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Prescribing trends over time by non-medical independent prescribers (NMIPs) in primary care settings across Wales (2011-2018): a secondary database analysis

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ABSTRACT

Introduction: As of 2015, as part of the implementation of the Welsh Government Primary Care Plan and primary care clusters the Welsh Government has encouraged non-medical healthcare professionals working in primary care to train as independent prescribers (IPs).

Objectives This research aimed to identify the number of non-medical independent prescribers (NMIPs) and their associated trend of prescribed items in primary care in Wales between 2011 and 2018, which incorporates the period when primary care clusters came into practice.

Design Retrospective secondary data analyses and Autoregressive Integrated Moving Average Interrupted Time Series analyses in order to compare prescribing by NMIPs pre and post-implementation of primary care clusters between HBs, as well as all Wales.

Results Over the study period, 600 NMIPs (nurses n=474 and pharmacists n=104) had prescribed at least one item. The number of nurse IPs increased by 108% and pharmacists by 325% (pharmacists had the largest increase between July 2015 and March 2018). The total number of items/100,000 population per year prescribed by NMIPs increased over time by 200% and the largest increase was between the end of 2015 and March 2018 (90%). The differences in pre and post-implementation of primary care clusters of the prescribing trends by NMIPs in all Wales, as well as in Betsi Cadwaladr University Health Board (HB), Aneurin Bevan University HB, Cardiff and Vale University HB, Hywel Dda University HB and Powys Teaching HB were statistically significant (p value < 0.05).

Conclusion The number of NMIPs and their volume of prescribing in primary care in Wales has increased, with the largest increase for pharmacist IPs occurring post 2015. This suggests that the Government's recommendations of utilising NMIPs in primary care have been implemented. Future studies should focus on efficiency and quality of prescribing by NMIPs in primary care.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study that has used a secondary database analysis, which has provided insights and empirical findings on the prescribing pattern of medicines by non-medical independent prescribers (NMIPs) over time in primary care in Wales.
- Although this study has achieved its aim and objectives, it has a number of limitations. Firstly, the data provided via the CASPA software system was limited to the last seven years. Secondly, this system was designed for financial reimbursement purposes for community pharmacies, which means that holding investigations at the level of patients or prescribers, such as stopping or changing patients' medications, as well as clinical safety issues or other prescribing activities, were not possible. In addition, this system only captured prescriptions that were dispensed in community pharmacies. Therefore, prescriptions issued by those prescribers that have not been dispensed were not captured by the system. Finally, the professions of NMIPs as pharmacist, nurse, physiotherapist or other were not identified on the prescriptions and, consequently, in the CASPA system.
- The limitation of the retrospective ARIMA design is considered the major one in this study because of the lack of the researcher control over the exposure to the intervention. In addition, unknown confounding variables, which are outside of the researcher's control, may have happened at the same time of the intervention and this leads to the difficulty of establishing causal effects[45]. However, the ARIMA analysis has the strength of evaluating data at the whole population level[46], which allowed the researchers to evaluate the utilisation of NMIPs in primary care across all of Wales.

INTRODUCTION

The right to prescribe medicines was traditionally restricted to physicians, dentists and veterinary surgeons[1]. Prescribing practice has changed over the last 50 years to involve not only physicians and dentists (medical prescribers) but also other health care professionals, known as non-medical prescribers. The adoption of non-medical prescribing fundamentally began in the USA in the 1960s[2] and has extended to the UK, Canada, New Zealand, Australia, and other European and African nations[3]. Beyond the UK, solely nurses and pharmacists have been granted the authority to prescribe medicines collaboratively (dependently) under a physician's supervision or independently from a limited lists of medicines[4-7]. The drive to extend the medicines prescribing mandate to non-medical healthcare professionals was related to a variety of aspects within every nation.

In the UK, non-medical prescribing was introduced as part of the National Health Service (NHS) plans, which intended to improve and modernise the health care system[8,9]. The aim of introducing non-medical prescribing was to enhance patient care and safety, improve patient access and choice of appropriate medicines for their conditions, use the already gained skills of health care professionals in the most effective way, and promote a more flexible teamwork environment in the NHS[10]. Pharmacists, nurses, and Allied Health Professionals (AHPs) can qualify as non-medical prescribers after completing an advanced prescribing training programme[10]. This programme lawfully allows these healthcare professionals to prescribe medicines, appliances, and wound dressings as either independent or supplementary prescribers within their clinical area of competence.

Independent prescribing is defined as 'prescribing by a practitioner (e.g. a doctor, dentist, nurse, or a pharmacist) responsible and accountable for the

assessment of patients with undiagnosed or diagnosed conditions and for decisions about the clinical management required, including prescribing'[10]. Whereas, supplementary prescribing is a 'voluntary partnership between the responsible independent prescriber and a supplementary prescriber, to implement an agreed patient-specific clinical management plan with the patient's agreement, particularly but not only in relation to prescribing for a specific non-acute medical condition or health need affecting the patient'[11]. Non-medical independent prescribing was introduced in the UK in 2002 after a change in the legislation made by the UK Government allowing the first level registered nurses who have at least 3 years of experience to prescribe independently from a limited list of medicines[12]. In 2006, independent prescribing extended for qualified nurses and pharmacists who completed the necessary training to prescribe any medicines within their area of competence with few exceptions[10]. This was followed by the introduction of optometrist independent prescribing in 2007[13], and more recently, independent prescribing by AHPs including podiatrists and physiotherapists independent prescribing in 2013[14], and therapeutic radiographers independent prescribing in 2016[15]. In 2017, the estimated number of non-medical independent prescribers (NMIPs) in the UK was as follows: 30,000 nurse independent prescribers (IPs); 3,000 pharmacist IPs and 600 AHP IPs[16]. All NMIPs are responsible and accountable for their own prescribing and limiting their prescribing to their therapeutic area of expertise[9]. Moreover, these healthcare professionals are required to seek appropriate advice or referral if they lack the confidence to manage patients' conditions or prescribe the suitable medicines for their patients[9].

In Wales, the NHS provides its services via three NHS Trusts and seven health boards (HBs). The seven HBs are Swansea Bay University HB (SBUHB), Cardiff and

Vale University HB (CVUHB), Cwm Taf Morgannwg University HB (CTMUHB), Hywel Dda University HB (HDUHB), Powys Teaching HB (PTHB), Betsi Cadwaladr University HB (BCUHB) and Aneurin Bevan University HB (ABUHB). The SBUHB was formerly known as Abertawe Bro Morgannwg University HB (ABMUHB), having being renamed in 2019.

Primary health care services are the initial point of care for patients in the NHS. In Wales, it has been estimated that around 90% of people's contact with the NHS is with primary care services with General Practices the main point of contact[17]. In 2016, there were 441 General Practices in Wales and 2,009 General Practitioners (GPs) (excluding, locums, retainers, and registrars)[18]. The Welsh Government and HBs have focused upon improving primary care services[17] and this has included the development of primary care clusters. Clusters comprise groups of adjacent general practices that have linked together to provide advanced medical services locally in order to relieve pressure on hospitals[19]. The aims of these clusters include improving patients' access to their medicines and information as well as the provision of advice and support to manage medicines. These clusters came into being in the last quarter of 2015[19]. Currently, there are 64 primary care clusters in Wales which provide services for a population of 30,000 to 50,000 patients per cluster[19]. In order to overcome GP shortages[20,21], these clusters are supported by high numbers of hospital pharmacists, nurses and other professionals. In addition, the Welsh Government and HBs have prioritised funding for new posts and training of other health care professionals, such as pharmacist and nurse IPs[17]. Consequently, the number of non-medical prescribers in primary care has increased in recent years and is expected to rise further[16,21].

Only one published study has investigated the implementation of non-medical

prescribing in Wales[16]. This study aimed to provide an overview of the implementation and utilisation of non-medical prescribing in all health care sectors through a national questionnaire survey. The results of this study indicated that the majority of non-medical prescribers in Wales were based in secondary care settings. Moreover, these researchers stated that the utilisation of non-medical prescribers across Wales, particularly in primary care, was inconsistent and had not been implemented in all services. In addition, it was suggested that there was a need to investigate and recognise the development of primary care services in Wales, with support required for non-medical prescribers[16].

The aim of this study was to describe changes in the number of NMIPs in Wales and their prescribing volume (from April 2011 to March 2018) as a whole, as well as within the seven HBs, before and after the implementation of primary care clusters. This is the first study in Wales to use data obtained through a national database to review prescribing volume by NMIPs in primary care. No equivalent studies have been published internationally.

METHODOLOGY

The study design was a retrospective secondary data analysis of monthly data for prescriptions issued by NMIPs in primary care in Wales and dispensed in community pharmacies, as well as the data on the number of NMIPs within primary care in Wales.

The number of NMIPs who prescribed each month and who prescribed at least one item from April 2011 to March 2018 was obtained through the NHS Wales Shared Services Partnership, Primary Care Services. Prescribing data were obtained from the Comparative Analysis System for Prescribing Audit (CASPA) software system (Version 5), provided by the NHS Wales Shared Services. Data were fully anonymised and recorded as part of routine practice, as such, the study did not require ethical approval. CASPA records all dispensed WP10 prescriptions (Welsh prescriptions for use in primary care), to allow financial reimbursement to community pharmacies[9]. Whilst it is acknowledged that dispensing may not fully reflect prescribing, due to patients not taking their prescriptions to a pharmacy for dispensing, the impact of this is likely to be small[22], and therefore dispensing was used as a surrogate marker for prescribing in this study.

The number of items refers to a single item prescribed by a prescriber on a prescription form[23]. All recorded WP10 prescriptions issued by GPs and NMIPs in Wales and dispensed by community pharmacists from April 2011 to March 2018 were extracted and included in the study. The number of prescribed items by NMIPs were extracted from the CASPA system on a monthly basis, the total number of items per 100,000 population per year (the population data in Wales as a whole and in each HB obtained from the Welsh Government Stats Wales[24]) was calculated in order to illustrate changes in the prescribing rate in each financial year (April to March).

Percentages were calculated for the total number of prescribed items by NMIPs in each HB. The name of ABMUHB was used to illustrate the findings in this HB as this was its name over the study period.

Although Randomised Controlled Trails (RCTs) are considered the gold standard method to evaluate longitudinal effects of interventions over time[25-27], they lack the ability to evaluate the already implemented service retrospectively[27]. Therefore, prescribing data were compared by using a series of Autoregressive Integrated Moving Average (ARIMA) Interrupted Time Series (ITS) analyses. ITS analysis has been used to assess healthcare interventions over time in previous studies[26-30]. Cochrane Effective Practice and Organisation of Care (EPOC) guidance[31] was followed and IBM SPSS software (Version 25) was used to conduct the ARIMA statistical analysis.

The difference in slope between the pre and post-intervention (pre and post-implementation of primary care clusters) regression lines is the change in the trend of prescribing by NMIPs. In order to understand whether the changes in prescribing over time occurred at a gradual or abrupt onset, step changes were investigated at five time points after the intervention (3, 6, 9, 12 and 24-month time points). The step change, which is also known as the change in the level of prescribing by NMIPs, is the difference between the outcome at the first post-intervention time point and that anticipated by the pre-intervention trend. The findings were assumed significant at p value <0.05. Confidence intervals (CIs) were calculated in order to be 95% certain that the range of values contained the true mean of the data[32].

Data were organised in three periods as follows: pre-intervention phase (April 2011 to September 2015), intervention phase (October 2015 to December 2015) and post-intervention phase (January 2016 to March 2018). The Welsh Government

plan[17] encouraged local HBs to prioritise funding and development of primary care clusters. However, the implementation of these clusters is the responsibility of each individual local HB and there are no definitive time points of their establishment. To accommodate this, the researcher engaged with the relevant stakeholders (e.g. policy makers and Chief of Pharmaceutical Officer) to determine the appropriate length of an intervention phase. They agreed the intervention phase should be three months.

RESULTS

Trend of the total number of items prescribed by all prescribers

The total number of items prescribed by all health care professionals (GPs and non-medical prescribers) from April 2011 to March 2018 was 540,781,584 items (17,482,150 per 100,000 population). The total number of prescribed items per 100,000 population per year increased by 7.1% between 2011-2012 (n= 2,371,511) and 2014-2015 (n= 2,539,192) and increased by 0.7% between 2014-2015 (n= 2,539,192) and 2017-2018 (n= 2,556,784]) (Figure 1).

Trend of the total number of items prescribed by NMIPs

The total number of items prescribed by NMIPs in primary care in Wales between April 2011 and March 2018 was 5,088,405 items (n= 164,130 per 100,000 population). The number of items prescribed as a percentage of all items prescribed by all health care professionals (except items prescribed by dentists) increased from 0.57% in 2011-2012 to 1.7% in 2017-2018. The total prescribed items per 100,000 population per year increased from 2011-2012 (n= 13,622) to 2017-2018 (n= 40,1234) by 194.5%, while the largest increase was from the last quarter of 2015 to 17-18 (Figure 2).

The total number of NMIPs

Data obtained from the NHS Wales Shared Services Partnership shows that the total number of NMIPs who prescribed at least one item from April 2011 to March 2018 was 600 prescribers (474 nurses, 104 pharmacists, 21 physiotherapists and 1 with unknown profession). The number of NMIPs in each HB is illustrated in figure 3.

The number of prescribing NMIPs per month increased by approximately 140% between April 2011 (n=174) and March 2018 (n=414). Of those, the number of nurses increased from 158 in April 2011 to 328 in March 2018 (an increase of 108%). The number of pharmacists increased from 16 in April 2011 to 68 in March 2018 (an increase of 325%), the largest increase was from July 2015 (n=20) to March 2018 (n=68) by 240%. In January 2015, the first physiotherapist IP started to prescribe with the number increasing to 17 by March 2018.

Trend of the total number of prescribed items by NMIPs in different HBs pre and post-intervention

Table 1 presents the total number of items prescribed by NMIPs, as well as the number per 100,000 population and percentage of all items prescribed, per HB. Approximately one third of the items prescribed by NMIPs was within BCUHB (Table 1) with only 4% in PTHB. Figure 4 illustrates the trends of the total number of items per 100,000 population prescribed from April 2011 to March 2018. Table 2 summarises the eight ARIMA analyses findings, in order to compare between HBs, as well as all Wales. The positive values represent the increase in the average of the number of items prescribed by NMIPs per month, while the decrease is represented by negative values. The differences in pre and post-intervention of the prescribing trends of all Wales, as well as in BCUHB, ABUHB, CVUHB, HDUHB and PTHB were statistically significant (Table 2).

Table 1 Total number of items prescribed by NMIPs, as well as the number per 100,000 population and percentage of all items prescribed, per HB in primary care in Wales and dispensed in community pharmacies since April 2011 until March 2018

Number	Health Board	Total number of items prescribed by NMIPs	% of the prescribed items by NMIPs	Prescribed items by NMIPs per 100,000 population
1	BCUHB	1,711,949	33.64%	240,742.5
2	ABUHB	834,879	16.41%	139,396.5
3	CVUHB	711,805	13.99%	145,069.9
4	HDUHB	686,166	13.48%	172,782.9
5	ABMUHB	573,624	11.27%	106,813.2
6	CTMUHB	371,315	7.30%	122,620.2
7	PTHB	198,667	3.91%	137,000.6

ABMUHB (Abertawe Bro Morgannwg University HB); **ABUHB** (Aneurin Bevan University HB); **BCUHB** (Betsi Cadwaladr University HB); **CTMUHB** (Cwm Taf Morgannwg University HB); **CVUHB** (Cardiff and Vale University HB); **HDUHB** (Hywel Dda University HB); **PTHB** (Powys Teaching HB)

Table 2 Pre and post-intervention differences of the prescribing trends carried out by NMIPs in primary care in Wales. Statistically significant results (p value < 0.05 is significant) are in the white shading, whereas non-significant results are in the dark grey shading

Number	All Wales and HBs	Pre-intervention slope	Post-intervention slope	Difference in p value	95% CI
1	All Wales	497	1732	<0.001	1,016 to 1,454
2	BCUHB	243	430	0.014	38 to 337
3	ABUHB	110	245	0.001	54 to 217
4	CVUHB	6	68	0.043	13 to 122
5	HDUHB	45	431	<0.001	262 to 510
6	PTHB	-20	518	0.004	180 to 897
7	ABMUHB	75	140	0.188	-32 to 162
8	CTMUHB	-525	-501	0.473	-43 to 91

ABMUHB (Abertawe Bro Morgannwg University HB); **ABUHB** (Aneurin Bevan University HB); **BCUHB** (Betsi Cadwaladr University HB); **CTMUHB** (Cwm Taf Morgannwg University HB); **CVUHB** (Cardiff and Vale University HB); **HDUHB** (Hywel Dda University HB); **PTHB** (Powys Teaching HB)

Step changes analysis for NMIPs

Table 3 demonstrates the step changes in the prescribed number of items by NMIPs in all Wales and in each HB at five post-intervention time points. At all post-intervention time points, step changes were significant in all Wales, BCUHB and HDUHB. Step changes in PTHB were significant at 9, 12 and 24 post-intervention months' points, whereas step changes in ABMUHB and ABUHB were significant at 12 and 24 post-intervention months' points. Step changes in CVUHB and CTMUHB were not statistically significant.

Table 3 step changes in the prescribed number of items by NMIPs in primary care and dispensed in community pharmacies in all Wales and in each HB. Statistically significant results are in the white shading, while non-significant results are in the dark grey shading

	post-intervention time points: n (p value)				
All Wales and HBs	**3 months**	**6 months**	**9 months**	**12 months**	**24 months**
All Wales	6801 (0.001)	10506 (<0.001)	14211 (<0.001)	17917 (<0.001)	32738 (<0.001)
BCUHB	2821 (0.032)	3384 (0.008)	3947 (0.002)	4509 (0.001)	6759 (<0.001)
HDUHB	1796 (0.049)	2955 (0.001)	4113 (<0.001)	5272 (<0.001)	9907 (<0.001)
PTHB	730 (0.586)	2346 (0.133)	3961 (0.040)	5577 (0.018)	12039 (0.006)
ABMUHB	950 (0.177)	1145 (0.100)	1340 (0.063)	1535 (0.047)	2314 (0.046)
ABUHB	364 (0.575)	770 (0.225)	1176 (0.068)	1582 (0.020)	3206 (0.001)
CVUHB	-96 (0.857)	89 (0.861)	274 (0.587)	458 (0.373)	1197 (0.082)
CTMUHB	852 (0.138)	925 (0.095)	997 (0.071)	1070 (0.061)	1360 (0.080)

ABMUHB (Abertawe Bro Morgannwg University HB); **ABUHB** (Aneurin Bevan University HB); **BCUHB** (Betsi Cadwaladr University HB); **CTMUHB** (Cwm Taf Morgannwg University HB); **CVUHB** (Cardiff and Vale University HB); **HDUHB** (Hywel Dda University HB); **PTHB** (Powys Teaching HB)

DISCUSSION

Overview

This study investigated the number and associated prescribing trends of NMIPs before and after the implementation of primary care clusters in Wales.

Number of NMIPs

The majority of NMIPs in primary care in Wales were nurses, followed by pharmacists, and physiotherapists. Although the number of nurse IPs is much greater than pharmacist IPs, they only represent 5% of the nursing workforce[33], while pharmacist IPs represent 7% of the pharmacist profession[34]. The fact that there are more nurse IPs than other professions is in line with the findings of other studies that have investigated the implementation of non-medical prescribing in England[35,36] and Wales[16]. Interestingly, the database did not identify other health care professionals who have prescribing authorisation in Wales, including therapeutic radiographers, chiropodists and podiatrists, and optometrists[16]. Therapeutic radiographer IPs are based within secondary or tertiary care settings in Wales and therefore, they would be unlikely to be included in the database. However, the other professions could potentially be working in primary care settings but do not appear to have issued NHS prescriptions. This is wasteful in terms of the time and expenses incurred for training and failure to deliver an improved service to patients.

The increase in the number of NMIPs in primary care in Wales may suggest that the primary care sector has recognised the skills of these practitioners, improving the skill-mix in this sector, and hopefully reducing the pressure on GPs i.e. the benefits described in the second Crown Report[37]. Since the last quarter of 2015, the increase

in the percentage of pharmacist IPs was higher than the increase in the percentage of nurse IPs (325% vs 108%). This could be explained by the implementation of the Welsh Government Plan[17], introduction of primary care clusters[19], and the shortage of GPs in Wales, particularly in BCUHB[15,36,37,38]. All of these factors may have contributed to recruitment of more pharmacist IPs[17]. Pharmacist independent prescribing is a new role for pharmacists within clusters, with many secondary care based pharmacist IPs moving into these positions[21]. This may lead to a shortage of pharmacists within secondary care and has highlighted the need for a pharmacy workforce plan for Wales

Prescribing by NMIPs over the study period

The increase in the number of NMIPs, particularly pharmacist IPs, may explain the increased rate of prescribing of medicines by these practitioners over the same period. The high number of prescribed items by NMIPs in BCUHB (34%) compared to other HBs could be explained by the high number of NMIPs in BCUHB (246 NMIPs).

Prescribing by NMIPs before and after the implementation of primary care clusters

It is evident that the utilisation of NMIPs is inconsistent across the seven HBs in Wales, which supports previous research[16]. Step changes in the prescribed number of items by NMIPs before and after the implementation of primary care clusters were observed after 3 months in all Wales, BCUHB and HDUHB. However, step changes were not seen until much later in PTHB (after 9 months) and after 12 months in ABUHB and ABMUHB. In contrast, step changes were absent in CTMUHB and CVUHB within the same time period. HBs can therefore be classified in relation

to the intervention in this study into the following categories: early adopters (BCUHB and HDUHB), a mid-term adopter (PTHB), and late adopters (ABUHB, ABMUHB, CTMUHB and CVUHB) of NMIPs.

BCUHB and HDUHB represent the largest geographical areas in Wales compared to other HBs[41], but have the lowest number of GPs per 10,000 population (6.1 and 5.8, retrospectively)[42]. The low number of GPs in these HBs could be related to issues of recruitment, as well as the difficulty in keeping those who are already employed in their positions[38,39]. The shortage of GPs in these HBs, may explain the early adoption of non-medical independent prescribing.

Although there is a lack of evidence with regards to the barriers to implementing non-medical independent prescribing in Wales, reasons that may have contributed to the lack of utilisation of this service in the late adopter HBs could include the lack of funding[16, 35, 43, 44] and lack of a plan or strategy to develop this service[35]. However, these studies are outdated given the pace of change and may not reflect recent practice and policies. Due to the lack of evidence regarding the impact of these barriers on the implementation of non-medical independent prescribing in each HB, further research is required to investigate this matter. This study provides the initial evidence for such research, as well as providing the opportunity to share learning among HBs.

FUTURE STUDIES

This study provides a research agenda for further investigation to examine questions related to efficiency, quality of prescribing, cost effectiveness, and improved access to services provided by NMIPs. With the presence of some variety and inconsistency in the prescribing trend of NMIPs across different HBs, this provides an

opportunity to share the knowledge on advanced and novel services provided by these prescribers as well as to investigate the reasons behind it.

CONCLUSION

The number of NMIPs and their prescribing trends of medicines increased in the majority of HBs, particularly the number of pharmacist IPs since the last quarter of 2015. This could be related to the implementation of the Welsh Government Plan[17] and the introduction of primary care clusters. The findings of this study may suggest that the increased number of NMIPs in the primary care sector in Wales over time may help to reduce the pressure on GPs and improve the skill-mix across different therapeutic areas. This aligns with the main reasons for the implementation of non-medical prescribing in the UK, as outlined in the second Crown Report[37]. Future studies should focus on efficiency and quality of prescribing by NMIPs in primary care.

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Competing interests - All authors the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

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DATA SHARING STATEMENT - No additional data available

Transparency declaration - The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

INTEGRITY OF THE DATA AND ACCURACY OF THE DATA ANALYSIS - All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Ethics approval - No ethical approval required.

Patient and public involvement - This research was done without patient and public involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

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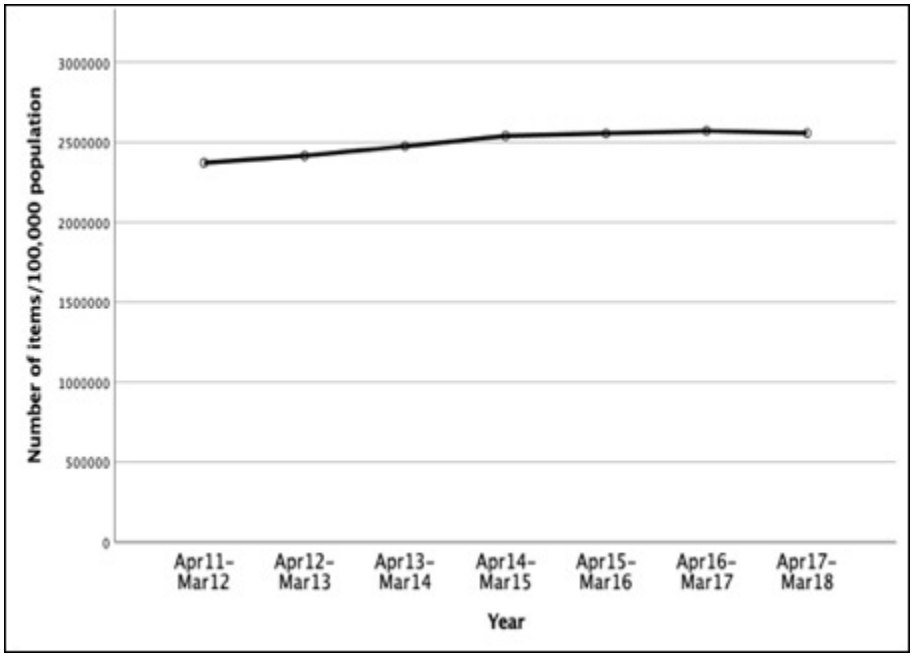

Figure 1 Trend of the total number of items per 100,000 population prescribed by all prescribers in primary care in Wales and dispensed in community pharmacies by year

38x27mm (300 x 300 DPI)

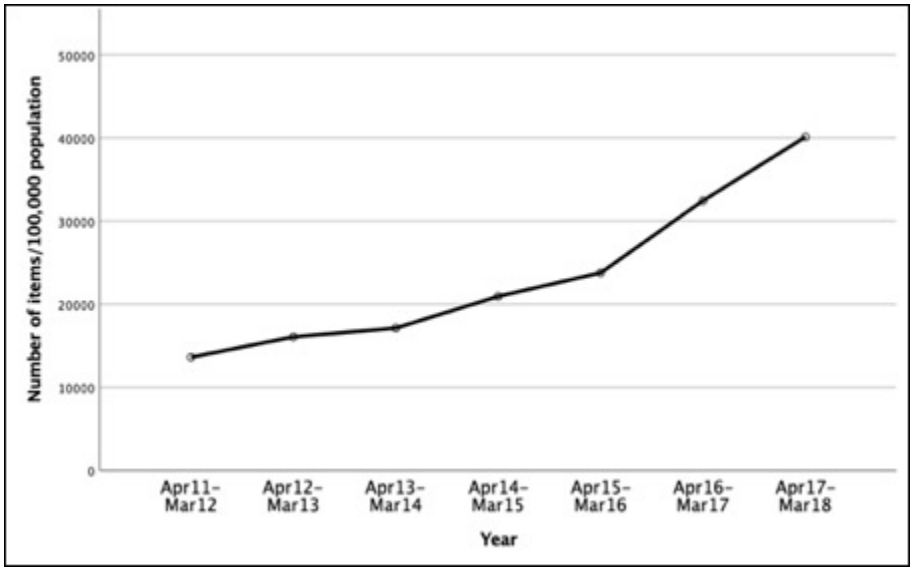

Figure 2 Trend of the total number of items per 100,000 population prescribed by NMIPs in primary care in Wales and dispensed in community pharmacies by year

38x23mm (300 x 300 DPI)

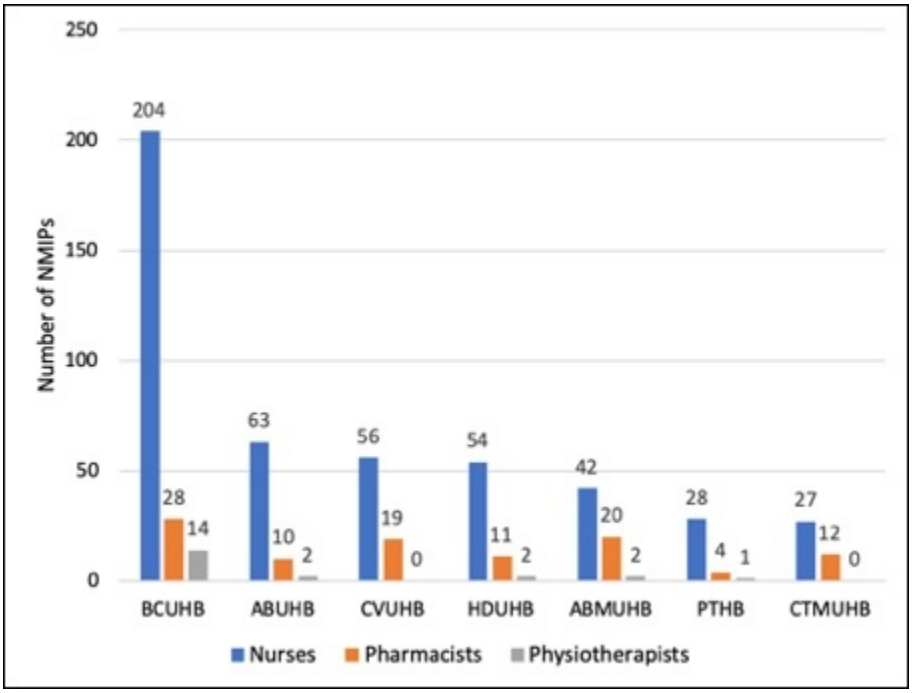

Figure 3 The total number of NMIPs (pharmacists, nurses and physiotherapists) who prescribed at least one item from April 2011 to March 2018 in primary care in Wales in different HBs
ABMUHB (Abertawe Bro Morgannwg University HB); ABUHB (Aneurin Bevan University HB); BCUHB (Betsi Cadwaladr University HB); CTMUHB (Cwm Taf Morgannwg University HB); CVUHB (Cardiff and Vale University HB); HDUHB (Hywel Dda University HB); PTHB (Powys Teaching HB)

38x28mm (300 x 300 DPI)

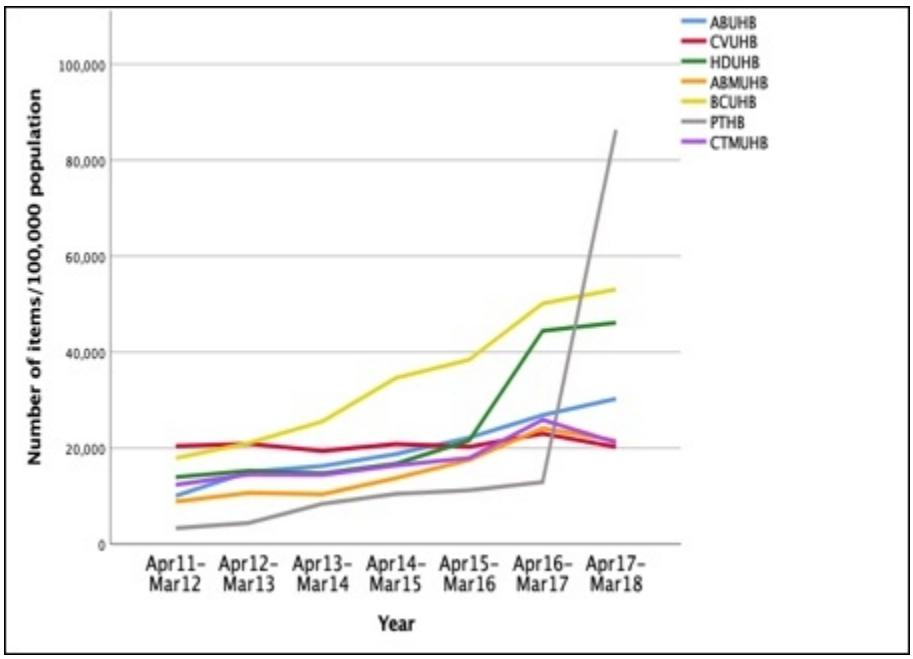

Figure 4 Trend of the total number of items/100,000 population prescribed by NMIPs in primary care in Wales and dispensed in community pharmacies in different HBs by year
ABMUHB (Abertawe Bro Morgannwg University HB); ABUHB (Aneurin Bevan University HB); BCUHB (Betsi Cadwaladr University HB); CTMUHB (Cwm Taf Morgannwg University HB); CVUHB (Cardiff and Vale University HB); HDUHB (Hywel Dda University HB); PTHB (Powys Teaching HB)

38x27mm (300 x 300 DPI)

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Prescribing trends over time by non-medical independent prescribers (NMIPs) in primary care settings across Wales (2011-2018): a secondary database analysis

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ABSTRACT

Introduction As of 2015, as part of the implementation of the Welsh Government Primary Care Plan and primary care clusters, the Welsh Government has encouraged non-medical healthcare professionals working in primary care to train as independent prescribers (IPs).

Design Retrospective secondary data analysis and Interrupted Time Series (ITS) analysis in order to compare prescribing by NMIPs pre and post-implementation of primary care clusters across Wales.

Objectives This research aimed to identify the number of non-medical independent prescribers (NMIPs) in primary care in Wales and describe their prescribing trend of items between 2011 and 2018, in order to compare their prescribing pattern before and after the implementation of primary care clusters for Wales.

Results Over the study period, 600 NMIPs (nurses n=474 and pharmacists n=104) had prescribed at least one item. The number of nurse IPs increased by 108% and pharmacists by 325% (pharmacists had the largest increase between July 2015 and March 2018). The number of items prescribed by NMIPs increased over time by an average of 1,380 per month (95% CI: 904 to 1855, $p < 0.001$) after the implementation of primary care clusters compared to 496 (95% CI: 445 to 548, $p < 0.001$) prior its implementation. Approximately one third of the items prescribed by NMIPs was within Betsi Cadwaladr University Health Board (HB) with only 4% in Powys Teaching HB.

Conclusion The number of NMIPs and their volume of prescribing in primary care in Wales has increased following the implementation of primary care clusters in 2015. This suggests that the Government's recommendations of utilising NMIPs in primary care have been implemented. Future studies should focus on efficiency and quality of prescribing by NMIPs in primary care.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study that has used a secondary database analysis, which has provided insights and empirical findings on the prescribing pattern of medicines by non-medical independent prescribers (NMIPs) over time in primary care in Wales.
- The data provided via the CASPA software system was limited to the last seven years and only captured prescriptions that were dispensed in community pharmacies.
- The CASPA system was designed for financial reimbursement purposes for community pharmacies, which means that holding investigations at the level of patients or prescribers, such as stopping or changing patients' medications, as well as clinical safety issues or other prescribing activities, were not possible.
- The professions of NMIPs as pharmacist, nurse, physiotherapist or others were not identified on the prescriptions and, consequently, in the CASPA system.
- The ITS analysis has the strength of evaluating data at the whole population level, which allowed the researchers to evaluate the utilisation of NMIPs in primary care across all of Wales.

INTRODUCTION

The right to prescribe medicines was traditionally restricted to physicians, dentists and veterinary surgeons[1]. Prescribing practice has changed over the last 50 years to involve not only physicians and dentists (medical prescribers) but also other health care professionals, known as non-medical prescribers. The adoption of non-medical prescribing fundamentally began in the USA in the 1960s[2] and has extended to the UK, Canada, New Zealand, Australia, and other European and African nations[3]. Beyond the UK, solely nurses and pharmacists have been granted the authority to prescribe medicines collaboratively (dependently) under a physician's supervision or independently from a limited lists of medicines[4-7]. The drive to extend the medicines prescribing mandate to non-medical healthcare professionals was related to a variety of aspects within every nation.

In the UK, non-medical prescribing was introduced as part of the National Health Service (NHS) plans, which intended to improve and modernise the health care system[8,9]. The aim of introducing non-medical prescribing was to enhance patient care and safety, improve patient access and choice of appropriate medicines for their conditions, use the already gained skills of health care professionals in the most effective way, and promote a more flexible teamwork environment in the NHS[10]. Pharmacists, nurses, optometrists and Allied Health Professionals can qualify as non-medical prescribers after completing an advanced prescribing training programme[9,10]. This programme lawfully allows these healthcare professionals to prescribe within their area of competence. such as that pharmacists and nurses can prescribe medicines, appliances, and wound dressings as either independent or supplementary prescribers within their clinical area of practice. Some NMIPs are limited to prescribe certain medications within their clinical of speciality, such as

optometrists who can only prescribe for eye conditions and surrounding tissues[9].

Independent prescribing is defined as 'prescribing by a practitioner (e.g. a doctor, dentist, nurse, or a pharmacist) responsible and accountable for the assessment of patients with undiagnosed or diagnosed conditions and for decisions about the clinical management required, including prescribing'[10]. Whereas, supplementary prescribing is a 'voluntary partnership between the responsible independent prescriber and a supplementary prescriber, to implement an agreed patient-specific clinical management plan with the patient's agreement, particularly but not only in relation to prescribing for a specific non-acute medical condition or health need affecting the patient'[11]. Non-medical independent prescribing was introduced in the UK in 2002 after a change in the legislation made by the UK Government allowing the first level registered nurses who have at least 3 years of experience to prescribe independently from a limited list of medicines[12]. In 2006, independent prescribing extended for qualified nurses and pharmacists who completed the necessary training to prescribe any medicines within their area of competence with few exceptions[10]. This was followed by the introduction of optometrist independent prescribing in 2007[13], and more recently, independent prescribing by Allied Health Professionals including podiatrists and physiotherapists independent prescribing in 2013[14], and therapeutic radiographers independent prescribing in 2016[15]. The recent healthcare professionals who gained the prescribing authority in Wales were paramedics in 2019. In 2017, the estimated number of non-medical independent prescribers (NMIPs) in the UK was as follows: 30,000 nurse independent prescribers (IPs); 3,000 pharmacist IPs and 600 Allied Health Professionals IPs[16]. All NMIPs are responsible and accountable for their own prescribing and limiting their prescribing to their therapeutic area of expertise[9]. Moreover, these healthcare professionals are

required to seek appropriate advice or referral if they lack the confidence to manage patients' conditions or prescribe the suitable medicines for their patients[9].

In Wales, the NHS provides its services via three NHS Trusts and seven health boards (HBs). The seven HBs are Swansea Bay University HB (SBUHB), Cardiff and Vale University HB (CVUHB), Cwm Taf Morgannwg University HB (CTMUHB), Hywel Dda University HB (HDUHB), Powys Teaching HB (PTHB), Betsi Cadwaladr University HB (BCUHB) and Aneurin Bevan University HB (ABUHB). The SBUHB was formerly known as Abertawe Bro Morgannwg University HB (ABMUHB), having being renamed in 2019.

Primary health care services are the initial point of care for patients in the NHS. In Wales, it has been estimated that around 90% of people's contact with the NHS is with primary care services, with General Practices the main point of contact[17]. In 2016, there were 441 General Practices in Wales and 2,009 General Practitioners (GPs) (excluding, locums, retainers, and registrars)[18]. The Welsh Government and HBs have focused upon improving primary care services[17], and this has included the development of primary care clusters. Clusters comprise groups of adjacent general practices that have linked together to provide advanced medical services locally in order to relieve pressure on hospitals[19]. The aims of these clusters include improving patients' access to their medicines and information as well as the provision of advice and support to manage medicines. These clusters came into being in the last quarter of 2015[19]. Currently, there are 64 primary care clusters in Wales which provide services for a population of 30,000 to 50,000 patients per cluster[19]. In order to overcome GP shortages[20,21], these clusters are supported by high numbers of hospital pharmacists, nurses and other professionals. In addition, the Welsh Government and HBs have prioritised funding for new posts and training of other

health care professionals, such as pharmacist and nurse IPs[17]. Consequently, the number of non-medical prescribers in primary care has increased in recent years and is expected to rise further[16,21].

Only one published study has investigated the implementation of non-medical prescribing in Wales[16]. This study aimed to provide an overview of the implementation and utilisation of non-medical prescribing in all health care sectors through a national questionnaire survey. The results of this study indicated that the majority of non-medical prescribers in Wales were based in secondary care settings. Moreover, these researchers stated that the utilisation of non-medical prescribers across Wales, particularly in primary care, was inconsistent and had not been implemented in all services. In addition, it was suggested that there was a need to investigate and recognise the development of primary care services in Wales, with support required for non-medical prescribers[16].

The aim of this study was to identify the number of NMIPs in Wales and describe their prescribing volume (from April 2011 to March 2018) as a whole, as well as within the seven HBs, before and after the implementation of primary care clusters. This is the first study in Wales to use data obtained through a national database to review prescribing volume by NMIPs in primary care. No equivalent studies have been published internationally.

METHODOLOGY

The study design was a retrospective secondary data analysis of monthly data for prescriptions issued by NMIPs in primary care in Wales and dispensed in community pharmacies, as well as the data on the number of NMIPs within primary care in Wales.

The number of NMIPs who prescribed each month and who prescribed at least one item from April 2011 to March 2018 was obtained through the NHS Wales Shared Services Partnership, Primary Care Services. Prescribing data were obtained from the Comparative Analysis System for Prescribing Audit (CASPA) software system (Version 5), provided by the NHS Wales Shared Services. Data were fully anonymised and recorded as part of routine practice, as such, the study did not require ethical approval. CASPA records all dispensed WP10 prescriptions (NHS Welsh prescriptions for use in primary care), to allow financial reimbursement to community pharmacies[9]. Whilst it is acknowledged that dispensing may not fully reflect prescribing, due to patients not taking their prescriptions to a pharmacy for dispensing, the impact of this is likely to be small. This is due to that the prescription charge for people in Wales was abolished in 2007 allowing all patients who were registered with their Welsh GPs to get their prescriptions dispensed from a pharmacy in Wales free of charge[22]. As a result, the impact of non-dispensed items would have been reduced by this policy, which also limits the financial burden to patients. Therefore, dispensing was used as a surrogate marker for prescribing in this study.

The number of items refers to each single item prescribed by a prescriber on a prescription form to a patient[23]. All recorded WP10 prescriptions issued by GPs and NMIPs in Wales and dispensed by community pharmacists from April 2011 to March 2018 were extracted and included in the study. The number of prescribed items by

NMIPs were extracted from the CASPA system on a monthly basis, the total number of items per 100,000 population (the population data in Wales as a whole and in each HB obtained from the Welsh Government Stats Wales[24]) was calculated in order to take the population into consideration. Percentages were calculated for the total number of prescribed items by NMIPs in each HB. The name of ABMUHB was used to illustrate the findings in this HB as this was its name over the study period.

Although Randomised Controlled Trials (RCTs) are considered the gold standard method to evaluate longitudinal effects of interventions over time[25-27], they lack the ability to evaluate the already implemented service retrospectively[27]. Therefore, prescribing trend data were compared before and after the introduction of primary care clusters (the intervention) by using an interrupted time series (ITS) analysis. This analysis was performed using ordinary-least squares regression with Newey-West standard errors and a lag for the autocorrelation structure. The Cumby-Huizinga test for autocorrelation was examined to determine the appropriate autocorrelation structure to be accounted for in the model. The model included pre- and post-intervention trends, as well as a coefficient to examine a change in level immediately post-intervention. The parameter estimates are presented alongside 95% confidence intervals and p-values. The counterfactual trend (i.e. the trend in the absence of the intervention) was examined, and this was compared to the actual observed trend to calculate absolute and relative differences at the end of the observed period (March 2018). Analysis was performed using the *itsa* command in Stata V16.0[28]. The findings were assumed significant at p value <0.05. Confidence intervals (CIs) were calculated in order to be 95% certain that the range of values contained the true mean of the data[29].

The Welsh Government plan[17] encouraged local HBs to prioritise funding and

development of primary care clusters in April 2015. However, the implementation of these clusters is the responsibility of each individual local HB and there are no definitive time points of their establishment. To accommodate this, the researchers engaged with the relevant stakeholders (e.g. policy makers and Chief Pharmaceutical Officer) to determine the appropriate time for the intervention phase. They agreed the intervention phase should be after six months of the provided funding by the Government to HBs, which means the October 2015, to allow for an appropriate time for each HB to train NMIPs.

Patient and public involvement - This research was done without patient and public involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

RESULTS

Trend of the total number of items prescribed by all prescribers

The total number of items prescribed by all health care professionals (GPs and non-medical prescribers) from April 2011 to March 2018 was 540,781,584 items (17,482,150 per 100,000 population). The total number of prescribed items per 100,000 population per year increased by 7.1% between 2011-2012 (n= 2,371,511) and 2014-2015 (n= 2,539,192) and increased by 0.7% between 2014-2015 (n= 2,539,192) and 2017-2018 (n= 2,556,784]) (Figure 1).

Trend of the total number of items prescribed by NMIPs

The total number of items prescribed by NMIPs in primary care in Wales between April 2011 and March 2018 was 5,088,405 items (n= 164,130 per 100,000 population). The number of items prescribed as a percentage of all items prescribed by all health care professionals (except items prescribed by dentists) increased from 0.57% in 2011-2012 to 1.7% in 2017-2018. As shown in Table 1 and Figure 2, dispensed prescriptions by NMIPs in primary care started at 31,756 and increased on average per month prior to the implementation of primary care clusters by 496 (95% CI: 445 to 548, $p < 0.001$). There was no evidence to suggest a change in the level immediately following the implementation of primary care clusters in October 2015. However, following this implementation, there was an increase in dispensed prescriptions per month, relative to pre-implementation trends, of 1,380 on average (95% CI: 904 to 1855, $p < 0.001$).

Table 1: Parameter estimates from the interrupted time series analysis examining the change in level and slope of dispensed prescriptions in primary care by NMIPs following the implementation of primary care clusters in October 2015 (N = 84 months)

Variable	Coefficient	Lower 95% CI	Upper 95% CI	p-value
Intercept	31755.5	30208.3	33302.8	<0.001
Pre-intervention slope	496.3	444.8	547.8	<0.001
Level change	3023.4	-2151.5	8198.2	0.248
Post-intervention slope	1379.7	904.4	1855.1	<0.001

Assuming the pre-implementation trend would have continued in the absence of the introduction of primary care clusters, the expected number of dispensed prescriptions by NMIPs at the end of the observation period (March 2018) was 73,443 (95% CI: 70,260 to 76,627), and with the model predicting an expected number (in the presence of primary care clusters) of 117,859 (95% CI: 108,049 to 127,670), there was a 60% relative increase in the number of dispensed prescriptions by NMIPs following the implementation of primary care clusters over and above what would have been expected in the absence of such a scheme (95% CI: 46 to 75, p < 0.001).

The total number of NMIPs

Data obtained from the NHS Wales Shared Services Partnership shows that the total number of NMIPs who prescribed at least one item from April 2011 to March 2018 was 600 prescribers (474 nurses, 104 pharmacists, 21 physiotherapists and 1 with unknown profession). The number of NMIPs in each HB is illustrated in Figure 3. The number of prescribing NMIPs per month increased by approximately 140% between April 2011 (n=174) and March 2018 (n=414). Of those, the number of nurses increased from 158 in April 2011 to 328 in March 2018 (an increase of 108%). The number of pharmacists increased from 16 in April 2011 to 68 in March 2018 (an

increase of 325%), the largest increase was from July 2015 (n=20) to March 2018 (n=68) by 240%. In January 2015, the first physiotherapist IP started to prescribe with the number increasing to 17 by March 2018.

Trend of the total number of prescribed items by NMIPs in different HBs pre and post-intervention

Table 2 presents the total number of items prescribed by NMIPs, as well as the number per 100,000 population and percentage of all items prescribed, per HB. Approximately one third of the items prescribed by NMIPs was within BCUHB (Table 2) with only 4% in PTHB. Data by HBs are illustrated in Figure 4 and Figure 5, and it can also be seen in the supplementary file.

Table 2 Total number of items prescribed by NMIPs, as well as the number per 100,000 population and percentage of all items prescribed, per HB in primary care in Wales and dispensed in community pharmacies since April 2011 until March 2018

Health Board	Total number of items prescribed by NMIPs	% of the prescribed items by NMIPs in each HB*	Prescribed items by NMIPs per 100,000 population
BCUHB	1,711,949	33.64%	240,742.5
ABUHB	834,879	16.41%	139,396.5
CVUHB	711,805	13.99%	145,069.9
HDUHB	686,166	13.48%	172,782.9
ABMUHB	573,624	11.27%	106,813.2
CTMUHB	371,315	7.30%	122,620.2
PTHB	198,667	3.91%	137,000.6

ABMUHB (Abertawe Bro Morgannwg University HB); **ABUHB** (Aneurin Bevan University HB); **BCUHB** (Betsi Cadwaladr University HB); **CTMUHB** (Cwm Taf Morgannwg University HB); **CVUHB** (Cardiff and Vale University HB); **HDUHB** (Hywel Dda University HB); **PTHB** (Powys Teaching HB)

* The percentage of the prescribed items by NMIPs in each HB was calculated based on the total number of items prescribed by NMIPs in all Wales

DISCUSSION

Statement of the principal findings

This study investigated the number and associated prescribing volume of NMIPs before and after the implementation of primary care clusters in Wales. The number of NMIPs has increased in primary care in Wales over the study period and the majority of them were nurses, followed by pharmacists, and physiotherapists. Interestingly, the database did not identify other health care professionals who have prescribing authorisation in Wales, including therapeutic radiographers, chiropodists and podiatrists, and optometrists[16].

The analysis of the prescribed number of items by NMIPs before and after the implementation of primary care clusters showed a 60% relative increase following the implementation of the primary care clusters in Wales. However, the prescribing of items by NMIPs was inconsistent across the seven HBs.

Strengths and weaknesses

This is the first study that has used a secondary database analysis, which has provided insights and empirical findings on the prescribing pattern of medicines by non-medical independent prescribers (NMIPs) over time in primary care in Wales. Although this study has achieved its aim and objectives, it has a number of limitations. Firstly, the data provided via the CASPA software system was limited to the last seven years. Secondly, this system was designed for financial reimbursement purposes for community pharmacies, which means that holding investigations at the level of patients or prescribers, such as stopping or changing patients' medications, as well as clinical safety issues or other prescribing activities, were not possible. In addition, this

system only captured NHS prescriptions that were dispensed in community pharmacies. Therefore, prescriptions issued by those prescribers that have not been dispensed as well as private prescriptions that have been prescribed by NMIPs, such as optometrists, were not captured by the system. Finally, the professions of NMIPs as pharmacist, nurse, physiotherapist or other were not identified on the prescriptions and, consequently, in the CASPA system. The ITS analysis may have the limitation of the presence of unknown confounding variables, which are outside of the researcher's control, that may have happened at the same time of the intervention and this leads to the difficulty of establishing causal effects[30]. However, this analysis has the strength of evaluating data at the whole population level[31], which allowed the researchers to evaluate the utilisation of NMIPs in primary care across all of Wales.

Comparison with other studies

The increase in the number of NMIPs in primary care in Wales may suggest that the primary care sector has recognised the skills of these practitioners, improving the skill-mix in this sector, and hopefully reducing the pressure on GPs i.e. the benefits described in the second Crown Report[32]. Since the last quarter of 2015, the increase in the percentage of pharmacist IPs was higher than the increase in the percentage of nurse IPs (325% vs 108%). This could be explained by the implementation of the Welsh Government Plan[17], introduction of primary care clusters[19], and the shortage of GPs in Wales, particularly in BCUHB[15,32,33,34]. All of these factors may have contributed to recruitment of more pharmacist IPs[17]. Pharmacist independent prescribing is a new role for pharmacists within clusters, with many secondary care based pharmacist IPs moving into these positions[21]. This may lead to a shortage of pharmacists within secondary care and has highlighted the need for

a pharmacy workforce plan for Wales.

Although the number of nurse IPs is much greater than pharmacist IPs, they only represent 5% of the nursing workforce[*35*], while pharmacist IPs represent 7% of the pharmacist profession[*36*]. The fact that there are more nurse IPs than other professions is in line with the findings of other studies that have investigated the implementation of non-medical prescribing in England[*33*,*37*] and Wales[16]. Therapeutic radiographer IPs are based within secondary or tertiary care settings in Wales and therefore, they would be unlikely to be included in the database. However, the other professions, such as chiropodists, podiatrists and optometrists, could potentially be working in primary care settings but do not appear to have issued NHS prescriptions as they could have been prescribing medications for their patients within private hospitals, at point of care or not using their prescribing qualification. If they were not using their prescribing qualification, this may suggest that HBs need to investigate the reasons for that in order to prevent wasting the time and expenses incurred for training and failure to deliver an improved service to patients.

The increase in the number of NMIPs, particularly pharmacist IPs, may explain the increased rate of prescribing of medicines by these practitioners over the same period. The high number of prescribed items by NMIPs in BCUHB (34%) compared to other HBs could be explained by the high number of NMIPs in BCUHB (246 NMIPs). It is evident that the utilisation of NMIPs is inconsistent across the seven HBs in Wales, which supports previous research[16]. BCUHB and HDUHB represent the largest geographical areas in Wales compared to other HBs[38], but have the lowest number of GPs per 10,000 population (6.1 and 5.8, retrospectively)[39]. The low number of GPs in these HBs could be related to issues of recruitment, as well as the difficulty in

keeping those who are already employed in their positions[34,40]. The shortage of GPs in these HBs, may explain the early adoption of non-medical independent prescribing. Although PTHB showed the lowest number of items prescribed by NMIPs over the study period, it is the smallest geographical area in Wales that has the lowest number of populations compared to other HBs. An equivalent increase in the number of prescribers and items would therefore produce a bigger percentage change than in a larger HB. However, the largest increase in the trend of the prescribing items in this HB over the last two years of the study period may be explained by the increase in the number of NMIPs. Moreover, PTHB only has primary care services, so whilst other HBs may have been training IPs in both primary and secondary care settings, the focus in PTHB would have been primary care only, which may have resulted in a greater change. However, due to the nature of the database used, it was not possible to investigate this further and this could be the focus of future work.

The meaning of the study: possible explanations and implications for clinicians and policymakers

The findings of this study showed inconsistency in terms of the implementation of the NMIPs' services between HBs in primary care in Wales, particularly after the primary care clusters' implementation. Although there is a lack of evidence with regards to the reasons and barriers behind this, some reasons that may have contributed to lower utilisation of this service in some HBs may include the lack of funding[16, 37, 41, 42] and lack of a plan or strategy to develop this service[37]. However, these studies are outdated given the pace of change as well as not been conducted in Wales in particular, which may not reflect recent practice and policies. Due to the lack of evidence regarding the impact of these barriers on the

implementation of non-medical independent prescribing in each HB, further research is required to investigate this matter. This study provides the initial evidence for such research, as well as providing the opportunity to share learning among HBs.

Unanswered questions and future studies

This study provides a research agenda for further investigation to examine questions related to efficiency, quality of prescribing, cost effectiveness, and improved access to services provided by NMIPs. With the presence of some variety and inconsistency in the prescribing trend of NMIPs across different HBs, this provides an opportunity to share the knowledge on advanced and novel services provided by these prescribers as well as to investigate the reasons behind it.

CONCLUSION

The number of NMIPs and their prescribing trends of medicines increased in all Wales, as well as in the majority of HBs, particularly the number of pharmacist IPs since the implementation of primary care clusters. This could be related to the implementation of the Welsh Government Plan[17] and the introduction of primary care clusters. The findings of this study may suggest that the increased number of NMIPs in the primary care sector in Wales over time may help to reduce the pressure on GPs and improve the skill-mix across different therapeutic areas. This aligns with the main reasons for the implementation of non-medical prescribing in the UK, as outlined in the second Crown Report[32]. Future studies should focus on efficiency and quality of prescribing by NMIPs in primary care.

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Competing interests - All authors the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

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DATA SHARING STATEMENT - No additional data available

Transparency declaration - The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

INTEGRITY OF THE DATA AND ACCURACY OF THE DATA ANALYSIS - All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Ethics approval - No ethical approval required.

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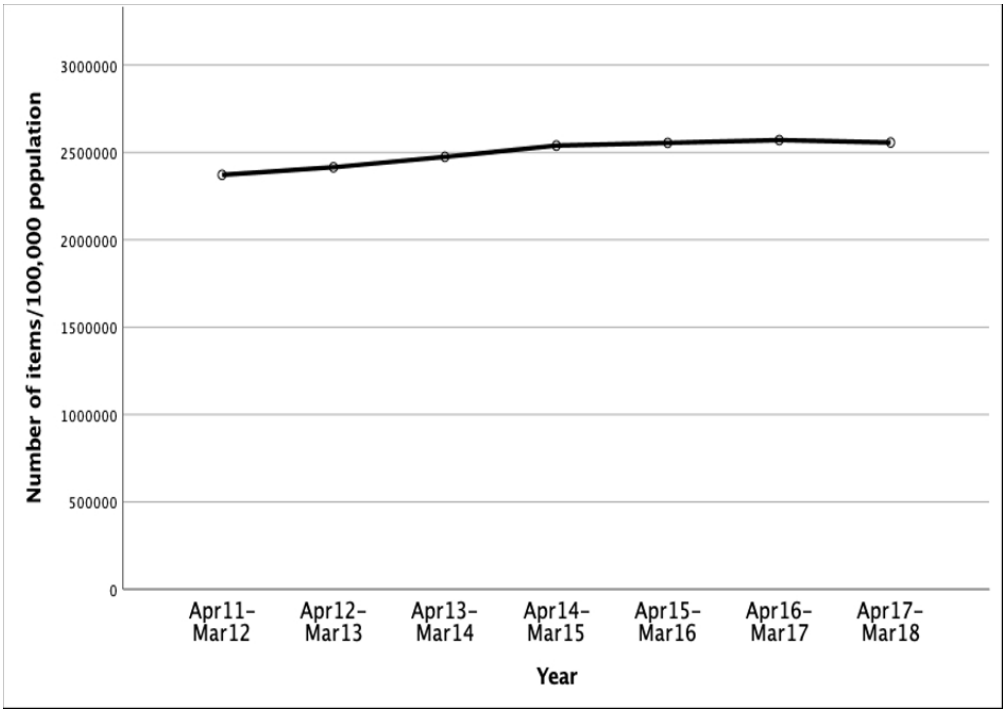

Figure 1 Trend of the total number of items per 100,000 population prescribed by all prescribers in primary care in Wales and dispensed in community pharmacies by year

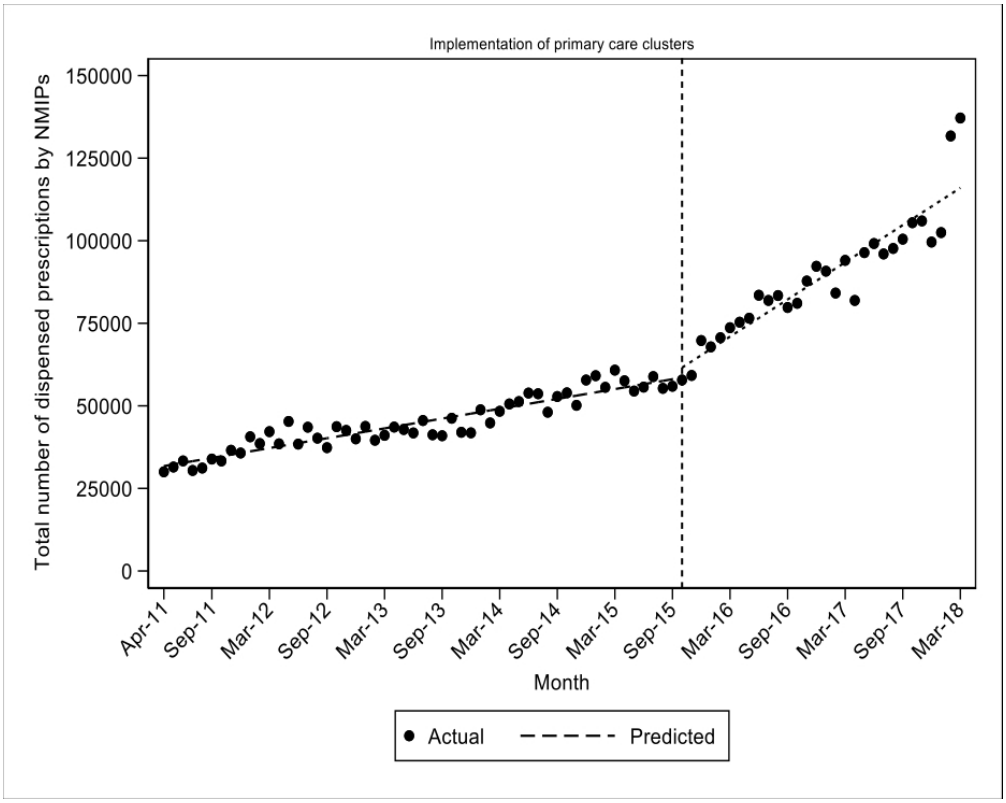

Figure 2 Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (All Wales)

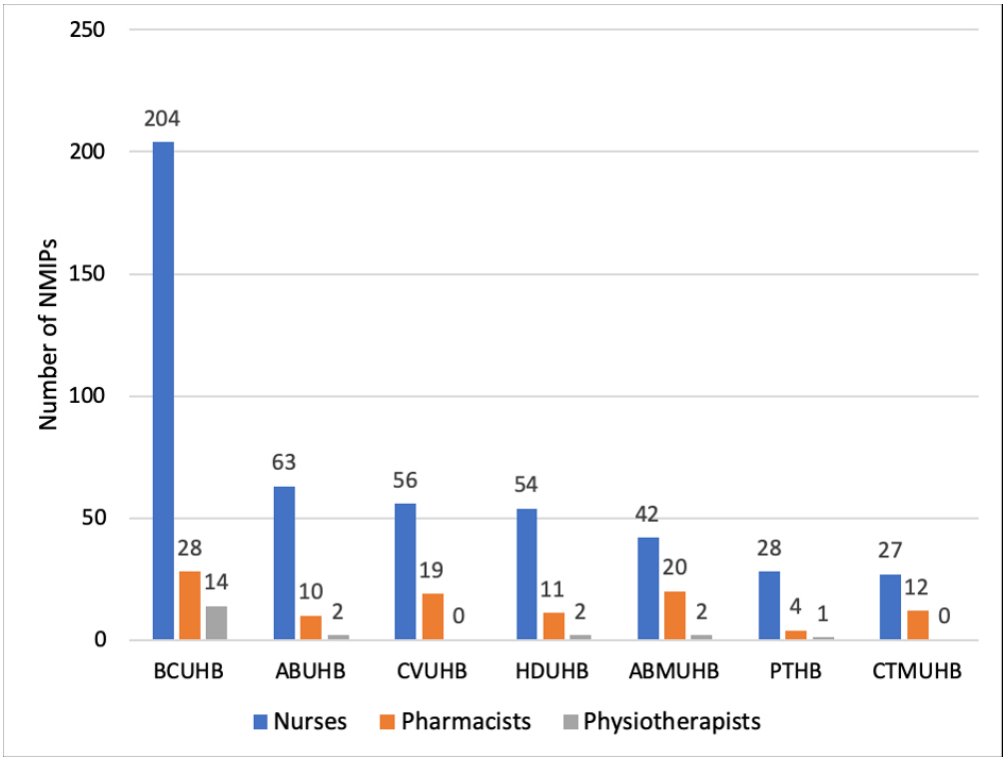

Figure 3 The total number of NMIPs (pharmacists, nurses and physiotherapists) who prescribed at least one item from April 2011 to March 2018 in primary care in Wales in different HBs

*ABMUHB (Abertawe Bro Morgannwg University HB); ABUHB (Aneurin Bevan University HB); BCUHB (Betsi Cadwaladr University HB); CTMUHB (Cwm Taf Morgannwg University HB); CVUHB (Cardiff and Vale University HB); HDUHB (Hywel Dda University HB); PTHB (Powys Teaching HB)

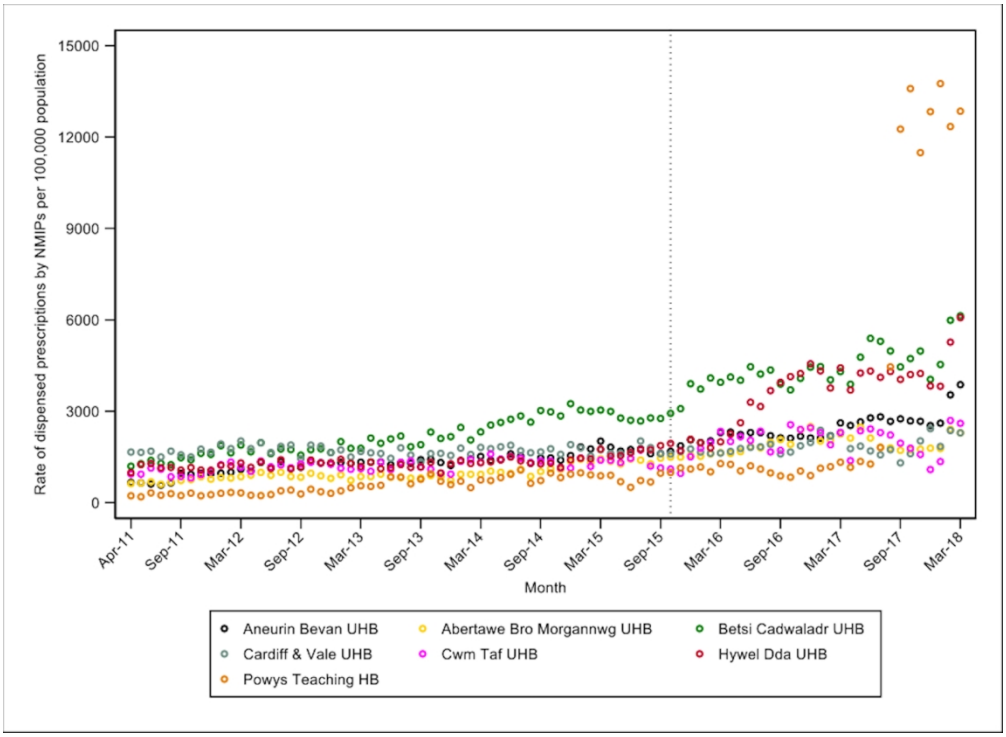

Figure 4 Trend of the total number of dispensed items per 100,000 population prescribed by NMIPs in primary care by health board (dashed line denotes the introduction of primary care clusters in October 2015)

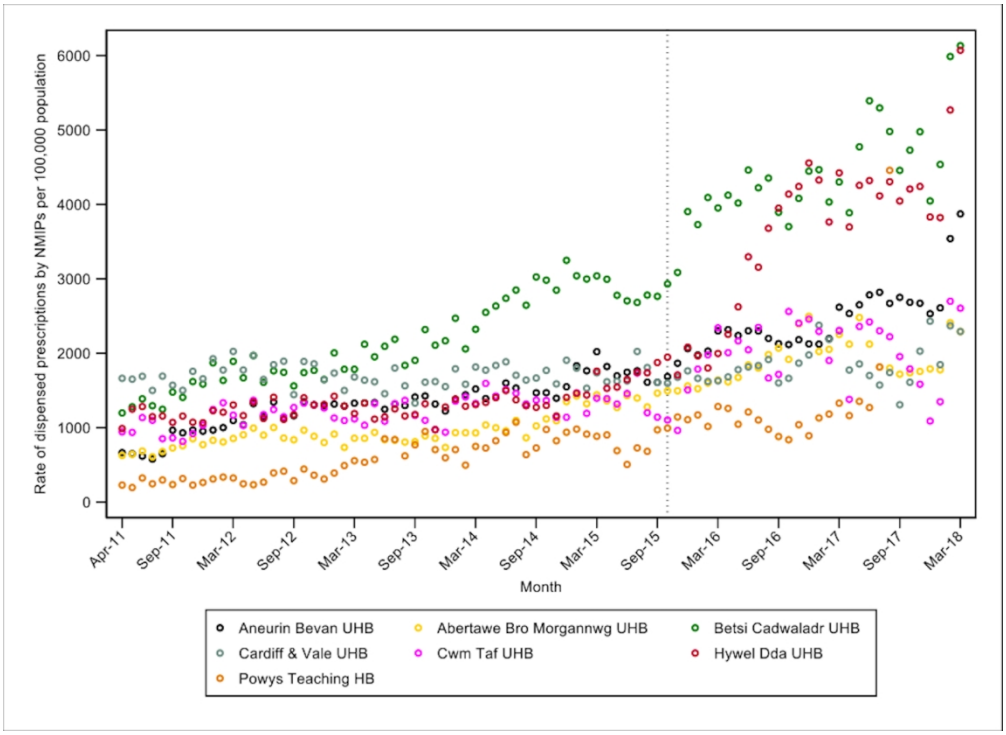

Figure 5 Trend of the total number of dispensed items per 100,000 population prescribed by NMIPs in primary care by health board (dashed line denotes introduction of primary care clusters in October 2015) * *Final seven outlying data points in Powys Teaching Health Board removed to illustrate trends in other Health Boards.

Prescribing trends over time by non-medical independent prescribers (NMIPs) in primary care settings across Wales (2011-2018): a secondary database analysis

Supplementary material

Health board trends in dispensed prescriptions by non-medical prescribers across health boards in Wales

Table S1: Health Board-specific parameter estimates from the interrupted time series analysis examining the change in level and slope of dispensed prescriptions in primary care by NMIPs following the implementation of primary care clusters in October 2015 (N = 84 months) *

Health board	Variable	Coefficient	Lower 95% CI	Upper 95% CI	p-value
Aneurin Bevan University Health Board	Intercept	4639.4	4019.8	5259.0	<0.001
	Pre-intervention slope	109.9	89.7	130.1	<0.001
	Level change	-27.5	-1321.8	1266.8	0.966
	Post-intervention slope	144.7	40.9	248.5	0.007
Abertawe Bro Morgannwg University Health Board (lag 3)	Intercept	3268.9	2833.5	3704.3	<0.001
	Pre-intervention slope	65.4	47.2	83.6	<0.001
	Level change	1954.3	534.6	3374.0	0.008
	Post-intervention slope	28.6	-52.4	109.7	0.484
Betsi Cadwaladr University Health Board	Intercept	8480.1	7791.3	9168.9	<0.001
	Pre-intervention slope	239.7	208.3	271.1	<0.001
	Level change	2634.6	3.1	5266.0	0.050
	Post-intervention slope	195.4	2.7	388.1	0.047
Cardiff and Vale University Health Board (lag 8)	Intercept	7976.3	7458.2	8494.4	<0.001
	Pre-intervention slope	6.1	-6.6	18.9	0.342
	Level change	-266.1	-876.5	344.4	0.388
	Post-intervention slope	65.4	12.6	118.1	0.016
Cwm Taf University Health Board (lag 4)	Intercept	2998.4	2689.6	3307.4	<0.001
	Pre-intervention slope	22.7	13.1	32.3	<0.001
	Level change	1104.3	-310.2	2518.7	0.124
	Post-intervention slope	16.6	-75.0	108.2	0.720

*Models fitted with a lag of order 1 unless otherwise specified. Note that linear modelling assumptions were not fulfilled for Hywel Dda and Powys Health Boards and Findings are illustrated graphically in Figures S6 and S7.

Table S2: Comparison between actual and counterfactual dispensed prescriptions in primary care by NMIPs*

Health board	Estimate	Coefficient	Lower 95% CI	Upper 95% CI
All Wales	Absolute difference at March 2018	44415.5	34086.8	54744.1
	Relative difference at March 2018	60.5	45.6	75.3
Aneurin Bevan University Health Board	Absolute difference at March 2018	4313.3	1924.1	6702.5
	Relative difference at March 2018	31.1	12.7	49.5
Abertawe Bro Morgannwg University Health Board	Absolute difference at March 2018	2813.2	751.1	4875.4
	Relative difference at March 2018	32.1	6.1	58.1
Betsi Cadwaladr University Health Board	Absolute difference at March 2018	8496.7	4136.1	12857.3
	Relative difference at March 2018	29.7	13.5	45.9
Cardiff and Vale University Health Board	Absolute difference at March 2018	1694.8	332.9	3056.7
	Relative difference at March 2018	20.0	3.4	36.5
Cwm Taf University Health Board	Absolute difference at March 2018	1601.9	-78.1	3281.9
	Relative difference at March 2018	32.7	-2.9	68.2

*The counterfactual represents predicted values and trends in the absence of the implementation of primary care clusters in October 2015 (i.e. making the assumption that pre-implementation trends would have continued in the same way).

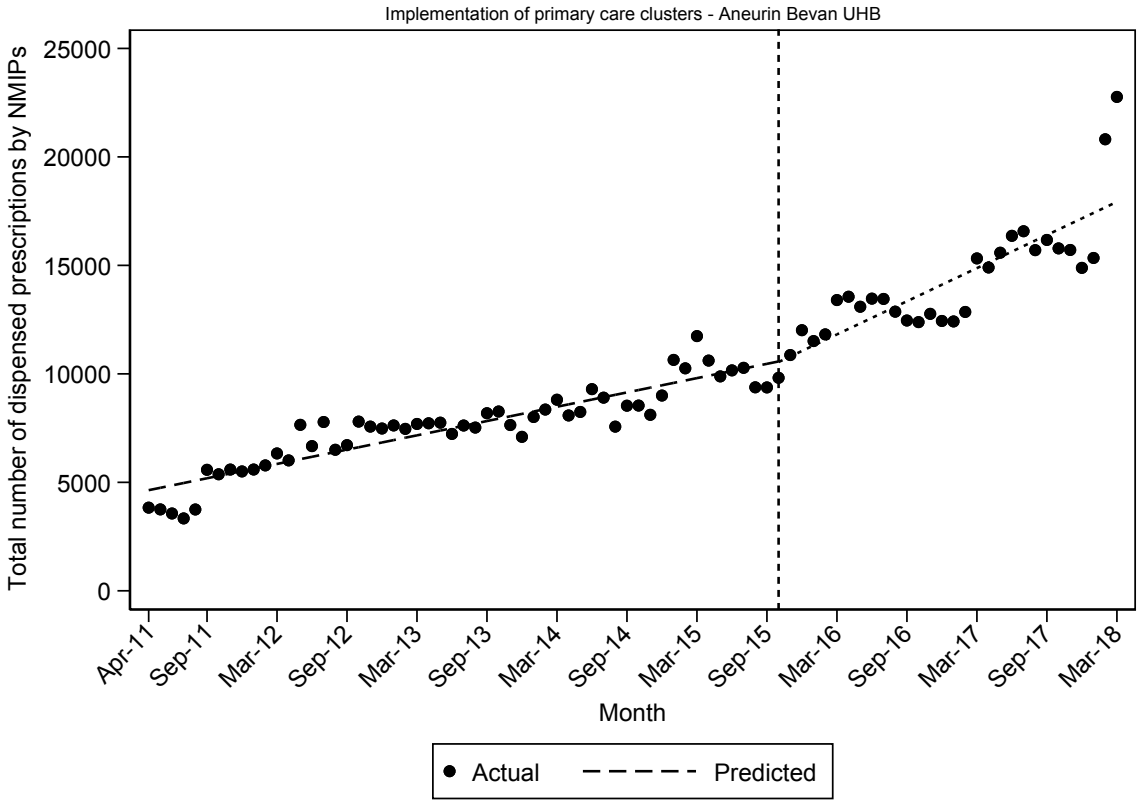

Figure S1: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Aneurin Bevan University Health Board)

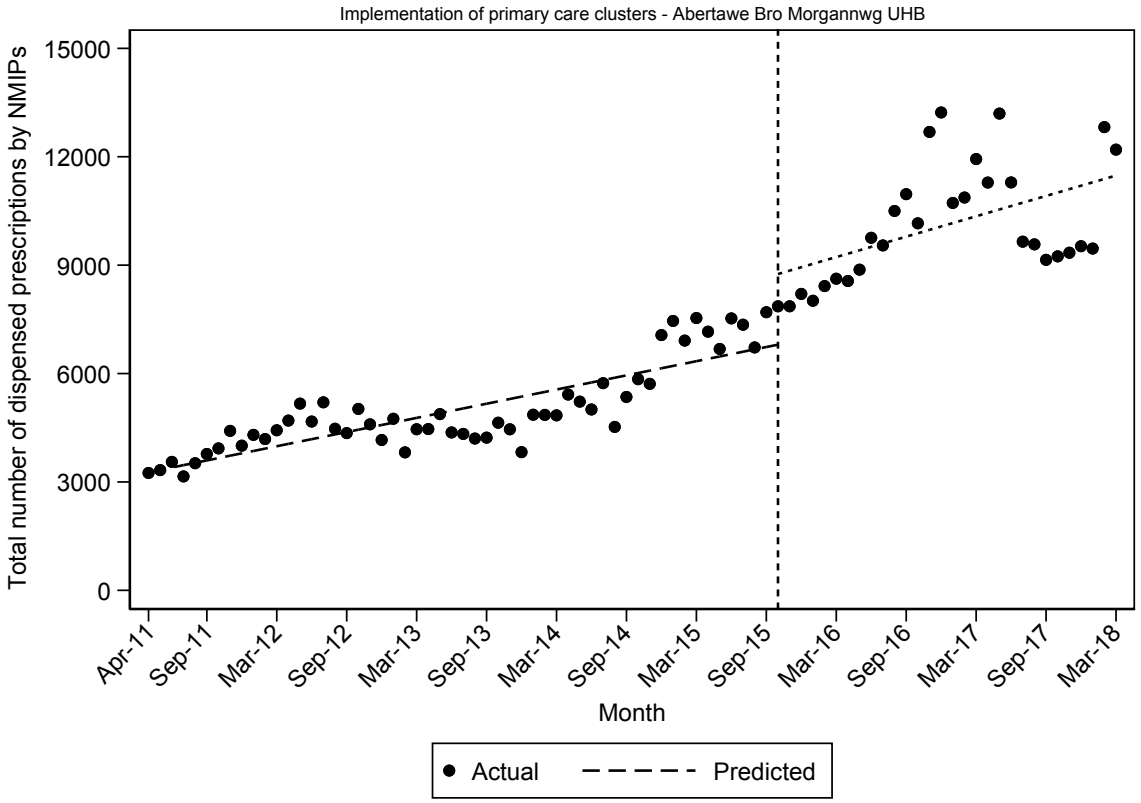

Figure S2: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Abertawe Bro Morgannwg University Health Board)

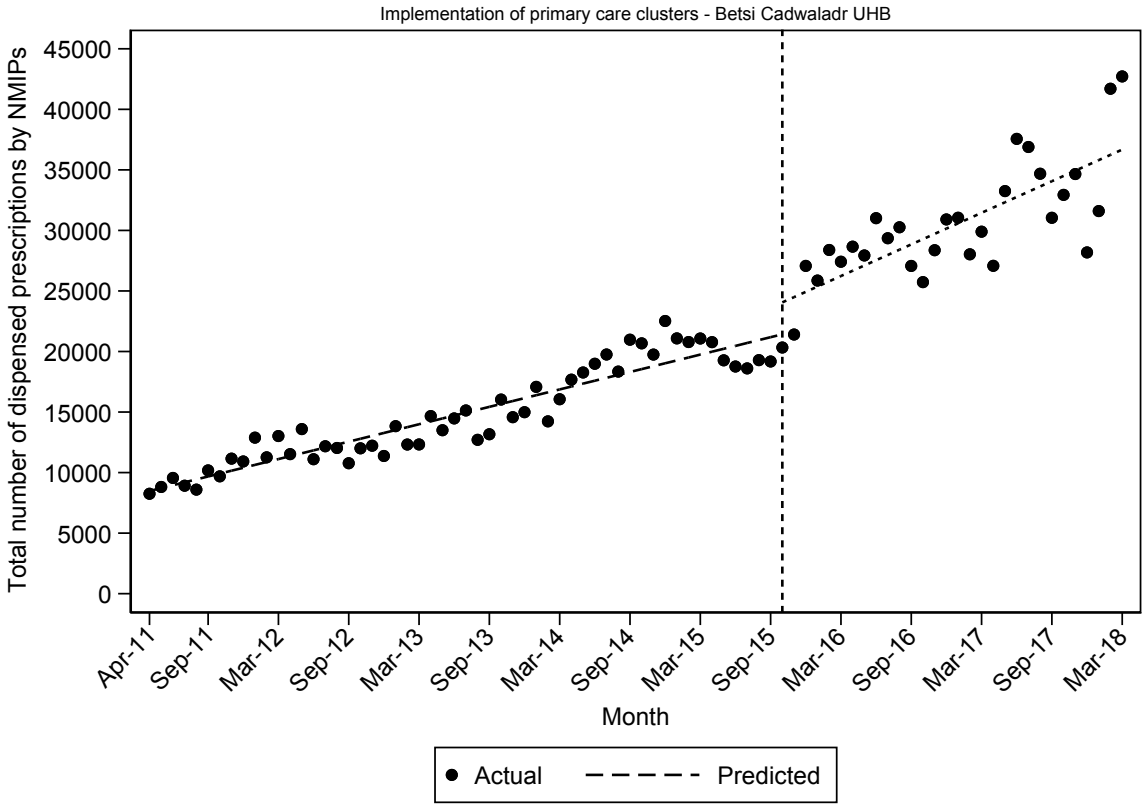

Figure S3: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Betsi Cadwaladr University Health Board)

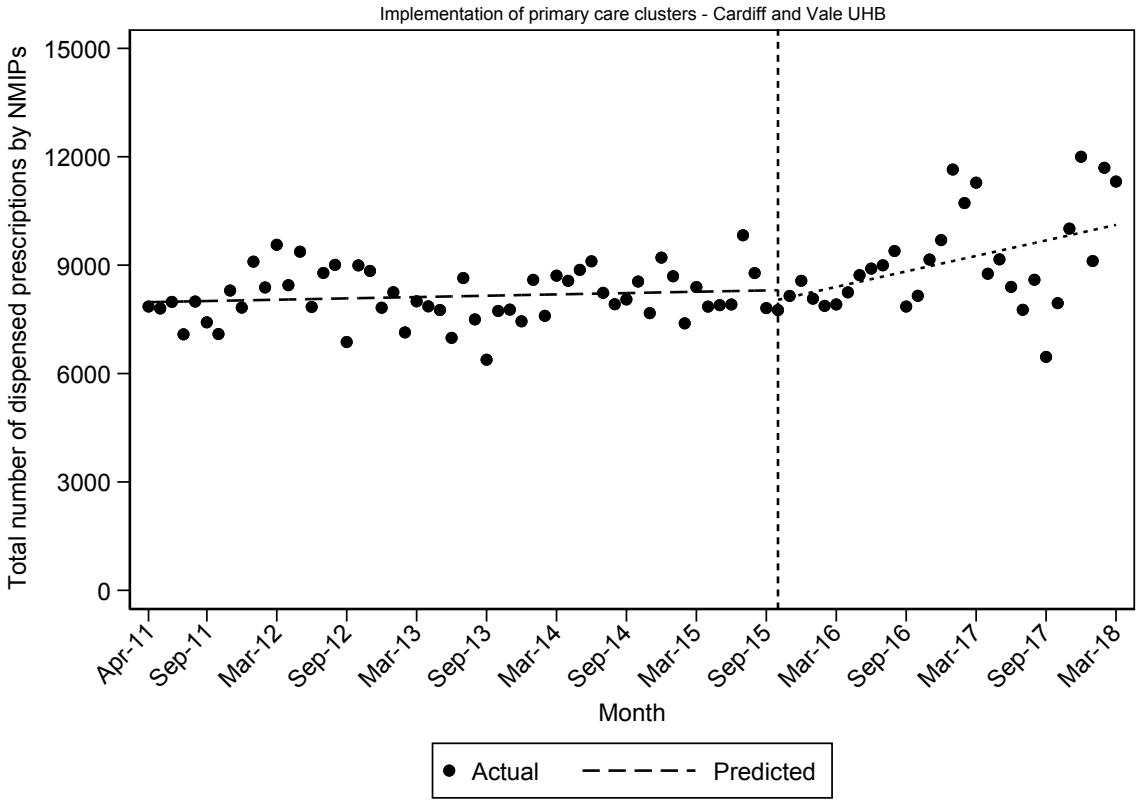

Figure S4: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Cardiff and Vale University Health Board)

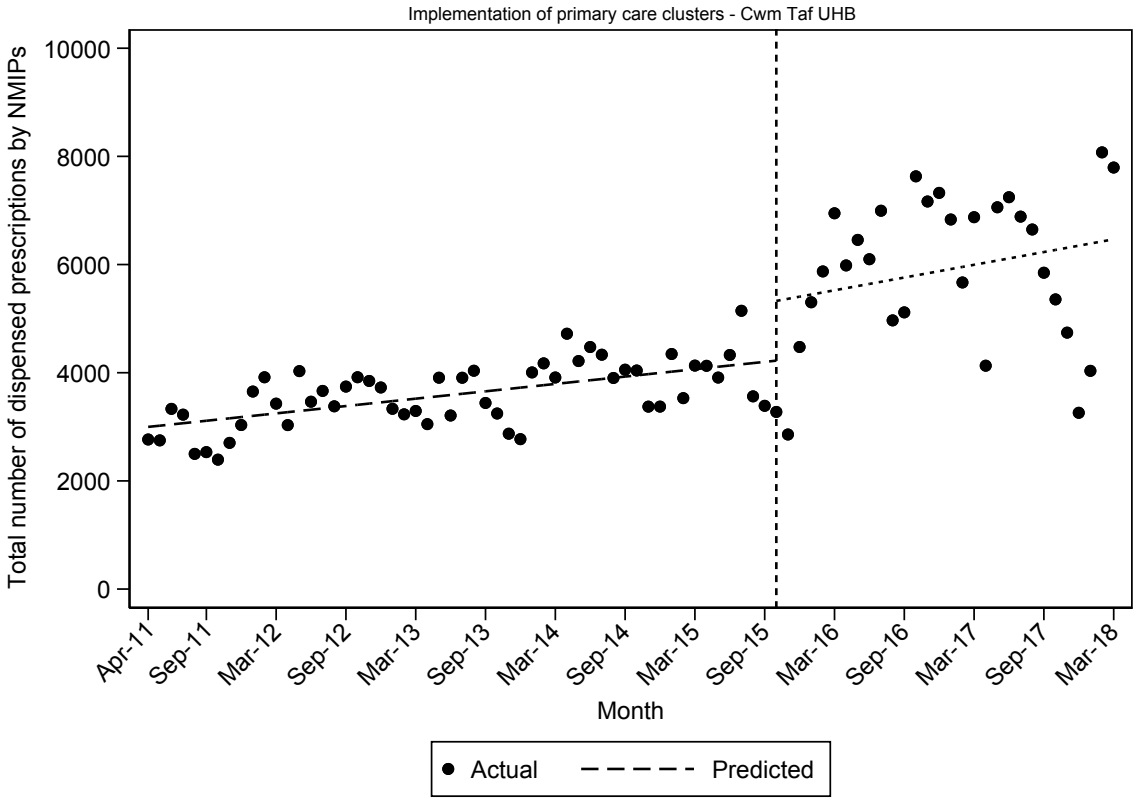

Figure S5: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Cwm Taf University Health Board)

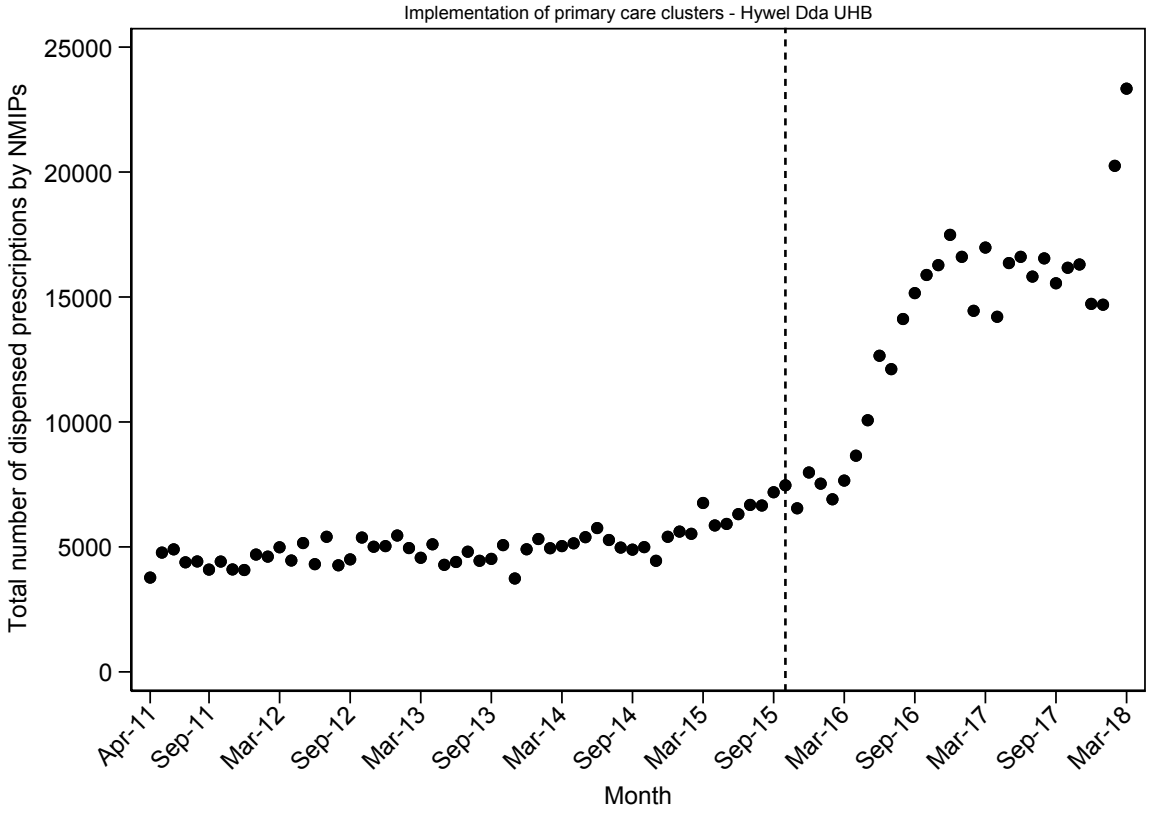

Figure S6: Observed dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Hywel Dda University Health Board)

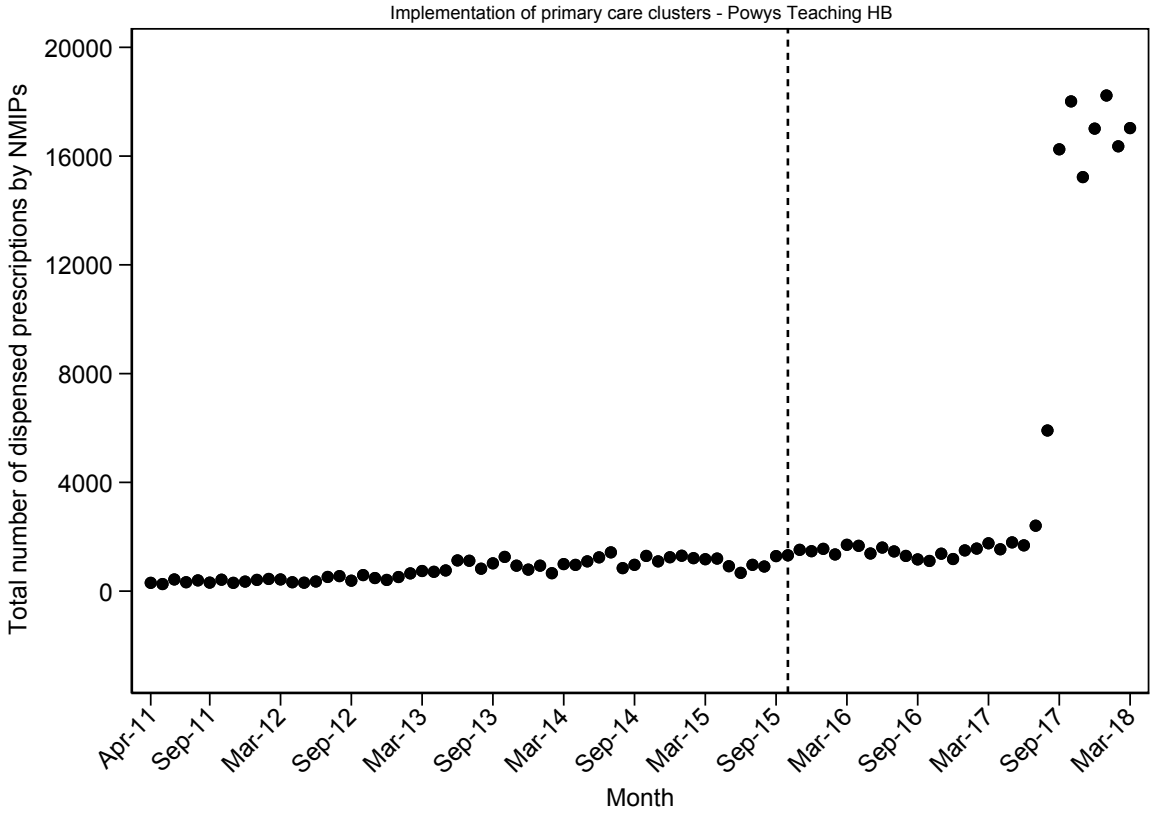

Figure S7: Observed dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Powys Teaching Health Board)

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Prescribing trends over time by non-medical independent prescribers (NMIPs) in primary care settings across Wales (2011-2018): a secondary database analysis

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Prescribing trends over time by non-medical independent prescribers (NMIPs) in primary care settings across Wales (2011-2018): a secondary database analysis

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ABSTRACT

Introduction As of 2015, as part of the implementation of the Welsh Government Primary Care Plan and primary care clusters, the Welsh Government has encouraged non-medical healthcare professionals working in primary care to train as independent prescribers (IPs).

Design Retrospective secondary data analysis and Interrupted Time Series (ITS) analysis in order to compare prescribing by non-medical independent prescribers (NMIPs) pre and post-implementation of primary care clusters across Wales.

Objectives This research aimed to identify the number of NMIPs in primary care in Wales and describe their prescribing trend of items between 2011 and 2018, in order to compare their prescribing pattern before and after the implementation of primary care clusters for Wales.

Results Over the study period, 600 NMIPs (nurses n=474 and pharmacists n=104) had prescribed at least one item. The number of nurse IPs increased by 108% and pharmacists by 325% (pharmacists had the largest increase between July 2015 and March 2018). The number of items prescribed by NMIPs increased over time by an average of 1,380 per month (95% CI: 904 to 1855, $p < 0.001$) after the implementation of primary care clusters compared to 496 (95% CI: 445 to 548, $p < 0.001$) prior its implementation. Approximately one third of the items prescribed by NMIPs was within Betsi Cadwaladr University Health Board (HB) with only 4% in Powys Teaching HB.

Conclusion The number of NMIPs and their volume of prescribing in primary care in Wales has increased following the implementation of primary care clusters in 2015. This suggests that the Government's recommendations of utilising NMIPs in primary care have been implemented. Future studies should focus on efficiency and quality of prescribing by NMIPs in primary care.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first study using a secondary database analysis, which has provided insights and empirical findings on the prescribing pattern of medicines by non-medical independent prescribers (NMIPs) over time in primary care in Wales.
- The data provided via the Comparative Analysis System for Prescribing Audit (CASPA) software system was limited to the last seven years and only captured prescriptions that were dispensed in community pharmacies.
- The CASPA system was designed for financial reimbursement purposes for community pharmacies, which means that holding investigations at the level of patients or prescribers, such as stopping or changing patients' medications, as well as clinical safety issues or other prescribing activities, were not possible.
- The professions of NMIPs as pharmacist, nurse, physiotherapist or others were not identified on the prescriptions and, consequently, in the CASPA system.
- The ITS analysis has the strength of evaluating data at the whole population level, which allowed the researchers to evaluate the utilisation of NMIPs in primary care across all of Wales.

INTRODUCTION

The right to prescribe medicines was traditionally restricted to physicians, dentists and veterinary surgeons[1]. Prescribing practice has changed over the last 50 years to involve not only physicians and dentists (medical prescribers) but also other health care professionals, known as non-medical prescribers. The adoption of non-medical prescribing fundamentally began in the USA in the 1960s[2] and has extended to the UK, Canada, New Zealand, Australia, and other European and African nations[3]. Beyond the UK, solely nurses and pharmacists have been granted the authority to prescribe medicines collaboratively (dependently) under a physician's supervision or independently from a limited lists of medicines[4-7]. The drive to extend the medicines prescribing mandate to non-medical healthcare professionals was related to a variety of aspects within every nation.

In the UK, non-medical prescribing was introduced as part of the National Health Service (NHS) plans, which intended to improve and modernise the health care system[8,9]. The aim of introducing non-medical prescribing was to enhance patient care and safety, improve patient access and choice of appropriate medicines for their conditions, use the already gained skills of health care professionals in the most effective way, and promote a more flexible teamwork environment in the NHS[10]. Pharmacists, nurses, optometrists and Allied Health Professionals can qualify as non-medical prescribers after completing an advanced prescribing training programme[9,10]. This programme lawfully allows these healthcare professionals to prescribe within their area of competence. such as that pharmacists and nurses can prescribe medicines, appliances, and wound dressings as either independent or supplementary prescribers within their clinical area of practice. Some NMIPs are limited to prescribe certain medications within their clinical of speciality, such as

optometrists who can only prescribe for eye conditions and surrounding tissues[9].

Independent prescribing is defined as 'prescribing by a practitioner (e.g. a doctor, dentist, nurse, or a pharmacist) responsible and accountable for the assessment of patients with undiagnosed or diagnosed conditions and for decisions about the clinical management required, including prescribing'[10]. Whereas, supplementary prescribing is a 'voluntary partnership between the responsible independent prescriber and a supplementary prescriber, to implement an agreed patient-specific clinical management plan with the patient's agreement, particularly but not only in relation to prescribing for a specific non-acute medical condition or health need affecting the patient'[11]. Non-medical independent prescribing was introduced in the UK in 2002 after a change in the legislation made by the UK Government allowing the first level registered nurses who have at least 3 years of experience to prescribe independently from a limited list of medicines[12]. In 2006, independent prescribing extended for qualified nurses and pharmacists who completed the necessary training to prescribe any medicines within their area of competence with few exceptions[10]. This was followed by the introduction of optometrist independent prescribing in 2007[13], and more recently, independent prescribing by Allied Health Professionals including podiatrists and physiotherapists independent prescribing in 2013[14], and therapeutic radiographers independent prescribing in 2016[15]. The recent healthcare professionals who gained the prescribing authority in Wales were paramedics in 2019. In 2017, the estimated number of non-medical independent prescribers (NMIPs) in the UK was as follows: 30,000 nurse independent prescribers (IPs); 3,000 pharmacist IPs and 600 Allied Health Professionals IPs[16]. All NMIPs are responsible and accountable for their own prescribing and limiting their prescribing to their therapeutic area of expertise[9]. Moreover, these healthcare professionals are

required to seek appropriate advice or referral if they lack the confidence to manage patients' conditions or prescribe the suitable medicines for their patients[9].

In Wales, the NHS provides its services via three NHS Trusts and seven health boards (HBs). The seven HBs are Swansea Bay University HB (SBUHB), Cardiff and Vale University HB (CVUHB), Cwm Taf Morgannwg University HB (CTMUHB), Hywel Dda University HB (HDUHB), Powys Teaching HB (PTHB), Betsi Cadwaladr University HB (BCUHB) and Aneurin Bevan University HB (ABUHB). The SBUHB was formerly known as Abertawe Bro Morgannwg University HB (ABMUHB), having being renamed in 2019.

Primary health care services are the initial point of care for patients in the NHS. In Wales, it has been estimated that around 90% of people's contact with the NHS is with primary care services, with General Practices the main point of contact[17]. In 2016, there were 441 General Practices in Wales and 2,009 General Practitioners (GPs) (excluding, locums, retainers, and registrars)[18]. The Welsh Government and HBs have focused upon improving primary care services[17], and this has included the development of primary care clusters. Clusters comprise groups of adjacent general practices that have linked together to provide advanced medical services locally in order to relieve pressure on hospitals[19]. The aims of these clusters include improving patients' access to their medicines and information as well as the provision of advice and support to manage medicines. These clusters came into being in the last quarter of 2015[19]. Currently, there are 64 primary care clusters in Wales which provide services for a population of 30,000 to 50,000 patients per cluster[19]. In order to overcome GP shortages[20,21], these clusters are supported by high numbers of hospital pharmacists, nurses and other professionals. In addition, the Welsh Government and HBs have prioritised funding for new posts and training of other

health care professionals, such as pharmacist and nurse IPs[17]. Consequently, the number of non-medical prescribers in primary care has increased in recent years and is expected to rise further[16,21].

Only one published study has investigated the implementation of non-medical prescribing in Wales[16]. This study aimed to provide an overview of the implementation and utilisation of non-medical prescribing in all health care sectors through a national questionnaire survey. The results of this study indicated that the majority of non-medical prescribers in Wales were based in secondary care settings. Moreover, these researchers stated that the utilisation of non-medical prescribers across Wales, particularly in primary care, was inconsistent and had not been implemented in all services. In addition, it was suggested that there was a need to investigate and recognise the development of primary care services in Wales, with support required for non-medical prescribers[16].

The aim of this study was to identify the number of NMIPs in Wales and describe their prescribing volume (from April 2011 to March 2018) as a whole, as well as within the seven HBs, before and after the implementation of primary care clusters. This is the first study in Wales to use data obtained through a national database to review prescribing volume by NMIPs in primary care. No equivalent studies have been published internationally.

METHODOLOGY

The study design was a retrospective secondary data analysis of monthly data for prescriptions issued by NMIPs in primary care in Wales and dispensed in community pharmacies, as well as the data on the number of NMIPs within primary care in Wales.

The number of NMIPs who prescribed each month and who prescribed at least one item from April 2011 to March 2018 was obtained through the NHS Wales Shared Services Partnership, Primary Care Services. Prescribing data were obtained from the Comparative Analysis System for Prescribing Audit (CASPA) software system (Version 5), provided by the NHS Wales Shared Services. Data were fully anonymised and recorded as part of routine practice, as such, the study did not require ethical approval. CASPA records all dispensed WP10 prescriptions (NHS Welsh prescriptions for use in primary care), to allow financial reimbursement to community pharmacies[9]. Whilst it is acknowledged that dispensing may not fully reflect prescribing, due to patients not taking their prescriptions to a pharmacy for dispensing, the impact of this is likely to be small. This is due to that the prescription charge for people in Wales was abolished in 2007 allowing all patients who were registered with their Welsh GPs to get their prescriptions dispensed from a pharmacy in Wales free of charge[22]. As a result, the impact of non-dispensed items would have been reduced by this policy, which also limits the financial burden to patients. Therefore, dispensing was used as a surrogate marker for prescribing in this study.

The number of items refers to each single item prescribed by a prescriber on a prescription form to a patient[23]. All recorded WP10 prescriptions issued by GPs and NMIPs in Wales and dispensed by community pharmacists from April 2011 to March 2018 were extracted and included in the study. The number of prescribed items by

NMIPs were extracted from the CASPA system on a monthly basis, the total number of items per 100,000 population (the population data in Wales as a whole and in each HB obtained from the Welsh Government Stats Wales[24]) was calculated in order to take the population into consideration. Percentages were calculated for the total number of prescribed items by NMIPs in each HB. The name of ABMUHB was used to illustrate the findings in this HB as this was its name over the study period.

Although Randomised Controlled Trials (RCTs) are considered the gold standard method to evaluate longitudinal effects of interventions over time[25-27], they lack the ability to evaluate the already implemented service retrospectively[27]. Therefore, prescribing trend data were compared before and after the introduction of primary care clusters (the intervention) by using an interrupted time series (ITS) analysis. This analysis was performed using ordinary-least squares regression with Newey-West standard errors and a lag for the autocorrelation structure. The Cumby-Huizinga test for autocorrelation was examined to determine the appropriate autocorrelation structure to be accounted for in the model. The model included pre- and post-intervention trends, as well as a coefficient to examine a change in level immediately post-intervention. The parameter estimates are presented alongside 95% confidence intervals and p-values. The counterfactual trend (i.e. the trend in the absence of the intervention) was examined, and this was compared to the actual observed trend to calculate absolute and relative differences at the end of the observed period (March 2018). Analysis was performed using the *itsa* command in Stata V16.0[28]. The findings were assumed significant at p value <0.05. Confidence intervals (CIs) were calculated in order to be 95% certain that the range of values contained the true mean of the data[29].

The Welsh Government plan[17] encouraged local HBs to prioritise funding and

development of primary care clusters in April 2015. However, the implementation of these clusters is the responsibility of each individual local HB and there are no definitive time points of their establishment. To accommodate this, the researchers engaged with the relevant stakeholders (e.g. policy makers and Chief Pharmaceutical Officer) to determine the appropriate time for the intervention phase. They agreed the intervention phase began six months after the provided funding by the Government to HBs, meaning October 2015, to allow for an appropriate time for each HB to train NMIPs.

Patient and public involvement - This research was done without patient and public involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

RESULTS

Trend of the total number of items prescribed by all prescribers

The total number of items prescribed by all health care professionals (GPs and non-medical prescribers) from April 2011 to March 2018 was 540,781,584 items (17,482,150 per 100,000 population). The total number of prescribed items per 100,000 population per year increased by 7.1% between 2011-2012 (n= 2,371,511) and 2014-2015 (n= 2,539,192) and increased by 0.7% between 2014-2015 (n= 2,539,192) and 2017-2018 (n= 2,556,784]) (Figure 1).

Trend of the total number of items prescribed by NMIPs

The total number of items prescribed by NMIPs in primary care in Wales between April 2011 and March 2018 was 5,088,405 items (n= 164,130 per 100,000 population). The number of items prescribed as a percentage of all items prescribed by all health care professionals (except items prescribed by dentists) increased from 0.57% in 2011-2012 to 1.7% in 2017-2018. As shown in Table 1 and Figure 2, dispensed prescriptions by NMIPs in primary care started at 31,756 and increased on average per month prior to the implementation of primary care clusters by 496 (95% CI: 445 to 548, $p < 0.001$). There was no evidence to suggest a change in the level immediately following the implementation of primary care clusters in October 2015. However, following this implementation, there was an increase in dispensed prescriptions per month, relative to pre-implementation trends, of 1,380 on average (95% CI: 904 to 1855, $p < 0.001$).

Table 1: Parameter estimates from the interrupted time series analysis examining the change in level and slope of dispensed prescriptions in primary care by NMIPs following the implementation of primary care clusters in October 2015 (N = 84 months)

Variable	Coefficient	Lower 95% CI	Upper 95% CI	p-value
Intercept	31755.5	30208.3	33302.8	<0.001
Pre-intervention slope	496.3	444.8	547.8	<0.001
Level change	3023.4	-2151.5	8198.2	0.248
Post-intervention slope	1379.7	904.4	1855.1	<0.001

Assuming the pre-implementation trend would have continued in the absence of the introduction of primary care clusters, the expected number of dispensed prescriptions by NMIPs at the end of the observation period (March 2018) was 73,443 (95% CI: 70,260 to 76,627), and with the model predicting an expected number (in the presence of primary care clusters) of 117,859 (95% CI: 108,049 to 127,670), there was a 60% relative increase in the number of dispensed prescriptions by NMIPs following the implementation of primary care clusters over and above what would have been expected in the absence of such a scheme (95% CI: 46 to 75, $p < 0.001$).

The total number of NMIPs

Data obtained from the NHS Wales Shared Services Partnership shows that the total number of NMIPs who prescribed at least one item from April 2011 to March 2018 was 600 prescribers (474 nurses, 104 pharmacists, 21 physiotherapists and 1 with unknown profession). The total number of NMIPs in each HB is illustrated in Figure 3. The number of prescribing NMIPs per month increased by approximately 140% between April 2011 (n=174) and March 2018 (n=414). Of those, the number of nurses increased from 158 in April 2011 to 328 in March 2018 (an increase of 108%). The number of pharmacists increased from 16 in April 2011 to 68 in March 2018 (an

increase of 325%), the largest increase was from July 2015 (n=20) to March 2018 (n=68) by 240%. In January 2015, the first physiotherapist IP started to prescribe with the number increasing to 17 in March 2018.

Trend of the total number of prescribed items by NMIPs in different HBs pre and post-intervention

Table 2 presents the total number of items prescribed by NMIPs, as well as the number per 100,000 population and percentage of all items prescribed, per HB. Approximately one third of the items prescribed by NMIPs was within BCUHB (Table 2) with only 4% in PTHB. Data by HBs are illustrated in Figure 4 and Figure 5, and it can also be seen in the supplementary file.

Table 2 Total number of items prescribed by NMIPs, as well as the number per 100,000 population and percentage of all items prescribed, per HB in primary care in Wales and dispensed in community pharmacies since April 2011 until March 2018

Health Board	Total number of items prescribed by NMIPs	% of the prescribed items by NMIPs in each HB*	Prescribed items by NMIPs per 100,000 population
BCUHB	1,711,949	33.64%	240,742.5
ABUHB	834,879	16.41%	139,396.5
CVUHB	711,805	13.99%	145,069.9
HDUHB	686,166	13.48%	172,782.9
ABMUHB	573,624	11.27%	106,813.2
CTMUHB	371,315	7.30%	122,620.2
PTHB	198,667	3.91%	137,000.6

ABMUHB (Abertawe Bro Morgannwg University HB); **ABUHB** (Aneurin Bevan University HB); **BCUHB** (Betsi Cadwaladr University HB); **CTMUHB** (Cwm Taf Morgannwg University HB); **CVUHB** (Cardiff and Vale University HB); **HDUHB** (Hywel Dda University HB); **PTHB** (Powys Teaching HB)

* The percentage of the prescribed items by NMIPs in each HB was calculated based on the total number of items prescribed by NMIPs in all Wales

DISCUSSION

Statement of the principal findings

This study investigated the number and associated prescribing volume of NMIPs before and after the implementation of primary care clusters in Wales. The number of NMIPs has increased in primary care in Wales over the study period and the majority of them were nurses, followed by pharmacists, and physiotherapists. Interestingly, the database did not identify other health care professionals who have prescribing authorisation in Wales, including therapeutic radiographers, chiropodists and podiatrists, and optometrists[16].

The analysis of the prescribed number of items by NMIPs before and after the implementation of primary care clusters showed a 60% relative increase following the implementation of the primary care clusters in Wales. However, the prescribing of items by NMIPs was inconsistent across the seven HBs.

Strengths and weaknesses

This is the first study that has used a secondary database analysis, which has provided insights and empirical findings on the prescribing pattern of medicines by non-medical independent prescribers (NMIPs) over time in primary care in Wales. Although this study has achieved its aim and objectives, it has a number of limitations. Firstly, the data provided via the CASPA software system was limited to the last seven years. Secondly, this system was designed for financial reimbursement purposes for community pharmacies, which means that holding investigations at the level of patients or prescribers, such as stopping or changing patients' medications, as well as clinical safety issues or other prescribing activities, were not possible. In addition, this

system only captured NHS prescriptions that were dispensed in community pharmacies. Therefore, prescriptions issued by those prescribers that have not been dispensed as well as private prescriptions that have been prescribed by NMIPs, such as optometrists, were not captured by the system. Finally, the professions of NMIPs as pharmacist, nurse, physiotherapist or other were not identified on the prescriptions and, consequently, in the CASPA system. The ITS analysis may have the limitation of the presence of unknown confounding variables, which are outside of the researcher's control, that may have happened at the same time of the intervention and this leads to the difficulty of establishing causal effects[30]. However, this analysis has the strength of evaluating data at the whole population level[31], which allowed the researchers to evaluate the utilisation of NMIPs in primary care across all of Wales.

Comparison with other studies

The increase in the number of NMIPs in primary care in Wales may suggest that the primary care sector has recognised the skills of these practitioners, improving the skill-mix in this sector, and hopefully reducing the pressure on GPs i.e. the benefits described in the second Crown Report[32]. Since the last quarter of 2015, the increase in the percentage of pharmacist IPs was higher than the increase in the percentage of nurse IPs (325% vs 108%). This could be explained by the implementation of the Welsh Government Plan[17], introduction of primary care clusters[19], and the shortage of GPs in Wales, particularly in BCUHB[15,32,33,34]. All of these factors may have contributed to recruitment of more pharmacist IPs[17]. Pharmacist independent prescribing is a new role for pharmacists within clusters, with many secondary care based pharmacist IPs moving into these positions[21]. This may lead to a shortage of pharmacists within secondary care and has highlighted the need for

a pharmacy workforce plan for Wales.

Although the number of nurse IPs is much greater than pharmacist IPs, they only represent 5% of the nursing workforce[*35*], while pharmacist IPs represent 7% of the pharmacist profession[*36*]. The fact that there are more nurse IPs than other professions is in line with the findings of other studies that have investigated the implementation of non-medical prescribing in England[*33*,*37*] and Wales[16]. Therapeutic radiographer IPs are based within secondary or tertiary care settings in Wales and therefore, they would be unlikely to be included in the database. However, the other professions, such as chiropodists, podiatrists and optometrists, could potentially be working in primary care settings but do not appear to have issued NHS prescriptions as they could have been prescribing medications for their patients within private hospitals, at point of care or not using their prescribing qualification. If they were not using their prescribing qualification, this may suggest that HBs need to investigate the reasons for that in order to prevent wasting the time and expenses incurred for training and failure to deliver an improved service to patients.

The increase in the number of NMIPs, particularly pharmacist IPs, may explain the increased rate of prescribing of medicines by these practitioners over the same period. The high number of prescribed items by NMIPs in BCUHB (34%) compared to other HBs could be explained by the high number of NMIPs in BCUHB (246 NMIPs). It is evident that the utilisation of NMIPs is inconsistent across the seven HBs in Wales, which supports previous research[16]. BCUHB and HDUHB represent the largest geographical areas in Wales compared to other HBs[38], but have the lowest number of GPs per 10,000 population (6.1 and 5.8, retrospectively)[39]. The low number of GPs in these HBs could be related to issues of recruitment, as well as the difficulty in

keeping those who are already employed in their positions[34,40]. The shortage of GPs in these HBs, may explain the early adoption of non-medical independent prescribing. Although PTHB showed the lowest number of items prescribed by NMIPs over the study period, it is the smallest geographical area in Wales with the lowest population compared to other HBs. An equivalent increase in the number of prescribers and items would therefore produce a bigger percentage change than in a larger HB. However, the large increase in the trend of the prescribing items in this HB over the last two years of the study period may be explained by the increase in the number of NMIPs. Moreover, PTHB only has primary care services, so whilst other HBs may have been training IPs in both primary and secondary care settings, the focus in PTHB would have been primary care only, which may have resulted in a greater change. However, due to the nature of the database used, it was not possible to investigate this further and this could be the focus of future work.

The meaning of the study: possible explanations and implications for clinicians and policymakers

The findings of this study showed inconsistency in terms of the implementation of the NMIPs' services between HBs in primary care in Wales, particularly after the primary care clusters' implementation. Although there is a lack of evidence with regards to the reasons and barriers behind this, some reasons that may have contributed to lower utilisation of this service in some HBs may include the lack of funding[16, 37, 41, 42] and lack of a plan or strategy to develop this service[37]. However, these studies are outdated given the pace of change. Moreover, it has not been conducted in Wales in particular, which may not reflect recent practice and policies in this country. Due to the lack of evidence regarding the impact of these

barriers on the implementation of non-medical independent prescribing in each HB, further research is required to investigate this matter. This study provides the initial evidence for such research, as well as providing the opportunity to share learning among HBs.

Unanswered questions and future studies

This study provides a research agenda for further investigation to examine questions related to efficiency, quality of prescribing, cost effectiveness, and improved access to services provided by NMIPs. With the presence of some variety and inconsistency in the prescribing trend of NMIPs across different HBs, this provides an opportunity to share the knowledge on advanced and novel services provided by these prescribers as well as to investigate the reasons behind it.

CONCLUSION

The number of NMIPs and their prescribing trends of medicines increased in all Wales, as well as in the majority of HBs, particularly the number of pharmacist IPs since the implementation of primary care clusters. This could be related to the implementation of the Welsh Government Plan[17] and the introduction of primary care clusters. The findings of this study may suggest that the increased number of NMIPs in the primary care sector in Wales over time may help to reduce the pressure on GPs and improve the skill-mix across different therapeutic areas. This aligns with the main reasons for the implementation of non-medical prescribing in the UK, as outlined in the second Crown Report[32]. Future studies should focus on efficiency and quality of prescribing by NMIPs in primary care.

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Competing interests - All authors the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

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DATA SHARING STATEMENT - No additional data available

Transparency declaration - The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

INTEGRITY OF THE DATA AND ACCURACY OF THE DATA ANALYSIS - All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Ethics approval - No ethical approval required.

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Figure 1 Trend of the total number of items per 100,000 population prescribed by all prescribers in primary care in Wales and dispensed in community pharmacies by year

Figure 2 Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (All Wales)

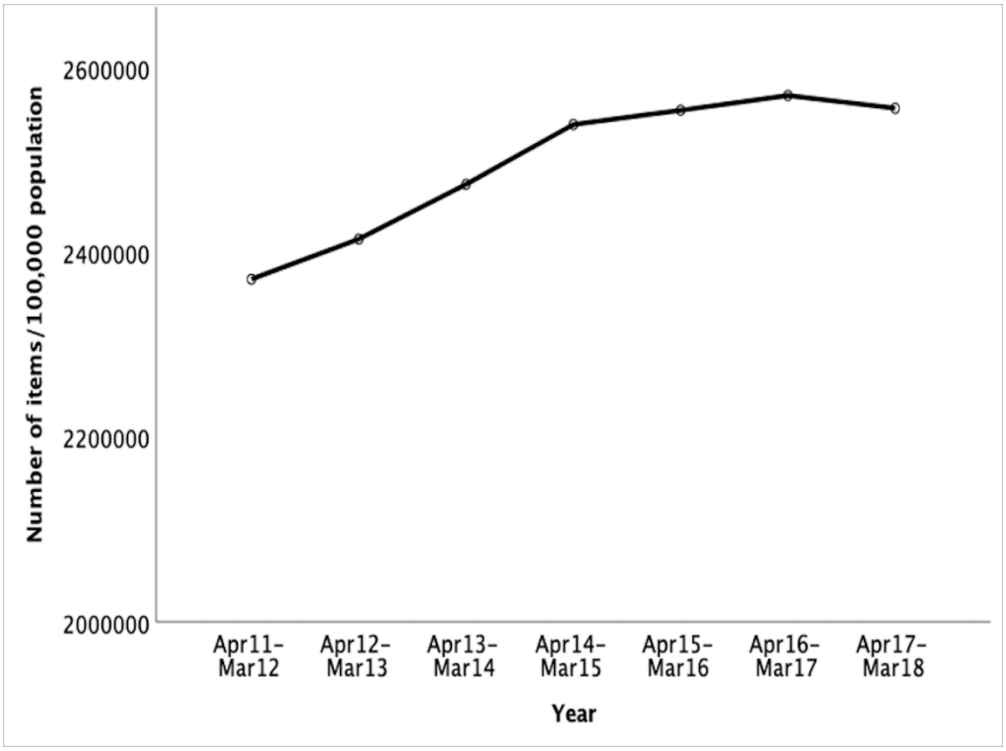
Figure 3 The total number of NMIPs (pharmacists, nurses and physiotherapists) who prescribed at least one item from April 2011 to March 2018 in primary care in Wales in different HBs

** **ABMUHB** (Abertawe Bro Morgannwg University HB); **ABUHB** (Aneurin Bevan University HB); **BCUHB** (Betsi Cadwaladr University HB); **CTMUHB** (Cwm Taf Morgannwg University HB); **CVUHB** (Cardiff and Vale University HB); **HDUHB** (Hywel Dda University HB); **PTHB** (Powys Teaching HB)*

Figure 4 Trend of the total number of dispensed items per 100,000 population prescribed by NMIPs in primary care by health board (dashed line denotes introduction of primary care clusters in October 2015)

*Figure 5 Trend of the total number of dispensed items per 100,000 population prescribed by NMIPs in primary care by health board (dashed line denotes introduction of primary care clusters in October 2015) **

* Final seven outlying data points in Powys Teaching Health Board removed to illustrate trends in other Health Boards.



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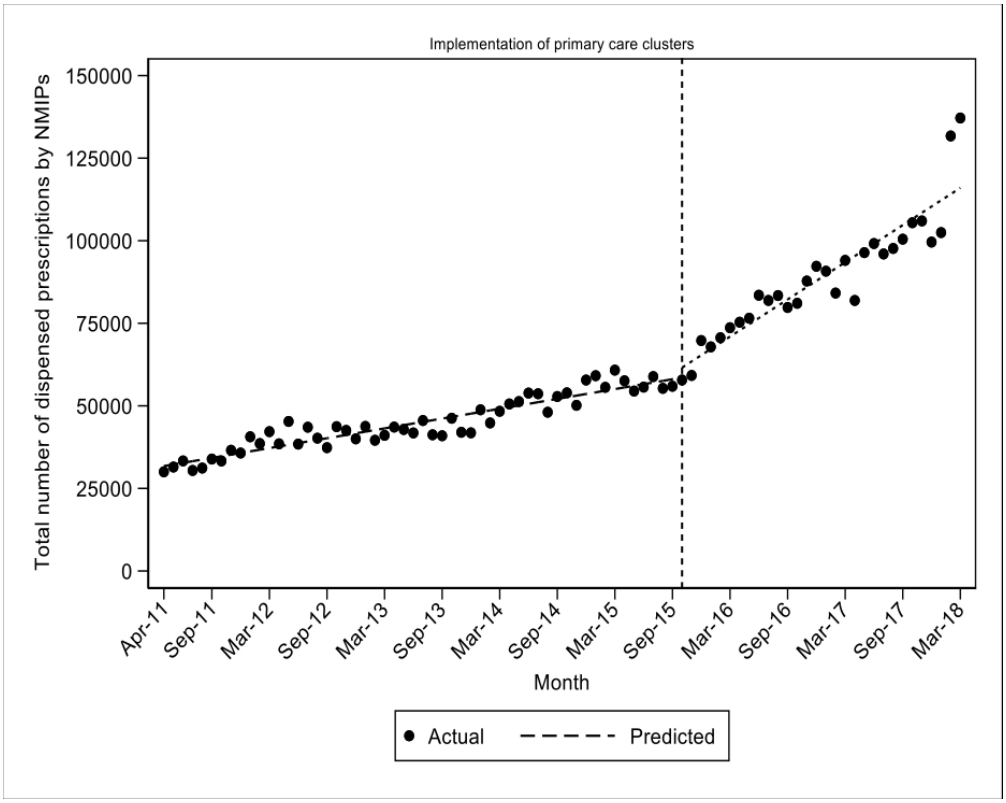
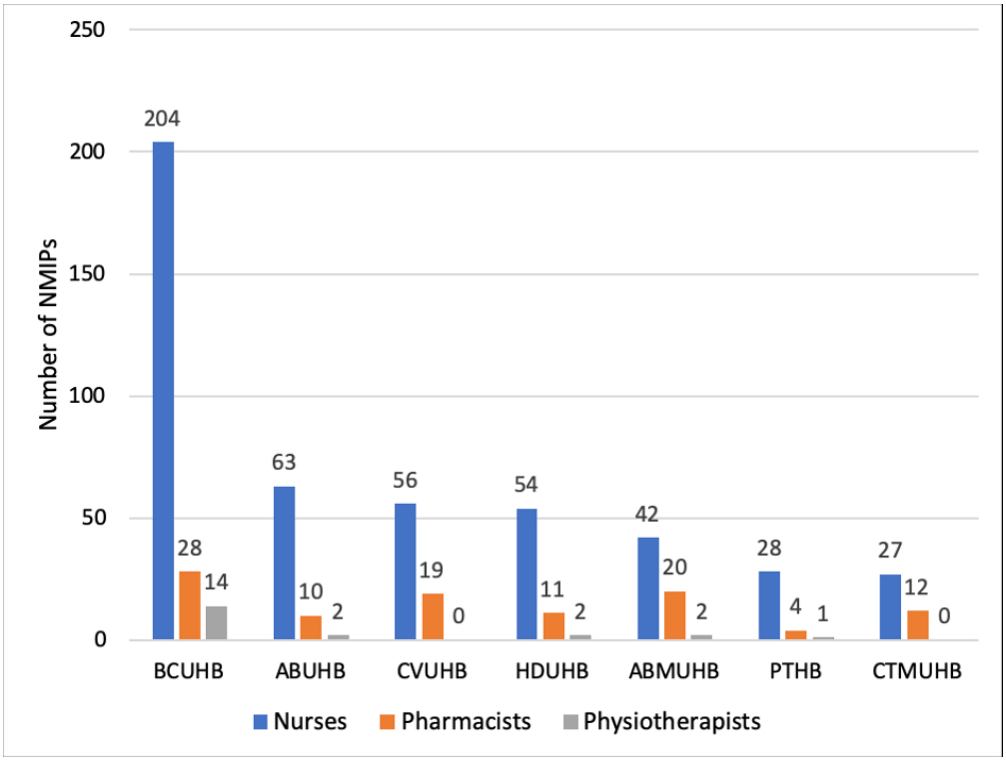


Figure 2 Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (All Wales)



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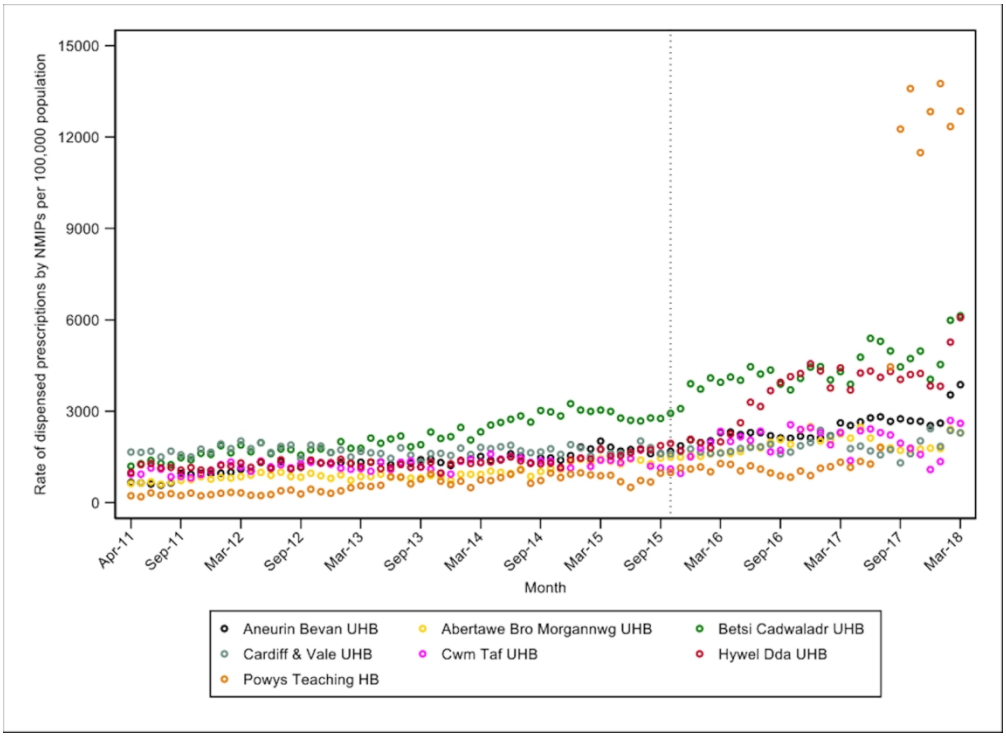

Figure 4 Trend of the total number of dispensed items per 100,000 population prescribed by NMIPs in primary care by health board (dashed line denotes the introduction of primary care clusters in October 2015)

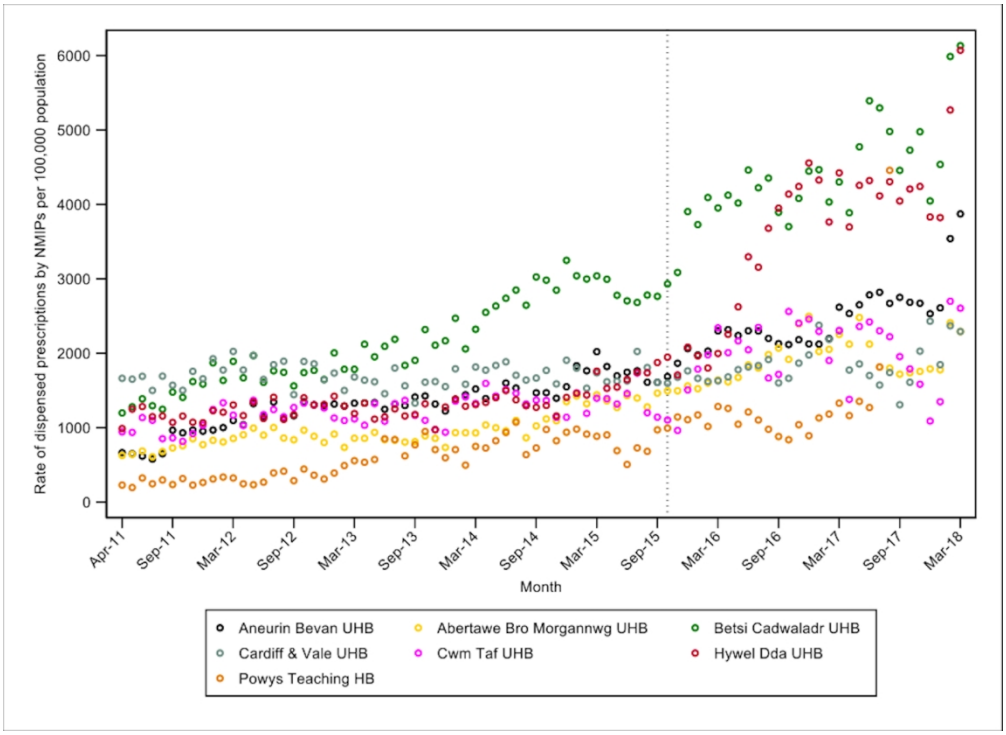

Figure 5 Trend of the total number of dispensed items per 100,000 population prescribed by NMIPs in primary care by health board (dashed line denotes introduction of primary care clusters in October 2015) * *Final seven outlying data points in Powys Teaching Health Board removed to illustrate trends in other Health Boards.

Prescribing trends over time by non-medical independent prescribers (NMIPs) in primary care settings across Wales (2011-2018): a secondary database analysis

Supplementary material

Health board trends in dispensed prescriptions by non-medical prescribers across health boards in Wales

Table S1: Health Board-specific parameter estimates from the interrupted time series analysis examining the change in level and slope of dispensed prescriptions in primary care by NMIPs following the implementation of primary care clusters in October 2015 (N = 84 months) *

Health board	Variable	Coefficient	Lower 95% CI	Upper 95% CI	p-value
Aneurin Bevan University Health Board	Intercept	4639.4	4019.8	5259.0	<0.001
	Pre-intervention slope	109.9	89.7	130.1	<0.001
	Level change	-27.5	-1321.8	1266.8	0.966
	Post-intervention slope	144.7	40.9	248.5	0.007
Abertawe Bro Morgannwg University Health Board (lag 3)	Intercept	3268.9	2833.5	3704.3	<0.001
	Pre-intervention slope	65.4	47.2	83.6	<0.001
	Level change	1954.3	534.6	3374.0	0.008
	Post-intervention slope	28.6	-52.4	109.7	0.484
Betsi Cadwaladr University Health Board	Intercept	8480.1	7791.3	9168.9	<0.001
	Pre-intervention slope	239.7	208.3	271.1	<0.001
	Level change	2634.6	3.1	5266.0	0.050
	Post-intervention slope	195.4	2.7	388.1	0.047
Cardiff and Vale University Health Board (lag 8)	Intercept	7976.3	7458.2	8494.4	<0.001
	Pre-intervention slope	6.1	-6.6	18.9	0.342
	Level change	-266.1	-876.5	344.4	0.388
	Post-intervention slope	65.4	12.6	118.1	0.016
Cwm Taf University Health Board (lag 4)	Intercept	2998.4	2689.6	3307.4	<0.001
	Pre-intervention slope	22.7	13.1	32.3	<0.001
	Level change	1104.3	-310.2	2518.7	0.124
	Post-intervention slope	16.6	-75.0	108.2	0.720

*Models fitted with a lag of order 1 unless otherwise specified. Note that linear modelling assumptions were not fulfilled for Hywel Dda and Powys Health Boards and Findings are illustrated graphically in Figures S6 and S7.

Table S2: Comparison between actual and counterfactual dispensed prescriptions in primary care by NMIPs*

Health board	Estimate	Coefficient	Lower 95% CI	Upper 95% CI
All Wales	Absolute difference at March 2018	44415.5	34086.8	54744.1
	Relative difference at March 2018	60.5	45.6	75.3
Aneurin Bevan University Health Board	Absolute difference at March 2018	4313.3	1924.1	6702.5
	Relative difference at March 2018	31.1	12.7	49.5
Abertawe Bro Morgannwg University Health Board	Absolute difference at March 2018	2813.2	751.1	4875.4
	Relative difference at March 2018	32.1	6.1	58.1
Betsi Cadwaladr University Health Board	Absolute difference at March 2018	8496.7	4136.1	12857.3
	Relative difference at March 2018	29.7	13.5	45.9
Cardiff and Vale University Health Board	Absolute difference at March 2018	1694.8	332.9	3056.7
	Relative difference at March 2018	20.0	3.4	36.5
Cwm Taf University Health Board	Absolute difference at March 2018	1601.9	-78.1	3281.9
	Relative difference at March 2018	32.7	-2.9	68.2

*The counterfactual represents predicted values and trends in the absence of the implementation of primary care clusters in October 2015 (i.e. making the assumption that pre-implementation trends would have continued in the same way).

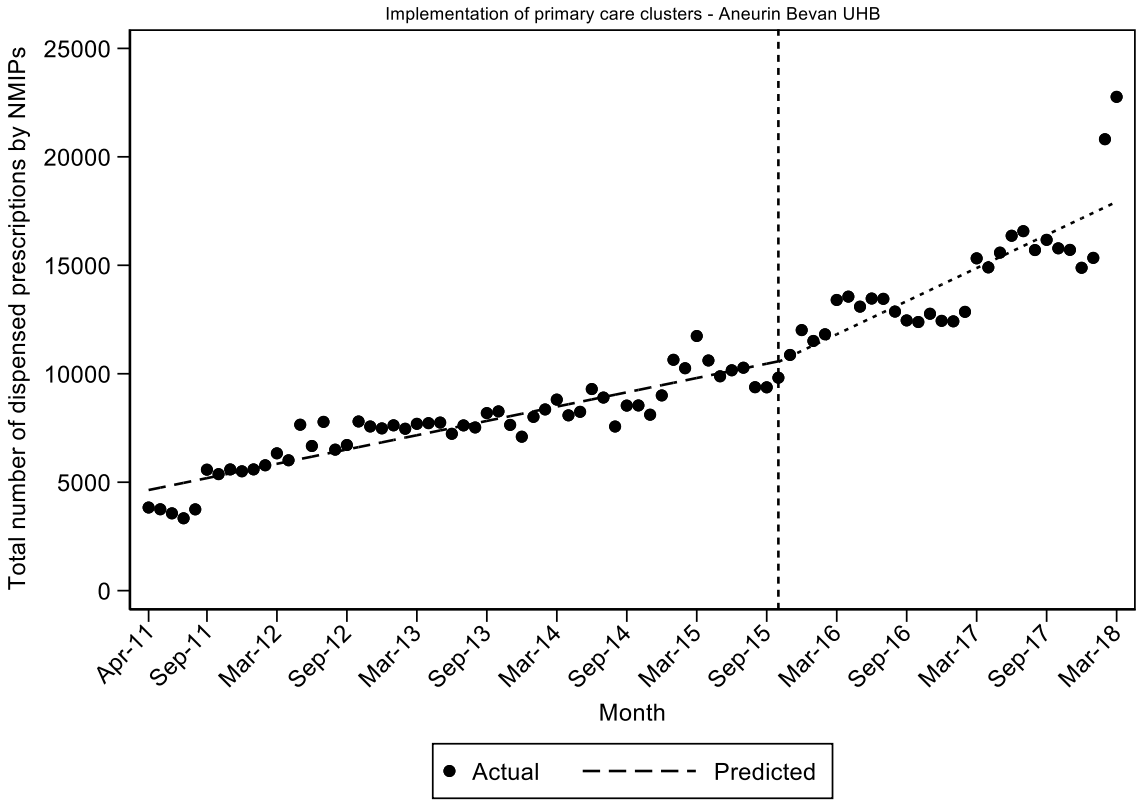

Figure S1: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Aneurin Bevan University Health Board)

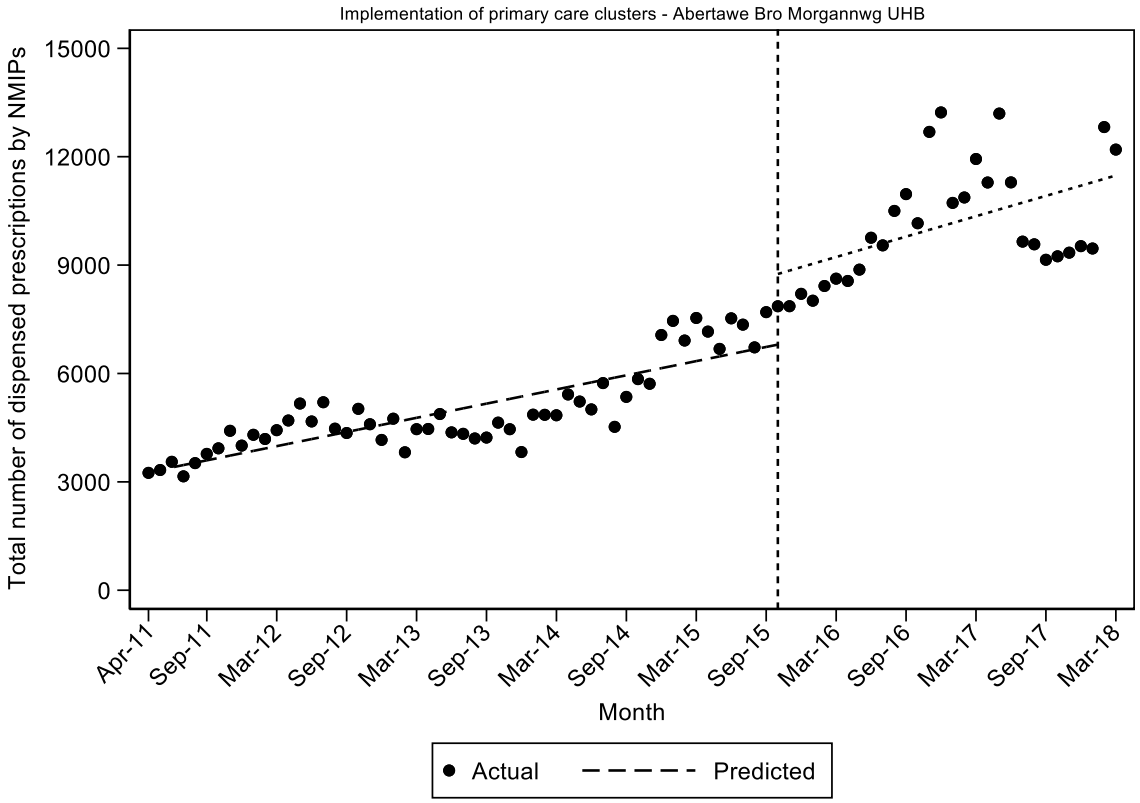

Figure S2: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Abertawe Bro Morgannwg University Health Board)

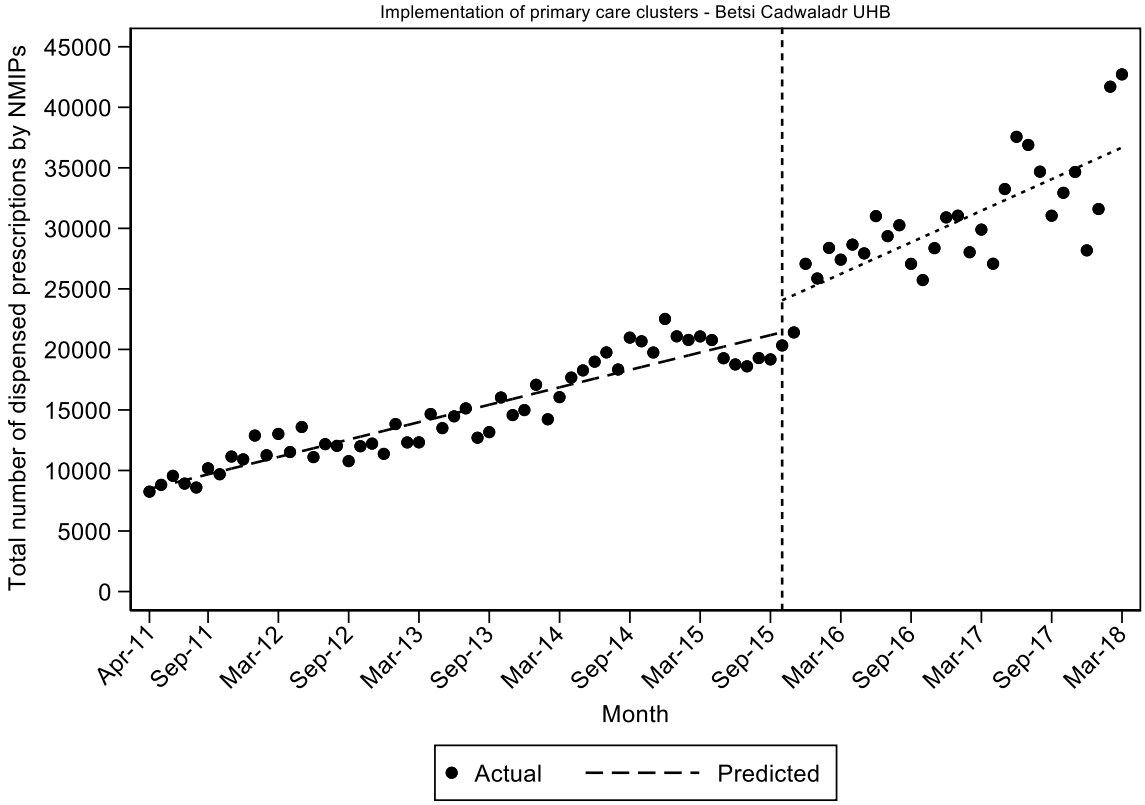

Figure S3: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Betsi Cadwaladr University Health Board)

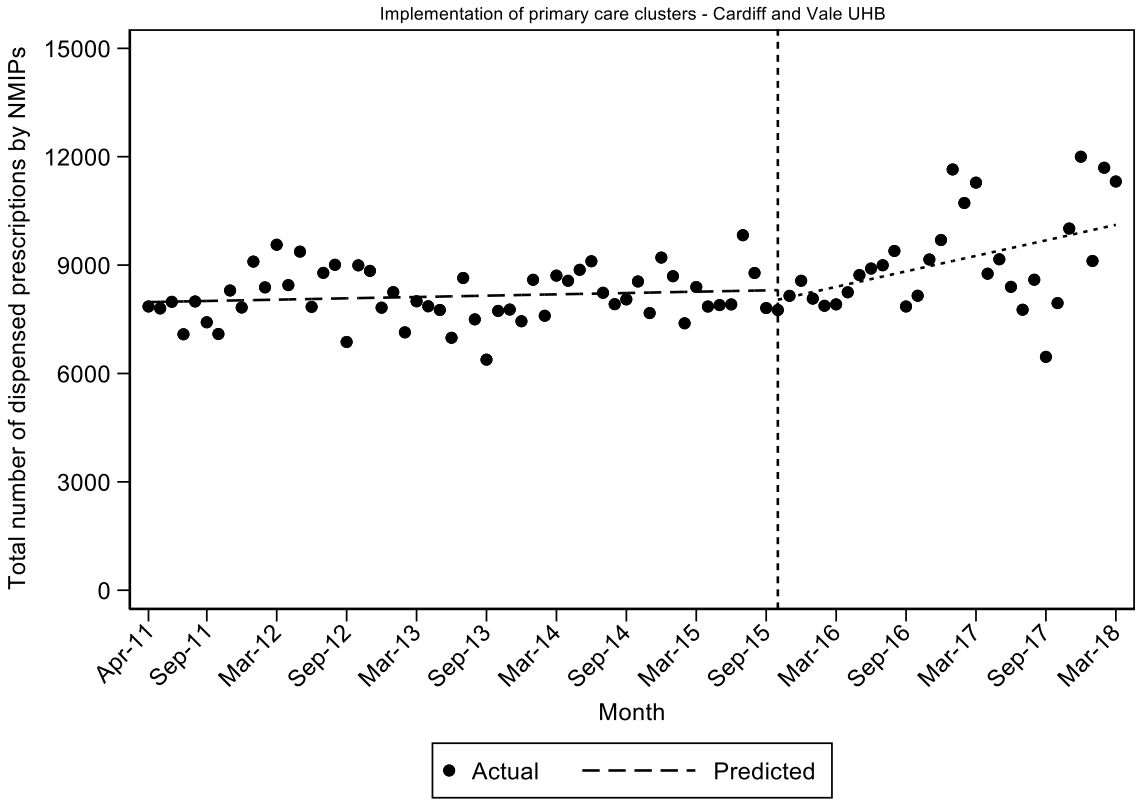

Figure S4: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Cardiff and Vale University Health Board)

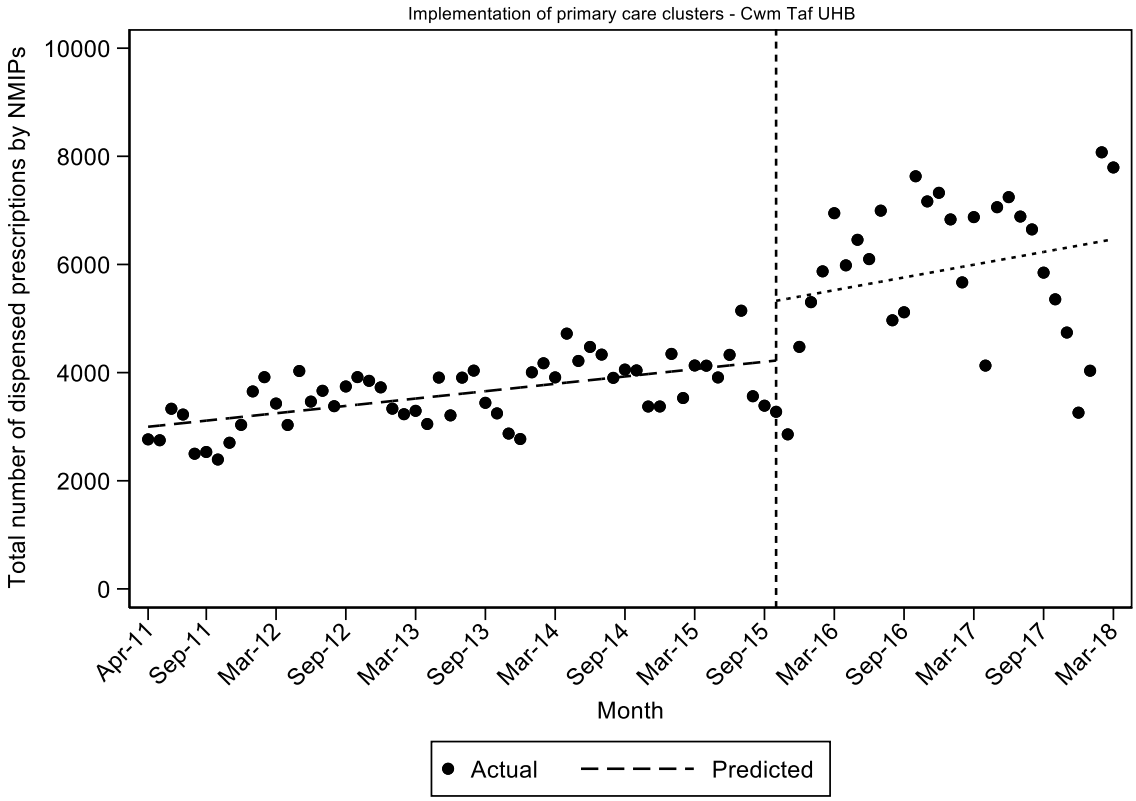

Figure S5: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Cwm Taf University Health Board)

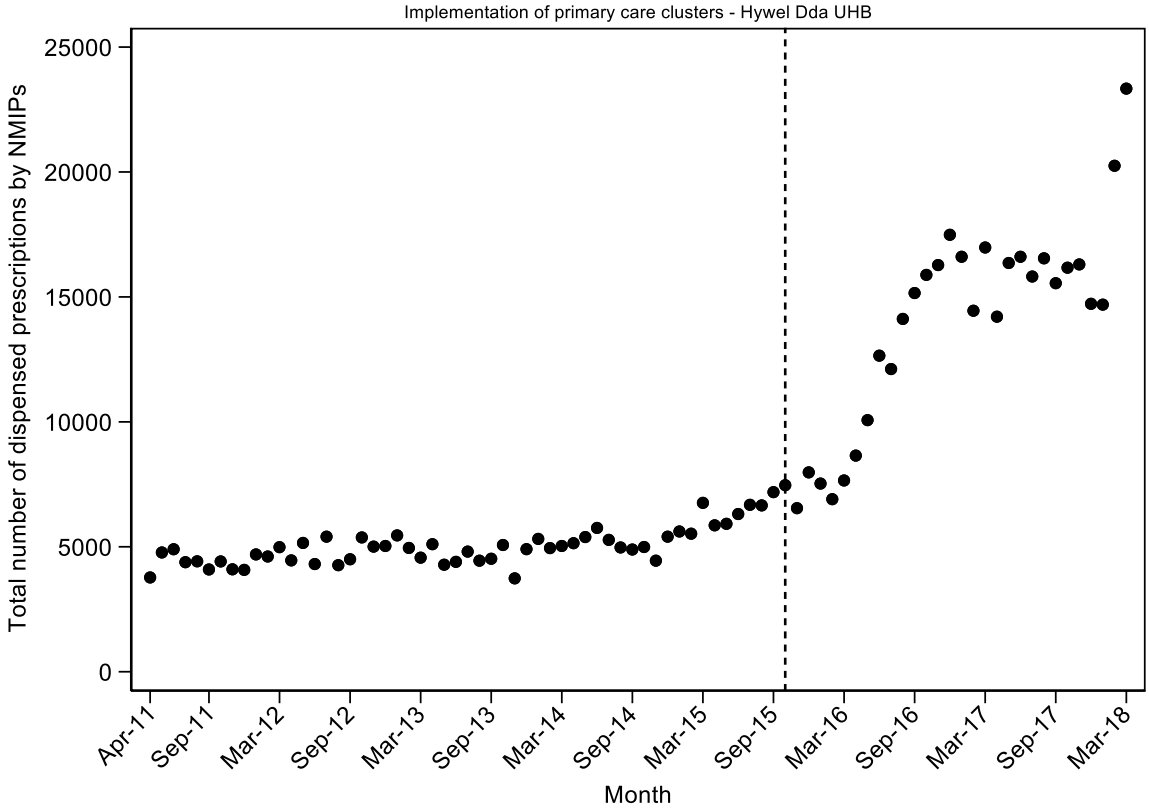

Figure S6: Observed dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Hywel Dda University Health Board)

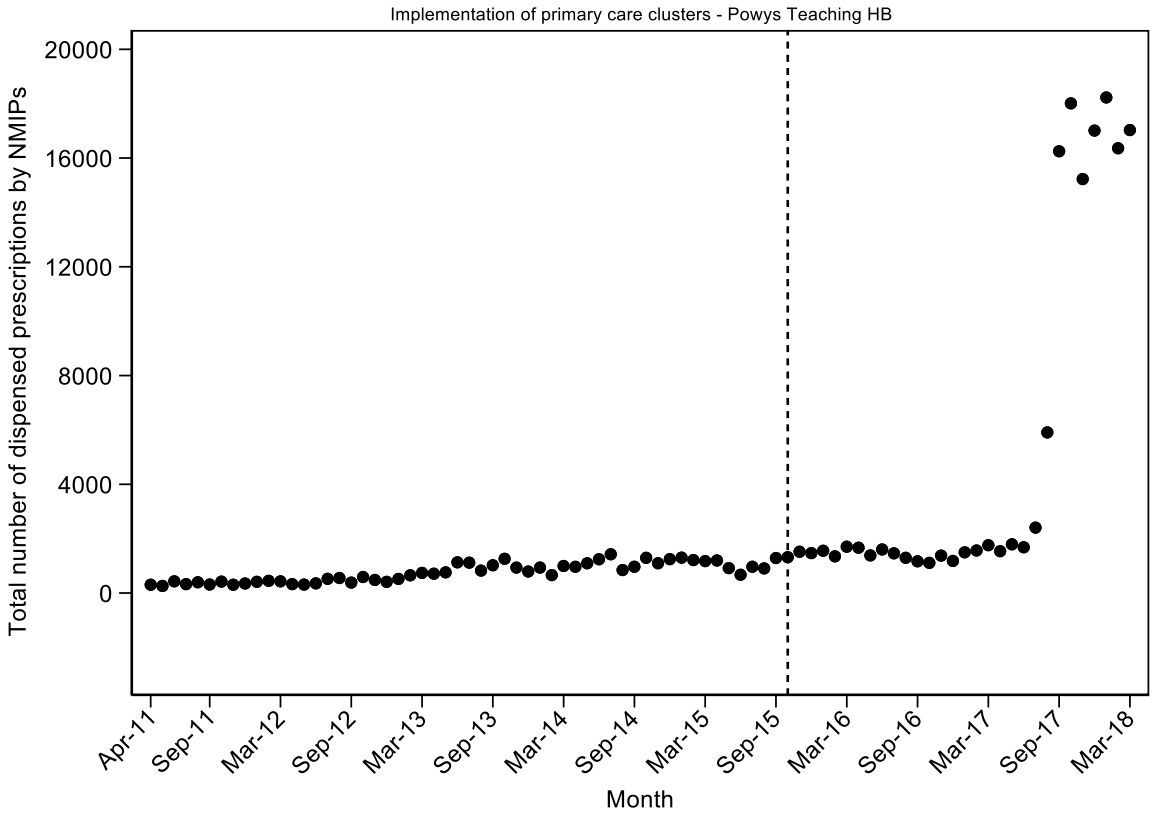

Figure S7: Observed dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (Powys Teaching Health Board)

Sensitivity analysis 1: Excluding Powys teaching health board from the All Wales analysis

Table S3: All Wales analysis excluding Powys Teaching Health Board

Variable	Coefficient	Lower 95% CI	Upper 95% CI	p-value
Intercept	31490.9	29914.3	33067.5	<0.001
Pre-intervention slope	477.5	426.4	528.5	<0.001
Level change	7353.0	1450.0	13255.9	0.015
Post-intervention slope	826.4	314.7	1338.1	0.002

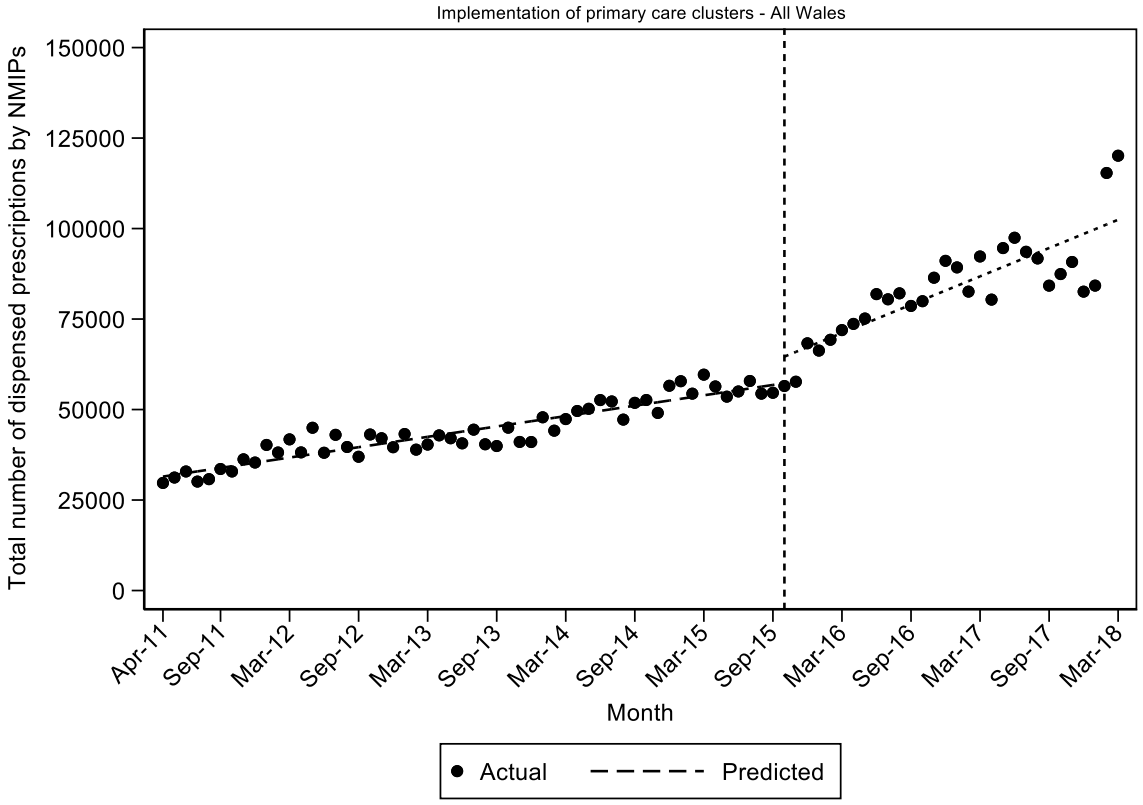

Figure S8: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (All Wales, excluding Powys Teaching Health Board)

Sensitivity analysis 2: Excluding Powys teaching health board and the final two months of data points from the All Wales analysis

Table S4: All Wales analysis excluding Powys Teaching Health Board and the final two months of observations

Variable	Coefficient	Lower 95% CI	Upper 95% CI	p-value
Intercept	31490.9	29489.3	33492.6	<0.001
Pre-intervention slope	477.5	416.1	538.8	<0.001
Level change	9762.5	2570.3	16954.6	0.008
Post-intervention slope	563.5	44.0	1083.1	0.034

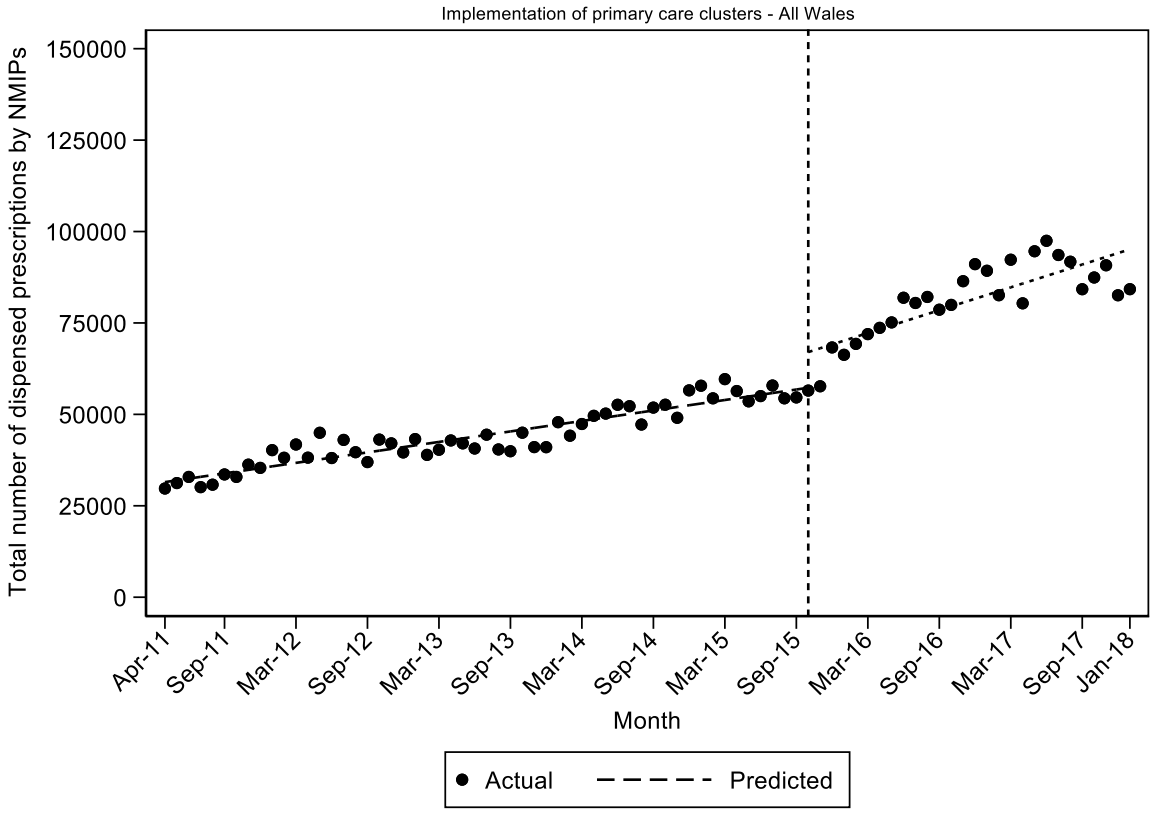

Figure S9: Observed and predicted dispensed prescriptions in primary care by NMIPs prior to and following the implementation of primary care clusters in October 2015 (All Wales, excluding Powys Teaching Health Board and the final two months of observations)

Findings were robust to the two sensitivity analyses 1: excluding PTHB (Table S3 and Figure S8) and 2: excluding PTHB and the final two months of observations (Table S4 and Figure S9) as presented above.