

# FEATURES OF CANCER IN TEENAGERS AND YOUNG ADULTS PRESENTING TO PRIMARY CARE IN THE UK: A POPULATION-BASED NESTED CASE-CONTROL STUDY

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## INTRODUCTION

Teenagers and Young Adults (TYA - 15-24 years) with cancer frequently report repeated visits to primary care before referral for investigation. Improving early diagnosis is a priority for TYA, reflected in UK cancer policy. Perceived or actual diagnostic delay can be a major preoccupation, influencing reaction and adaptation to the diagnosis.

Potential cancer diagnoses are diverse in TYA, early symptoms are often non-specific, may be explained by more common illnesses, and, because cancer is rare, are low on the list of differential diagnoses for a general practitioner (GP).

The aim of this study was to investigate the risk of cancer in TYA presenting to primary care with symptoms and/or increased consultation frequency.

## METHODS

### Study design

Population-based case-control study nested within a cohort of TYA registered with the UK Clinical Practice Research Datalink (CPRD) (www.cprd.com)

CPRD is a prospectively gathered, anonymised database that holds longitudinal administrative, clinical and prescribing records (including all consultations and diagnoses) from over 600 general practices across the UK (covering approximately 8% of the population).

### Study Population

TYA 15-24 years, inclusive, drawn from all GP practices contributing research-standard data to the CPRD between 01/01/1988 and 31/12/2010.

### Cases and controls

Cases were diagnosed with cancer and identified using pre-defined medical codes in the CPRD  
Controls- Up to 13 controls (TYA with no diagnosis of cancer at any time) per case, matched on age, sex, and practice; and had to be currently registered on the date of diagnosis of their matched case (the index date).

### Symptoms and consultations

Libraries of codes representing individual features of possible cancer in TYA were assembled. Acne was considered to be unrelated to cancer and was included as a control condition to identify any recording bias.  
Consultations in the year before diagnosis were identified.

### Analysis

Magnitude of associations of symptoms and consultation frequency with cancer were identified using univariable conditional logistic regression.

Only variables occurring in  $\geq 2\%$  of either cases or controls, and with a univariable p-value  $\leq 0.1$  entered the multivariable analyses. We used a 'conservative' p-value of  $<0.01$  for retention in the final model.

To assess the value of symptoms and consultation patterns in diagnosing cancer, likelihood ratios (LR) and positive predictive values (PPVs).

PPVs were calculated using Bayes' theorem, whereby posterior odds = prior odds x likelihood ratio

Prior odds were estimated from national incidence figures, expressed as the odds of developing cancer in one year. Annual incidence figures were divided by 4 for the analyses of 3-month time periods.

All analyses were performed using Stata, version 10. (StataCorp, 2008)

## RESULTS

**Study population** 1,064 cases of cancer, 13,206 controls

### Consultation frequency

In the year before diagnosis, cases had a median of five consultations (interquartile range, IQR: 3-9) compared to two (IQR: 0-4) in controls ( $p<0.001$ ).

Differences in consultation rates were most apparent in the 3 months immediately before diagnosis with cases having a median of three consultations (interquartile range (IQR) 1-5) compared to zero consultations (IQR 0-1) in controls ( $p<0.001$ ). This difference was consistent across all diagnostic groups in both cases and controls

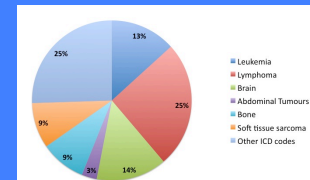
95% of cases consulted in the year before diagnosis compared to 71% of controls (Odds Ratio 9; 95%CI: 7, 12)

87% of all cases consulted in the 3 months before diagnosis compared to 39% of controls (OR: 12; 10, 15)

### The association between number of consultations and a diagnosis of cancer, 0-3 months prior to diagnosis

Number of consultations	Case N=1,064		Control N=13,206		OR <sup>3</sup>	LR	PPV (per 10000) (95% CI)
	Freq	% <sup>2</sup>	Freq	% <sup>2</sup>			
0-3 months prior to index date							
No consultations	139	13.06	8,071	61.12	1.0		
With consultations	925	86.94	5,135	38.88	12.4 (10.3-15.0)	2.2	1.1 (1.07-1.14)
1	195	21.05	2,860	55.70	1.0		
2	190	20.54	1,150	22.40	2.6 (2.1-3.2)	0.9	0.45 (0.39-0.52)
3	143	15.46	532	10.36	4.5 (3.5-5.8)	1.5	0.73 (0.62-0.87)
4 or more	397	42.92	593	11.55	12.1 (9.7-15.1)	3.7	1.83 (1.65-2.04)

<sup>1</sup>All primary care consultations including out of hours and telephone consultations  
<sup>2</sup>For categories 1, 2, 3 and 4 or more, proportions reflect only patients with consultations  
<sup>3</sup>Odds Ratio: Represents the odds of being diagnosed with cancer given more consultations with the GP; computed using conditional logistic regression



### Identification of independent associations with cancer

Due to the diversity of diagnoses in our cohort, symptom analysis was limited to four disease groups: leukaemia (annual incidence 0.21 per 10,000); lymphoma (annual incidence 0.47 per 10,000); CNS tumours (annual incidence 0.17 per 10,000); bone/soft tissue sarcoma (annual incidence 0.21 per 10,000) (Birch et al, 2002).

### Multivariable analysis of the features of specific TYA cancers

#### Leukaemia

lymphadenopathy had the highest PPV of 1.51 per 10,000

#### Lymphoma

lump/mass/swelling of the head and neck had the highest PPV of 50.34 per 10,000

#### CNS tumours

seizure had the highest PPV of 2.38 per 10,000

In this group, 8.4% of cases had visual symptoms, but a PPV could not be calculated as no controls had this feature

#### Bone/soft tissue sarcomas

lump/mass/swelling below neck, excluding abdomen, had the highest PPV of 4.15 per 10,000

The OR and LR for the control condition, acne, was 1.32 (95% CI: 0.8, 2.19) and 1.31 (95% CI: 0.8, 2.14) respectively, indicating little evidence of recording bias (data not shown).

Symptom*	Cases N=143		Control N=1799		LR	95% CI	PPV (per 10000)	95% CI
	Freq	%	Freq	%				
Lymphadenopathy <sup>1</sup>	7	4.90	3	0.17	29.4	7.7 - 112.3	1.51	0.4 - 5.8
Fatigue	15	10.49	8	0.44	23.6	10.2 - 54.7	1.21	0.5 - 2.8
Bruising	9	6.29	5	0.28	22.6	7.7 - 66.7	1.17	0.4 - 3.4
3 or more consultations	74	51.75	125	6.95	7.5	5.9 - 9.4	0.38	0.3 - 0.5

Symptom*	Cases N=270		Control N=3350		LR	95% CI	PPV (per 10000)	95% CI
	Freq	%	Freq	%				
Lump Mass Swelling head and neck	35	12.96	1	0.03	434.3	59.7 - 3157.6	50.34	7.0 - 367.9
Lymphadenopathy	77	28.52	4	0.12	238.8	88.1 - 647.6	27.75	10.3 - 75.4
Lump mass swelling <sup>2</sup>	29	10.74	15	0.45	24.0	13.0 - 44.2	2.79	1.5 - 5.2
3 or more consultations	175	64.81	294	8.78	7.4	6.4 - 8.5	0.86	0.8 - 1.0

Symptom*	Cases N=154		Control N=1906		LR	95% CI	PPV (per 10000)	95% CI
	Freq	%	Freq	%				
Seizure	18	11.69	4	0.21	55.7	19.1 - 162.5	2.38	0.8 - 7.0
Headache	33	21.43	12	0.63	34.0	18.0 - 64.6	1.45	0.8 - 2.8
Vomiting	11	7.14	5	0.26	27.2	9.6 - 77.4	1.16	0.4 - 3.3
Pain	11	7.14	20	1.05	6.8	3.3 - 14.0	0.29	0.1 - 0.6
3 or more consultations	73	47.4	165	8.66	5.5	4.4 - 6.8	0.23	0.2 - 0.3

Symptom*	Cases N=196		Control N=2438		LR	95% CI	PPV (per 10000)	95% CI
	Freq	%	Freq	%				
Lump mass swelling	19	9.69	3	0.12	78.8	23.5 - 263.9	4.15	1.2 - 13.9
Musculoskeletal symptoms	37	18.88	26	1.07	17.7	11.0 - 28.6	0.93	0.6 - 1.5
3 or more consultations	86	43.88	189	7.75	5.7	4.6 - 7.0	0.3	0.2 - 0.4
Chest pain <sup>1</sup>	5	2.55	12	0.49	5.2	1.8 - 14.6	0.27	0.1 - 0.8

\*Symptoms are ordered by PPV

<sup>1</sup>has a p-value below the threshold but is needed in the model based on the LR test.

<sup>2</sup>Lump Mass Swelling below neck not including abdomen

## CONCLUSIONS

- TYA with cancer consulted more frequently than controls before diagnosis
- Primary care features of cancer match secondary care reports
- Most symptoms were very low risk but some increased the likelihood of cancer substantially and should be taken seriously when assessing TYA

This work is now published

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