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The management of chronic headache with referral from primary care to direct access to Magnetic Resonance Imaging (MRI) compared to Neurology services: an observational prospective study.

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Abstract

Objectives. To evaluate the cost, accessibility and patient satisfaction implications of two clinical pathways used in the management of chronic headache.

Intervention. Management of chronic headache following referral from Primary Care that differed in the first appointment, either a Neurology appointment or an MRI brain scan.

Design and setting. A pragmatic, non-randomised, prospective, single-center study at a Central Hospital in London.

Participants. Adult patients with chronic headache referred from Primary to Secondary Care.

Primary and secondary outcome measures. Participants' use of health care services and costs were estimated using primary and secondary care databases and questionnaires quarterly up to 12 months post-recruitment. Cost analyses were compared using generalised linear models (GLM). Secondary outcomes assessed: access to care, patient satisfaction, headache burden and self-perceived quality of life using headache-specific (MIDAS, HIT-6) and a generic questionnaire (EQ-5D-5L).

Results. Mean (SD) cost up to 6 months post-recruitment per participant was £578 (£420) for the Neurology group (n=128) and £245 (£172) for the MRI group (n=95), leading to an estimated mean cost difference of £333 (95% CI £253 to £413, p<0.001). The mean cost difference at 12 months increased to £518 (95% CI £401 to £637, p<0.001). When adjusted for baseline and follow-up imbalances between groups, this remained statistically significant. The utilisation of brain MRI improved access to care compared to the Neurology group (p<0.001). Participants in the Neurology group reported higher levels of satisfaction associated with the pathway and led to greater change in care management.

Conclusion. Direct referral to brain MRI from Primary Care led to cost-savings and quicker access to care but lower satisfaction levels when compared with referral to Neurology services. Further research into the use of brain MRI for a subset of patient population more likely to be reassured by a negative brain scan should be considered.

Keywords: Chronic headache; migraine; direct access; magnetic resonance imaging; cost analysis.

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Strengths and limitations of this study

- The estimate of health care resource use was based on comprehensive and complete data retrieved from hospital databases supplemented by both primary care utilisation data and self-reported participant data. Any chronic headache related event was costed regardless of the healthcare provider and location.
- The evaluation of the intervention's impact across different dimensions of analysis (efficiency, quality of care, access to care and patient satisfaction).
- This was a single-centre study with participants recruited from one central hospital in London. A multi-centre study would be necessary to explore the generalisability of the results.

Introduction

Globally, the percentage of the adult population with an active headache disorder is 47% for episodic headache and 3% for chronic headache (lasting more than 15 days per month) [1]. Headache is in the top ten international causes of disability [2], with nearly half of sufferers reporting it affects work, home or social activities [3–5]. Most headaches are primary headache disorders, such as migraine or tension-type headaches. Secondary headaches, due to an underlying serious pathology (e.g. tumour, brain aneurysm) are far less common [6]. In fact, less than 0.1% of the lifetime headache prevalence is associated with a life-threatening condition, which can include primary or secondary brain tumours [2,3].

Most headache sufferers self-manage, but over 4% of adults each year consult their General Practitioner (GP) [7,8]. GPs manage 97% of headache presentations, with 2% of these referred to neurologists and 1% to other specialists [7]. Headache is the most common cause for GP referrals to neurologists accounting for up to 20-30% [9–12], the vast majority of these are for migraine. Chronic migraine sufferers (>15 days/month) had more emergency department/hospital visits, and diagnostic tests than those with episodic migraine and consequently the medical costs were three times higher [13]. Hence, despite the benign nature of most headaches, headache management is associated with high health care utilisation. Between 2012 and 2014, patients presenting to headache specialists (either neurologists or GPs with special interest in headache) costed £959 million in the UK [12].

GP direct access to imaging has been defined as a priority within the National Health Service (NHS), with direct access to brain Magnetic Resonance Imaging (MRI) for the diagnosis of brain cancer identified as a specific initiative [8]. GPs have reported referrals for secondary care, both for a neurologist consultation or neuroimaging, when they were unable to reassure the patient [14,15]. Furthermore, Morgan et al. (2007) found that referral for headache is often the outcome of patient pressure and anxiety interacting with GP characteristics, organisational factors and service availability rather than the headache severity itself [14]. This contrasts with the recommendations from the National Institute for Health and Care Excellence (NICE) that does not recommend the use of neuroimaging for reassurance purposes [16]. A US study estimated that patients with new onset migraine headache or a flare-up of chronic headache had, respectively, a 39% (95% CI 24–54%) and 51% (95% CI 32–68%) probability of having neuroimaging routinely ordered even where guidelines specifically recommended against this approach [17]. A UK-based randomised controlled trial evaluated the cost implications of using brain MRI for reassurance purposes and found that it led to a decrease in health care costs, in particular for patients with higher levels of psychiatric morbidity [18].

In summary, despite proportionately low level of referrals to secondary care, high prevalence makes headache the most frequently listed reason for referral to neurologists and thus, utilises capacity that is severely constrained. The potential decrease of referral rates to Neurology specialists as a result of direct access to imaging holds the potential release resources. On the other hand, direct access may be associated with a transfer of workload to Radiology, as not all patients directly referred to brain MRI would

routinely undergo an MRI scan as part of the management of their chronic headache. This study aims to evaluate the health care utilisation and associated costs of GPs using direct access to brain MRI for the management of chronic headache patients compared to referral to a Neurologist.

Patients and Methods

Study design and patient selection

The study was an independent single-centre site, prospective, observational study. The study compared two existing clinical pathways in the management of patients with chronic headache from either GP referral to the Neurology Department or to direct access to brain MRI. No change to clinical practice was involved. Participants were allocated to two groups, the Neurology group or the MRI group. The allocation was decided *a priori*, i.e. the referrer (in this case the GP) decided which referral route would suit each participant. Subsequent care was consistent with standard of care for each clinical pathway and depicted in Figure 1.

Patients eligible for the study included adults aged 16 years or over with chronic headache defined as occurring ≥ 15 days per month for more than 3 months and referred from GP practices to a local Hospital in Central London, either for a Neurology outpatient appointment or an MRI exam. Participants were excluded if there were secondary causes for the headache, if they were prisoners, lacked capacity to give consent or participate in the study, not fluent in English or already taking part in a clinical trial of an investigational medicinal product. Following eligibility assessment, participants completed a written informed consent. The Health Research Authority and Research Ethics Committee (West of Scotland – REC 4) approved the study research on 12th April 2016 (REC reference 16/WS/0028).

This study has involved Patient and Public Involvement (PPI) during the design and dissemination phase. Prior to the start of the research, a group of patients suffering from chronic headache were consulted to co-produce the study mobile app that was used to monitor symptoms and triggers of chronic headache. The patients who were involved in the study design, as well as all study participants, will receive a lay summary of the research findings as per their preferences, either via post or e-mail.

Study outcomes

The primary outcome was to estimate the 6-month health care costs associated with two existing clinical pathways in the management of chronic headaches. Secondary outcomes comprised: the extension of the cost analysis up to 12 months, the evaluation of access to care, patient satisfaction, headache burden and time off work associated with both clinical pathways.

Service use costs

Total costs were calculated based on the multiplication of any headache-related healthcare events by the unit cost of each event. Resource use data included contacts with any NHS healthcare provider associated with the management of chronic headache. These included, among others, visits to GPs or headache clinical nurse specialist, inpatient care, neurologist or other headache-related outpatient visits (e.g. psychiatry), physiotherapist, visits to the Emergency Department (ED), advanced imaging such as Computed Tomography (CT) and MRI. Resource use data was retrieved from multiple hospital and primary care databases as well as self-reported data from participants using a participant headache diary (either paper-based or a headache mobile app). For the purposes of the primary outcome, the valuation of unit costs was, whenever possible, based on NHS Reference Costs 2016-17 [19]. Medication costs were derived from Prescription Cost Analysis [20] and estimated from clinical data, specifically secondary care clinic letters and information provided by primary care. Participants were also asked to record time off work due to headache using the weekly participant diary.

Quality of life and headache burden

Headache burden was assessed using validated headache questionnaires and headache diaries. The HIT-6 questionnaire measured the headache burden based on 6 questions, leading to a score range from 36 to 78. The MIDAS questionnaire assessed the disability associated with the headache (ranges from 0 to 90). Furthermore, along with the headache diaries completed by participants, the MIDAS questionnaire allowed the estimate of the number of headache days per quarter (maximum of 90 days) and self-reported headache pain scores (ranging from 0, no pain at all, to 10, the worst pain ever).

Access to care

The time elapsed between the GP referral and the first appointment in each group, either the Neurology appointment or the MRI scan, was measured as a proxy for access to care. Furthermore, in the MRI group, the availability of the MRI report to the GP, rather than the actual timing of the diagnostic scan, was considered.

Change in care management

Change in care management in both groups was evaluated. It was considered that a change in care management occurred when patients underwent new treatment options (medication or otherwise, e.g. new headache medication, Botox treatment).

Patient satisfaction

Patient satisfaction was evaluated at month 3 post-recruitment using a non-validated questionnaire. This questionnaire evaluated three dimensions of analysis: (a) referral process (time elapsed between referral

from primary care to initial secondary care appointment); (b) initial appointment; and (c) overall experience three months after recruitment.

Statistical analyses

This study was observational but all analyses were based on the principle of 'intention-to-treat' so that participants recruited were included in the analysis as per the group they were recruited to, regardless of whether they actually received the intended treatment, any protocol deviations or potential losses to follow-up [21]. Given the study's time horizon of 12 months, no discounting of costs or effects were considered. Descriptive statistics on several socio-demographics baseline characteristics were included. Differences in baseline characteristics between treatment groups were compared using statistical tests: Chi-squared for categorical data, t test for Normal data and Mann-Whitney for non-Normal quantitative data. Given the skewness associated with the cost distribution, all cost differences between groups were assessed using generalised linear models (GLM) with an identity-link and gamma distribution. An identity link function instead of a log link was considered in order to avoid potential analytical biases [22,23]. An unadjusted GLM cost analysis with the study group (MRI group vs Neurology group) as only univariate analysis was performed as the first step. Given the study's observational design, the cost difference can be impacted due to the lack of randomisation [24]. Baseline variables that differenced between the two groups ($p<0.1$) were included in the multivariable (adjusted) GLM analyses. For all GLM analyses, group difference estimates and associated confidence intervals were reported, together with p-values. Analyses were conducted using Stata version 15.

Sample size

The sample size estimate was calculated based on the primary endpoint, total 6-month health care costs. A total of 150 participants were recruited in the Neurology group and 99 participants in the MRI group to achieve a detection a cost difference of £300 assuming standard deviations of £750 and £500, respectively, with 85% power at the 5% two-sided significance level. A 20% increase in sample size due to unknown cost distribution and attrition rate was considered.

Results

A total of 249 participants were recruited, 150 in the Neurology group and 99 in the MRI group. 100% (n=128) and 97% (n=96) of participants recruited received the treatment allocation in the Neurology and the MRI group, respectively (Figure 2). With regards to the follow-up duration, 15% (n=22) and 4.0% (n=4) participants withdrew from the Neurology and MRI group, respectively, and were considered lost to follow-up. Remaining participants (n=223) were included in the analysis, equivalent to 128 (85%) and 95 (96%) participants in the Neurology and MRI group, respectively.

Baseline socio-demographic, clinical variables and resource use in the twelve months pre-recruitment are detailed in Table 1. A higher proportion of females were recruited to the Neurology group compared to the MRI group (81% vs 68%, p=0.039). Both groups were similar in mean age, ethnic mix, with more than half being White. No significant differences between the groups were found in terms of highest qualification and employment, with high-school and full-time employment being the most common. In terms of clinical variables, no significant difference between groups were found in terms of number of active health problems or number of headache triggers. Participants in the Neurology group reported lower utility and health scores using the generic EQ-5D-5L questionnaire, with a statistically significant difference in health scores (p=0.005). Lower health scores imply lower self-rated quality of life, while for the headache-specific questionnaires [Headache Impact Test (HIT-6) and Migraine Disability Assessment (MIDAS)], a higher score implies a higher headache burden. Compared to the MRI group, participants in the Neurology group reported significantly higher headache burden (HIT-6 mean score: 65 vs 63, p=0.006), number of headache days in the past 3 months (MIDAS questionnaire: 52 vs 43, p=0.038). Participants in the Neurology group also had significantly more primary care appointments (3.7 vs 2.4, p<0.001) and all NHS appointments (4.3 vs 2.5, p<0.001).

Service use

Table 2 summarises the NHS resource use of primary care and hospital-based services over a period of 12 months following recruitment. With regards to primary care utilisation, participants in the Neurology group had a significantly higher number of GP face-to-face appointments (mean number per participant: 1.82 vs 1.19, p=0.006). Regarding secondary care, participants in the Neurology group had a higher mean number of outpatient appointments (2.52 vs 0.26, p<0.001) and other treatments such as Botox and nerve root injection (mean 0.30 vs 0.05, p<0.001). In contrast, they had a lower mean number of brain MRIs (0.59 vs 1.05, p<0.001). There were no statistically significant differences in the utilisation levels of any of the other healthcare events.

The NHS resource use pre and post-recruitment for both groups was also compared. Table 3 summarises the difference between headache-related events 12 months post-recruitment compared to the 12 months pre-recruitment. A reduction of 197 and 87 GP visits (mean 1.54/0.92 per participant or a percentage reduction of 85%/77%) was noted in the Neurology and MRI group, respectively. Similarly, there was a reduction in emergency department utilisation with a decrease of 23 and 6 episodes (mean 0.18 and 0.07 per participant or a percentage reduction of 288% and 120%) in the Neurology and MRI group, respectively.

Cost analyses

The mean (SD) cost management per participant at 6 months post-recruitment was lower in the MRI group compared to the Neurology group [£245 (£172) vs £578 (£420)], leading to a mean cost difference between groups of -£333 per participant (95% CI: -£413 to -£253, p<0.001). The MRI group had a higher proportion

of participants with lower costs (£0 to £250 range) than the Neurology group (73% vs 4.7%). The initial cost analysis was extended to 12 months post-recruitment and the mean cost difference between groups increased, with the MRI group generating cost savings of £518 per participant (95% CI: -£637 to -£401, p<0.001).

Given the non-randomised study design, an additional GLM analysis was performed to adjust for baseline characteristics. The unadjusted 6-month cost difference between groups (-£333; 95% CI: -£413, -£253) hardly changed after adjustment (-£308; 95% CI: -£408, -£209). In all analyses, at both 6 and 12 months post-recruitment, direct access to MRI for the management of chronic headache was associated with statistically significant mean cost savings for the NHS.

Abnormal findings in the MRI group

Out of the 95 participants recruited in the MRI group, three MRIs were not performed during the initial appointment due to claustrophobia events. From a total number of 92 MRIs, 85 (92%) were normal and 7 (7.6%) presented abnormal findings (Table 4), with one diagnosis being particularly significant (two small intracranial aneurysms). This participant was referred to neurovascular team for assessment, at which point no intervention was performed during the follow-up period (participant included in an active surveillance group). Two other participants had a change in their clinical management for less significant findings, leading to either a follow-up appointment or scan. No brain malignancies were diagnosed.

Access to care

The mean time (SD) elapsed from GP referral to the initial Neurology and MRI scan was, respectively, 110 (35) days and 39 days (17), a statistically significant difference (p<0.001). Second, if the MRI report, than the actual scan, is considered as a proxy for access to care, the mean time elapsed was 70 days (35) (p<0.001).

Change in management

Participants in the Neurology group were more likely to have a change in therapeutic management compared to participants in the MRI group (97% vs 64%, p<0.001). Similarly, among participants that had not started on preventative medication pre-recruitment, a higher proportion of participants in the Neurology group were started on preventative medication as part of their clinical management (93% vs 53%, p<0.001).

Quality of life and headache burden

At baseline, mean utility was lower in the Neurology group but not significant (mean utility of 0.809 vs 0.830, p=0.097), while their self-perceived mean health score was significantly lower (EQ-5D-5L: visual analogue

scale score of 64.0 vs 70.8, p=0.005) (Table 5). There was no statistically significant differences between the groups at 6 months for to the utility and self-reported healthcare scores.

At baseline, participants in the Neurology group presented a higher headache burden compared to the MRI group (mean score of 65.0 vs 62.6, p=0.006) (Table 5). This trend seemed to be maintained over the follow-up period but was difficult to interpret due to high attrition rates: mean HIT-6 score at 6 months (60.0 vs 53.1, p=0.968). At baseline, participants in the Neurology group had higher headache severity compared to the MRI group, but this was not significant (mean MIDAS score of 57.8 vs 44.8, p=0.075) (Table 5). In both groups the headache severity decreased over the follow-up period. At baseline, participants in the Neurology group reported a significantly higher mean number of headache days compared to the MRI group (51.6 vs 42.8, p=0.038). This trend was observed at month 6 but was not significant (41.2 vs 26.5, p=0.152). A third variable assessed self-reported headache pain scores. At baseline, participants at baseline showed almost identical mean headache pain scores (6.9 vs 6.9, p=0.827). During the follow-up period, no statistical differences were found at month 6 (4.5 vs 4.2, p=0.663).

Time off work

Participants in the Neurology group (n=83) had higher mean number of days off work due to headache compared to participants in the MRI group (n=35) but these were not statistically significant at 6 (13.9 vs 9.7, p=0.563) or 12 months (27.9 vs 19.1, p=0.808) post-recruitment.

Patient satisfaction

Patient satisfaction was evaluated at month 3 post-recruitment using a non-validated questionnaire (Appendix I). Participants in both groups reported no difference in terms of receiving an appointment in a suitable timeframe (p=0.193). Participants in the MRI group reported higher satisfaction levels (p=0.005) compared to the Neurology group associated with the information received prior to the actual appointment. No statistically significant difference (p=0.366) between the groups was found regarding the satisfaction levels of both appointments (either MRI scan or Neurologist appointment) but a higher proportion of participants in the Neurology group reported a better experience compared to their expectation (p=0.002). At month 3 post-recruitment in all variables, except frequency of appointments (p=0.166), participants in the Neurology group reported higher levels of satisfaction with: amount of time spent with clinical staff (p=0.001); consistency of care (p=0.028); how informed you felt about your condition (p=0.010) / your treatment (p=0.004); and the overall experience (p<0.001).

Discussion

Previous UK studies assessed the use of direct access to advanced imaging in the management of chronic headache patients [9,18]. Howard et al. (2005) performed a randomised controlled trial, which showed that the use of imaging in patients led to a reduction of referral rates to Neurology services in secondary care from 23% to 1.3% (1/76) in the treatment group (i.e. patients being scanned) [18]. Thomas et al. (2010) estimated that direct access to brain imaging, in this case CT, reduced referral rates to Neurology in 86% of the cases during the follow-up period (average of 1.3 years per patient) [9].

The study's underlying hypothesis was that the early use of an advanced and accurate diagnostic tool (in this case MRI) would reassure both patients and GPs that no serious underlying cause (particularly brain tumour) is present. This would in turn reduce the headache burden and NHS resource use associated with the patient's subsequent management. Given the high prevalence of headache and the increased referral of patients with chronic headaches and other neurological conditions from primary care to hospital based care [7], it is relevant to assess the implications of using different management strategies. To our knowledge, no previous prospective study in the UK has assessed the economic implications of these two coexisting management strategies based on GP referral decision.

The primary outcome was total costs at six months post-recruitment. The study showed that the use of advanced imaging produced cost-savings to the NHS compared to referral to Neurology, with mean cost-savings per participant of £333 and £518 at month 6 and 12 post-recruitment, respectively ($p<0.001$). These cost differences were multifactorial but primarily driven by: (i) the lower unit cost of a brain MRI scan (£146) compared to the initial Neurology appointment (£240); (ii) the lower number of outpatient appointments in the MRI group (25 vs 322); (iii) the fact that 75/128 (59%) of participants in the Neurology group ended up having a brain MRI scan in the 12-month period of follow-up; and (iv) the increased likelihood of patients in the Neurology arm receiving management with Botox injections or nerve block procedures (39 vs 5 events). Direct access to brain MRI seemed to reassure most participants as only 17 (18%) participants in the MRI group ended up being referred to a neurologist. Furthermore over 66% of participants in the MRI group had no further hospital-based care, compared to 5% in the Neurology group. Similarly, at primary care level, participants in the MRI group presented lower utilisation rates per participant when compared to the Neurology group (mean GP appointments of 1.82 vs 1.19, $p=0.006$). All cost differences between groups remained statistically significant ($p<0.001$) when adjusted for differences in baseline characteristics or follow-up attrition rates.

At baseline, participants in the Neurology group presented lower self-reported quality of life and higher headache burden. HIT-6 scores did improve over time but we were unable to assess whether there was a statistically significant difference in both groups due to the high attrition rates, particularly in the MRI group. As mentioned, out of the 95 participants recruited to the MRI group, 17 (18%) were subsequently referred to a Neurologist. Interestingly, at baseline, these 17 patients reported higher headache burden compared to all 95 patients recruited to the MRI group (MIDAS score: 51.2 vs 44.8; MIDAS headache days: 55.8 vs

42.8). This finding seems to suggest that this data might be useful to risk stratify patients and support GPs in their referral criteria. However, further research into this area is required.

Participants in the Neurology group presented a higher probability of being started on a preventative medication and had a change in therapeutic management following referral from primary care. A small proportion (7.6%) of participants in the MRI group had abnormal findings in the initial brain MRI. Only one participant had clinically significant lesions (two small aneurysms) which were also incidental and no brain tumour was diagnosed.

Time off work was also evaluated as a proxy of headache burden. Participants in the Neurology group presented a trend ($p>0.05$) of higher number of days off work due to headache compared to participants in the MRI group. This difference was not however statistically significant.

Lastly, patient satisfaction in both groups was compared based on three dimensions of analysis: during the referral period, the initial appointment and overall satisfaction. Twenty five percent of participants in the Neurology group (vs 18% in the MRI group) reported dissatisfaction with the waiting time. This finding is not unexpected as the mean waiting time associated with the Neurology appointment was almost three times of the one associated with the MRI scan (110 vs 39 days). Contrary to the referral period, participants in the Neurology group reported trends of higher satisfaction levels associated with the first appointment (neurology outpatient visit vs MRI scan) and a better experience compared to their expectations (60% vs 29% in the Neurology and MRI group, respectively). Participants in the Neurology group reported improved satisfaction levels at 3 months across different variables (time spent with clinician, consistency of care, information about the condition and its treatment). Almost three quarters of Neurology participants reported being satisfied or very satisfied with their headache management compared to only 21% in the MRI group ($p<.001$). Both participants and GP referrers in the MRI group reported dissatisfaction associated with the waiting time elapsed between the MRI scan and the availability of results (mean time of 31 days). This might have contributed to increased anxiety in some participants.

Strengths of this study:

The estimate of NHS resource use data was primarily based on comprehensive and complete data retrieved from hospital-based databases that captured both the acute and elective elements of the pathway associated with the management of patients with chronic headache. This data was supplemented by both primary care utilisation data, collected from each participant's GP, and self-reported participant data. The aim was to guarantee that any chronic headache related NHS event was costed regardless of the healthcare provider and its location. The prospective collection of health care utilisation and the evaluation of the impact of the interventions across different dimensions of analysis (efficiency, quality of care, access to care and patient satisfaction) were other key factors that contributed to the overall strength of the study.

Limitations of this study:

There were some limitations to this study. First, this was a single-centre study with participants recruited from one central hospital in London. A multi-centre study would be necessary to explore the generalisability of the results. Second, as with any observational study, no randomisation between groups was performed and there were significant differences in baseline of headache burden and health-scores and utilisation of resources, reflecting potential selection bias. Third, specific inclusion and exclusion criteria were considered and as such the study sample might not be representative of all patients with chronic headache. Fourth, for the purpose of secondary outcomes, most data was self-reported and hence prone to recall bias. Lastly, there were high follow-up attrition rates particularly for participants in the MRI group, which affected some of the study's secondary outcomes.

Conclusions

This study found that the referral from primary care to direct access to brain MRI compared to referral for a neurologist for patients with chronic headache was associated with lower NHS overall costs at 6 and 12 months post-recruitment. Despite waiting longer from referral to appointment, participants in the Neurology group reported higher satisfaction levels associated with the care received compared to the MRI group and were more likely to benefit from changes to their therapeutic management.

Implications for further research and clinical practice

Baseline measures of headache burden, such as the HIT-6 or MIDAS, could potentially be used to determine which pathway may be suitable for patients but further research into the risk stratification of chronic headache patients is required. With regards to clinical practice, and based on the study findings, we plan to provide GPs with headache management advice along with the MRI report.

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Figure 1. High-level illustration of two existing clinical pathways associated with the referral from GP due to chronic headache.

Figure 2. Participant flow chart for the headache study.

Table 1. Baseline characteristics of the population analysed.

Variable	Neurology group (n=128)	MRI group (n=95)	p-value
Age, years: mean (SD)	38.4 (14.1)	40.0 (14.6)	0.514
Gender Female, n (%)	103 (81)	65 (68)	0.039
Ethnicity			0.079
Asian	13 (10)	6 (6.3)	
Black	40 (31)	17 (18)	
White	68 (53)	60 (63)	
Mixed	5 (3.9)	8 (8.4)	
Other	2 (1.6)	4 (4.2)	
Qualification, n (%)			0.565
Advanced work or PhD	3 (2.3)	4 (4.2)	
Master's Degree	15 (12)	12 (13)	
Bachelor's Degree	31 (24)	29 (31)	
High School	57 (45)	33 (35)	
Did not finish High School	8 (6.3)	10 (11)	
Prefer not to answer	14 (11)	7 (7.4)	
Employment, n (%)			0.839
Employee in full time job (30 hours or more a week)	50 (39)	36 (38)	
Employee in part-time job (under 30 hours a week)	18 (14)	18 (19)	
Self-employed, full or part time	12 (9.4)	8 (8.4)	
Full-time education at school, college or university	16 (13)	9 (9.5)	
Doing something else	2 (1.6)	2 (2.1)	
Permanently sick/ disabled	8 (6.3)	6 (6.3)	
Looking after the home	4 (3.1)	6 (6.3)	
Unemployed and available for work	12 (9.4)	6 (6.3)	
Wholly retired from work	4 (3.1)	4 (4.2)	
Prefer not to answer	2 (1.6)	0 (0)	
Presence of mental health condition, n (%)	22 (17)	11 (12)	0.243
Number of active health problems: mean (SD)	2.0 (1.5)	1.8 (1.4)	0.277
Number of headache triggers: mean (SD)	2.1 (1.8)	1.8 (1.4)	0.378
Self-reported questionnaires			
EQ-5D-5L: mean utility (SD)	0.809 (0.182)	0.830 (0.195)	0.097
EQ-5D-5L: mean score (SD)	64 (19)	71 (20)	0.005
HIT-6: mean score (SD)	65 (5.3)	63 (7.3)	0.006
MIDAS, mean score (SD)	58 (54)	45 (45)	0.075
MIDAS, mean headache days (SD)	52 (32)	43 (31)	0.038
MIDAS, mean pain score (SD)	6.9 (1.8)	6.9 (1.9)	0.778
Resource use in the 12 months prior to recruitment			
GP appointments: mean (SD)	3.7 (2.9)	2.4 (1.5)	<0.001
All NHS events: mean (SD)	4.3 (3.7)	2.5 (1.5)	<0.001

SD= Standard deviation; EQ-5D-5L - 5 level EQ-5D; HIT-6 = headache impact test; MIDAS = Migraine Disability assessment scale

Table 2. Breakdown of number of NHS appointments per type of activity organised per group and respective number of participants responsible for these appointments (12 months post-recruitment).

	Neurology group (n=128)			MRI group (n=95)			p-value
Type of NHS appointment	**Total of episodes**	**Mean (SD)**	**N (%)**	**Total of episodes**	**Mean (SD)**	**N (%)**	
Primary Care services							
GP face-to-face appointment	233	1.82 (2.11)	91 (71)	113	1.19 (1.64)	57 (60)	0.006
GP phone appointment	37	0.29 (0.75)	24 (19)	25	0.26 (0.49)	23 (24)	0.420
Hospital based services							
Hospital outpatient appointment	322	2.52 (1.19)	128 (100)	25	0.26 (0.55)	20 (21)	<0.001
Inpatient episode	4	0.03 (0.35)	1 (0.8)	1	0.01 (0.10)	1 (1.1)	0.837
Emergency Department episode	8	0.06 (0.24)	8 (6.3)	5	0.05 (0.22)	5 (5.3)	0.756
Head CT	1	0.01 (0.09)	1 (0.8)	1	0.01 (0.10)	1 (1.1)	0.832
Brain MRI	75	0.59 (0.49)	75 (59)	100	1.05 (0.30)	95 (100)	<0.001
Others (e.g. botox and nerve injection treatments)	39	0.30 (0.79)	25 (20)	5	0.05 (0.30)	3 (3.2)	<0.001

Table 3. Difference in the number, mean and percentage reduction of NHS appointments per type of activity organised per group 12 months post-recruitment compared to the 12 months pre-recruitment (note: a negative/positive percentage denotes a decrease/increase in activity following recruitment).

	Neurology group (n=128)			**MRI group (n=95)**		
Type of NHS appointment	**Total of episodes**	**Mean**	**%**	**Total of episodes**	**Mean**	**%**
Primary Care services						
GP face-to-face appointment	-197	-1.54	-85%	-87	-0.92	-77%
GP phone appointment	-11	-0.09	-30%	5	0.05	20%
Hospital-based services						
Hospital outpatient appointment	301	2.36	93%	23	0.24	92%
Inpatient episode	3	0.02	75%	1	0.01	100%
Emergency Department episode	-23	-0.18	-288%	-6	-0.07	-120%
Head CT	-9	-0.07	-12%	1	0.01	1.0%
Brain MRI	55	0.43	141%	100	1.05	N/A

Table 4. Description of incidental findings, its clinical relevance and subsequent pathway.

Abnormal findings	**Significant (Yes/No)?**	**Changes in diagnostic or treatment pathway**
Mature striatocapsular lacune	No	
Sinusitis with complete opacification	No	ENT review only.
Pituitary abnormality (T1)	No	
Low lying cerebellar tonsils	No	
Previous petrous surgery noted	No	
Two aneurysms AcomA (anterior communicating artery) and right ICA	Yes	Referred to neurovascular – no coiling (no intervention).
No definite lesion	No	Follow-up MRI only.

Table 5. Descriptive statistics for one generic questionnaire (EQ-5D-5L) and two headache-specific questionnaires (HIT-6 and MIDAS) at baseline and 6 months post-recruitment.

				N	Mean	Standard Deviation	p-value
BASELINE	**EQ-5D-5L**	Utility	Neurology	127	0.809	0.182	0.097
			Radiology	95	0.830	0.195	
		Score	Neurology	126	64.0	18.8	0.005
			Radiology	95	70.8	20.2	
	HIT-6	Score	Neurology	128	65.0	5.3	0.006
			Radiology	92	62.6	7.3	
	MIDAS	Score	Neurology	124	57.8	54.0	0.075
			Radiology	90	44.8	44.9	
		Headache days	Neurology	124	51.6	31.5	0.038
			Radiology	90	42.8	30.7	
		Pain score	Neurology	124	6.9	1.8	0.778
			Radiology	90	6.9	1.9	
MONTH 6	**EQ-5D-5L**	Utility	Neurology	55	0.770	0.263	0.243
			Radiology	26	0.681	0.346	
		Score	Neurology	53	68.2	20.6	0.463
			Radiology	23	62.5	24.7	
	HIT-6	Score	Neurology	35	60.0	8.7	0.968
			Radiology	12	53.1	22.8	
	MIDAS	Score	Neurology	32	52.6	58.1	0.827
			Radiology	12	40.7	36.0	
		Headache days	Neurology	46	41.2	28.6	0.152
			Radiology	15	26.5	28.1	
		Pain score	Neurology	44	4.5	2.3	0.663
			Radiology	15	4.2	2.0	

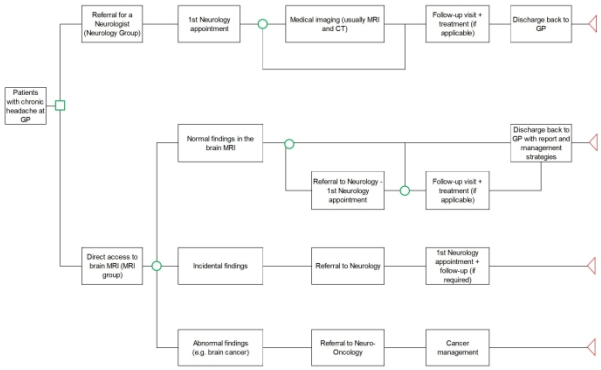

Figure 1. High-level illustration of two existing clinical pathways associated with the referral from GP due to chronic headache.

338x190mm (300 x 300 DPI)

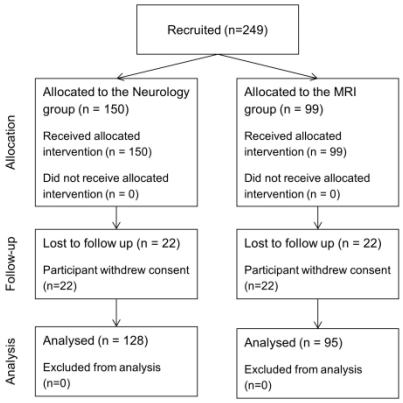

Figure 2. Participant flow chart for the headache study.

338x190mm (300 x 300 DPI)

Appendix I. Patient satisfaction.

This questionnaire evaluated three dimensions of analysis: (a) referral process (time elapsed between referral from primary care to initial secondary care appointment); (b) initial appointment; and (c) overall experience three months after recruitment.

(a): Patient experience questionnaire associated with the referral process to either Neurology (n=99) or Radiology (n=79).

		Not sure		Yes		No		p-value
		N	%	N	%	N	%	
Did you receive your appointment within a timeframe acceptable to you?	Neurology (n=99)	8	8.1%	66	67%	25	25%	0.193
	Radiology (n=79)	3	3.8%	62	79%	14	18%	

		Very satisfied		Satisfied		Neutral		Dissatisfied		Very dissatisfied		p-value
		N	%	N	%	N	%	N	%	N	%	
How satisfied were with the information you received beforehand?	Neurology (n=98)	25	26%	48	49%	22	22%	3	3.1%	0	0%	0.005
	Radiology (n=79)	38	50%	24	32%	10	13%	2	2.6%	2	2.6%	

(b): Patient experience questionnaire associated with either the Neurology (n=99) or the Radiology (n=50) appointment.

		Very satisfied		Satisfied		Neutral		Dissatisfied		Very dissatisfied		p-value
		N	%	N	%	N	%	N	%	N	%	
How you found the process overall?	Neurology (n=98)	55	56%	36	36%	5	5.1%	3	3.0%	0	0%	0.366
	Radiology (n=50)	27	54%	22	44%	0	0.0%	1	2.0%	0	0%	

		A better experience		About the same as expected		A worse experience		p-value
		N	%	N	%	N	%	
How did you find the experience in comparison to what you had expected?	Neurology (n=95)	57	60%	35	37%	3	3.2%	0.002
	Radiology (n=45)	13	29%	31	69%	1	2.2%	

(c): Overall patient experience questionnaire at 3 months post-recruitment with either the Neurology (n=56) or the Radiology (n=14) appointment.

		Very satisfied		Satisfied		Neutral		Dissatisfied		Very dissatisfied		p-value
		N	%	N	%	N	%	N	%	N	%	
Amount of time spent with clinical staff	Neurology (n=56)	20	36%	30	54%	6	11%	0	0%	0	0%	0.001
	Radiology (n=14)	3	21%	3	21%	5	36%	1	7.1%	2	14%	
Consistency of care	Neurology (n=29)	16	55%	0	0%	12	41%	1	3.4%	0	0%	0.028
	Radiology (n=14)	2	14%	3	21%	6	43%	2	14.3%	1	7.1%	
Frequency of appointments	Neurology (n=55)	9	16%	19	35%	22	40%	4	7.3%	1	1.8%	0.166
	Radiology (n=14)	2	14%	1	7.1%	7	50%	3	21%	1	7.1%	
How informed you felt about your condition	Neurology (n=54)	15	28%	24	44%	9	17%	5	9.3%	1	1.9%	0.010
	Radiology (n=13)	2	15%	2	15%	5	39%	1	7.7%	3	23%	
How informed you felt about your treatment	Neurology (n=55)	15	27%	18	33%	17	31%	4	7.3%	1	1.8%	0.004
	Radiology (n=14)	1	7.1%	1	7.1%	5	36%	5	36%	2	14%	
Your overall experience	Neurology (n=55)	13	24%	32	58%	7	13%	3	5.5%	0	0%	<0.001
	Radiology (n=14)	2	14%	1	7.1%	9	64%	1	7.1%	1	7.1%	

Reporting checklist for quality improvement study.

Based on the SQUIRE guidelines.

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	Reporting Item	Page Number
Title		
#1	Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patientcenteredness, timeliness, cost, efficiency, and equity of healthcare)	1

Abstract			
	#02a	Provide adequate information to aid in searching and indexing	4
	#02b	Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions	4
Introduction			
Problem description	#3	Nature and significance of the local problem	6
Available knowledge	#4	Summary of what is currently known about the problem, including relevant previous studies	6
Rationale	#5	Informal or formal frameworks, models, concepts, and / or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work	6-7
Specific aims	#6	Purpose of the project and of this report	7
Methods			
Context	#7	Contextual elements considered important at the outset of introducing the intervention(s)	7
Intervention(s)	#08a	Description of the intervention(s) in sufficient detail that others could reproduce it	7

Intervention(s)	#08b	Specifics of the team involved in the work	7
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Study of the Intervention(s)	#09b	Approach used to establish whether the observed outcomes were due to the intervention(s)	8-9
Measures	#10a	Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability	7-8
Measures	#10b	Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost	7-8
Measures	#10c	Methods employed for assessing completeness and accuracy of data	7-8
Analysis	#11a	Qualitative and quantitative methods used to draw inferences from the data	8-9
Analysis	#11b	Methods for understanding variation within the data, including the effects of time as a variable	8-9
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	#13b	Details of the process measures and outcome	10, 11,19
	#13c	Contextual elements that interacted with the intervention(s)	
	#13d	Observed associations between outcomes, interventions, and relevant contextual elements	10,11,20-,23
	#13e	Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s).	
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Limitations	#16b	Factors that might have limited internal validity such as confounding, bias, or imprecision in the design, methods, measurement, or analysis	14,15
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Conclusion	#17b	Sustainability	15
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Conclusion	#17e	Suggested next steps	15
Other information			
Funding	#18	Sources of funding that supported this work. Role, if any, of the funding organization in the design, implementation, interpretation, and reporting	5

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The management of chronic headache with referral from primary care to direct access to Magnetic Resonance Imaging (MRI) compared to Neurology services: an observational prospective study in London.

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The management of chronic headache with referral from primary care to direct access to Magnetic Resonance Imaging (MRI) compared to Neurology services: an observational prospective study in London.

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Abstract

Objectives. To evaluate the cost, accessibility and patient satisfaction implications of two clinical pathways used in the management of chronic headache.

Intervention. Management of chronic headache following referral from Primary Care that differed in the first appointment, either a Neurology appointment or an MRI brain scan.

Design and setting. A pragmatic, non-randomised, prospective, single-center study at a Central Hospital in London.

Participants. Adult patients with chronic headache referred from Primary to Secondary Care.

Primary and secondary outcome measures. Participants' use of health care services and costs were estimated using primary and secondary care databases and questionnaires quarterly up to 12 months post-recruitment. Cost analyses were compared using generalised linear models (GLM). Secondary outcomes assessed: access to care, patient satisfaction, headache burden and self-perceived quality of life using headache-specific (MIDAS, HIT-6) and a generic questionnaire (EQ-5D-5L).

Results. Mean (SD) cost up to 6 months post-recruitment per participant was £578 (£420) for the Neurology group (n=128) and £245 (£172) for the MRI group (n=95), leading to an estimated mean cost difference of £333 (95% CI £253 to £413, p<0.001). The mean cost difference at 12 months increased to £518 (95% CI £401 to £637, p<0.001). When adjusted for baseline and follow-up imbalances between groups, this remained statistically significant. The utilisation of brain MRI improved access to care compared to the Neurology group (p<0.001). Participants in the Neurology group reported higher levels of satisfaction associated with the pathway and led to greater change in care management.

Conclusion. Direct referral to brain MRI from Primary Care led to cost-savings and quicker access to care but lower satisfaction levels when compared with referral to Neurology services. Further research into the use of brain MRI for a subset of patient population more likely to be reassured by a negative brain scan should be considered.

Keywords: Chronic headache; migraine; direct access; magnetic resonance imaging; cost analysis.

Strengths and limitations of this study

- The estimate of health care resource use was based on comprehensive and complete data retrieved from hospital databases supplemented by both primary care utilisation data and self-reported participant data.

- The evaluation of the intervention's impact considered different dimensions of analysis (efficiency, quality of care, access to care and patient satisfaction).
- This was a single-centre study with participants recruited from one central hospital in London, therefore a multi-centre study would be necessary to explore the generalisability of the results.

Introduction

Globally, the percentage of the adult population with an active headache disorder is 47% for episodic headache and 3% for chronic headache (lasting more than 15 days per month) [1]. Headache is in the top ten international causes of disability [2], with nearly half of sufferers reporting it affects work, home or social activities [3–5]. Most headaches are primary headache disorders, such as migraine or tension-type headaches. Secondary headaches, due to an underlying serious pathology (e.g. tumour, brain aneurysm) are far less common [6]. In fact, less than 0.1% of the lifetime headache prevalence is associated with a life-threatening condition, which can include primary or secondary brain tumours [2,3].

Most headache sufferers self-manage, but over 4% of adults each year consult their General Practitioner (GP) [7, 8]. GPs manage 97% of headache presentations, particularly GPs with special interest and training in headache training initiatives [9], with 2% of these referred to neurologists and 1% to other specialists [7]. Headache is the most common cause for GP referrals to neurologists accounting for up to 20-30% [10–13], the vast majority of these are for migraine. Chronic migraine sufferers (>15 days/month) had more emergency department/hospital visits, and diagnostic tests than those with episodic migraine and consequently the medical costs were three times higher [14]. Hence, despite the benign nature of most headaches, headache management is associated with high health care utilisation. Furthermore, a study in multiple countries of the European Union found that headache management was variable in terms of visits with GPs and specialists and medication use [15]. Between 2012 and 2014, patients presenting to headache specialists (either neurologists or GPs with special interest in headache) costed £956 million in the UK [13, 16].

GP direct access to imaging has been defined as a priority within the National Health Service (NHS), with direct access to brain Magnetic Resonance Imaging (MRI) for the diagnosis of brain cancer identified as a specific initiative [8]. GPs have reported referrals for secondary care, both for a neurologist consultation or neuroimaging, when they were unable to reassure the patient [17, 18]. Furthermore, Morgan et al. (2007) found that referral for headache is often the outcome of patient pressure and anxiety interacting with GP characteristics, organisational factors and service availability rather than the headache severity itself [17]. This contrasts with the recommendations from the National Institute for Health and Care Excellence (NICE) that does not recommend the use of neuroimaging for reassurance purposes [19]. A US study estimated that patients with new onset migraine headache or a flare-up of chronic headache had, respectively, a 39% (95% CI 24–54%) and 51% (95% CI 32–68%) probability of having neuroimaging routinely ordered even where guidelines specifically recommended against this approach [20]. A UK-based randomised controlled trial evaluated the cost implications of using brain MRI for reassurance purposes and found that it led to a decrease in health care costs, in particular for patients with higher levels of psychiatric morbidity [21].

In summary, despite proportionately low level of referrals to secondary care, high prevalence makes headache the most frequently listed reason for referral to neurologists and thus, utilises capacity that is

severely constrained. The potential decrease of referral rates to Neurology specialists as a result of direct access to imaging holds the potential release resources. On the other hand, direct access may be associated with a transfer of workload to Radiology, as not all patients directly referred to brain MRI would routinely undergo an MRI scan as part of the management of their chronic headache. This study aims to evaluate the health care utilisation and associated costs of GPs using direct access to brain MRI for the management of chronic headache patients compared to referral to a Neurologist.

Patients and Methods

Study design and patient selection

The study was an independent single-centre site, prospective, observational study. The study compared two existing clinical pathways in the management of patients with chronic headache from either GP referral to the Neurology Department or to direct access to brain MRI. No change to clinical practice was involved. Participants were allocated to two groups, the Neurology group or the MRI group. The allocation was decided *a priori*, i.e. the referrer (in this case the GP) decided which referral route would suit each participant. Subsequent care was consistent with standard of care for each clinical pathway and depicted in Figure 1.

Patients eligible for the study included adults aged 16 years or over with chronic headache defined as occurring ≥ 15 days per month for more than 3 months (as per ICHD-3 criteria) and referred from GP practices to a local Hospital in Central London, either for a Neurology outpatient appointment or an MRI exam. Participants were excluded if there were secondary causes for the headache, if they were prisoners, lacked capacity to give consent or participate in the study, not fluent in English or already taking part in a clinical trial of an investigational medicinal product. Following eligibility assessment, participants completed a written informed consent. The Health Research Authority and Research Ethics Committee (West of Scotland – REC 4) approved the study research on 12th April 2016 (REC reference 16/WS/0028).

This study has involved Patient and Public Involvement (PPI) during the design and dissemination phase. Prior to the start of the research, a group of patients suffering from chronic headache were consulted to co-produce the study mobile app that was used to monitor symptoms and triggers of chronic headache. The patients who were involved in the study design, as well as all study participants, received a lay summary of the research findings as per their preferences, either via post or e-mail. Research data are available upon reasonable request.

Study outcomes

The primary outcome was to estimate the 6-month health care costs associated with two existing clinical pathways in the management of chronic headaches. Secondary outcomes comprised: the extension of the

cost analysis up to 12 months, the evaluation of access to care, patient satisfaction, headache burden and time off work associated with both clinical pathways.

Service use costs

Total costs were calculated based on the multiplication of any headache-related healthcare events by the unit cost of each event. Resource use data included contacts with any NHS healthcare provider associated with the management of chronic headache. These included, among others, visits to GPs or headache clinical nurse specialist, inpatient care, neurologist or other headache-related outpatient visits (e.g. psychiatry), physiotherapist, visits to the Emergency Department (ED), advanced imaging such as Computed Tomography (CT) and MRI. Resource use data was retrieved from multiple hospital and primary care databases as well as self-reported data from participants using a participant headache diary (either paper-based or a headache mobile app). For the purposes of the primary outcome, the valuation of unit costs was, whenever possible, based on NHS Reference Costs 2016-17 [22]. Medication costs were derived from Prescription Cost Analysis [23] and estimated from clinical data, specifically secondary care clinic letters and information provided by primary care. Participants were also asked to record time off work due to headache using the weekly participant diary.

Quality of life and headache burden

Headache burden was assessed using validated headache questionnaires and headache diaries. The HIT-6 questionnaire measured the headache burden based on 6 questions, leading to a score range from 36 to 78. The MIDAS questionnaire assessed the disability associated with the headache (ranges from 0 to 90). Furthermore, along with the headache diaries completed by participants, the MIDAS questionnaire allowed the estimate of the number of headache days per quarter (maximum of 90 days) and self-reported headache pain scores (ranging from 0, no pain at all, to 10, the worst pain ever).

Access to care

The time elapsed between the GP referral and the first appointment in each group, either the Neurology appointment or the MRI scan, was measured as a proxy for access to care. Furthermore, in the MRI group, the availability of the MRI report to the GP, rather than the actual timing of the diagnostic scan, was considered.

Change in care management

Change in care management in both groups was evaluated. It was considered that a change in care management occurred when patients underwent new treatment options (medication or otherwise, e.g. new headache medication, Botox treatment).

Patient satisfaction

Patient satisfaction was evaluated at month 3 post-recruitment using a non-validated questionnaire. This questionnaire evaluated three dimensions of analysis: (a) referral process (time elapsed between referral from primary care to initial secondary care appointment); (b) initial appointment; and (c) overall experience three months after recruitment.

Statistical analyses

This study was observational but all analyses were based on the principle of 'intention-to-treat' so that participants recruited were included in the analysis as per the group they were recruited to, regardless of whether they actually received the intended treatment, any protocol deviations or potential losses to follow-up [24]. Given the study's time horizon of 12 months, no discounting of costs or effects were considered. Descriptive statistics on several socio-demographics baseline characteristics were included. Differences in baseline characteristics between treatment groups were compared using statistical tests: Chi-squared for categorical data, t test for Normal data and Mann-Whitney for non-Normal quantitative data. Given the skewness associated with the cost distribution, all cost differences between groups were assessed using generalised linear models (GLM) with an identity-link and gamma distribution. An identity link function instead of a log link was considered in order to avoid potential analytical biases [25, 26]. An unadjusted GLM cost analysis with the study group (MRI group vs Neurology group) as only univariate analysis was performed as the first step. Given the study's observational design, the cost difference can be impacted due to the lack of randomisation [27]. Baseline variables that differenced between the two groups ($p<0.1$) were included in the multivariable (adjusted) GLM analyses. For all GLM analyses, group difference estimates and associated confidence intervals were reported, together with p-values. Analyses were conducted using Stata version 15.

Sample size

The sample size estimate was calculated based on the primary endpoint, total 6-month health care costs. A total of 150 participants were recruited in the Neurology group and 99 participants in the MRI group to achieve a detection a cost difference of £300 assuming standard deviations of £750 and £500, respectively, with 85% power at the 5% two-sided significance level. A 20% increase in sample size due to unknown cost distribution and attrition rate was considered.

Results

A total of 249 participants were recruited, 150 in the Neurology group and 99 in the MRI group. 100% (n=128) and 97% (n=96) of participants recruited received the treatment allocation in the Neurology and the MRI group, respectively (Figure 2). With regards to the follow-up duration, 15% (n=22) and 4.0% (n=4)

participants withdrew from the Neurology and MRI group, respectively, and were considered lost to follow-up. Remaining participants (n=223) were included in the analysis, equivalent to 128 (85%) and 95 (96%) participants in the Neurology and MRI group, respectively.

Baseline socio-demographic, clinical variables and resource use in the twelve months pre-recruitment are detailed in Table 1. A higher proportion of females were recruited to the Neurology group compared to the MRI group (81% vs 68%, p=0.039). Both groups were similar in mean age, ethnic mix, with more than half being White. No significant differences between the groups were found in terms of highest qualification and employment, with high-school and full-time employment being the most common. In terms of clinical variables, no significant difference between groups were found in terms of number of active health problems or number of headache triggers. Participants in the Neurology group reported lower utility and health scores using the generic EQ-5D-5L questionnaire, with a statistically significant difference in health scores (p=0.005). Lower health scores imply lower self-rated quality of life, while for the headache-specific questionnaires [Headache Impact Test (HIT-6) and Migraine Disability Assessment (MIDAS)], a higher score implies a higher headache burden. Compared to the MRI group, participants in the Neurology group reported significantly higher headache burden (HIT-6 mean score: 65 vs 63, p=0.006), number of headache days in the past 3 months (MIDAS questionnaire: 52 vs 43, p=0.038). Participants in the Neurology group also had significantly more primary care appointments (3.7 vs 2.4, p<0.001) and all NHS appointments (4.3 vs 2.5, p<0.001).

Service use

Table 2 summarises the NHS resource use of primary care and hospital-based services over a period of 12 months following recruitment. With regards to primary care utilisation, participants in the Neurology group had a significantly higher number of GP face-to-face appointments (mean number per participant: 1.82 vs 1.19, p=0.006). Regarding secondary care, participants in the Neurology group had a higher mean number of outpatient appointments (2.52 vs 0.26, p<0.001) and other treatments such as Botox and nerve root injection (mean 0.30 vs 0.05, p<0.001). In contrast, they had a lower mean number of brain MRIs (0.59 vs 1.05, p<0.001). There were no statistically significant differences in the utilisation levels of any of the other healthcare events.

The NHS resource use pre and post-recruitment for both groups was also compared. Table 3 summarises the difference between headache-related events 12 months post-recruitment compared to the 12 months pre-recruitment. A reduction of 197 and 87 GP visits (mean 1.54/0.92 per participant or a percentage reduction of 85%/77%) was noted in the Neurology and MRI group, respectively. Similarly, there was a reduction in emergency department utilisation with a decrease of 23 and 6 episodes (mean 0.18 and 0.07 per participant or a percentage reduction of 288% and 120%) in the Neurology and MRI group, respectively.

Cost analyses

The mean (SD) cost management per participant at 6 months post-recruitment was lower in the MRI group compared to the Neurology group [£245 (£172) vs £578 (£420)], leading to a mean cost difference between groups of -£333 per participant (95% CI: -£413 to -£253, p<0.001). The MRI group had a higher proportion of participants with lower costs (£0 to £250 range) than the Neurology group (73% vs 4.7%). The initial cost analysis was extended to 12 months post-recruitment and the mean cost difference between groups increased, with the MRI group generating cost savings of £518 per participant (95% CI: -£637 to -£401, p<0.001).

Given the non-randomised study design, an additional GLM analysis was performed to adjust for baseline characteristics. The unadjusted 6-month cost difference between groups (-£333; 95% CI: -£413, -£253) hardly changed after adjustment (-£308; 95% CI: -£408, -£209). In all analyses, at both 6 and 12 months post-recruitment, direct access to MRI for the management of chronic headache was associated with statistically significant mean cost savings for the NHS.

Abnormal findings in the MRI group

Out of the 95 participants recruited in the MRI group, three MRIs were not performed during the initial appointment due to claustrophobia events. From a total number of 92 MRIs, 85 (92%) were normal and 7 (7.6%) presented abnormal findings (Table 4), with one diagnosis being particularly significant (two small intracranial aneurysms). This participant was referred to neurovascular team for assessment, at which point no intervention was performed during the follow-up period (participant included in an active surveillance group). Two other participants had a change in their clinical management for less significant findings, leading to either a follow-up appointment or scan. No brain malignancies were diagnosed.

Access to care

The mean time (SD) elapsed from GP referral to the initial Neurology and MRI scan was, respectively, 110 (35) days and 39 days (17), a statistically significant difference (p<0.001). Second, if the MRI report, than the actual scan, is considered as a proxy for access to care, the mean time elapsed was 70 days (35) (p<0.001).

Change in management

Participants in the Neurology group were more likely to have a change in therapeutic management compared to participants in the MRI group (97% vs 64%, p<0.001). Similarly, among participants that had not started on preventative medication pre-recruitment, a higher proportion of participants in the Neurology group were started on preventative medication as part of their clinical management (93% vs 53%, p<0.001).

Quality of life and headache burden

At baseline, mean utility was lower in the Neurology group but not significant (mean utility of 0.809 vs 0.830, p=0.097), while their self-perceived mean health score was significantly lower (EQ-5D-5L: visual analogue scale score of 64.0 vs 70.8, p=0.005) (Table 5). There was no statistically significant differences between the groups at 6 months for to the utility and self-reported healthcare scores.

At baseline, participants in the Neurology group presented a higher headache burden compared to the MRI group (mean score of 65.0 vs 62.6, p=0.006) (Table 5). This trend seemed to be maintained over the follow-up period but was difficult to interpret due to high attrition rates: mean HIT-6 score at 6 months (60.0 vs 53.1, p=0.968). At baseline, participants in the Neurology group had higher headache severity compared to the MRI group, but this was not significant (mean MIDAS score of 57.8 vs 44.8, p=0.075) (Table 5). In both groups the headache severity decreased over the follow-up period. At baseline, participants in the Neurology group reported a significantly higher mean number of headache days compared to the MRI group (51.6 vs 42.8, p=0.038). This trend was observed at month 6 but was not significant (41.2 vs 26.5, p=0.152). A third variable assessed self-reported headache pain scores. At baseline, participants at baseline showed almost identical mean headache pain scores (6.9 vs 6.9, p=0.827). During the follow-up period, no statistical differences were found at month 6 (4.5 vs 4.2, p=0.663).

Time off work

Participants in the Neurology group (n=83) had higher mean number of days off work due to headache compared to participants in the MRI group (n=35) but these were not statistically significant at 6 (13.9 vs 9.7, p=0.563) or 12 months (27.9 vs 19.1, p=0.808) post-recruitment.

Patient satisfaction

Patient satisfaction was evaluated at month 3 post-recruitment using a non-validated questionnaire (Appendix I). Participants in both groups reported no difference in terms of receiving an appointment in a suitable timeframe (p=0.193). Participants in the MRI group reported higher satisfaction levels (p=0.005) compared to the Neurology group associated with the information received prior to the actual appointment. No statistically significant difference (p=0.366) between the groups was found regarding the satisfaction levels of both appointments (either MRI scan or Neurologist appointment) but a higher proportion of participants in the Neurology group reported a better experience compared to their expectation (p=0.002). At month 3 post-recruitment in all variables, except frequency of appointments (p=0.166), participants in the Neurology group reported higher levels of satisfaction with: amount of time spent with clinical staff (p=0.001); consistency of care (p=0.028); how informed you felt about your condition (p=0.010) / your treatment (p=0.004); and the overall experience (p<0.001).

Discussion

Previous UK studies assessed the use of direct access to advanced imaging in the management of chronic headache patients [10, 21]. Howard et al. (2005) performed a randomised controlled trial, which showed that the use of imaging in patients led to a reduction of referral rates to Neurology services in secondary care from 23% to 1.3% (1/76) in the treatment group (i.e. patients being scanned) [21]. Thomas et al. (2010) estimated that direct access to brain imaging, in this case CT, reduced referral rates to Neurology in 86% of the cases during the follow-up period (average of 1.3 years per patient) [10].

The study's underlying hypothesis was that the early use of an advanced and accurate diagnostic tool (in this case MRI) would reassure both patients and GPs that no serious underlying cause (particularly brain tumour) is present. This would in turn reduce the headache burden and NHS resource use associated with the patient's subsequent management. Given the high prevalence of headache and the increased referral of patients with chronic headaches and other neurological conditions from primary care to hospital based care [7], it is relevant to assess the implications of using different management strategies. To our knowledge, no previous prospective study in the UK has assessed the economic implications of these two coexisting management strategies based on GP referral decision.

The primary outcome was total costs at six months post-recruitment. The study showed that the use of advanced imaging produced cost-savings to the NHS compared to referral to Neurology, with mean cost-savings per participant of £333 and £518 at month 6 and 12 post-recruitment, respectively ($p<0.001$). These cost differences were multifactorial but primarily driven by: (i) the lower unit cost of a brain MRI scan (£146) compared to the initial Neurology appointment (£240); (ii) the lower number of outpatient appointments in the MRI group (25 vs 322); (iii) the fact that 75/128 (59%) of participants in the Neurology group ended up having a brain MRI scan in the 12-month period of follow-up; and (iv) the increased likelihood of patients in the Neurology arm receiving management with Botox injections or nerve block procedures (39 vs 5 events). Direct access to brain MRI seemed to reassure most participants as only 17 (18%) participants in the MRI group ended up being referred to a neurologist. Furthermore over 66% of participants in the MRI group had no further hospital-based care, compared to 5% in the Neurology group. Similarly, at primary care level, participants in the MRI group presented lower utilisation rates per participant when compared to the Neurology group (mean GP appointments of 1.82 vs 1.19, $p=0.006$). In order to mitigate the potential confounding by indication introduced by GPs referring patients to both clinical pathways, adjusted GLMs were conducted. All cost differences between groups remained statistically significant ($p<0.001$) when adjusted for differences in baseline characteristics or follow-up attrition rates.

At baseline, participants in the Neurology group presented lower self-reported quality of life and higher headache burden. HIT-6 scores did improve over time but we were unable to assess whether there was a statistically significant difference in both groups due to the high attrition rates, particularly in the MRI group. As mentioned, out of the 95 participants recruited to the MRI group, 17 (18%) were subsequently referred to a Neurologist. Interestingly, at baseline, these 17 patients reported higher headache burden compared

to all 95 patients recruited to the MRI group (MIDAS score: 51.2 vs 44.8; MIDAS headache days: 55.8 vs 42.8). This finding seems to suggest that this data might be useful to risk stratify patients and support GPs in their referral criteria. However, further research into this area is required.

Participants in the Neurology group presented a higher probability of being started on a preventative medication and had a change in therapeutic management following referral from primary care. A small proportion (7.6%) of participants in the MRI group had abnormal findings in the initial brain MRI. Only one participant had clinically significant lesions (two small aneurysms) which were also incidental and no brain tumour was diagnosed.

Time off work was also evaluated as a proxy of headache burden. Participants in the Neurology group presented a trend ($p>0.05$) of higher number of days off work due to headache compared to participants in the MRI group. This difference was not however statistically significant.

Lastly, patient satisfaction in both groups was compared based on three dimensions of analysis: during the referral period, the initial appointment and overall satisfaction. Twenty five percent of participants in the Neurology group (vs 18% in the MRI group) reported dissatisfaction with the waiting time. This finding is not unexpected as the mean waiting time associated with the Neurology appointment was almost three times of the one associated with the MRI scan (110 vs 39 days). Contrary to the referral period, participants in the Neurology group reported trends of higher satisfaction levels associated with the first appointment (neurology outpatient visit vs MRI scan) and a better experience compared to their expectations (60% vs 29% in the Neurology and MRI group, respectively). Participants in the Neurology group reported improved satisfaction levels at 3 months across different variables (time spent with clinician, consistency of care, information about the condition and its treatment). Almost three quarters of Neurology participants reported being satisfied or very satisfied with their headache management compared to only 21% in the MRI group ($p<.001$). Both participants and GP referrers in the MRI group reported dissatisfaction associated with the waiting time elapsed between the MRI scan and the availability of results (mean time of 31 days). This might have contributed to increased anxiety in some participants.

Strengths of this study:

The estimate of NHS resource use data was primarily based on comprehensive and complete data retrieved from hospital-based databases that captured both the acute and elective elements of the pathway associated with the management of patients with chronic headache. This data was supplemented by both primary care utilisation data, collected from each participant's GP, and self-reported participant data. The aim was to guarantee that any chronic headache related NHS event was costed regardless of the healthcare provider and its location. The prospective collection of health care utilisation and the evaluation of the impact of the interventions across different dimensions of analysis (efficiency, quality of care, access to care and patient satisfaction) were other key factors that contributed to the overall strength of the study.

Limitations of this study:

There were some limitations to this study. First, this was a single-centre study with participants recruited from one central hospital in London. A multi-centre study would be necessary to explore the generalisability of the results. Second, as with any observational study, no randomisation between groups was performed and there were significant differences in baseline of headache burden and health-scores and utilisation of resources. In order to mitigate potential confounding factors, adjusted multivariate analyses showed that the primary outcome was hardly affected and remained statistically significant. Nevertheless, residual confounding factors remain a limitation of the study. Third, specific inclusion and exclusion criteria were considered and as such the study sample might not be representative of all patients with chronic headache. Fourth, for the purpose of secondary outcomes, most data was self-reported and hence prone to recall bias. Lastly, there were high follow-up attrition rates particularly for participants in the MRI group, which affected some of the study's secondary outcomes.

Conclusions

This study found that the referral from primary care to direct access to brain MRI compared to referral for a neurologist for patients with chronic headache was associated with lower NHS overall costs at 6 and 12 months post-recruitment. Despite waiting longer from referral to appointment, participants in the Neurology group reported higher satisfaction levels associated with the care received compared to the MRI group and were more likely to benefit from changes to their therapeutic management.

Implications for further research and clinical practice

Baseline measures of headache burden, such as the HIT-6 or MIDAS, could potentially be used to determine which pathway may be suitable for patients but further research into the risk stratification of chronic headache patients is required. Future study designs should consider the confounding by indication introduced by recruiting participants referred to the two pathways based on GP decision. With regards to clinical practice, and based on the study findings, we plan to provide GPs with headache management advice along with the MRI report.

Author contributions:

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Figure 1. High-level illustration of two existing clinical pathways associated with the referral from GP due to chronic headache.

Figure 2. Participant flow chart for the headache study.

Table 1. Baseline characteristics of the population analysed.

Variable	Neurology group (n=128)	MRI group (n=95)	p-value
Age, years: mean (SD)	38.4 (14.1)	40.0 (14.6)	0.514
Gender Female, n (%)	103 (81)	65 (68)	0.039
Ethnicity			0.079
Asian	13 (10)	6 (6.3)	
Black	40 (31)	17 (18)	
White	68 (53)	60 (63)	
Mixed	5 (3.9)	8 (8.4)	
Other	2 (1.6)	4 (4.2)	
Qualification, n (%)			0.565
Advanced work or PhD	3 (2.3)	4 (4.2)	
Master's Degree	15 (12)	12 (13)	
Bachelor's Degree	31 (24)	29 (31)	
High School	57 (45)	33 (35)	
Did not finish High School	8 (6.3)	10 (11)	
Prefer not to answer	14 (11)	7 (7.4)	
Employment, n (%)			0.839
Employee in full time job (30 hours or more a week)	50 (39)	36 (38)	
Employee in part-time job (under 30 hours a week)	18 (14)	18 (19)	
Self-employed, full or part time	12 (9.4)	8 (8.4)	
Full-time education at school, college or university	16 (13)	9 (9.5)	
Doing something else	2 (1.6)	2 (2.1)	
Permanently sick/ disabled	8 (6.3)	6 (6.3)	
Looking after the home	4 (3.1)	6 (6.3)	
Unemployed and available for work	12 (9.4)	6 (6.3)	
Wholly retired from work	4 (3.1)	4 (4.2)	
Prefer not to answer	2 (1.6)	0 (0)	
Presence of mental health condition, n (%)	22 (17)	11 (12)	0.243
Number of active health problems: mean (SD)	2.0 (1.5)	1.8 (1.4)	0.277
Number of headache triggers: mean (SD)	2.1 (1.8)	1.8 (1.4)	0.378
Self-reported questionnaires			
EQ-5D-5L: mean utility (SD)	0.809 (0.182)	0.830 (0.195)	0.097
EQ-5D-5L: mean score (SD)	64 (19)	71 (20)	0.005
HIT-6: mean score (SD)	65 (5.3)	63 (7.3)	0.006
MIDAS, mean score (SD)	58 (54)	45 (45)	0.075
MIDAS, mean headache days (SD)	52 (32)	43 (31)	0.038
MIDAS, mean pain score (SD)	6.9 (1.8)	6.9 (1.9)	0.778
Resource use in the 12 months prior to recruitment			
GP appointments: mean (SD)	3.7 (2.9)	2.4 (1.5)	<0.001
All NHS events: mean (SD)	4.3 (3.7)	2.5 (1.5)	<0.001

SD= Standard deviation; EQ-5D-5L - 5 level EQ-5D; HIT-6 = headache impact test; MIDAS = Migraine Disability assessment scale

Table 2. Breakdown of number of NHS appointments per type of activity organised per group and respective number of participants responsible for these appointments (12 months post-recruitment).

	Neurology group (n=128)			MRI group (n=95)			p-value
Type of NHS appointment	**Total of episodes**	**Mean (SD)**	**N (%)**	**Total of episodes**	**Mean (SD)**	**N (%)**	
Primary Care services							
GP face-to-face appointment	233	1.82 (2.11)	91 (71)	113	1.19 (1.64)	57 (60)	0.006
GP phone appointment	37	0.29 (0.75)	24 (19)	25	0.26 (0.49)	23 (24)	0.420
Hospital based services							
Hospital outpatient appointment	322	2.52 (1.19)	128 (100)	25	0.26 (0.55)	20 (21)	<0.001
Inpatient episode	4	0.03 (0.35)	1 (0.8)	1	0.01 (0.10)	1 (1.1)	0.837
Emergency Department episode	8	0.06 (0.24)	8 (6.3)	5	0.05 (0.22)	5 (5.3)	0.756
Head CT	1	0.01 (0.09)	1 (0.8)	1	0.01 (0.10)	1 (1.1)	0.832
Brain MRI	75	0.59 (0.49)	75 (59)	100	1.05 (0.30)	95 (100)	<0.001
Others (e.g. botox and nerve injection treatments)	39	0.30 (0.79)	25 (20)	5	0.05 (0.30)	3 (3.2)	<0.001

Table 3. Difference in the number, mean and percentage reduction of NHS appointments per type of activity organised per group 12 months post-recruitment compared to the 12 months pre-recruitment (note: a negative/positive percentage denotes a decrease/increase in activity following recruitment).

	Neurology group (n=128)			MRI group (n=95)		
Type of NHS appointment	**Total of episodes**	**Mean**	**%**	**Total of episodes**	**Mean**	**%**
Primary Care services						
GP face-to-face appointment	-197	-1.54	-85%	-87	-0.92	-77%
GP phone appointment	-11	-0.09	-30%	5	0.05	20%
Hospital-based services						
Hospital outpatient appointment	301	2.36	93%	23	0.24	92%
Inpatient episode	3	0.02	75%	1	0.01	100%
Emergency Department episode	-23	-0.18	-288%	-6	-0.07	-120%
Head CT	-9	-0.07	-12%	1	0.01	1.0%
Brain MRI	55	0.43	141%	100	1.05	N/A

Table 4. Description of incidental findings, its clinical relevance and subsequent pathway.

Abnormal findings	**Significant (Yes/No)?**	**Changes in diagnostic or treatment pathway**
Mature striatocapsular lacune	No	
Sinusitis with complete opacification	No	ENT review only.
Pituitary abnormality (T1)	No	
Low lying cerebellar tonsils	No	
Previous petrous surgery noted	No	
Two aneurysms AcomA (anterior communicating artery) and right ICA	Yes	Referred to neurovascular – no coiling (no intervention).
No definitive lesion	No	Follow-up MRI only.

Table 5. Descriptive statistics for one generic questionnaire (EQ-5D-5L) and two headache-specific questionnaires (HIT-6 and MIDAS) at baseline and 6 months post-recruitment.

				N	Mean	Standard Deviation	p-value
BASELINE	**EQ-5D-5L**	Utility	Neurology	127	0.809	0.182	0.097
			Radiology	95	0.830	0.195	
		Score	Neurology	126	64.0	18.8	0.005
			Radiology	95	70.8	20.2	
	HIT-6	Score	Neurology	128	65.0	5.3	0.006
			Radiology	92	62.6	7.3	
	MIDAS	Score	Neurology	124	57.8	54.0	0.075
			Radiology	90	44.8	44.9	
		Headache days	Neurology	124	51.6	31.5	0.038
			Radiology	90	42.8	30.7	
		Pain score	Neurology	124	6.9	1.8	0.778
			Radiology	90	6.9	1.9	
MONTH 6	**EQ-5D-5L**	Utility	Neurology	55	0.770	0.263	0.243
			Radiology	26	0.681	0.346	
		Score	Neurology	53	68.2	20.6	0.463
			Radiology	23	62.5	24.7	
	HIT-6	Score	Neurology	35	60.0	8.7	0.968
			Radiology	12	53.1	22.8	
	MIDAS	Score	Neurology	32	52.6	58.1	0.827
			Radiology	12	40.7	36.0	
		Headache days	Neurology	46	41.2	28.6	0.152
			Radiology	15	26.5	28.1	
		Pain score	Neurology	44	4.5	2.3	0.663
			Radiology	15	4.2	2.0	

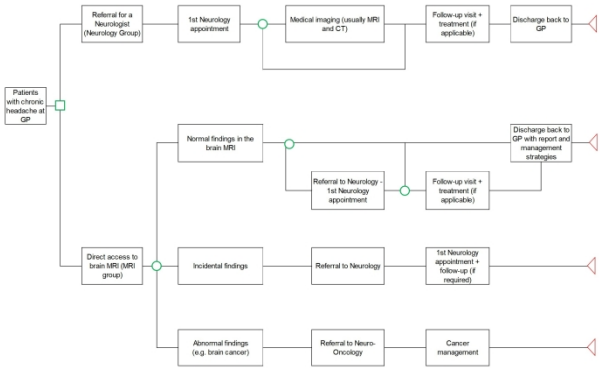

Figure 1. High-level illustration of two existing clinical pathways associated with the referral from GP due to chronic headache.

338x190mm (300 x 300 DPI)

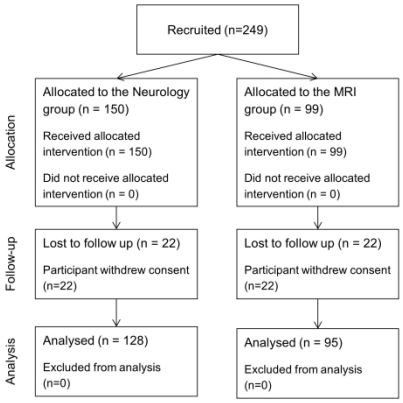

Figure 2. Participant flow chart for the headache study.

338x190mm (300 x 300 DPI)

Appendix I. Patient satisfaction.

This questionnaire evaluated three dimensions of analysis: (a) referral process (time elapsed between referral from primary care to initial secondary care appointment); (b) initial appointment; and (c) overall experience three months after recruitment.

(a): Patient experience questionnaire associated with the referral process to either Neurology (n=99) or Radiology (n=79).

		Not sure		Yes		No		p-value
		N	%	N	%	N	%	
Did you receive your appointment within a timeframe acceptable to you?	Neurology (n=99)	8	8.1%	66	67%	25	25%	0.193
	Radiology (n=79)	3	3.8%	62	79%	14	18%	

		Very satisfied		Satisfied		Neutral		Dissatisfied		Very dissatisfied		p-value
		N	%	N	%	N	%	N	%	N	%	
How satisfied were with the information you received beforehand?	Neurology (n=98)	25	26%	48	49%	22	22%	3	3.1%	0	0%	0.005
	Radiology (n=79)	38	50%	24	32%	10	13%	2	2.6%	2	2.6%	

(b): Patient experience questionnaire associated with either the Neurology (n=99) or the Radiology (n=50) appointment.

		Very satisfied		Satisfied		Neutral		Dissatisfied		Very dissatisfied		p-value
		N	%	N	%	N	%	N	%	N	%	
How you found the process overall?	Neurology (n=98)	55	56%	36	36%	5	5.1%	3	3.0%	0	0%	0.366
	Radiology (n=50)	27	54%	22	44%	0	0.0%	1	2.0%	0	0%	

		A better experience		About the same as expected		A worse experience		p-value
		N	%	N	%	N	%	
How did you find the experience in comparison to what you had expected?	Neurology (n=95)	57	60%	35	37%	3	3.2%	0.002
	Radiology (n=45)	13	29%	31	69%	1	2.2%	

(c): Overall patient experience questionnaire at 3 months post-recruitment with either the Neurology (n=56) or the Radiology (n=14) appointment.

		Very satisfied		Satisfied		Neutral		Dissatisfied		Very dissatisfied		p-value
		N	%	N	%	N	%	N	%	N	%	
Amount of time spent with clinical staff	Neurology (n=56)	20	36%	30	54%	6	11%	0	0%	0	0%	0.001
	Radiology (n=14)	3	21%	3	21%	5	36%	1	7.1%	2	14%	
Consistency of care	Neurology (n=29)	16	55%	0	0%	12	41%	1	3.4%	0	0%	0.028
	Radiology (n=14)	2	14%	3	21%	6	43%	2	14.3%	1	7.1%	
Frequency of appointments	Neurology (n=55)	9	16%	19	35%	22	40%	4	7.3%	1	1.8%	0.166
	Radiology (n=14)	2	14%	1	7.1%	7	50%	3	21%	1	7.1%	
How informed you felt about your condition	Neurology (n=54)	15	28%	24	44%	9	17%	5	9.3%	1	1.9%	0.010
	Radiology (n=13)	2	15%	2	15%	5	39%	1	7.7%	3	23%	
How informed you felt about your treatment	Neurology (n=55)	15	27%	18	33%	17	31%	4	7.3%	1	1.8%	0.004
	Radiology (n=14)	1	7.1%	1	7.1%	5	36%	5	36%	2	14%	
Your overall experience	Neurology (n=55)	13	24%	32	58%	7	13%	3	5.5%	0	0%	<0.001
	Radiology (n=14)	2	14%	1	7.1%	9	64%	1	7.1%	1	7.1%	

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Title		
#1	Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patientcenteredness, timeliness, cost, efficiency, and equity of healthcare)	1

Abstract			
	#02a	Provide adequate information to aid in searching and indexing	4
	#02b	Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions	4
Introduction			
Problem description	#3	Nature and significance of the local problem	6
Available knowledge	#4	Summary of what is currently known about the problem, including relevant previous studies	6
Rationale	#5	Informal or formal frameworks, models, concepts, and / or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work	6-7
Specific aims	#6	Purpose of the project and of this report	7
Methods			
Context	#7	Contextual elements considered important at the outset of introducing the intervention(s)	7
Intervention(s)	#08a	Description of the intervention(s) in sufficient detail that others could reproduce it	7

Intervention(s)	#08b	Specifics of the team involved in the work	7
Study of the Intervention(s)	#09a	Approach chosen for assessing the impact of the intervention(s)	7-8
Study of the Intervention(s)	#09b	Approach used to establish whether the observed outcomes were due to the intervention(s)	8-9
Measures	#10a	Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability	7-8
Measures	#10b	Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost	7-8
Measures	#10c	Methods employed for assessing completeness and accuracy of data	7-8
Analysis	#11a	Qualitative and quantitative methods used to draw inferences from the data	8-9
Analysis	#11b	Methods for understanding variation within the data, including the effects of time as a variable	8-9
Ethical considerations	#12	Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest	7

Results

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	#13b	Details of the process measures and outcome	10, 11,19
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	#13d	Observed associations between outcomes, interventions, and relevant contextual elements	10,11,20-,23
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	#13f	Details about missing data	9
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Other information			
Funding	#18	Sources of funding that supported this work. Role, if any, of the funding organization in the design, implementation, interpretation, and reporting	5

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The management of chronic headache with referral from primary care to direct access to Magnetic Resonance Imaging (MRI) compared to Neurology services: an observational prospective study in London.

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The management of chronic headache with referral from primary care to direct access to Magnetic Resonance Imaging (MRI) compared to Neurology services: an observational prospective study in London.

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Abstract

Objectives. To evaluate the cost, accessibility and patient satisfaction implications of two clinical pathways used in the management of chronic headache.

Intervention. Management of chronic headache following referral from Primary Care that differed in the first appointment, either a Neurology appointment or an MRI brain scan.

Design and setting. A pragmatic, non-randomised, prospective, single-center study at a Central Hospital in London.

Participants. Adult patients with chronic headache referred from Primary to Secondary Care.

Primary and secondary outcome measures. Participants' use of health care services and costs were estimated using primary and secondary care databases and questionnaires quarterly up to 12 months post-recruitment. Cost analyses were compared using generalised linear models (GLM). Secondary outcomes assessed: access to care, patient satisfaction, headache burden and self-perceived quality of life using headache-specific (MIDAS, HIT-6) and a generic questionnaire (EQ-5D-5L).

Results. Mean (SD) cost up to 6 months post-recruitment per participant was £578 (£420) for the Neurology group (n=128) and £245 (£172) for the MRI group (n=95), leading to an estimated mean cost difference of £333 (95% CI £253 to £413, p<0.001). The mean cost difference at 12 months increased to £518 (95% CI £401 to £637, p<0.001). When adjusted for baseline and follow-up imbalances between groups, this remained statistically significant. The utilisation of brain MRI improved access to care compared to the Neurology group (p<0.001). Participants in the Neurology group reported higher levels of satisfaction associated with the pathway and led to greater change in care management.

Conclusion. Direct referral to brain MRI from Primary Care led to cost-savings and quicker access to care but lower satisfaction levels when compared with referral to Neurology services. Further research into the use of brain MRI for a subset of patient population more likely to be reassured by a negative brain scan should be considered.

Keywords: Chronic headache; migraine; direct access; magnetic resonance imaging; cost analysis.

Strengths and limitations of this study

- The estimate of health care resource use was based on comprehensive and complete data retrieved from hospital databases supplemented by both primary care utilisation data and self-reported participant data.

- The evaluation of the intervention's impact considered different dimensions of analysis (efficiency, quality of care, access to care and patient satisfaction).
- This was a single-centre study with participants recruited from one central hospital in London, therefore a multi-centre study would be necessary to explore the generalisability of the results.

Introduction

Globally, the percentage of the adult population with an active headache disorder is 47% for episodic headache and 3% for chronic headache (lasting more than 15 days per month) [1]. Headache is in the top ten international causes of disability [2], with nearly half of sufferers reporting it affects work, home or social activities [3–5]. Most headaches are primary headache disorders, such as migraine or tension-type headaches. Secondary headaches, due to an underlying serious pathology (e.g. tumour, brain aneurysm) are far less common [6]. In fact, less than 0.1% of the lifetime headache prevalence is associated with a life-threatening condition, which can include primary or secondary brain tumours [2,3].

Most headache sufferers self-manage, but over 4% of adults each year consult their General Practitioner (GP) [7, 8]. GPs manage 97% of headache presentations, particularly GPs with special interest and training in headache training initiatives [9], with 2% of these referred to neurologists and 1% to other specialists [7]. Headache is the most common cause for GP referrals to neurologists accounting for up to 20-30% [10–13], the vast majority of these are for migraine. Chronic migraine sufferers (>15 days/month) had more emergency department/hospital visits, and diagnostic tests than those with episodic migraine and consequently the medical costs were three times higher [14]. Hence, despite the benign nature of most headaches, headache management is associated with high health care utilisation. Furthermore, a study in multiple countries of the European Union found that headache management was variable in terms of visits with GPs and specialists and medication use [15]. Between 2012 and 2014, patients presenting to headache specialists (either neurologists or GPs with special interest in headache) costed £956 million in the UK [13, 16].

GP direct access to imaging has been defined as a priority within the National Health Service (NHS), with direct access to brain Magnetic Resonance Imaging (MRI) for the diagnosis of brain cancer identified as a specific initiative [8]. GPs have reported referrals for secondary care, both for a neurologist consultation or neuroimaging, when they were unable to reassure the patient [17, 18]. Furthermore, Morgan et al. (2007) found that referral for headache is often the outcome of patient pressure and anxiety interacting with GP characteristics, organisational factors and service availability rather than the headache severity itself [17]. This contrasts with the recommendations from the National Institute for Health and Care Excellence (NICE) that does not recommend the use of neuroimaging for reassurance purposes [19]. A US study estimated that patients with new onset migraine headache or a flare-up of chronic headache had, respectively, a 39% (95% CI 24–54%) and 51% (95% CI 32–68%) probability of having neuroimaging routinely ordered even where guidelines specifically recommended against this approach [20]. A UK-based randomised controlled trial evaluated the cost implications of using brain MRI for reassurance purposes and found that it led to a decrease in health care costs, in particular for patients with higher levels of psychiatric morbidity [21].

In summary, despite proportionately low level of referrals to secondary care, high prevalence makes headache the most frequently listed reason for referral to neurologists and thus, utilises capacity that is

severely constrained. The potential decrease of referral rates to Neurology specialists as a result of direct access to imaging holds the potential release resources. On the other hand, direct access may be associated with a transfer of workload to Radiology, as not all patients directly referred to brain MRI would routinely undergo an MRI scan as part of the management of their chronic headache. This study aims to evaluate the health care utilisation and associated costs of GPs using direct access to brain MRI for the management of chronic headache patients compared to referral to a Neurologist.

Patients and Methods

Study design and patient selection

The study was an independent single-centre site, prospective, observational study. The study compared two existing clinical pathways in the management of patients with chronic headache from either GP referral to the Neurology Department or to direct access to brain MRI. No change to clinical practice was involved. Participants were allocated to two groups, the Neurology group or the MRI group. The allocation was decided *a priori*, i.e. the referrer (in this case the GP) decided which referral route would suit each participant. Subsequent care was consistent with standard of care for each clinical pathway and depicted in Figure 1.

Patients eligible for the study included adults aged 16 years or over with chronic migraine defined as occurring ≥ 15 days per month for more than 3 months (as per ICHD-3 criteria) and referred from GP practices to a local Hospital in Central London, either for a Neurology outpatient appointment or an MRI exam. Participants were excluded if there were secondary causes for the headache, if they were prisoners, lacked capacity to give consent or participate in the study, not fluent in English or already taking part in a clinical trial of an investigational medicinal product. Following eligibility assessment, participants completed a written informed consent. The Health Research Authority and Research Ethics Committee (West of Scotland – REC 4) approved the study research on 12th April 2016 (REC reference 16/WS/0028).

Patient and Public Involvement statement

This study has involved Patient and Public Involvement (PPI) during the design and dissemination phase. Prior to the start of the research, a group of patients suffering from chronic headache were consulted to co-produce the study mobile app that was used to monitor symptoms and triggers of chronic headache. The patients who were involved in the study design, as well as all study participants, received a lay summary of the research findings as per their preferences, either via post or e-mail. Research data are available upon reasonable request.

Study outcomes

The primary outcome was to estimate the 6-month health care costs associated with two existing clinical pathways in the management of chronic headaches. Secondary outcomes comprised: the extension of the

cost analysis up to 12 months, the evaluation of access to care, patient satisfaction, headache burden and time off work associated with both clinical pathways.

Service use costs

Total costs were calculated based on the multiplication of any headache-related healthcare events by the unit cost of each event. Resource use data included contacts with any NHS healthcare provider associated with the management of chronic headache. These included, among others, visits to GPs or headache clinical nurse specialist, inpatient care, neurologist or other headache-related outpatient visits (e.g. psychiatry), physiotherapist, visits to the Emergency Department (ED), advanced imaging such as Computed Tomography (CT) and MRI. Resource use data was retrieved from multiple hospital and primary care databases as well as self-reported data from participants using a participant headache diary (either paper-based or a headache mobile app). For the purposes of the primary outcome, the valuation of unit costs was, whenever possible, based on NHS Reference Costs 2016-17 [22]. Medication costs were derived from Prescription Cost Analysis [23] and estimated from clinical data, specifically secondary care clinic letters and information provided by primary care. Participants were also asked to record time off work due to headache using the weekly participant diary.

Quality of life and headache burden

Headache burden was assessed using validated headache questionnaires and headache diaries. The HIT-6 questionnaire measured the headache burden based on 6 questions, leading to a score range from 36 to 78. The MIDAS questionnaire assessed the disability associated with the headache (ranges from 0 to 90). Furthermore, along with the headache diaries completed by participants, the MIDAS questionnaire allowed the estimate of the number of headache days per quarter (maximum of 90 days) and self-reported headache pain scores (ranging from 0, no pain at all, to 10, the worst pain ever).

Access to care

The time elapsed between the GP referral and the first appointment in each group, either the Neurology appointment or the MRI scan, was measured as a proxy for access to care. Furthermore, in the MRI group, the availability of the MRI report to the GP, rather than the actual timing of the diagnostic scan, was considered.

Change in care management

Change in care management in both groups was evaluated. It was considered that a change in care management occurred when patients underwent new treatment options (medication or otherwise, e.g. new headache medication, Botox treatment).

Patient satisfaction

Patient satisfaction was evaluated at month 3 post-recruitment using a non-validated questionnaire. This questionnaire evaluated three dimensions of analysis: (a) referral process (time elapsed between referral from primary care to initial secondary care appointment); (b) initial appointment; and (c) overall experience three months after recruitment.

Statistical analyses

This study was observational but all analyses were based on the principle of 'intention-to-treat' so that participants recruited were included in the analysis as per the group they were recruited to, regardless of whether they actually received the intended treatment, any protocol deviations or potential losses to follow-up [24]. Given the study's time horizon of 12 months, no discounting of costs or effects were considered. Descriptive statistics on several socio-demographics baseline characteristics were included. Differences in baseline characteristics between treatment groups were compared using statistical tests: Chi-squared for categorical data, t test for Normal data and Mann-Whitney for non-Normal quantitative data. Given the skewness associated with the cost distribution, all cost differences between groups were assessed using generalised linear models (GLM) with an identity-link and gamma distribution. An identity link function instead of a log link was considered in order to avoid potential analytical biases [25, 26]. An unadjusted GLM cost analysis with the study group (MRI group vs Neurology group) as only univariate analysis was performed as the first step. Given the study's observational design, the cost difference can be impacted due to the lack of randomisation [27]. Baseline variables that differenced between the two groups ($p<0.1$) were included in the multivariable (adjusted) GLM analyses. For all GLM analyses, group difference estimates and associated confidence intervals were reported, together with p-values. Analyses were conducted using Stata version 15.

Sample size

The sample size estimate was calculated based on the primary endpoint, total 6-month health care costs. A total of 150 participants were recruited in the Neurology group and 99 participants in the MRI group to achieve a detection a cost difference of £300 assuming standard deviations of £750 and £500, respectively, with 85% power at the 5% two-sided significance level. A 20% increase in sample size due to unknown cost distribution and attrition rate was considered.

Results

A total of 249 participants were recruited, 150 in the Neurology group and 99 in the MRI group. 100% (n=128) and 97% (n=96) of participants recruited received the treatment allocation in the Neurology and the MRI group, respectively (Figure 2). With regards to the follow-up duration, 15% (n=22) and 4.0% (n=4)

participants withdrew from the Neurology and MRI group, respectively, and were considered lost to follow-up. Remaining participants (n=223) were included in the analysis, equivalent to 128 (85%) and 95 (96%) participants in the Neurology and MRI group, respectively.

Baseline socio-demographic, clinical variables and resource use in the twelve months pre-recruitment are detailed in Table 1. A higher proportion of females were recruited to the Neurology group compared to the MRI group (81% vs 68%, p=0.039). Both groups were similar in mean age, ethnic mix, with more than half being White. No significant differences between the groups were found in terms of highest qualification and employment, with high-school and full-time employment being the most common. In terms of clinical variables, no significant difference between groups were found in terms of number of active health problems or number of headache triggers. Participants in the Neurology group reported lower utility and health scores using the generic EQ-5D-5L questionnaire, with a statistically significant difference in health scores (p=0.005). Lower health scores imply lower self-rated quality of life, while for the headache-specific questionnaires [Headache Impact Test (HIT-6) and Migraine Disability Assessment (MIDAS)], a higher score implies a higher headache burden. Compared to the MRI group, participants in the Neurology group reported significantly higher headache burden (HIT-6 mean score: 65 vs 63, p=0.006), number of headache days in the past 3 months (MIDAS questionnaire: 52 vs 43, p=0.038). Participants in the Neurology group also had significantly more primary care appointments (3.7 vs 2.4, p<0.001) and all NHS appointments (4.3 vs 2.5, p<0.001).

Service use

Table 2 summarises the NHS resource use of primary care and hospital-based services over a period of 12 months following recruitment. With regards to primary care utilisation, participants in the Neurology group had a significantly higher number of GP face-to-face appointments (mean number per participant: 1.82 vs 1.19, p=0.006). Regarding secondary care, participants in the Neurology group had a higher mean number of outpatient appointments (2.52 vs 0.26, p<0.001) and other treatments such as Botox and nerve root injection (mean 0.30 vs 0.05, p<0.001). In contrast, they had a lower mean number of brain MRIs (0.59 vs 1.05, p<0.001). There were no statistically significant differences in the utilisation levels of any of the other healthcare events.

The NHS resource use pre and post-recruitment for both groups was also compared. Table 3 summarises the difference between headache-related events 12 months post-recruitment compared to the 12 months pre-recruitment. A reduction of 197 and 87 GP visits (mean 1.54/0.92 per participant or a percentage reduction of 85%/77%) was noted in the Neurology and MRI group, respectively. Similarly, there was a reduction in emergency department utilisation with a decrease of 23 and 6 episodes (mean 0.18 and 0.07 per participant or a percentage reduction of 288% and 120%) in the Neurology and MRI group, respectively.

Cost analyses

The mean (SD) cost management per participant at 6 months post-recruitment was lower in the MRI group compared to the Neurology group [£245 (£172) vs £578 (£420)], leading to a mean cost difference between groups of -£333 per participant (95% CI: -£413 to -£253, p<0.001). The MRI group had a higher proportion of participants with lower costs (£0 to £250 range) than the Neurology group (73% vs 4.7%). The initial cost analysis was extended to 12 months post-recruitment and the mean cost difference between groups increased, with the MRI group generating cost savings of £518 per participant (95% CI: -£637 to -£401, p<0.001).

Given the non-randomised study design, an additional GLM analysis was performed to adjust for baseline characteristics. The unadjusted 6-month cost difference between groups (-£333; 95% CI: -£413, -£253) hardly changed after adjustment (-£308; 95% CI: -£408, -£209). In all analyses, at both 6 and 12 months post-recruitment, direct access to MRI for the management of chronic headache was associated with statistically significant mean cost savings for the NHS.

Abnormal findings in the MRI group

Out of the 95 participants recruited in the MRI group, three MRIs were not performed during the initial appointment due to claustrophobia events. From a total number of 92 MRIs, 85 (92%) were normal and 7 (7.6%) presented abnormal findings (Table 4), with one diagnosis being particularly significant (two small intracranial aneurysms). This participant was referred to neurovascular team for assessment, at which point no intervention was performed during the follow-up period (participant included in an active surveillance group). Two other participants had a change in their clinical management for less significant findings, leading to either a follow-up appointment or scan. No brain malignancies were diagnosed.

Access to care

The mean time (SD) elapsed from GP referral to the initial Neurology and MRI scan was, respectively, 110 (35) days and 39 days (17), a statistically significant difference (p<0.001). Second, if the MRI report, than the actual scan, is considered as a proxy for access to care, the mean time elapsed was 70 days (35) (p<0.001).

Change in management

Participants in the Neurology group were more likely to have a change in therapeutic management compared to participants in the MRI group (97% vs 64%, p<0.001). Similarly, among participants that had not started on preventative medication pre-recruitment, a higher proportion of participants in the Neurology group were started on preventative medication as part of their clinical management (93% vs 53%, p<0.001).

Quality of life and headache burden

At baseline, mean utility was lower in the Neurology group but not significant (mean utility of 0.809 vs 0.830, p=0.097), while their self-perceived mean health score was significantly lower (EQ-5D-5L: visual analogue scale score of 64.0 vs 70.8, p=0.005) (Table 5). There was no statistically significant differences between the groups at 6 months for to the utility and self-reported healthcare scores.

At baseline, participants in the Neurology group presented a higher headache burden compared to the MRI group (mean score of 65.0 vs 62.6, p=0.006) (Table 5). This trend seemed to be maintained over the follow-up period but was difficult to interpret due to high attrition rates: mean HIT-6 score at 6 months (60.0 vs 53.1, p=0.968). At baseline, participants in the Neurology group had higher headache severity compared to the MRI group, but this was not significant (mean MIDAS score of 57.8 vs 44.8, p=0.075) (Table 5). In both groups the headache severity decreased over the follow-up period. At baseline, participants in the Neurology group reported a significantly higher mean number of headache days compared to the MRI group (51.6 vs 42.8, p=0.038). This trend was observed at month 6 but was not significant (41.2 vs 26.5, p=0.152). A third variable assessed self-reported headache pain scores. At baseline, participants at baseline showed almost identical mean headache pain scores (6.9 vs 6.9, p=0.827). During the follow-up period, no statistical differences were found at month 6 (4.5 vs 4.2, p=0.663).

Time off work

Participants in the Neurology group (n=83) had higher mean number of days off work due to headache compared to participants in the MRI group (n=35) but these were not statistically significant at 6 (13.9 vs 9.7, p=0.563) or 12 months (27.9 vs 19.1, p=0.808) post-recruitment.

Patient satisfaction

Patient satisfaction was evaluated at month 3 post-recruitment using a non-validated questionnaire (Appendix I). Participants in both groups reported no difference in terms of receiving an appointment in a suitable timeframe (p=0.193). Participants in the MRI group reported higher satisfaction levels (p=0.005) compared to the Neurology group associated with the information received prior to the actual appointment. No statistically significant difference (p=0.366) between the groups was found regarding the satisfaction levels of both appointments (either MRI scan or Neurologist appointment) but a higher proportion of participants in the Neurology group reported a better experience compared to their expectation (p=0.002). At month 3 post-recruitment in all variables, except frequency of appointments (p=0.166), participants in the Neurology group reported higher levels of satisfaction with: amount of time spent with clinical staff (p=0.001); consistency of care (p=0.028); how informed you felt about your condition (p=0.010) / your treatment (p=0.004); and the overall experience (p<0.001).

Discussion

Previous UK studies assessed the use of direct access to advanced imaging in the management of chronic headache patients [10, 21]. Howard et al. (2005) performed a randomised controlled trial, which showed that the use of imaging in patients led to a reduction of referral rates to Neurology services in secondary care from 23% to 1.3% (1/76) in the treatment group (i.e. patients being scanned) [21]. Thomas et al. (2010) estimated that direct access to brain imaging, in this case CT, reduced referral rates to Neurology in 86% of the cases during the follow-up period (average of 1.3 years per patient) [10].

The study's underlying hypothesis was that the early use of an advanced and accurate diagnostic tool (in this case MRI) would reassure both patients and GPs that no serious underlying cause (particularly brain tumour) is present. This would in turn reduce the headache burden and NHS resource use associated with the patient's subsequent management. Given the high prevalence of headache and the increased referral of patients with chronic headaches and other neurological conditions from primary care to hospital based care [7], it is relevant to assess the implications of using different management strategies. To our knowledge, no previous prospective study in the UK has assessed the economic implications of these two coexisting management strategies based on GP referral decision.

The primary outcome was total costs at six months post-recruitment. The study showed that the use of advanced imaging produced cost-savings to the NHS compared to referral to Neurology, with mean cost-savings per participant of £333 and £518 at month 6 and 12 post-recruitment, respectively ($p<0.001$). These cost differences were multifactorial but primarily driven by: (i) the lower unit cost of a brain MRI scan (£146) compared to the initial Neurology appointment (£240); (ii) the lower number of outpatient appointments in the MRI group (25 vs 322); (iii) the fact that 75/128 (59%) of participants in the Neurology group ended up having a brain MRI scan in the 12-month period of follow-up; and (iv) the increased likelihood of patients in the Neurology arm receiving management with Botox injections or nerve block procedures (39 vs 5 events). Direct access to brain MRI seemed to reassure most participants as only 17 (18%) participants in the MRI group ended up being referred to a neurologist. Furthermore over 66% of participants in the MRI group had no further hospital-based care, compared to 5% in the Neurology group. Similarly, at primary care level, participants in the MRI group presented lower utilisation rates per participant when compared to the Neurology group (mean GP appointments of 1.82 vs 1.19, $p=0.006$). In order to mitigate the potential confounding by indication introduced by GPs referring patients to both clinical pathways, adjusted GLMs were conducted. All cost differences between groups remained statistically significant ($p<0.001$) when adjusted for differences in baseline characteristics or follow-up attrition rates.

At baseline, participants in the Neurology group presented lower self-reported quality of life and higher headache burden. HIT-6 scores did improve over time but we were unable to assess whether there was a statistically significant difference in both groups due to the high attrition rates, particularly in the MRI group. As mentioned, out of the 95 participants recruited to the MRI group, 17 (18%) were subsequently referred to a Neurologist. Interestingly, at baseline, these 17 patients reported higher headache burden compared

to all 95 patients recruited to the MRI group (MIDAS score: 51.2 vs 44.8; MIDAS headache days: 55.8 vs 42.8). This finding seems to suggest that this data might be useful to risk stratify patients and support GPs in their referral criteria. However, further research into this area is required.

Participants in the Neurology group presented a higher probability of being started on a preventative medication and had a change in therapeutic management following referral from primary care. A small proportion (7.6%) of participants in the MRI group had abnormal findings in the initial brain MRI. Only one participant had clinically significant lesions (two small aneurysms) which were also incidental and no brain tumour was diagnosed.

Time off work was also evaluated as a proxy of headache burden. Participants in the Neurology group presented a trend ($p>0.05$) of higher number of days off work due to headache compared to participants in the MRI group. This difference was not however statistically significant.

Lastly, patient satisfaction in both groups was compared based on three dimensions of analysis: during the referral period, the initial appointment and overall satisfaction. Twenty five percent of participants in the Neurology group (vs 18% in the MRI group) reported dissatisfaction with the waiting time. This finding is not unexpected as the mean waiting time associated with the Neurology appointment was almost three times of the one associated with the MRI scan (110 vs 39 days). Contrary to the referral period, participants in the Neurology group reported trends of higher satisfaction levels associated with the first appointment (neurology outpatient visit vs MRI scan) and a better experience compared to their expectations (60% vs 29% in the Neurology and MRI group, respectively). Participants in the Neurology group reported improved satisfaction levels at 3 months across different variables (time spent with clinician, consistency of care, information about the condition and its treatment). Almost three quarters of Neurology participants reported being satisfied or very satisfied with their headache management compared to only 21% in the MRI group ($p<.001$). Both participants and GP referrers in the MRI group reported dissatisfaction associated with the waiting time elapsed between the MRI scan and the availability of results (mean time of 31 days). This might have contributed to increased anxiety in some participants.

Strengths of this study:

The estimate of NHS resource use data was primarily based on comprehensive and complete data retrieved from hospital-based databases that captured both the acute and elective elements of the pathway associated with the management of patients with chronic headache. This data was supplemented by both primary care utilisation data, collected from each participant's GP, and self-reported participant data. The aim was to guarantee that any chronic headache related NHS event was costed regardless of the healthcare provider and its location. The prospective collection of health care utilisation and the evaluation of the impact of the interventions across different dimensions of analysis (efficiency, quality of care, access to care and patient satisfaction) were other key factors that contributed to the overall strength of the study.

Limitations of this study:

There were some limitations to this study. First, this was a single-centre study with participants recruited from one central hospital in London. A multi-centre study would be necessary to explore the generalisability of the results. Second, as with any observational study, no randomisation between groups was performed and there were significant differences in baseline of headache burden and health-scores and utilisation of resources. In order to mitigate potential confounding factors, adjusted multivariate analyses showed that the primary outcome was hardly affected and remained statistically significant. Nevertheless, residual confounding factors remain a limitation of the study. Third, specific inclusion and exclusion criteria were considered and as such the study sample might not be representative of all patients with chronic headache. Fourth, for the purpose of secondary outcomes, most data was self-reported and hence prone to recall bias. Lastly, there were high follow-up attrition rates particularly for participants in the MRI group, which affected some of the study's secondary outcomes.

Conclusions

This study found that the referral from primary care to direct access to brain MRI compared to referral for a neurologist for patients with chronic headache was associated with lower NHS overall costs at 6 and 12 months post-recruitment. Despite waiting longer from referral to appointment, participants in the Neurology group reported higher satisfaction levels associated with the care received compared to the MRI group and were more likely to benefit from changes to their therapeutic management.

Implications for further research and clinical practice

Baseline measures of headache burden, such as the HIT-6 or MIDAS, could potentially be used to determine which pathway may be suitable for patients but further research into the risk stratification of chronic headache patients is required. Future study designs should consider the confounding by indication introduced by recruiting participants referred to the two pathways based on GP decision. With regards to clinical practice, and based on the study findings, we plan to provide GPs with headache management advice along with the MRI report.

Author contributions:

Conception and design: T. Rua, A. A. Mazumder, Y. Akande, J. Turville, R. Razavi, JL. Peacock, P. McCrone, S. K. Afridi

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Figure 1. High-level illustration of two existing clinical pathways associated with the referral from GP due to chronic headache.

Figure 2. Participant flow chart for the headache study.

Table 1. Baseline characteristics of the population analysed.

Variable	Neurology group (n=128)	MRI group (n=95)	p-value
Age, years: mean (SD)	38.4 (14.1)	40.0 (14.6)	0.514
Gender Female, n (%)	103 (81)	65 (68)	0.039
Ethnicity			0.079
Asian	13 (10)	6 (6.3)	
Black	40 (31)	17 (18)	
White	68 (53)	60 (63)	
Mixed	5 (3.9)	8 (8.4)	
Other	2 (1.6)	4 (4.2)	
Qualification, n (%)			0.565
Advanced work or PhD	3 (2.3)	4 (4.2)	
Master's Degree	15 (12)	12 (13)	
Bachelor's Degree	31 (24)	29 (31)	
High School	57 (45)	33 (35)	
Did not finish High School	8 (6.3)	10 (11)	
Prefer not to answer	14 (11)	7 (7.4)	
Employment, n (%)			0.839
Employee in full time job (30 hours or more a week)	50 (39)	36 (38)	
Employee in part-time job (under 30 hours a week)	18 (14)	18 (19)	
Self-employed, full or part time	12 (9.4)	8 (8.4)	
Full-time education at school, college or university	16 (13)	9 (9.5)	
Doing something else	2 (1.6)	2 (2.1)	
Permanently sick/ disabled	8 (6.3)	6 (6.3)	
Looking after the home	4 (3.1)	6 (6.3)	
Unemployed and available for work	12 (9.4)	6 (6.3)	
Wholly retired from work	4 (3.1)	4 (4.2)	
Prefer not to answer	2 (1.6)	0 (0)	
Presence of mental health condition, n (%)	22 (17)	11 (12)	0.243
Number of active health problems: mean (SD)	2.0 (1.5)	1.8 (1.4)	0.277
Number of headache triggers: mean (SD)	2.1 (1.8)	1.8 (1.4)	0.378
Self-reported questionnaires			
EQ-5D-5L: mean utility (SD)	0.809 (0.182)	0.830 (0.195)	0.097
EQ-5D-5L: mean score (SD)	64 (19)	71 (20)	0.005
HIT-6: mean score (SD)	65 (5.3)	63 (7.3)	0.006
MIDAS, mean score (SD)	58 (54)	45 (45)	0.075
MIDAS, mean headache days (SD)	52 (32)	43 (31)	0.038
MIDAS, mean pain score (SD)	6.9 (1.8)	6.9 (1.9)	0.778
Resource use in the 12 months prior to recruitment			
GP appointments: mean (SD)	3.7 (2.9)	2.4 (1.5)	<0.001
All NHS events: mean (SD)	4.3 (3.7)	2.5 (1.5)	<0.001

SD= Standard deviation; EQ-5D-5L - 5 level EQ-5D; HIT-6 = headache impact test; MIDAS = Migraine Disability assessment scale

Table 2. Breakdown of number of NHS appointments per type of activity organised per group and respective number of participants responsible for these appointments (12 months post-recruitment).

	Neurology group (n=128)			MRI group (n=95)			p-value
Type of NHS appointment	**Total of episodes**	**Mean (SD)**	**N (%)**	**Total of episodes**	**Mean (SD)**	**N (%)**	
Primary Care services							
GP face-to-face appointment	233	1.82 (2.11)	91 (71)	113	1.19 (1.64)	57 (60)	0.006
GP phone appointment	37	0.29 (0.75)	24 (19)	25	0.26 (0.49)	23 (24)	0.420
Hospital based services							
Hospital outpatient appointment	322	2.52 (1.19)	128 (100)	25	0.26 (0.55)	20 (21)	<0.001
Inpatient episode	4	0.03 (0.35)	1 (0.8)	1	0.01 (0.10)	1 (1.1)	0.837
Emergency Department episode	8	0.06 (0.24)	8 (6.3)	5	0.05 (0.22)	5 (5.3)	0.756
Head CT	1	0.01 (0.09)	1 (0.8)	1	0.01 (0.10)	1 (1.1)	0.832
Brain MRI	75	0.59 (0.49)	75 (59)	100	1.05 (0.30)	95 (100)	<0.001
Others (e.g. botox and nerve injection treatments)	39	0.30 (0.79)	25 (20)	5	0.05 (0.30)	3 (3.2)	<0.001

Table 3. Difference in the number, mean and percentage reduction of NHS appointments per type of activity organised per group 12 months post-recruitment compared to the 12 months pre-recruitment (note: a negative/positive percentage denotes a decrease/increase in activity following recruitment).

	Neurology group (n=128)			MRI group (n=95)		
Type of NHS appointment	**Total of episodes**	**Mean**	**%**	**Total of episodes**	**Mean**	**%**
Primary Care services						
GP face-to-face appointment	-197	-1.54	-85%	-87	-0.92	-77%
GP phone appointment	-11	-0.09	-30%	5	0.05	20%
Hospital-based services						
Hospital outpatient appointment	301	2.36	93%	23	0.24	92%
Inpatient episode	3	0.02	75%	1	0.01	100%
Emergency Department episode	-23	-0.18	-288%	-6	-0.07	-120%
Head CT	-9	-0.07	-12%	1	0.01	1.0%
Brain MRI	55	0.43	141%	100	1.05	N/A

Table 4. Description of incidental findings, its clinical relevance and subsequent pathway.

Abnormal findings	**Significant (Yes/No)?**	**Changes in diagnostic or treatment pathway**
Mature striatocapsular lacune	No	
Sinusitis with complete opacification	No	ENT review only.
Pituitary abnormality (T1)	No	
Low lying cerebellar tonsils	No	
Previous petrous surgery noted	No	
Two aneurysms AcomA (anterior communicating artery) and right ICA	Yes	Referred to neurovascular – no coiling (no intervention).
No definitive lesion	No	Follow-up MRI only.

Table 5. Descriptive statistics for one generic questionnaire (EQ-5D-5L) and two headache-specific questionnaires (HIT-6 and MIDAS) at baseline and 6 months post-recruitment.

				N	Mean	Standard Deviation	p-value
BASELINE	**EQ-5D-5L**	Utility	Neurology	127	0.809	0.182	0.097
			Radiology	95	0.830	0.195	
		Score	Neurology	126	64.0	18.8	0.005
			Radiology	95	70.8	20.2	
	HIT-6	Score	Neurology	128	65.0	5.3	0.006
			Radiology	92	62.6	7.3	
	MIDAS	Score	Neurology	124	57.8	54.0	0.075
			Radiology	90	44.8	44.9	
		Headache days	Neurology	124	51.6	31.5	0.038
			Radiology	90	42.8	30.7	
		Pain score	Neurology	124	6.9	1.8	0.778
			Radiology	90	6.9	1.9	
MONTH 6	**EQ-5D-5L**	Utility	Neurology	55	0.770	0.263	0.243
			Radiology	26	0.681	0.346	
		Score	Neurology	53	68.2	20.6	0.463
			Radiology	23	62.5	24.7	
	HIT-6	Score	Neurology	35	60.0	8.7	0.968
			Radiology	12	53.1	22.8	
	MIDAS	Score	Neurology	32	52.6	58.1	0.827
			Radiology	12	40.7	36.0	
		Headache days	Neurology	46	41.2	28.6	0.152
			Radiology	15	26.5	28.1	
		Pain score	Neurology	44	4.5	2.3	0.663
			Radiology	15	4.2	2.0	

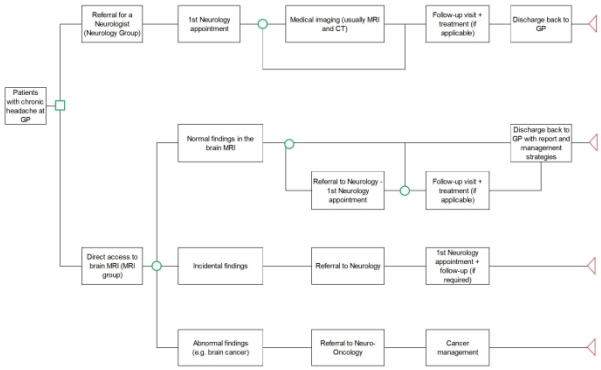

Figure 1. High-level illustration of two existing clinical pathways associated with the referral from GP due to chronic headache.

338x190mm (300 x 300 DPI)

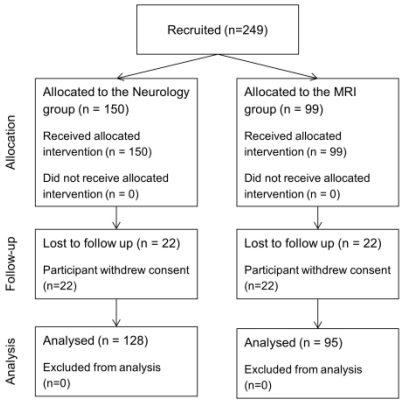

Figure 2. Participant flow chart for the headache study.

338x190mm (300 x 300 DPI)

Appendix I. Patient satisfaction.

This questionnaire evaluated three dimensions of analysis: (a) referral process (time elapsed between referral from primary care to initial secondary care appointment); (b) initial appointment; and (c) overall experience three months after recruitment.

(a): Patient experience questionnaire associated with the referral process to either Neurology (n=99) or Radiology (n=79).

		Not sure		Yes		No		p-value
		N	%	N	%	N	%	
Did you receive your appointment within a timeframe acceptable to you?	Neurology (n=99)	8	8.1%	66	67%	25	25%	0.193
	Radiology (n=79)	3	3.8%	62	79%	14	18%	

		Very satisfied		Satisfied		Neutral		Dissatisfied		Very dissatisfied		p-value
		N	%	N	%	N	%	N	%	N	%	
How satisfied were with the information you received beforehand?	Neurology (n=98)	25	26%	48	49%	22	22%	3	3.1%	0	0%	0.005
	Radiology (n=79)	38	50%	24	32%	10	13%	2	2.6%	2	2.6%	

(b): Patient experience questionnaire associated with either the Neurology (n=99) or the Radiology (n=50) appointment.

		Very satisfied		Satisfied		Neutral		Dissatisfied		Very dissatisfied		p-value
		N	%	N	%	N	%	N	%	N	%	
How you found the process overall?	Neurology (n=98)	55	56%	36	36%	5	5.1%	3	3.0%	0	0%	0.366
	Radiology (n=50)	27	54%	22	44%	0	0.0%	1	2.0%	0	0%	

		A better experience		About the same as expected		A worse experience		p-value
		N	%	N	%	N	%	
How did you find the experience in comparison to what you had expected?	Neurology (n=95)	57	60%	35	37%	3	3.2%	0.002
	Radiology (n=45)	13	29%	31	69%	1	2.2%	

(c): Overall patient experience questionnaire at 3 months post-recruitment with either the Neurology (n=56) or the Radiology (n=14) appointment.

		Very satisfied		Satisfied		Neutral		Dissatisfied		Very dissatisfied		p-value
		N	%	N	%	N	%	N	%	N	%	
Amount of time spent with clinical staff	Neurology (n=56)	20	36%	30	54%	6	11%	0	0%	0	0%	0.001
	Radiology (n=14)	3	21%	3	21%	5	36%	1	7.1%	2	14%	
Consistency of care	Neurology (n=29)	16	55%	0	0%	12	41%	1	3.4%	0	0%	0.028
	Radiology (n=14)	2	14%	3	21%	6	43%	2	14.3%	1	7.1%	
Frequency of appointments	Neurology (n=55)	9	16%	19	35%	22	40%	4	7.3%	1	1.8%	0.166
	Radiology (n=14)	2	14%	1	7.1%	7	50%	3	21%	1	7.1%	
How informed you felt about your condition	Neurology (n=54)	15	28%	24	44%	9	17%	5	9.3%	1	1.9%	0.010
	Radiology (n=13)	2	15%	2	15%	5	39%	1	7.7%	3	23%	
How informed you felt about your treatment	Neurology (n=55)	15	27%	18	33%	17	31%	4	7.3%	1	1.8%	0.004
	Radiology (n=14)	1	7.1%	1	7.1%	5	36%	5	36%	2	14%	
Your overall experience	Neurology (n=55)	13	24%	32	58%	7	13%	3	5.5%	0	0%	<0.001
	Radiology (n=14)	2	14%	1	7.1%	9	64%	1	7.1%	1	7.1%	

Reporting checklist for quality improvement study.

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	Reporting Item	Page Number
Title		
#1	Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patientcenteredness, timeliness, cost, efficiency, and equity of healthcare)	1

Abstract			
	#02a	Provide adequate information to aid in searching and indexing	4
	#02b	Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions	4
Introduction			
Problem description	#3	Nature and significance of the local problem	6
Available knowledge	#4	Summary of what is currently known about the problem, including relevant previous studies	6
Rationale	#5	Informal or formal frameworks, models, concepts, and / or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work	6-7
Specific aims	#6	Purpose of the project and of this report	7
Methods			
Context	#7	Contextual elements considered important at the outset of introducing the intervention(s)	7
Intervention(s)	#08a	Description of the intervention(s) in sufficient detail that others could reproduce it	7

Intervention(s)	#08b	Specifics of the team involved in the work	7
Study of the Intervention(s)	#09a	Approach chosen for assessing the impact of the intervention(s)	7-8
Study of the Intervention(s)	#09b	Approach used to establish whether the observed outcomes were due to the intervention(s)	8-9
Measures	#10a	Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability	7-8
Measures	#10b	Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost	7-8
Measures	#10c	Methods employed for assessing completeness and accuracy of data	7-8
Analysis	#11a	Qualitative and quantitative methods used to draw inferences from the data	8-9
Analysis	#11b	Methods for understanding variation within the data, including the effects of time as a variable	8-9
Ethical considerations	#12	Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest	7

Results

	#13a	Initial steps of the intervention(s) and their evolution over time (e.g., time-line diagram, flow chart, or table), including modifications made to the intervention during the project	9, 17,18
	#13b	Details of the process measures and outcome	10, 11,19
	#13c	Contextual elements that interacted with the intervention(s)	
	#13d	Observed associations between outcomes, interventions, and relevant contextual elements	10,11,20-,23
	#13e	Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s).	
	#13f	Details about missing data	9
Discussion			
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Summary	#14b	Particular strengths of the project	14
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Interpretation	#15b	Comparison of results with findings from other publications	12
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