception andfertilityrates/datasets/conceptionstatisticsenglandandwalesreferencetables [Accessed: 15 August 2017].

9. International Statistical Classification of Diseases and Related Health Problems (1CD-10) 10th Revision. World Health Organization, 2010.

10. Department for Communities and Local Government: The English Indices of Deprivation 2015 Technical report. Available from: www.gov.uk/government/publications/english-indices-of-deprivation-2015-technical-report [Accessed: 11 October 2017].

11. Sobin LH, Gospodarowicz MK, Wittekind CH. editors. TNM Classification of Malignant Tumours. 7th ed. Wiley-Blackwell; Oxford 2009.

12. Office for National Statistics. Revised European Standard Population 2013 (2013 ESP). 2014. Available from: www.ons.gov.uk/ons/guide-method/user-guidance/health-and-life-events/revised-european-standard-population-2013--2013-esp-/index.html [Accessed: 11 October 2017].

13. Eayres D. APHO Technical Briefing 3: Commonly used public health statistics and their confidence intervals York: APHO; 2008. Available from; fingertips.phe.org.uk/documents/APHO%20Tech%20Briefing%203%20Common%20 PH%20Stats%20and%20CIs.pdf [Accessed: 13 March 2018].

14. NCRAS (2016). Deprivation and cancer: in search of a common measure across England, Wales, Scotland, Northern Ireland and Ireland, Based on cancer incidence and mortality data, 2008-2012. Available from: www.ncin.org.uk/view?rid=3278 [Accessed: 26 September 2017]

15. Min Hee Shim, Chi-Won Mok, Kylie Hae-Jin Chang et al. Clinical characteristics and outcome of cancer diagnosed during pregnancy. Obstet Gynecol Sci 2016;59(1):1-8. Available from: ogscience.org/Synapse/Data/PDFData/3021OGS/ogs-59-1.pdf [Accessed: 23rd August 2017].

16. Bonnier P, Romain S, Dilhuydy JM, Bonichon F, Julien JP, Charpin C, et al. Influence of pregnancy on the outcome of breast cancer: a case-control study. Int J Cancer 1997;72:720–7. Available from: onlinelibrary.wiley.com/doi/10.1002/(SICI)1097-0215(19970904)72:5%3C720::AID-IJC3%3E3.0.CO;2-U/epdf [Accessed: 24 August 2017]

17. Khosrotehrani K, Huu SN, Prignon A, et al. Pregnancy Promotes Melanoma Metastasis through Enhanced Lymphangiogenesis. The American Journal of Pathology. 2011; 178: 1870-80. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC3078435 [Accessed: 23 August 2017].

18. Shack L, Jordan C, Catherine S, Thomson SC, Mak V, Møller H. Variation in incidence of breast, lung and cervical cancer and malignant melanoma of skin by socioeconomic group in England. BMC Cancer. 2008, 8:271. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC2577116 [Accessed: 3 November 2016].

19. Rodriguez AO, Chew H, Cress R, Xing G, McElvy S, Danielsen B, Smith L. Evidence of poorer survival in pregnancy-associated breast cancer. Obstetrics and Gynecology 2008 , 112 (1):71-8. Available from: www.ncbi.nlm.nih.gov/pubmed/18591310 [Accessed: 14 March 2018].

20. Keyser EA, Staat MBC, Fausett MB, Shields AD (2012) Pregnancy-associated breast cancer, Rev Obstet Gynecol. 5(2):94–99: Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC3410508 [Accessed: 13 March 2018].

21. Popovic L, Grgic Z, Popovic M. Melanoma During Pregnancy; in book: Advances in Malignant Melanoma - Clinical and Research Perspectives, 2011. Available from: cdn.intechopen.com/pdfs-wm/20081.pdf [Accessed: 23 August 2017].

22. Zemlickis D, Lishner M, Degendorfer P, Panzarella T, Sutcliffe SB, Koren G. J Clin Oncol. 1991, 9(11):1956-61. Available from: www.ncbi.nlm.nih.gov/pubmed/1941053 [Accessed: 13 March 2018].

23. NHS Digital, Maternity Services Data Set Data Dictionary. Available from: www.datadictionary.nhs.uk/data_dictionary/messages/clinical_data_sets/data_sets/maternity_services_data_set/maternity_services_data_set_fr.asp?shownav=1 [Accessed: 13 October 2017].

24. Hebert A, Wijlars L, Zylbersztejn A, Cromwell D, Hardelid P. Data Resource Profile: Hospital Episode Statistics Admitted Patient Care (HES APC). Available from: doi.org/10.1093/ije/dyx015 [Accessed: 13 October 2017].

Appendix

Cancer site ICD10 groups

Group or site name	Site name	ICD10 codes
Colorectal and anus	Colon	C18
	Rectosigmoid junction	C19
	Rectum	C20
	Anus and anal canal	C21
Lung	Trachea	C33
	Bronchus and lung	C34
Melanoma of skin	Malignant melanoma of skin	C43
Female breast	Breast	C50
Cervix uteri	Cervix	C53
Ovary	Ovary	C56
Other gynaecological	Vulva	C51
	Vagina	C52
	Corpus uteri	C54
	Uterus, part unspecified	C55
	Other and unspecified female genital organs	C57
	Placenta	C58
Urological	Kidney	C64
	Renal pelvis	C65
	Ureter	C66
	Bladder	C67
	Other and unspecified urinary organs	C68
Brain and Central Nervous System (CNS)	Peripheral nerves and autonomic nervous system	C47
	Eye and adnexa	C69
	Meninges	C70
	Brain	C71
	Spinal cord, cranial nerves and other parts of central nervous system	C72
Haematological	Lymphoma	C81-C85
	Immunoproliferative disease	C88
	Myeloma and leukaemia	C90-C95
	Other and unspecified lymphoid and haematopoietic tissues	C96

Cancer site ICD10 groups

Group or site name	Site name	ICD10 codes
Other malignant neoplasm	Lip	C00
	Base of tongue	C01
	Oral cavity and pharynx	C02-C14
	Oesophagus	C15
	Stomach	C16
	Small intestine	C17
	Liver and intrahepatic bile ducts	C22
	Gallbladder	C23
	Other and unspecified parts of biliary tract	C24
	Pancreas	C25
	Other and ill-defined digestive organs	C26
	Nasal cavity and middle ear	C30
	Accessory sinuses	C31
	Larynx	C32
	Thymus	C37
	Heart, mediastinum and pleura	C38
	Other and ill-defined sites in the respiratory system and intrathoracic organs	C39
	Bone and articular cartilage of limbs	C40
	Bone and articular cartilage of other and unspecified sites	C41
	Mesothelioma	C45
	Kaposi's sarcoma	C46
	Retroperitonuem and peritonuem	C48
	Other connective and soft tissues	C49
	Thyroid gland	C73
	Adrenal and other endocrine glands	C74-C75
	Ill-defined secondary and unspecified sites	C76-C80
	Indipendent (primary) multiple sites	C97

ICD10 codes - Pregnancy, childbirth and the puerperium

O00	Ectopic pregnancy
O01	Hydatidiform mole
O02	Other abnormal products of conception
O03	Spontaneous abortion
O04	Medical abortion
O05	Other abortion
O06	Unspecified abortion
O07	Failed attempted abortion
O08	Complications following abortion and ectopic and molar pregnancy
O10	Pre-existing hypertension complicating pregnancy, childbirth and the puerperium
O11	Pre-existing hypertensive disorder with superimposed proteinuria
O12	Gestational [pregnancy-induced] oedema and proteinuria without hypertension
O13	Gestational [pregnancy-induced] hypertension without significant proteinuria
O14	Gestational [pregnancy-induced] hypertension with significant proteinuria
O15	Eclampsia
O16	Unspecified maternal hypertension
O20	Haemorrhage in early pregnancy
O21	Excessive vomiting in pregnancy
O22	Venous complications in pregnancy
O23	Infections of genitourinary tract in pregnancy
O24	Diabetes mellitus in pregnancy
O25	Malnutrition in pregnancy
O26	Maternal care for other conditions predominantly related to pregnancy
O28	Abnormal findings on antenatal screening of mother
O29	Complications of anaesthesia during pregnancy
O30	Multiple gestation
O31	Complications specific to multiple gestation
O32	Maternal care for known or suspected malpresentation of fetus
O33	Maternal care for known or suspected disproportion
O34	Maternal care for known or suspected abnormality of pelvic organs
O35	Maternal care for known or suspected fetal abnormality and damage
O36	Maternal care for other known or suspected fetal problems
O40	Polyhydramnios
O41	Other disorders of amniotic fluid and membranes
O42	Premature rupture of membranes
O43	Placental disorders
O44	Placenta praevia
O45	Premature separation of placenta [abruptio placentae]
O46	Antepartum haemorrhage, not elsewhere classified
O47	False labour
O48	Prolonged pregnancy
O60	Preterm labour and delivery

ICD10 codes - Pregnancy, childbirth and the puerperium

O61	Failed induction of labour
O62	Abnormalities of forces of labour
O63	Long labour
O64	Obstructed labour due to malposition and malpresentation of fetus
O65	Obstructed labour due to maternal pelvic abnormality
O66	Other obstructed labour
O67	Labour and delivery complicated by intrapartum haemorrhage, not elsewhere classified
O68	Labour and delivery complicated by fetal stress [distress]
O69	Labour and delivery complicated by umbilical cord complications
O70	Perineal laceration during delivery
O71	Other obstetric trauma
O72	Postpartum haemorrhage
O73	Retained placenta and membranes, without haemorrhage
O74	Complications of anaesthesia during labour and delivery
O75	Other complications of labour and delivery, not elsewhere classified
O80	Single spontaneous delivery
O81	Single delivery by forceps and vacuum extractor
O82	Single delivery by caesarean section
O83	Other assisted single delivery
O85	Puerperal sepsis
O86	Other puerperal infections
O87	Venous complications in the puerperium
O88	Obstetric embolism
O89	Complications of anaesthesia during the puerperium
O90	Complications of the puerperium, not elsewhere classified
O91	Infections of breast associated with childbirth
O92	Other disorders of breast and lactation associated with childbirth
O98	Maternal infectious and parasitic diseases classifiable elsewhere but complicating pregnancy, childbirth and the puerperium
O99	Other maternal diseases classifiable elsewhere but complicating pregnancy, childbirth and the puerperium

ICD10 codes - Persons encountering health services in circumstances related to reproduction

Z321	Pregnancy confirmed
Z33	Pregnant state, incidental
Z34	Supervision of normal pregnancy
Z35	Supervision of high-risk pregnancy
Z36	Antenatal screening
Z37	Outcome of delivery
Z38	Liveborn infants according to place of birth
Z39	Postpartum care and examination