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The influence of chronic conditions and the environment on pubertal development. An example from medieval England.

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Abstract

Adolescence is a unique period in human development encompassing sexual maturation (puberty) and the physical and psychological transition into adulthood. It is a crucial time for healthy development and any adverse environmental conditions, poor nutrition, or chronic infection can alter the timing of these physical changes; delaying menarche in girls or the age of peak height velocity in boys. This study explores the impact of chronic illness on the tempo of puberty in 607 adolescent skeletons from medieval England (AD 900-1550).

A total of 135 (22.2%) adolescents showed some delay in their pubertal development, and this lag increased with age. Of those with a chronic condition, 40.0% (n=24/60) showed delay compared to only 20.3% (n=111/547) of the non-pathology group. This difference was statistically significant. A binary logistic regression model demonstrated a significant association between increasing delay in pubertal stage attainment with age in the pathology group.

This is the first time that chronic conditions have been directly associated with a delay in maturation in the osteological record, using a new method to assess stages of puberty in skeletal remains.

1. Introduction

Today, adolescence (from the Latin 'adolescere', or "to grow up") is defined by the World Health Organisation (1993) as a period between the ages of 10 to 24 years. Adolescence is a crucial period in terms of healthy development when individuals gain 50% of their weight and 20% of their final adult stature (World Health Organisation 1993). This adolescent growth spurt is a uniquely human phenomenon and encompasses sexual maturation (puberty), marking a period of physiological and psychological transition into adulthood (Hochberg and Belsky 2013). Adolescent health is receiving increasing attention in modern populations, with their unique behaviour directly linked to morbidity. Alcohol abuse, drug-taking and sexual activity increases the risk of unwanted pregnancies, sexually transmitted diseases and deaths due to motor vehicle accidents and suicides (Grunbaum et al., 2004). Well-nourished and healthy adolescent females are seen as the key for overall population well-being, with the nutritional levels of women before their first pregnancy having a direct impact on the development and birth-weight of their child and its subsequent survival (EWEC 2015). Despite the importance of this period of human development, it has received scant attention in bioarchaeology.

Pubertal changes occur as the result of stimulation of the hypothalamic-pituitary-gonadal (HPG) axis and the hypothalamic-pituitary-adrenal (HPA) axis (Louis et al. 2008). The latter, although active during infancy, becomes latent during childhood and is reactivated by the release of gonadotropine into the hypothalamus during adolescence, stimulating the gonads. Sex steroid induced accelerated growth is in turn, reliant on the presence of insulin-like growth factors produced by the pituitary gland (or the GH/IGF-1 axis) (Mason et al. 2011). Within a year of peak height velocity (PHV) being reached, girls will menstruate indicating that the ovaries are capable of secreting sufficient levels of oestrogen. Sometime later, the brain emits neuro-endocrine signals in a 26-day cycle that stimulates the pituitary glands to release the hormones needed for ovulation (Zacharias and Wurtman 1969). In boys, the presence of gonotrophins stimulate the release of androgens (testosterone and androstenedione), a stage known as 'gonadarch' (Louis et al. 2008). The HPA axis is independent of HPG and signals adrenal activation, eventually stimulating the formation of secondary sexual characteristics (Louis et al. 2008), such as breast development in females, and the apperance of facial hair and voice 'breaking' in males.

Many factors have been shown to influence the onset of puberty, including genetic disorders, ancestry, social status, nutrition, exposure to pollutants, extreme physical exercise, psychological stress, increased or reduced body mass, and chronic illness (Louis et al. 2008). Successful progression through the pubertal stages relies on the height and weight of the individual, which in turn is influenced by nutrition and the absence of chronic disease (Proos and Gustafsson 2012). Hochberg and Belksky (2013) interpret this relationship in terms of evolutionary biology, demonstrating phenotypic adaptive plasticity in favourable environmental conditions that allow females to achieve the extremes of their genetic range for maturation. In less favourable conditions, females may delay sexual maturation until they have reached the required body weight, providing for later fecundity, fertility and greater longevity. In terms of health longer term, the importance of pubertal growth on peak bone mineral density is demonstrated by the observation that women who experience delayed menarche by as little as two years, are more vulnerable to bone loss before the age of 40 years and potentially, early osteoporosis (Karapanou and Papadimitriou 2010).

Adolescence is a time of increased susceptibility to chronic infections such as tuberculosis and leprosy, due to exposure to new diseases associated with a riskier lifestyle, and the maturation of the immune system (Marais et al. 2005; Patil 2013). The greater propensity for adolescents over younger children to develop chronic tuberculosis for instance, is explained by Marais et al. (2005). They point to the destructive containment of pathogens, characteristic of a maturing immune response, as producing an oxygen-rich environment that allows *M. tuberculosis* to flourish, producing adult-type cavitations in the lung tissue. Chronic bowel conditions such as Crohn's disease and colitis often manifest in early adolescence and are associated with a delay in puberty development, and in particular delay boys entering peak height velocity of the adolescent growth spurt (Proos and Gustafsson 2012). This is though to be due to the combined influence of poor nutrition and inflammation on the GH/IGF-1 axis (Mason et al. 2011). Juvenile idiopathic arthritis is

another condition that often develops around 11-14 years, and is associated with a delay in puberty due to chronic inflammation, with menarche often occurring two years later than in healthy adolescents (Tsatsoulis et al. 1999; Umlawska and Prusek-Dudkiewicz 2010). Stini (1985: 213) also argued that the difference in immune system capability between males and females arises during adolescence as female bodies prepare for pregnancy.

While the presence of chronic infections is known to delay pubertal attainment in modern populations, this has yet to be assessed in archaeological samples. The development of new osteological techniques to identify stages of puberty provides the potential for us to explore this important period of human development in much greater detail than ever before (Shapland and Lewis 2013, 2014). Recent analysis of 645 skeletons aged between 10-25 years from medieval England provided the first direct evidence for the age of the adolecent growth spurt and onset of puberty between the seventh to sixteenth centuries (Lewis et al. 2015). While both males and females began puberty around 10-12 years, as today, the tempo of pubertal growth was longer, with females achieving menarche between 13-16 years, and individuals being as old as 16-20 years before they were fully mature. In London, most females were not achieving menarche until they were 17 years of age, and many were dying between 22-25 years, before they have reached full maturation. These delays indicate that the age at which children achieve each maturational stage in adolescence may be useful as an indicator of environmental stress.

During that study it was noted that a number of children identified as being behind their peers in pubertal stage attainment also suffered from a chronic condition, including tuberculosis, treponemal disease, osteomyelitis, rickets, bowel infection, arm paralysis and severe congenital spinal curvature (Lewis et al. 2015). The current study explores this association in more detail to assess the impact of chronic conditions on the tempo of the adolescent growth spurt, peak height velocity and menarche in urban medieval England.

2. Materials and methods

Of the original study sample of 994 adolescent individuals (10-25 years) analysed by Shapland and Lewis (2013; 2014), 607 were preserved well enough for a pubertal stage and the presence or absence of a pathology to be observed with confidence and were included in the analysis. This medieval urban sample comprised skeletons from four cemetery sites in England dating from AD 900-1550; St Peter's Church, Barton-on-Humber (or Barton, n=109), a combined York sample of St. Helen-on-the-Walls and Fishergate House (n=71), with the majority derived from St Mary Spital, London (n=427) (Figure 1). The adolescents from Barton were considered to be relatively affluent in comparison to those from York and London (Tyszka 2006), and it is likely the London sample contained a more diverse migrant group (Connell et al. 2012). As the focus was on the physical development of individuals with chronic conditions rather than geographical location or social status, the samples were combined to represent one large urban medieval sample.

Figure 1. Location of the cemetery sites used in the study

2.1 Age and sex determination

In order to investigate the influence of skeletal pathology on adolescent development in the largest sample possible, individuals were each assigned a 'minimum' age (i.e. 14+ years, 17+ years etc.) based on the lowest estimates derived from their dental age or extent of skeletal maturation. Age was assessed independently of pubertal status, with any marker used to provide a pubertal stage (e.g. the canine, iliac crest fusion, radial fusion etc.) omitted from the age assessment. For the dentition, age-at-death was determined using ages of attainment for the calcification of the permanent mandibular dentition (Moorrees et al. 1963, tabulated in Scheuer and Black, 2000). A mean age was calculated by averaging the ages for all observed teeth, combining the male and female values where sex was unknown. When only the third molar was still developing, a mean age was assigned using Liversidge and Marsden (2010), with the mean value taken as the minimum age. Once dental development was complete, age was assigned based on skeletal maturation. Observations were based on fusion of the proximal humerus, proximal and distal tibia and femur; extension of the epiphysis of the ischio-pubic ramus; flaked epiphysis at the medial clavicle, fusion of the ischial epiphysis, sacrum and vertebral annular rings (Albert and McCallister 2004; Schaefer et al. 2009). Anyone with a fused S1-S2 junction or fused medial clavicle epiphysis was considered to be over 25 years of age and was excluded from the study sample. The assigned minimum age was used to assess any delay in pubertal attainment for each individual.

Where possible, a sex assessment was carried out for all individuals aged 10-25 years (Lewis et al. 2015). The youngest groups were sexed using traits that have been shown to provide between 70% to 85% accuracy or above on the distal humerus, mandible and ilium (Falys et al. 2005; Sutter 2003). Sex was assigned only when three of these estimates agreed, from at least two different areas (i.e. features from the ilium and humerus). After 15 years, standard methods to sex adults based on the pelvis were employed (Buikstra and Ubelaker 1994), although the cranium was only used to confirm a male assignment, to avoid problems of effeminate cranial morphology noted in younger males (Walker 1994).

2.2 Assessing pubertal stage from skeletal and dental markers

The changes associated with the adolescent growth spurt follow a regular pattern that in clinical practice is identified through a series of 'bone markers' (Tanner et al. 1975). First, skeletal growth accelerates until 'peak height velocity' (PHV) is reached (Marshall and Tanner 1986). Around one year after PHV, during the deceleration phase, girls will achieve menarche and boys develop a full adult voice (Hägg and Taranger 1982). The growth spurt ends with the fusion of the major long bone epiphyses and complete maturation is signalled by fusion of the iliac crest (Marshall and Tanner 1986). Shapland and Lewis (2013; 2014) and Lewis et al. (2015) provide a series of bone markers that can be applied to human skeletal remains in order to assess an individual's position within the adolescent growth spurt and pubertal maturation sequence. Following these methods, observations were made using the mandibular canine root, the cervical vertebrae, bones of the hand, elbow and wrist, and maturation of the iliac crest. A pubertal stage was only assigned where three or more features were in agreement. Two stages of development were of particular interest for this study of puberty and health and are outlined below.

2.2.1 Peak height velocity

Peak height velocity is a crucial developmental stage in adolescence. In boys it signals a corresponding increase in weight and musculature that improves their physical capacity (Philippaerts et al. 2006). In girls, PHV corresponds to an increase in breast size signalling their transition to womanhood (Marshall and Tanner 1969). This stage provides the development of the external secondary sexual characteristics of adulthood and may have promoted a change in the way individuals were perceived by their society. Peak height velocity in particular has been found to be delayed in the presence of chronic inflammatory disease, especially in boys (Proos and Gustafsson 2012). Peak height velocity was estimated to have been achieved (either at or past PHV) when the following features were present:

- Hook of hamate complete: Stage I occurs around six months before PHV (Grave and Brown 1976),
- Canine Stage G (root complete or apex 1/2): occurs between 0.4 years and 1.3 years before PHV in girls and boys, respectively (Coutinho et al. 1993).
- Cervical vertebral maturation at Stages 3 and 4 (Franchi et al., 2000; Shapland and Lewis, 2014).
- Fusion of the proximal ulna, capitulum of the humerus and phalangeal epiphyses: fusion of the proximal ulna epiphysis precedes PHV (Roche 1976), fusion of the phalangeal epiphyses and capitulum at the lateral distal humerus occurs shortly after PHV (Houston 1980; Roche 1976).

2.2.2 Menarche

Menarche is a standard measure of adolescent development in clinical practice and the historical data, and precedes fertility in women by about a year (Zhang et al. 2008). Studies have consistently shown a link between poor nutritional status and a delay in menarche regardless of the child's ancestry or climate (Gluckman and Hanson 2006; Goyal et al. 2012;

Zacharias and Wurtman 1969). Given the intricate link between malnutrition and disease, the age at which menarche was achieved in our medieval samples was estimated as follows (Buehl and Pyle 1942; Frisancho et al. 1969):

- Presence of an ossified iliac crest epiphyses or fusion (of any part) of the crest,
- Fusion of the distal phalanx of the second finger where possible or in lieu of this, fusion of any distal hand phalanges.

2.3 Assessment of chronic conditions

Any sign of a chronic condition was noted in the sample. In particular, tuberculosis (TB) was diagnosed when an individual displayed classic lytic spinal changes, with or without collapse (Pott's disease), which may be accompanied by widespread new bone formation on the ribs and long bones (Lewis 2011). Treponemal disease (e.g. endemic and venereal syphilis) was diagnosed with the presence of gummatous lesions on the skull and long bones (Buckley and Dias 2002). Osteomyelitis, evident through the presence of a cloaca, involucrum and sequestrum (Ortner 2003), was also taken as evidence for long term ill-health. In addition to chronic infections, individuals with a metabolic disease (i.e. rickets, scurvy, porotic hyperostosis), or severe congenital conditions were identified using the criteria set out by Brickley and Ives (2008) and Ortner (2003).

In order to test whether individuals harbouring chronic conditions were significantly delayed in their development compared to those with no evidence of disease, an expected age at which each pubertal Stage should have been attained was calculated (Table 1). These ages were based on the average age range of Stage attainment for medieval adolescents calculated by Lewis et al. (2015). In order to ensure only significantly delayed individuals were identified, the midpoint of this age range was taken for each Stage providing a generous expected age of attainment.

Table 1. Average age range (years) at which a Stage is expected to have been reached (adapted from Lewis et al. 2015).

Stage	Process	Range	Expected age (years) of attainment
1	Initiation	10-12	10
2	Acceleration	10-13	12
3	PHV	11-15	14
4	Deceleration/Maturation	15-17	16
5	Completion	16-22	19

The effect of a chronic condition on an individual's pubertal status, whether delayed or not delayed, was tested using a Pearson chi-squared test, and the ability to predict whether an individual with a condition would be more likely to be delayed as their age increased was assessed using a binary logistic regression model with SPSS (Peng et al. 2002).

3. Results

Of the 607 individuals in the sample, 50% were assigned a 'minimum age' based on their dental development with the rest aged based on their skeletal maturation. A total of 60 (9.9%) displayed a chronic condition, whether metabolic, congenital or infectious. The overwhelming majority (52/60 or 86.6%) of the affected adolescents were from the later medieval London site of St Mary Spital (Table A.1).

Of the 607, a total of 135 (22.2%) individuals demonstrated some delay in their pubertal stage compared to the expected average age of attainment (Tables 2 and 3). In the pathology group, 40.0% (n=24/60) were delayed compared to a lesser 25.4% (n=111/436) of those in the non-pathology group. This difference in the proportion of individuals delayed in two groups was statistically significant (X^2= 11.66, P=<0.001, d.f.1).

When the general pattern of pubertal attainment was compared between the pathology and non-pathology groups (Figures 2ab), it showed that while adolescents are all entering the acceleration phase of the growth spurt around the same age, and over a similar wide period of time, those with a chronic conditions appear to lag behind their healthier peers at PHV. When the delayed group (pathology and non-pathology individuals) was examined as a whole (Figure 3), this lag increased as individuals proceeded through the pubertal stages, being most evident at PHV (Stage 3) and Completion (Stage 5).

Table 2. Minimum age, sex and pathology status of the non-delayed group.

Minimum Age	Number of Individuals				Pathology Status	
	Male	Female	Not sexed	Total	Yes	No
10	16	14	21	51	1	50
11	15	7	14	36	3	33
12	9	4	6	19	3	16
13	20	5	12	37	2	35
14	3	12	23	38	3	35
15	28	14	22	64	7	57
16	21	12	7	40	1	39
17	40	18	4	62	5	57
18	12	12	0	24	0	24
19	6	7	0	13	0	13
20	4	9	0	13	0	13
21	-	-	-	0	-	-
22	51	24	0	75	11	64
Total	**225**	**138**	**109**	**472**	**36 (7.6%)**	**436 (92.3%)**

Table 3. Minimum age, sex and pathology status of the delayed puberty group.

Minimum Age	Number of Individuals				Pathology Status	
	Male	Female	Not sexed	Total	Yes	No
10	-	-	-	0	-	-
11	-	-	-	0	-	-
12	1	1	1	3	0	3
13	-	-	-	0	-	-
14	6	0	4	10	0	10
15	8	2	6	16	4	12
16	6	3	5	14	5	9
17	1	1	1	3	0	3
18	0	0	1	1	0	1
19	21	6	3	30	5	25
20	10	7	0	17	5	12
21	-	-	-	0	-	-
22	22	19	0	41	5	36
Total	**75**	**39**	**21**	**135**	**24 (17.7%)**	**111 (82.2%)**
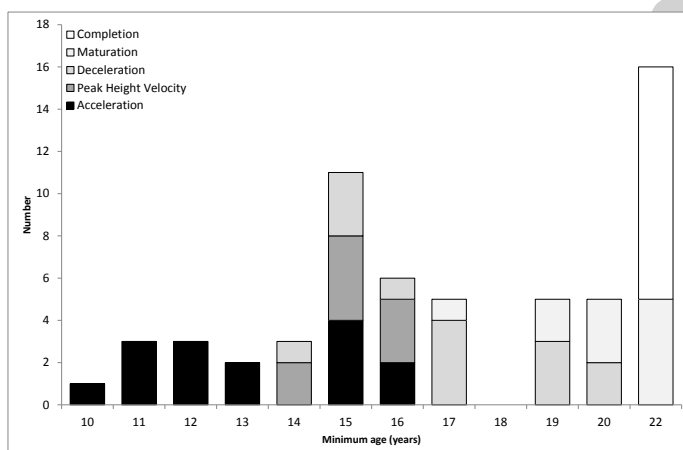
Figure 2a Age of pubertal stage attainment in non-pathology group (n=547)

Figure 2b Age of pubertal stage attainment in the pathology group (n=60)
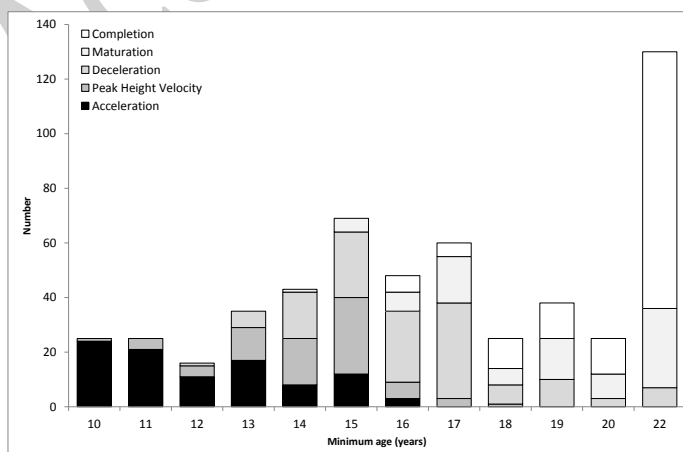
It is possible that the onset of the infectious disease or metabolic condition occurred after a pubertal stage had been reached in an individual and would therefore have had no impact on stage progression. For this reason, the stage attainment of the 47 individuals with identifiable chronic conditions was examined more closely (Tables 4-6). There were 19 clear cases of tuberculosis and treponemal disease, 16 individuals were probably suffering from either rickets or scurvy based on severe bowing of the long bones, frayed metaphyseal ends, porotic hyperostosis, or widespread new bone formation. Another 12 adolescents suffered from congenital conditions that may have affected their normal development or access to resources. Perthe's disease and slipped femoral epiphyses are included in the congenital group, despite their more complex aetiology including a circulatory disorder or traumatic event (Ortner, 2003), as both may have affected the physical ability of these individuals.

	1	2	3	4	5
■ Delayed	0	2.2	19.3	13.3	65.2
□ Not delayed	18.4	11.9	21.6	26.7	21.4
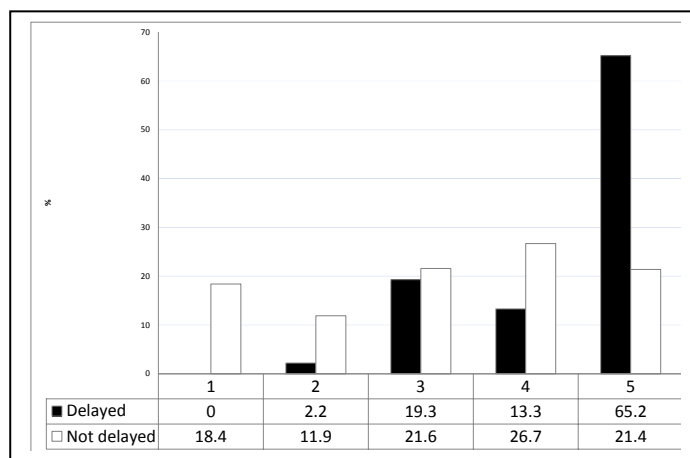
Figure 3. Percentage of individuals delayed at each stage of pubertal development.

Table 4: Pubertal development of adolescents with tuberculosis and treponemal disease, ordered by age (years). SP: St Mary Spital; B: Barton; Y: York. Delayed individuals are highlighted in bold.

Skeleton	Minimum age	Condition	Sex	Pubertal stage	Delayed?
SP30702	11	Tuberculosis	M?	Acceleration	No
SP25618	12	Tuberculosis		Acceleration	No
Y1205	**13**	**Tuberculosis**	**M?**	**Acceleration**	**Yes**
SP27615	14	Tuberculosis		Deceleration	No
SP13715	15	Treponematosis	M?	Deceleration	No
SP29986	**15**	**Tuberculosis**		**PHV**	**Yes**
SP22829	**15**	**Tuberculosis**		**Acceleration**	**Yes**
SP20634	16	Treponematosis	F?	Deceleration	No
SP5426	**16**	**Tuberculosis**		**PHV**	**Yes**
SP22345	**16**	**Tuberculosis**	**F?**	**PHV**	**Yes**

Skeleton	Minimum age	Condition	Sex	Pubertal stage	Delayed?
SP27544	**16**	**Treponematosis**		**PHV**	**Yes**
SP30931	**16**	**Tuberculosis**	**F**	**Acceleration**	**Yes**
SP7571	**19**	**Treponematosis**	**F**	**Maturation**	**Yes**
SP3975	**20**	**Tuberculosis**	**M**	**Deceleration**	**Yes**
SP22542	**20**	**Tuberculosis**	**M**	**Deceleration**	**Yes**
SP3144	**22**	**Tuberculosis**	**F**	**Maturation**	**Yes**
SP15030	22	Tuberculosis	F	Post	No
SP13232	**22**	**Treponematosis**	**F?**	**Maturation**	**Yes**
SP15575	**22**	**Tuberculosis**	**F**	**Maturation**	**Yes**

Table 5: Pubertal development of adolescents with possible metabolic conditions, ordered by age (years). SP: St Mary Spital; B: Barton; Y: York. Delayed individuals are highlighted in bold.

Skeleton	Minimum age	Condition	Sex	Pubertal stage	Delayed?
SP24009	10	Porotic hyperostosis	M?	Acceleration	No
Y1518	11	Rickets	M?	Pre-puberty	No
SP3933	11	Probable scurvy		Pre-puberty	No
B810	12	Rickets	M?	Acceleration	No
B961	14	Probable rickets	M?	Deceleration	No
SP3861	14	Rickets	F	Deceleration	No
Y1577	**15**	**Probable rickets**		**PHV**	**Yes**
SP2622	**15**	**Porotic hyperostosis**		**PHV**	**Yes**
SP15255	**15**	**Probable scurvy**	**F?**	**Acceleration**	**Yes**
SP32355	15	Probable scurvy	M	Deceleration	No
B704	16	Rickets		Maturation	No
SP15669	16	Probable rickets	F?	Deceleration	No
SP17072	17	Probable rickets	M?	Maturation	No
B131	19	Rickets	F	Complete	No
Y5409	22	Probable rickets	M	Complete	No
SP29152	**22**	**Probable rickets**	**M**	**Maturation**	**Yes**

Table 6: Pubertal development of adolescents with congenital conditions, ordered by age (years). SP: St Mary Spital; B: Barton. Delayed individuals are highlighted in bold.

Skeleton	Minimum age	Condition	Sex	Pubertal stage	Delayed?
SP13829	12	Familial idiopathic hyperphosphatia	M?	Acceleration	No
SP2917	13	Radial aplasia	F?	PHV	No
SP29964	15	Hyperbrachycephaly	F	Deceleration	No

SP12538	**17**	**Tarsal coalition**	**M**	**PHV**	**Yes**
SP20417	17	Talipes equinovarius	M?	Maturation	No
SP27661	17	Vertebral hypoplasia and kyphosis	M	Deceleration	No
SP32178	18	Tarsal coalition	M?	Deceleration	No
SP3816	22	Ulna dysplasia (glenoid)	M	Complete	No
SP20157	**22**	**Scaphocephaly**	**F**	**Deceleration**	**Yes**
SP31395	22	Perthe's disease	M	Complete	No
B1312	22	Spina bifida	M	Complete	No
B2340	22	Slipped femoral epiphysis	M	Complete	No

In the chronic infection group, 13 (68.4%) of the adolescents showed delay in their pubertal stage attainment compared to what might be expected for their age. Of the 14 individuals with tuberculosis, 71.4% (n=10) were delayed, compared to 60.0% (n=3/5) of those with treponematosis. For the metabolic group, four (25.0%) were showing delay compared to two (16.7%) individuals with congenital conditions. When these groups were compared, delay was significantly more likely to occur in individuals with an infectious disease, than in the metabolic and congenital group (X^2= 10.04, P=<0.01, d.f.2).

The general impression from these data is that as individuals grew older, the impact of the pathology exacerbated their delay, with chronically ill individuals falling further behind their healthier peers. In order to test whether this pattern was significant and could be predicted, a binary logistic regression model was applied to the data. The results are provided in Table 7. They show that increasing age is significantly associated with being delayed (the dependant), with individuals lagging further behind in the pubertal stage as they get progressively older, and that this pattern is more significant in individuals who have a pathological condition, than those who do not (P=0.005).

Table 7. Predicted probability of being delayed in pubertal development with increasing age when suffering from a chronic condition

	Predictor	ß(SE)	Wald's X^2	df	Significance	exp^ß (odds ratio)
Step 1	Delayed (dependant)	5.20 (0.55)	58.99	1	0.000	181.79
	Minimum age	-0.23 (0.03)	90.16	1	0.000	0.79
Step 2	Delayed (dependant)	4.40 (0.61)	52.09	1	0.000	81.79
	Minimum age by pathology status	0.85 (0.30)	7.79	1	0.005	2.34

3.1 Attaining peak height velocity and menarche

The pubertal stage PHV could be assigned to 85 individuals (including 13 females and 41 males). If 14 years is taken as the average minimum age for which PHV should be reached

(Table 1), then 31 adolescents were delayed, representing 21.9% (n=25/114) of the non-pathology group and 42.8% (n=6/14) of the pathology group, but this difference was not statistically significant (X^2=2.63, d.f.1, P=0.10). Only 18 of these individuals could be sexed, but it is interesting to note that in the non-pathological group, 14 of the 15 sexed individuals who were delayed for PHV were male.

Of the 355 females for whom a minimum age could be assigned, whether menarche had been passed could be estimated in 154 cases based on the maturation of the iliac crest and bones of the hand. Of these, 134 were in the non-pathology group and 20 had a chronic condition. In both groups, the youngest minimum age of menarche was 14 years, and one female in the non-pathology group showed the greatest delay having yet to reach menarche at least 17 years. If menarche is reached around 12 months after PHV, then the expected age of attainment is 15 years. No females in the pathology group for whom this status could be assessed, demonstrated delayed menarche.

4. Discussion

This study aimed to assess the affect of chronic conditions on pubertal development in a large group of adolescent skeletons from medieval England. The majority of individuals with pathology came from the later medieval contexts of St Mary Spital in London is not surprising given the highly industrial nature of the capital at the time. The London group would have been genetically diverse, with individuals migrating to London from rural areas in the UK and from Continental Europe (Wareing 1980; Youngs 2006), and it is also likely that both Barton and York experienced an influx of immigrants, although to a lesser extent (Goldberg 1992). Given the importance of genetics on the timing of maturation, and in particular menarche, generous average ages were provided for individuals to reach the specific stages along the puberty maturation scale. Although individuals were aged independently of the features used to assess puberty stage, skeletal maturation and pubertal development are inextricably linked, as both are affected by environmental and genetic factors. Hence, pubertal maturation provides a detailed map of maturational delay for each individual. The results indicated that a number of individuals took longer to reach the later stages of pubertal development, and this was particularly true for those suffering from a chronic condition.

The general lag of pubertal attainment with age may be an artefact of the ageing techniques employed. The majority of individuals up to Stage 3, or PHV, were aged using dental scores (76% , n=178/234) over skeletal maturation (23.9%, n=56/234), while after Stage 3 more individuals were provided a minimum age based on their skeletal development (67.0%, n=252/376). As dental ages are considered more environmentally robust than skeletal maturation, this may have resulted in an underestimation of the chronological age of the older individuals, exaggerating the amount of delay with age. While this may certainly be a factor, it does not explain the lag at PHV where 60% of individuals were dentally aged, or provide an explanation for the greater delay in the pathology group. For the latter, it indicates that the presence of a chronic condition was delaying both

general skeletal maturation reflected in the minimum age assigned, and pubertal development. Assigning a chronological age to these archaeological groups becomes particularly problematic when trying to compare their ages of pubertal attainment to that of modern children whose age is known rather than estimated, and this should be done with caution. Equally, the adolescents in this study are the non-survivors of their community, and it is possible their ages of pubertal attainment, and more importantly PHV and menarche, do not reflect the ages of pubertal attainment of the living population from which they derive. This is a common conundrum in bioarchaeology (Wood et al. 1992; Goodman 1993). It is likely, however, that the majority of the individuals in the study sample died from accidents or acute diseases that would not have affected their overall growth and development (Saunders and Hoppa 1993). Given that the expected ages of attainment were calculated using the ranges derived from the original medieval sample, rather than modern chronologies, individuals demonstrating delay are the true outliers within their peer group.

The results revealed that not only were individuals with a recognisable chronic pathology delayed in their pubertal attainment compared to their peers. This delay was particularly evident at peak height velocity and for completion. Where the individuals could be sexed, the majority of individuals failing to reach PHV by the expected time were male (77.8%, n=14/18) regardless of their pathological status. When these individuals were examined in detail, those suffering from the systemic chronic infections of tuberculosis or treponematosis that were the most delayed. Of the 19 individuals within this group, 13 (68.4%) showed a delay in their pubertal stage attainment compared to what might be expected. One London female (SP30931) with TB was only in the acceleration phase of her growth spurt by 16 years compared to the average age of 13 years, and two 20-year old males (SP3975, SP22542) also from London and suffering from TB, were still in their deceleration phase when most of their peers had completed puberty (three stages ahead) by 19 years.

While the adolescents with chronic conditions provide some explanation for developmental delay beyond the average expectations for medieval adolescents, 20.3% (n=111) of the delayed group showed no evidence of disease. A number will have suffered from a chronic disease that did not manifest on their skeleton before they died, for example, tuberculosis manifests in the skeleton in between 1-5% of cases (Resnick and Kransdorf 2005; Rankin and Tuli 2009), and treponemal disease in 5-15% (Steinbock 1976). For the rest, a series of urban environmental factors may be causing the delay in puberty attainment, and need to be considered. Strenuous child labour has associated with delayed adolescent development due to higher levels of energy expenditure (Thomas et al. 2001) and menarcheal delay has been demonstrated due to the psychological upheaval of war (Prebeg and Bralić 2000) as well as exposure to violence and fear in urban environments (Villamor et al. 2009). Malnutrition, acute infection and exposure to urban environmental pollutants may also have contributed to this pattern in these urban adolescents.

The average minimum age for menarche in medieval females was estimated at 15 years in a recent study (Lewis et al. 2015). In the current study sample, in both groups for

whom this could be assessed, the vast majority (98.7%, 152/154) experienced menarche between 14-15 years. Although not included in this study due to a lack of a definitive pubertal stage, one female from London (SP30711) died at 17.1 years (based on mean dental age) with unfused phalanges and an unfused iliac crest, suggesting she had yet to experience her menses. This female suffered from severe congenital kyphoscolosis (Walker 2012: 22). However, two females from the non-pathology group died before menarche at a mean dental age of 16.6 and 17.3. They may simply represent a normal distribution of development within the population, or it is possible that they were malnourished, or were carrying out strenuous physical activity at this critical period of their development. In modern developmental studies, age at first menarche is recorded from personal accounts of the girl or their mother, either at the time that they have their first 'period', or less accurately, from memory (Bean et al. 1979). Studies have consistently shown a link between poor nutritional status and a delay in menarche regardless of the child's ancestry or climate (Gluckman and Hanson 2006; Goyal et al. 2012; Karapanou and Papadimitriou 2010; Zacharias and Wurtman 1969). Swenne (2008) noted that girls with eating disorders and severe undernutrition were slow to progress through puberty and menarcheal delays have been demonstrated in times of famine (Van Noord and Kaaks 1991). Although carried out on a small sample of 60 North American girls, Dreizen and colleagues (1967) noted a delay in pubertal growth and menarche by as much as 24 months in undernourished girls compared to their well-nourished peers. The effects were most severe during the early stages of the adolescent growth spurt, after which 'catch-up' growth allows malnourished adolescents to achieve similar adult stature to their better nourished peers. Kaplowitz (2008) discusses the role of leptin, a protein released by fat cells, in stimulating the gonadotrophic secretion as a factor in the link between obesity in females and early menarche. A threshold level of leptin required for the initiation of menstruation suggests an evolutionary mechanism for ensuring pregnancy only occurs when an individual has achieved the right body weight (or adiposity) to ensure its success.

Karapanou and Papadimitriou (2010) argued that a delay in menarche by two years and over leaves women susceptible to developing osteoporosis at an earlier age due to a reduced peak bone mineral density at the time of maturation. While the current data has not shown any difference in menarcheal delay between the two groups under study, the onset of menarche at an average of 15 years in medieval women is three years behind modern estimates, despite starting puberty around the same age. It is possible that this later age of menarche is present in other medieval groups and may have contributed to the early bone loss in adult females identified in a later medieval site (Mays et al. 1998). Intriguingly, recent clinical studies have suggested a link between vitamin D deficiency and early menarche in females from Bogotá, Columbia (Villamor et al. 2011), and while this link has yet to be fully explained, it suggests a connection between vitamin D, sexual maturation and genetic variants in the oestrogen gene (Chew and Harris 2013). Of the five females diagnosed with probable rickets in the study sample and a pubertal status, one (SP3861) had reached menarche by a minimum age of 14 years, slightly earlier than her peers in

London, but her age actually ranged between 14-18 years so there is no evidence that we are seeing advanced pubertal development. The visibility of rickets in the archaeological record provides a tantalising glimpse into the potential of exploring vitamin D status and pubertal development in skeletal remains.

Due to their rapid growth, adolescents have different nutritional requirements to the rest of the population. The iron requirement rises from ~1.0 to 2.5 mg/d in boys, due to an increased blood volume and rise in haemoglobin concentration. At peak growth, females require ~1.5 mg/d iron, which finally decreases to 1.3 mg/d reflecting the need to supplement menstrual loss throughout adulthood (Brabin and Brabin 1992). Although some studies have shown iron deficiency has to be severe to affect growth (Ulijaszek 2006), others argue that iron coupled with vitamin A deficiencies may slow the tempo of growth, with any catch-up growth experienced later on in pubertal development further depleting stores of these nutrients (Brabin and Brabin 1992). Vitamin A, present in meat, poultry, fish and dairy products, fruits and vegetables is seen as essential for healthy fertility (Brabin and Brabin 1992). Acute infections such as malaria and intestinal parasites provoke a systemic response, and may affect the host over long periods of time. They can cause growth faltering due to the secondary effects undernutrition through a decreased appetite, impaired absorption or increased metabolic requirements (Ulijaszek 2006). The co-existence of disease and malnutrition have been frequently shown to cause delay in epiphyseal fusion at the end of the adolescent growth spurt, with some researchers suggesting females are less affected than males (Stini 1985).

High exposure to lead (3 µg/dL or 0.144 µmol/L blood levels) has been shown to delay physical growth, development and menarche, perhaps due to its affects on endocrine function (Selevan et al. 2003; Ulijaszek 2006; Wu et al. 2003). By contrast, exposure to mercury is thought to stimulate early menarche when compared to non-exposed adolescents (Denham et al. 2005). Environmental pollution had been noted in medieval urban environments since the 1250s (Bimblecombe 2011), and by the post-medieval period anthropomorphic lead levels reached as high as 90ppm (Millard et al. 2014). To explore the potential impact of generalised malnutrition, pollution and infection in the study sample, the prevalence of cribra orbitalia was used as a measure of anaemia of non-specific aetiology. Anaemia can be caused by malnutrition due to a lack of meat and leafy vegetables (resulting in iron, folic acid or vitamin B12 deficiency), as well as due to the secondary effects of lead exposure and infections such as malaria (Brown and Holden 2002; Bolton-Maggs and Thomas 2008; Walker et al. 2009; Oxenham and Cavill 2010). The results suggest general levels of anaemia were high, with 24.5% (n= 29/118 with orbits) of the delayed group, and 26.9% (n=75/279 with orbits) of the non-delayed group showing grades 3-5 (Stuart-Macadam 1991). Cases of the most severe manifestation of the lesion, grade 5, were slightly higher in the delayed group at 6.9% (n=2/29) compared to 4.0% (n=3/75). Direct study of lead levels in the teeth of the delayed group provides potential for future research.

5. Conclusions

This study is the first attempt to directly measure the impact of chronic conditions on the growth and development of adolescents, using a large sample of individuals from medieval England. The results showed that those with recognisable chronic pathology were delayed in their pubertal attainment compared to their peers and that this delay increased with age. Peak height velocity and age of completion were the stages most influenced by illness, with those suffering from tuberculosis and treponemal disease significantly affected. While chronic conditions provide some explanation for the developmental delay seen in the medieval group, 20.3% of the individuals showed no evidence of disease. Some may have harboured hidden infections, but other factors such as malnutrition, poverty, physiological stress and exposure to urban environmental pollutants may have all contributed to this pattern and are difficult to measure in archaeological populations.

While the study sample did not reveal any females with delayed menarche, there was evidence that severe congenital conditions could play a part, with the potential for rickets to actually induce earlier menarche. However, the numbers of females for whom menarche can be assessed is limited by the poor preservation of the iliac crest epiphysis, and until further methods can be developed to identify menarcheal status, this type of research will continue to be hindered by small sample sizes. Overall, the study has demonstrated the potential of the pubertal status method to provide valuable information on the impact of environmental and disease stress in past populations.

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Supplementary Table: Estimated and expected pubertal stages for the total study sample.

Site	Skeleton	Minimum age	Puberty Stage	Pathology Present	Expected Stage	Puberty Status
Barton-on-Humber	318	10	1	No	1	not delayed
Barton-on-Humber	339	10	2	No	1	not delayed
Barton-on-Humber	340	10	1	No	1	not delayed
Barton-on-Humber	366	10	2	No	1	not delayed
Barton-on-Humber	429	10	1	No	1	not delayed
Barton-on-Humber	856	10	1	No	1	not delayed
Barton-on-Humber	946	10	1	No	1	not delayed
Barton-on-Humber	1206	10	1	No	1	not delayed
Barton-on-Humber	1244	10	1	No	1	not delayed
Barton-on-Humber	2250	10	3	No	1	not delayed
Barton-on-Humber	2762	10	2	No	1	not delayed
St Helens	5669	10	2	No	1	not delayed
St Helens	5256	10	1	No	1	not delayed
St Helens	5138	10	1	No	1	not delayed
St Helens	6080	10	2	No	1	not delayed
St Helens	5873	10	1	No	1	not delayed
St Mary Spital	2923	10	1	No	1	not delayed
St Mary Spital	2966	10	1	No	1	not delayed
St Mary Spital	3492	10	2	No	1	not delayed
St Mary Spital	3844	10	1	No	1	not delayed
St Mary Spital	5705	10	1	No	1	not delayed
St Mary Spital	5809	10	2	No	1	not delayed
St Mary Spital	8181	10	1	No	1	not delayed
St Mary Spital	9658	10	2	No	1	not delayed
St Mary Spital	9845	10	1	No	1	not delayed
St Mary Spital	10606	10	2	No	1	not delayed
St Mary Spital	19120	10	1	No	1	not delayed
St Mary Spital	19379	10	2	No	1	not delayed
St Mary Spital	19441	10	1	No	1	not delayed
St Mary Spital	20421	10	1	No	1	not delayed
St Mary Spital	20446	10	1	No	1	not delayed
St Mary Spital	20463	10	1	No	1	not delayed
St Mary Spital	20924	10	2	No	1	not delayed
St Mary Spital	21518	10	2	No	1	not delayed
St Mary Spital	21730	10	2	No	1	not delayed
St Mary Spital	21872	10	2	No	1	not delayed
St Mary Spital	21969	10	2	Yes	1	not delayed
St Mary Spital	21989	10	1	No	1	not delayed
St Mary Spital	22253	10	1	No	1	not delayed
St Mary Spital	22479	10	2	No	1	not delayed
St Mary Spital	22898	10	2	No	1	not delayed

St Mary Spital	23615	10	2	No	1	not delayed
St Mary Spital	23948	10	2	No	1	not delayed
St Mary Spital	24009	10	2	No	1	not delayed
St Mary Spital	26496	10	2	No	1	not delayed
St Mary Spital	27250	10	2	No	1	not delayed
St Mary Spital	29297	10	2	No	1	not delayed
St Mary Spital	30136	10	2	No	1	not delayed
St Mary Spital	31004	10	2	No	1	not delayed
St Mary Spital	31294	10	1	No	1	not delayed
St Mary Spital	36026	10	1	No	1	not delayed
Barton-on-Humber	230	11	3	No	1	not delayed
Barton-on-Humber	514	11	3	No	1	not delayed
Barton-on-Humber	1490	11	2	No	1	not delayed
Barton-on-Humber	2650	11	1	No	1	not delayed
Fishergate House	1518	11	1	No	1	not delayed
Fishergate House	1106	11	2	No	1	not delayed
St Helens	5771	11	1	No	1	not delayed
St Helens	6034	11	1	No	1	not delayed
St Helens	5751	11	1	No	1	not delayed
St Helens	5510	11	2	No	1	not delayed
St Helens	5782	11	3	No	1	not delayed
St Mary Spital	3607	11	2	No	1	not delayed
St Mary Spital	30702	11	2	Yes	1	not delayed
St Mary Spital	3845	11	2	No	1	not delayed
St Mary Spital	3933	11	1	No	1	not delayed
St Mary Spital	5907	11	2	Yes	1	not delayed
St Mary Spital	11187	11	2	No	1	not delayed
St Mary Spital	14707	11	2	No	1	not delayed
St Mary Spital	14724	11	3	No	1	not delayed
St Mary Spital	15139	11	2	No	1	not delayed
St Mary Spital	19171	11	2	No	1	not delayed
St Mary Spital	19351	11	2	No	1	not delayed
St Mary Spital	17397	11	2	Yes	1	not delayed
St Mary Spital	19634	11	2	No	1	not delayed
St Mary Spital	20910	11	2	No	1	not delayed
St Mary Spital	20942	11	2	No	1	not delayed
St Mary Spital	21413	11	1	No	1	not delayed
St Mary Spital	21729	11	2	No	1	not delayed
St Mary Spital	21957	11	2	No	1	not delayed
St Mary Spital	22538	11	2	No	1	not delayed
St Mary Spital	24136	11	2	No	1	not delayed
St Mary Spital	29348	11	2	No	1	not delayed
St Mary Spital	30074	11	1	No	1	not delayed
St Mary Spital	31022	11	2	No	1	not delayed

St Mary Spital	32194	11	2	No	1	not delayed
St Mary Spital	32468	11	2	No	1	not delayed
St Helens	5814	12	1	No	2	delayed
St Helens	5599	12	1	No	2	delayed
St Mary Spital	12453	12	1	No	2	delayed
Barton-on-Humber	310	12	3	No	2	not delayed
Barton-on-Humber	810	12	2	No	2	not delayed
Barton-on-Humber	1676	12	2	No	2	not delayed
Barton-on-Humber	2186	12	3	No	2	not delayed
Fishergate House	1132	12	2	No	2	not delayed
St Helens	5121	12	3	No	2	not delayed
St Mary Spital	1064	12	2	No	2	not delayed
St Mary Spital	2845	12	4	No	2	not delayed
St Mary Spital	3846	12	2	No	2	not delayed
St Mary Spital	12403	12	2	No	2	not delayed
St Mary Spital	13829	12	2	No	2	not delayed
St Mary Spital	19880	12	3	No	2	not delayed
St Mary Spital	19920	12	2	No	2	not delayed
St Mary Spital	20132	12	2	Yes	2	not delayed
St Mary Spital	20712	12	2	Yes	2	not delayed
St Mary Spital	25618	12	2	Yes	2	not delayed
St Mary Spital	23496	12	2	No	2	not delayed
St Mary Spital	25219	12	2	No	2	not delayed
St Mary Spital	30175	12	2	No	2	not delayed
Barton-on-Humber	496	13	3	No	2	not delayed
Barton-on-Humber	745	13	2	No	2	not delayed
Barton-on-Humber	1160	13	3	No	2	not delayed
Barton-on-Humber	1753	13	4	No	2	not delayed
Barton-on-Humber	1913	13	2	No	2	not delayed
Barton-on-Humber	2397	13	2	No	2	not delayed
Barton-on-Humber	2753	13	2	No	2	not delayed
Fishergate House	1205	13	2	Yes	2	not delayed
St Helens	5518	13	2	No	2	not delayed
St Helens	5974	13	4	No	2	not delayed
St Helens	5252	13	2	No	2	not delayed
St Mary Spital	1067	13	3	No	2	not delayed
St Mary Spital	1149	13	4	No	2	not delayed
St Mary Spital	2621	13	2	No	2	not delayed
St Mary Spital	2917	13	3	No	2	not delayed
St Mary Spital	3623	13	3	No	2	not delayed
St Mary Spital	3695	13	2	No	2	not delayed
St Mary Spital	3561	13	2	Yes	2	not delayed
St Mary Spital	4139	13	3	No	2	not delayed
St Mary Spital	5674	13	2	No	2	not delayed

St Mary Spital	5757	13	2	No	2	not delayed
St Mary Spital	13433	13	2	No	2	not delayed
St Mary Spital	15647	13	4	No	2	not delayed
St Mary Spital	20845	13	2	No	2	not delayed
St Mary Spital	21068	13	3	No	2	not delayed
St Mary Spital	21235	13	3	No	2	not delayed
St Mary Spital	21870	13	2	No	2	not delayed
St Mary Spital	21878	13	2	No	2	not delayed
St Mary Spital	22717	13	3	No	2	not delayed
St Mary Spital	23004	13	2	No	2	not delayed
St Mary Spital	23390	13	2	No	2	not delayed
St Mary Spital	24138	13	3	No	2	not delayed
St Mary Spital	26243	13	4	No	2	not delayed
St Mary Spital	26636	13	4	No	2	not delayed
St Mary Spital	26802	13	3	No	2	not delayed
St Mary Spital	29134	13	2	No	2	not delayed
St Mary Spital	30964	13	3	No	2	not delayed
Barton-on-Humber	992	14	2	No	3	delayed
Barton-on-Humber	1378	14	2	No	3	delayed
Barton-on-Humber	2048	14	2	No	3	delayed
Barton-on-Humber	2690	14	2	No	3	delayed
St Helens	5586	14	1	No	3	delayed
St Helens	6025	14	1	No	3	delayed
St Mary Spital	3180	14	2	No	3	delayed
St Mary Spital	20254	14	2	No	3	delayed
St Mary Spital	22738	14	2	No	3	delayed
St Mary Spital	28391	14	2	No	3	delayed
Barton-on-Humber	41	14	4	No	3	not delayed
Barton-on-Humber	251	14	3	No	3	not delayed
Barton-on-Humber	281	14	4	No	3	not delayed
Barton-on-Humber	491	14	4	No	3	not delayed
Barton-on-Humber	961	14	4	No	3	not delayed
Barton-on-Humber	1582	14	4	No	3	not delayed
Barton-on-Humber	1876	14	4	No	3	not delayed
Barton-on-Humber	2419	14	4	No	3	not delayed
Barton-on-Humber	2489	14	4	No	3	not delayed
Barton-on-Humber	2702	14	3	No	3	not delayed
Fishergate House	1085	14	4	No	3	not delayed
St Mary Spital	3171	14	3	No	3	not delayed
St Mary Spital	3861	14	4	No	3	not delayed
St Mary Spital	27615	14	4	Yes	3	not delayed
St Mary Spital	21037	14	3	Yes	3	not delayed
St Mary Spital	8533	14	4	No	3	not delayed
St Mary Spital	9780	14	3	No	3	not delayed

St Mary Spital	12762	14	3	No	3	not delayed
St Mary Spital	19125	14	4	No	3	not delayed
St Mary Spital	19361	14	4	No	3	not delayed
St Mary Spital	20172	14	3	No	3	not delayed
St Mary Spital	20376	14	4	No	3	not delayed
St Mary Spital	20553	14	3	No	3	not delayed
St Mary Spital	20925	14	3	No	3	not delayed
St Mary Spital	21027	14	3	No	3	not delayed
St Mary Spital	21513	14	4	No	3	not delayed
St Mary Spital	23981	14	3	Yes	3	not delayed
St Mary Spital	22680	14	3	No	3	not delayed
St Mary Spital	23396	14	4	No	3	not delayed
St Mary Spital	23987	14	3	No	3	not delayed
St Mary Spital	25272	14	3	No	3	not delayed
St Mary Spital	25701	14	4	No	3	not delayed
St Mary Spital	25823	14	3	No	3	not delayed
St Mary Spital	26163	14	3	No	3	not delayed
St Mary Spital	28275	14	3	No	3	not delayed
St Mary Spital	29496	14	4	No	3	not delayed
St Mary Spital	29607	14	3	No	3	not delayed
St Mary Spital	31291	14	3	No	3	not delayed
Barton-on-Humber	1598	15	2	No	3	delayed
Barton-on-Humber	2694	15	2	No	3	delayed
Fishergate House	1410	15	2	No	3	delayed
St Helens	5931	15	2	No	3	delayed
St Mary Spital	1397	15	2	No	3	delayed
St Mary Spital	3876	15	2	No	3	delayed
St Mary Spital	5683	15	2	No	3	delayed
St Mary Spital	12100	15	2	No	3	delayed
St Mary Spital	15255	15	2	Yes	3	delayed
St Mary Spital	22415	15	2	No	3	delayed
St Mary Spital	23493	15	2	No	3	delayed
St Mary Spital	23090	15	2	Yes	3	delayed
St Mary Spital	28207	15	2	No	3	delayed
St Mary Spital	22829	15	2	Yes	3	delayed
St Mary Spital	29679	15	2	No	3	delayed
St Mary Spital	29075	15	2	Yes	3	delayed
Barton-on-Humber	485	15	3	Yes	3	not delayed
Barton-on-Humber	268	15	4	No	3	not delayed
Barton-on-Humber	785	15	4	No	3	not delayed
Barton-on-Humber	853	15	4	No	3	not delayed
Barton-on-Humber	968	15	4	No	3	not delayed
Barton-on-Humber	2159	15	3	Yes	3	not delayed
Barton-on-Humber	1803	15	3	No	3	not delayed

Barton-on-Humber	1820	15	4	No	3	not delayed
Barton-on-Humber	2344	15	3	No	3	not delayed
Fishergate House	1577	15	3	No	3	not delayed
Fishergate House	1039	15	3	No	3	not delayed
Fishergate House	1465	15	3	No	3	not delayed
St Helens	5168	15	4	No	3	not delayed
St Helens	5189a	15	4	No	3	not delayed
St Helens	5224	15	3	No	3	not delayed
St Mary Spital	2622	15	3	No	3	not delayed
St Mary Spital	2967	15	3	No	3	not delayed
St Mary Spital	3025	15	3	No	3	not delayed
St Mary Spital	3083	15	4	No	3	not delayed
St Mary Spital	3403	15	3	No	3	not delayed
St Mary Spital	3491	15	4	No	3	not delayed
St Mary Spital	3576	15	4	No	3	not delayed
St Mary Spital	6355	15	3	No	3	not delayed
St Mary Spital	6844	15	4	No	3	not delayed
St Mary Spital	8355	15	3	No	3	not delayed
St Mary Spital	10449	15	3	No	3	not delayed
St Mary Spital	11395	15	4	No	3	not delayed
St Mary Spital	12154	15	4	No	3	not delayed
St Mary Spital	12819	15	4	No	3	not delayed
St Mary Spital	12258	15	4	Yes	3	not delayed
St Mary Spital	14838	15	4	No	3	not delayed
St Mary Spital	13715	15	4	Yes	3	not delayed
St Mary Spital	15261	15	3	No	3	not delayed
St Mary Spital	15442	15	3	No	3	not delayed
St Mary Spital	15584	15	4	No	3	not delayed
St Mary Spital	17493	15	3	No	3	not delayed
St Mary Spital	17544	15	3	No	3	not delayed
St Mary Spital	19020	15	4	No	3	not delayed
St Mary Spital	19250	15	4	No	3	not delayed
St Mary Spital	19290	15	3	No	3	not delayed
St Mary Spital	19481	15	4	No	3	not delayed
St Mary Spital	19570	15	4	No	3	not delayed
St Mary Spital	19915	15	4	No	3	not delayed
St Mary Spital	20621	15	3	Yes	3	not delayed
St Mary Spital	21111	15	3	No	3	not delayed
St Mary Spital	21349	15	4	No	3	not delayed
St Mary Spital	29986	15	3	Yes	3	not delayed
St Mary Spital	22846	15	4	No	3	not delayed
St Mary Spital	23161	15	4	No	3	not delayed
St Mary Spital	24186	15	4	No	3	not delayed
St Mary Spital	26188	15	3	No	3	not delayed

St Mary Spital	27646	15	3	No	3	not delayed
St Mary Spital	28052	15	3	No	3	not delayed
St Mary Spital	28444	15	3	No	3	not delayed
St Mary Spital	29964	15	4	No	3	not delayed
St Mary Spital	30593	15	3	No	3	not delayed
St Mary Spital	30928	15	3	No	3	not delayed
St Mary Spital	31440	15	3	No	3	not delayed
St Mary Spital	32258	15	3	No	3	not delayed
St Mary Spital	32279	15	4	No	3	not delayed
St Mary Spital	32355	15	4	Yes	3	not delayed
St Mary Spital	32417	15	4	No	3	not delayed
St Mary Spital	36008	15	3	No	3	not delayed
St Mary Spital	36182	15	4	No	3	not delayed
Barton-on-Humber	1023	16	3	No	4	delayed
St Helens	5358	16	2	No	4	delayed
St Helens	5661	16	2	No	4	delayed
St Mary Spital	3800	16	3	No	4	delayed
St Mary Spital	7146	16	3	No	4	delayed
St Mary Spital	8187	16	3	No	4	delayed
St Mary Spital	19388	16	3	No	4	delayed
St Mary Spital	20764	16	2	No	4	delayed
St Mary Spital	21971	16	2	Yes	4	delayed
St Mary Spital	5426	16	3	Yes	4	delayed
St Mary Spital	26722	16	3	No	4	delayed
St Mary Spital	22345	16	3	Yes	4	delayed
St Mary Spital	27544	16	3	Yes	4	delayed
St Mary Spital	30931	16	2	Yes	4	delayed
Barton-on-Humber	454	16	5	No	4	not delayed
Barton-on-Humber	704	16	4	No	4	not delayed
Barton-on-Humber	766	16	4	No	4	not delayed
Barton-on-Humber	825	16	4	No	4	not delayed
Barton-on-Humber	864	16	5	No	4	not delayed
Barton-on-Humber	877	16	4	No	4	not delayed
Barton-on-Humber	1045	16	4	No	4	not delayed
Fishergate House	1421	16	4	No	4	not delayed
Fishergate House	1273	16	4	No	4	not delayed
Fishergate House	1322	16	5	No	4	not delayed
Fishergate House	1067	16	4	No	4	not delayed
St Helens	5435	16	5	No	4	not delayed
St Helens	5338	16	5	No	4	not delayed
St Helens	5790	16	5	No	4	not delayed
St Helens	5185	16	4	No	4	not delayed
St Mary Spital	3847	16	4	No	4	not delayed
St Mary Spital	6444	16	4	No	4	not delayed

St Mary Spital	10888	16	4	No	4	not delayed
St Mary Spital	11483	16	4	No	4	not delayed
St Mary Spital	13162	16	4	No	4	not delayed
St Mary Spital	13813	16	4	No	4	not delayed
St Mary Spital	14518	16	4	No	4	not delayed
St Mary Spital	15669	16	4	No	4	not delayed
St Mary Spital	17880	16	4	No	4	not delayed
St Mary Spital	19385	16	4	No	4	not delayed
St Mary Spital	20460	16	4	No	4	not delayed
St Mary Spital	20634	16	4	Yes	4	not delayed
St Mary Spital	21766	16	4	No	4	not delayed
St Mary Spital	21783	16	4	No	4	not delayed
St Mary Spital	22502	16	4	No	4	not delayed
St Mary Spital	22783	16	4	No	4	not delayed
St Mary Spital	23512	16	4	No	4	not delayed
St Mary Spital	23651	16	4	No	4	not delayed
St Mary Spital	25826	16	4	No	4	not delayed
St Mary Spital	26005	16	4	No	4	not delayed
St Mary Spital	26155	16	4	No	4	not delayed
St Mary Spital	29430	16	4	No	4	not delayed
St Mary Spital	29725	16	4	No	4	not delayed
St Mary Spital	31168	16	4	No	4	not delayed
St Mary Spital	31422	16	4	No	4	not delayed
St Mary Spital	12538	17	3	No	4	delayed
St Mary Spital	30168	17	3	No	4	delayed
St Mary Spital	33220	17	3	No	4	delayed
Barton-on-Humber	695	17	4	No	4	not delayed
Barton-on-Humber	885	17	4	No	4	not delayed
Barton-on-Humber	1088	17	5	No	4	not delayed
Barton-on-Humber	1184	17	4	No	4	not delayed
Barton-on-Humber	1592	17	4	No	4	not delayed
Barton-on-Humber	1706	17	4	No	4	not delayed
Barton-on-Humber	1714	17	5	No	4	not delayed
Barton-on-Humber	1738	17	4	No	4	not delayed
Barton-on-Humber	1883	17	5	No	4	not delayed
Barton-on-Humber	2233	17	4	No	4	not delayed
Barton-on-Humber	2384	17	4	No	4	not delayed
St Helens	5106	17	5	No	4	not delayed
St Helens	5083	17	4	No	4	not delayed
St Helens	5519	17	4	No	4	not delayed
St Helens	5209	17	4	No	4	not delayed
St Mary Spital	1405	17	4	No	4	not delayed
St Mary Spital	1773	17	4	No	4	not delayed
St Mary Spital	1841	17	4	No	4	not delayed

St Mary Spital	2469	17	4	No	4	not delayed
St Mary Spital	2541	17	4	No	4	not delayed
St Mary Spital	3145	17	4	No	4	not delayed
St Mary Spital	3838	17	4	No	4	not delayed
St Mary Spital	6924	17	4	No	4	not delayed
St Mary Spital	7054	17	4	No	4	not delayed
St Mary Spital	8412	17	4	No	4	not delayed
St Mary Spital	9417	17	4	No	4	not delayed
St Mary Spital	9555	17	4	No	4	not delayed
St Mary Spital	10464	17	4	No	4	not delayed
St Mary Spital	11254	17	4	No	4	not delayed
St Mary Spital	11812	17	4	Yes	4	not delayed
St Mary Spital	12279	17	4	No	4	not delayed
St Mary Spital	14129	17	4	No	4	not delayed
St Mary Spital	14865	17	4	No	4	not delayed
St Mary Spital	15253	17	4	Yes	4	not delayed
St Mary Spital	15832	17	4	No	4	not delayed
St Mary Spital	17072	17	4	No	4	not delayed
St Mary Spital	17014	17	4	Yes	4	not delayed
St Mary Spital	19093	17	4	No	4	not delayed
St Mary Spital	19579	17	4	No	4	not delayed
St Mary Spital	19604	17	4	No	4	not delayed
St Mary Spital	20417	17	4	No	4	not delayed
St Mary Spital	20435	17	4	No	4	not delayed
St Mary Spital	20789	17	4	No	4	not delayed
St Mary Spital	22021	17	4	No	4	not delayed
St Mary Spital	22254	17	4	No	4	not delayed
St Mary Spital	22413	17	4	Yes	4	not delayed
St Mary Spital	23409	17	4	No	4	not delayed
St Mary Spital	24005	17	4	No	4	not delayed
St Mary Spital	25217	17	4	No	4	not delayed
St Mary Spital	25619	17	4	No	4	not delayed
St Mary Spital	26559	17	4	No	4	not delayed
St Mary Spital	26661	17	4	No	4	not delayed
St Mary Spital	26719	17	4	No	4	not delayed
St Mary Spital	27661	17	4	No	4	not delayed
St Mary Spital	27673	17	4	No	4	not delayed
St Mary Spital	28199	17	4	No	4	not delayed
St Mary Spital	29053	17	4	No	4	not delayed
St Mary Spital	29386	17	4	No	4	not delayed
St Mary Spital	29461	17	5	No	4	not delayed
St Mary Spital	30997	17	4	Yes	4	not delayed
St Mary Spital	36034	17	4	No	4	not delayed
St Mary Spital	32108	17	4	No	4	not delayed

St Mary Spital	20970	18	3	No	4	delayed
Barton-on-Humber	549	18	5	No	4	not delayed
Barton-on-Humber	641	18	5	No	4	not delayed
Barton-on-Humber	669	18	5	No	4	not delayed
Barton-on-Humber	1175	18	5	No	4	not delayed
Barton-on-Humber	1318	18	5	No	4	not delayed
Barton-on-Humber	1322	18	5	No	4	not delayed
Barton-on-Humber	1903	18	5	No	4	not delayed
Barton-on-Humber	2100	18	5	No	4	not delayed
Barton-on-Humber	2774	18	5	No	4	not delayed
Fishergate House	1277	18	5	No	4	not delayed
St Helens	5592	18	4	No	4	not delayed
St Mary Spital	6381	18	4	No	4	not delayed
St Mary Spital	7104	18	4	No	4	not delayed
St Mary Spital	14109	18	5	No	4	not delayed
St Mary Spital	14629	18	4	No	4	not delayed
St Mary Spital	15441	18	4	No	4	not delayed
St Mary Spital	15655	18	4	No	4	not delayed
St Mary Spital	17380	18	4	No	4	not delayed
St Mary Spital	19173	18	4	No	4	not delayed
St Mary Spital	22758	18	4	No	4	not delayed
St Mary Spital	25753	18	4	No	4	not delayed
St Mary Spital	27674	18	4	No	4	not delayed
St Mary Spital	31404	18	4	No	4	not delayed
St Mary Spital	32178	18	4	No	4	not delayed
Barton-on-Humber	161	19	4	No	5	delayed
Barton-on-Humber	742	19	4	No	5	delayed
Fishergate House	1143	19	4	Yes	5	delayed
Fishergate House	1108	19	4	No	5	delayed
St Helens	5473	19	4	No	5	delayed
St Mary Spital	7571	19	4	Yes	5	delayed
St Mary Spital	3853	19	4	No	5	delayed
St Mary Spital	7158	19	4	Yes	5	delayed
St Mary Spital	9616	19	4	No	5	delayed
St Mary Spital	10767	19	4	No	5	delayed
St Mary Spital	11737	19	4	Yes	5	delayed
St Mary Spital	14568	19	4	No	5	delayed
St Mary Spital	15339	19	4	No	5	delayed
St Mary Spital	16961	19	4	No	5	delayed
St Mary Spital	16968	19	4	No	5	delayed
St Mary Spital	17207	19	4	No	5	delayed
St Mary Spital	17874	19	4	No	5	delayed
St Mary Spital	19027	19	4	No	5	delayed
St Mary Spital	19147	19	4	No	5	delayed

St Mary Spital	19165	19	4	No	5	delayed
St Mary Spital	19813	19	4	No	5	delayed
St Mary Spital	20207	19	4	No	5	delayed
St Mary Spital	20703	19	4	No	5	delayed
St Mary Spital	21250	19	4	No	5	delayed
St Mary Spital	21913	19	4	No	5	delayed
St Mary Spital	23674	19	4	No	5	delayed
St Mary Spital	25081	19	4	No	5	delayed
St Mary Spital	26231	19	4	No	5	delayed
St Mary Spital	26962	19	4	Yes	5	delayed
St Mary Spital	27450	19	4	No	5	delayed
Barton-on-Humber	131	19	5	No	5	not delayed
Barton-on-Humber	205	19	5	No	5	not delayed
Barton-on-Humber	1752	19	5	No	5	not delayed
Barton-on-Humber	2379	19	5	No	5	not delayed
Fishergate House	1328	19	5	No	5	not delayed
St Helens	5614	19	5	No	5	not delayed
St Mary Spital	7529	19	5	No	5	not delayed
St Mary Spital	11416	19	5	No	5	not delayed
St Mary Spital	17417	19	5	No	5	not delayed
St Mary Spital	20530	19	5	No	5	not delayed
St Mary Spital	20866	19	5	No	5	not delayed
St Mary Spital	25647	19	5	No	5	not delayed
St Mary Spital	31387	19	5	No	5	not delayed
Barton-on-Humber	2119	20	4	No	5	delayed
St Helens	5032	20	4	No	5	delayed
St Helens	5762	20	4	No	5	delayed
St Helens	6021	20	4	No	5	delayed
St Mary Spital	2627	20	4	No	5	delayed
St Mary Spital	2910	20	4	No	5	delayed
St Mary Spital	7744	20	4	Yes	5	delayed
St Mary Spital	11087	20	4	No	5	delayed
St Mary Spital	11591	20	4	No	5	delayed
St Mary Spital	22356	20	4	Yes	5	delayed
St Mary Spital	15656	20	4	No	5	delayed
St Mary Spital	15658	20	4	Yes	5	delayed
St Mary Spital	21808	20	4	No	5	delayed
St Mary Spital	22609	20	4	No	5	delayed
St Mary Spital	3975	20	4	Yes	5	delayed
St Mary Spital	23243	20	4	No	5	delayed
St Mary Spital	22542	20	4	Yes	5	delayed
Barton-on-Humber	16	20	5	No	5	not delayed
Barton-on-Humber	198	20	5	No	5	not delayed
Barton-on-Humber	580	20	5	No	5	not delayed

Barton-on-Humber	731	20	5	No	5	not delayed
Barton-on-Humber	1006	20	5	No	5	not delayed
Barton-on-Humber	1191	20	5	No	5	not delayed
Barton-on-Humber	1640	20	5	No	5	not delayed
Barton-on-Humber	1757	20	5	No	5	not delayed
Barton-on-Humber	2178	20	5	No	5	not delayed
Barton-on-Humber	2296	20	5	No	5	not delayed
Fishergate House	1055	20	5	No	5	not delayed
Fishergate House	1393	20	5	No	5	not delayed
St Helens	5677	20	5	No	5	not delayed
Barton-on-Humber	1042	22	4	No	5	delayed
St Helens	5631	22	4	No	5	delayed
St Mary Spital	3563	22	4	No	5	delayed
St Mary Spital	6706	22	4	No	5	delayed
St Mary Spital	7112	22	4	No	5	delayed
St Mary Spital	7377	22	4	No	5	delayed
St Mary Spital	8053	22	4	No	5	delayed
St Mary Spital	8454	22	4	No	5	delayed
St Mary Spital	9308	22	4	No	5	delayed
St Mary Spital	10819	22	4	No	5	delayed
St Mary Spital	10822	22	4	No	5	delayed
St Mary Spital	11091	22	4	No	5	delayed
St Mary Spital	12238	22	4	No	5	delayed
St Mary Spital	13070	22	4	No	5	delayed
St Mary Spital	13488	22	4	No	5	delayed
St Mary Spital	3144	22	4	Yes	5	delayed
St Mary Spital	14168	22	4	No	5	delayed
St Mary Spital	14726	22	4	No	5	delayed
St Mary Spital	13232	22	4	Yes	5	delayed
St Mary Spital	19280	22	4	No	5	delayed
St Mary Spital	19327	22	4	No	5	delayed
St Mary Spital	19404	22	4	No	5	delayed
St Mary Spital	15575	22	4	Yes	5	delayed
St Mary Spital	20086	22	4	Yes	5	delayed
St Mary Spital	20157	22	4	No	5	delayed
St Mary Spital	21363	22	4	No	5	delayed
St Mary Spital	21378	22	4	No	5	delayed
St Mary Spital	21803	22	4	No	5	delayed
St Mary Spital	21922	22	4	No	5	delayed
St Mary Spital	21984	22	4	No	5	delayed
St Mary Spital	22238	22	4	No	5	delayed
St Mary Spital	19405	22	4	Yes	5	delayed
St Mary Spital	22566	22	4	No	5	delayed
St Mary Spital	22597	22	4	No	5	delayed

St Mary Spital	23001	22	4	No	5	delayed
St Mary Spital	24127	22	4	No	5	delayed
St Mary Spital	26214	22	4	No	5	delayed
St Mary Spital	26914	22	4	No	5	delayed
St Mary Spital	28116	22	4	No	5	delayed
St Mary Spital	29152	22	4	No	5	delayed
St Mary Spital	30442	22	4	No	5	delayed
Barton-on-Humber	1505	22	5	Yes	5	not delayed
Barton-on-Humber	546	22	5	No	5	not delayed
Barton-on-Humber	813	22	5	No	5	not delayed
Barton-on-Humber	892	22	5	No	5	not delayed
Barton-on-Humber	1044	22	5	No	5	not delayed
Barton-on-Humber	1269	22	5	No	5	not delayed
Barton-on-Humber	1295	22	5	No	5	not delayed
Barton-on-Humber	1312	22	5	No	5	not delayed
Barton-on-Humber	1779	22	5	No	5	not delayed
Barton-on-Humber	1924	22	5	No	5	not delayed
Barton-on-Humber	2252	22	5	Yes	5	not delayed
Barton-on-Humber	2340	22	5	No	5	not delayed
Fishergate House	1083	22	5	No	5	not delayed
Fishergate House	1128	22	5	No	5	not delayed
Fishergate House	1165	22	5	No	5	not delayed
St Helens	5113	22	5	Yes	5	not delayed
St Helens	5593	22	5	No	5	not delayed
St Helens	5409	22	5	Yes	5	not delayed
St Helens	6104	22	5	No	5	not delayed
St Helens	5346	22	5	No	5	not delayed
St Helens	5653	22	5	No	5	not delayed
St Helens	5792	22	5	No	5	not delayed
St Helens	5850	22	5	No	5	not delayed
St Helens	5958	22	5	No	5	not delayed
St Mary Spital	1055	22	5	No	5	not delayed
St Mary Spital	1658	22	5	No	5	not delayed
St Mary Spital	1857	22	5	No	5	not delayed
St Mary Spital	2695	22	5	No	5	not delayed
St Mary Spital	3289	22	5	No	5	not delayed
St Mary Spital	1052	22	5	Yes	5	not delayed
St Mary Spital	3483	22	5	Yes	5	not delayed
St Mary Spital	3816	22	5	No	5	not delayed
St Mary Spital	3903	22	5	No	5	not delayed
St Mary Spital	7127	22	5	No	5	not delayed
St Mary Spital	7001	22	5	Yes	5	not delayed
St Mary Spital	7506	22	5	No	5	not delayed
St Mary Spital	7659a	22	5	No	5	not delayed

St Mary Spital	8279	22	5	No	5	not delayed
St Mary Spital	9448	22	5	No	5	not delayed
St Mary Spital	9533	22	5	No	5	not delayed
St Mary Spital	11248	22	5	No	5	not delayed
St Mary Spital	11371	22	5	No	5	not delayed
St Mary Spital	11659	22	5	No	5	not delayed
St Mary Spital	11775	22	5	No	5	not delayed
St Mary Spital	12714	22	5	No	5	not delayed
St Mary Spital	14567	22	5	No	5	not delayed
St Mary Spital	14705	22	5	No	5	not delayed
St Mary Spital	14945	22	5	No	5	not delayed
St Mary Spital	15030	22	5	Yes	5	not delayed
St Mary Spital	15587	22	5	No	5	not delayed
St Mary Spital	15588	22	5	No	5	not delayed
St Mary Spital	15830	22	5	No	5	not delayed
St Mary Spital	19580	22	5	Yes	5	not delayed
St Mary Spital	20905	22	5	No	5	not delayed
St Mary Spital	20993	22	5	No	5	not delayed
St Mary Spital	21062	22	5	No	5	not delayed
St Mary Spital	21099	22	5	No	5	not delayed
St Mary Spital	21560	22	5	No	5	not delayed
St Mary Spital	21879	22	5	No	5	not delayed
St Mary Spital	21588	22	5	Yes	5	not delayed
St Mary Spital	22247	22	5	No	5	not delayed
St Mary Spital	22420	22	5	No	5	not delayed
St Mary Spital	22709	22	5	No	5	not delayed
St Mary Spital	23373	22	5	No	5	not delayed
St Mary Spital	25776	22	5	No	5	not delayed
St Mary Spital	25946	22	5	No	5	not delayed
St Mary Spital	26560	22	5	No	5	not delayed
St Mary Spital	26639	22	5	No	5	not delayed
St Mary Spital	27014	22	5	No	5	not delayed
St Mary Spital	27035	22	5	No	5	not delayed
St Mary Spital	29726	22	5	No	5	not delayed
St Mary Spital	29981	22	5	No	5	not delayed
St Mary Spital	30448	22	5	Yes	5	not delayed
St Mary Spital	31328	22	5	No	5	not delayed
St Mary Spital	31395	22	5	No	5	not delayed