British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2017) **83** 1515–1520 1515

THERAPEUTICS

Multicompartment compliance aids in the community: the prevalence of potentially inappropriate medications

Correspondence Professor Dr James S. McLay, BPharm, PhD, MBChB, FRCP. FBHS, FBPhS, Department of Child Health, The Royal Aberdeen Children's Hospital, Westburn Road, Aberdeen, UK, AB24 3FX. Tel.: +44 (0)1224 438452; Fax: +44 (0)1224 438469; E-mail: j.mclay@abdn.ac.uk

Received 24 August 2016; **Revised** 21 November 2016; **Accepted** 12 December 2016

David Counter[1], Derek Stewart[2], Joan MacLeod[1] and James S. McLay[3]

[1]NHS Grampian, Aberdeen Royal Infirmary, Aberdeen, AB25 2ZB, [2]School of Pharmacy and Life Sciences, Robert Gordon University, Aberdeen, AB10 7GJ, UK, and [3]The Division of Applied Health Sciences, The University of Aberdeen, Aberdeen, AB25 2ZD, UK

Keywords drug interactions, multicompartment compliance aids, potentially inappropriate medications, prescription drugs, social class

AIMS

To assess the prevalence of potentially inappropriate medications (PIMs) use in a population of community-based multicompartment compliance aid (MCA) users in north-east Scotland.

METHODS

Data for MCAs dispensed by 48 of the 50 community pharmacies in Aberdeen City between 1st June to 31st October 2014, together with concurrently prescribed medications, patient demographics and Carstairs index of social deprivation were recorded. Drug-specific quality indicators for PIMs from the Swedish National Board of Health and Welfare were applied and bivariate logistic regression analysis used to assess for associations with demographic variables.

RESULTS

The median age was 82 years (range 12–105 years, 59% female). A total of 1977 PIMs were identified affecting 57.8% of patients. A quarter of patients were prescribed ≥10 medications and 43% had a prescription containing at least one clinically significant drug–drug interaction (DDI). Ten drug groups accounted for 76% of all DDIs. A significant increase in the risk for at least one PIM was associated with female sex (for all indicators of PIM use), age <80 years (three or more psychotropic medicines [OR 5.88, 2.96–11.70, $P < 0.001$]) and lower socioeconomic status (prescription of ≥10 medications [OR: 1.43, 95% CI: 1.16–1.78], prescription of a long-acting benzodiazepine [OR: 1.84, CI: 1.14–2.98]).

CONCLUSIONS

MCA use is associated with a significant incidence of PIMs particularly affecting those younger than 80 years and those living in deprived areas. Our findings indicate the need for a more aggressive multidisciplinary approach to the review of the medications prescribed to MCA users.

DOI:10.1111/bcp.13220

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Multicompartment compliance aid devices are used increasingly in the UK and Western Europe with the intention to maximize patient medication adherence, optimize treatment benefits and minimize economic waste.

WHAT THIS STUDY ADDS

- Multicompartment compliance aid use is associated with a significant number of potentially inappropriate medications including drug–drug interactions.
- These mainly affect those younger than 80 years and those living in the most socially deprived areas.
- To minimize potentially inappropriate medication prescribing and the potential for patient harm there is a need for a more aggressive multidisciplinary approach to the review of the medications prescribed to multicompartment compliance aid users.

Introduction

Multicompartment compliance aids (MCAs) are compartmentalized devices, with each discrete section denoting a single dosing occasion. Formation of an MCA therefore requires repackaging of solid dosage form medications, such as tablets and capsules, from the manufacturer's original packaging into an MCA. The primary aim of using an MCA is to maximize patient medication adherence and optimize treatment benefits [1, 2]. However, there is a lack of robust data to support the assumption that introduction of MCAs improves medication adherence, as measured by pill counts and patient self-reporting [3]. Indeed, while patient understanding of their own medications is widely viewed as a positive influence on medication adherence [4, 5], MCA use in older people has been associated with reduced knowledge of their medications, an effect that appears to be independent of patient cognitive function [6].

Despite a lack of robust evidence, MCAs are widely employed throughout western Europe and use appears to be rapidly increasing [7–9]. Currently, there are limited data available describing the prevalence of MCA use in the UK.

While the use of MCAs is conceptually appealing to prescribers, concerns exist regarding the safety of medication dispensing and the appropriateness of drug prescribing using this approach [10]. The requirement to remove medications from their original packaging and insert them into an MCA increases the opportunity for error within the dispensing pharmacy. Following an audit of MCA dispensing in Australia, Carruthers *et al.* [11] reported that the medication incident rate was 4.3% of issued packs with the most common causes being missing medications, supply of a ceased medication, wrong strength dispensed or incorrect dosage instructions.

There is also evidence that use of MCAs is adversely associated with quality of drug prescribing. Population-based studies comparing patients using an MCA with those receiving routinely dispensed medications have reported that MCA use is associated with an increase in potentially inappropriate medication (PIM) prescribing and potentially clinically significant drug–drug interactions (DDIs) [12, 13]. Belfrage *et al.* [14] reported recently on the results of a small study in 100 patients using the Screening Tool of Older Persons' Potentially inappropriate Prescriptions (STOPP) to assess medicines issued to older patients admitted to hospital. The authors reported a significantly greater proportion of PIMs in patients using an MCA [14]. Similarly, in a longitudinal study of older patients pre- and postcommencement of an MCA, Wallerstedt *et al.* [15] reported a sustained increase in PIMs following the introduction of an MCA, which the authors postulated may be related to reduced frequency of medication review once under the MCA system. The paucity of data supporting the use of MCAs as an aid to optimize medication adherence together with data indicating increased medication incidents and poorer quality prescribing, has led to growing concern over what may be seen as an increasingly untargeted approach to the use of MCAs [10].

The majority of studies assessing PIM use in MCA users have been conducted in Scandinavia and continental Europe [12–15]. The aim of this study was to investigate the extent of PIMs in a population of community-based MCA users in Scotland.

Methods

All community pharmacies (n = 50) in Aberdeen City, Grampian, UK were sent a study protocol and invitation to participate in the study by post and email with a follow-up phone call from the research pharmacist 1 week later. Forty-eight pharmacies (96%) gave consent to participate. For each MCA dispensed during the study period (1st June to 31st October 2014) the following information was recorded electronically: patient demographics, medications dispensed (name, strength, formulation) into an MCA, number of prescribed medications dispensed out with the MCA, frequency of MCA dispensing, MCA distribution method and pharmacy postal code as a surrogate for patient socioeconomic status. This information was collected from patient pharmacy records, prepared MCA packs and prescriptions. Patient socioeconomic status was determined using the Carstairs index score, a measure of social deprivation designed originally for use in Scotland and includes factors such as employment status, housing and overcrowding [16]. Patient socioeconomic status was expressed as a decile of the Carstairs index score with decile 1 being the most deprived and decile 10 the least deprived.

Because clinical data were absent and to permit international comparison, PIMs were assessed using the National

Table 1

Indicators of potentially inappropriate medicines with qualifying drug classes. Presence of a potentially inappropriate medicine was dependent solely on the prescription of a qualifying medication regardless of preparation, dose or indication. (ATC denotes anatomical therapeutic chemical – World Health Organization Classification System)

Indicator	Qualifying drug types	ATC codes
Long-acting benzodiazepines	Diazepam	N05BA01
	Nitrazepam	N05 DC02
Drugs with anticholinergic effects	Drugs for gastrointestinal disorders	A03AB, A03B, A04AD
	Urinary antispasmodics	G04BD
	Anti-Parkinson drugs	N04A
	Low potency antipsychotics	N05AA, N05AB04, N05AF03
	Hydroxyzine	N05BB01
	Nonselective monoamine oxidase reuptake inhibitors	N06AA
	Other antihistamines	R05CA10, R06AA02, R06AB, R06AD, R06AX02
Three or more psychotropic medicines	Antipsychotics	N05A
	Anxiolytics	N05B
	Hypnotics and sedatives	N05C
	Antidepressants	N06A
Potentially significant drug–drug interaction 10 or more distinct medicines	Class-D & X interactions	

Indicators for Quality of Drug Therapy in Older Persons issued by the Swedish National Board of Health and Welfare [13, 15, 17] as listed in Table 1. Potential DDIs for medications dispensed via the MCA were assessed using the drug interaction software package Lexi-Interact Lexicomp [18], which classifies DDIs into five classes (A- no interaction, B- no action needed, C- monitor therapy, D- modify regimen and X- avoid combination). Only drug combinations classified as class-D or class-X interactions, both denoting potential for clinically significant interaction, were recorded. PIMs and DDIs were assessed by two independent researchers (Specialist Registrar in Clinical Pharmacology D.C. and Research Pharmacist D.S.) and disagreements were reviewed by a third researcher (Consultant Clinical Pharmacologist J.S.M.).

Statistical analysis

Binary logistic regression analysis was used in the multivariate analysis of associations between indicators of PIM and demographic variables of sex, age and Carstairs index of social deprivation (expressed as odds ratio with 95% confidence intervals).

Ethics statement

This study was registered as an audit with the Quality Governance and Risk Unit, NHS Grampian (ID: 3044), and was therefore exempted from NHS Ethical review. Patient data were anonymized at the time of data collection and stored electronically as an encrypted password-protected file.

Results

During the study period, MCAs were issued to 2060 patients (59% female, median age 82 years [interquartile range: 70–87], range 12–105 years). The majority (60.3%) of MCAs users were in the top 50% for socioeconomic status (Carstairs deciles 6–10).

Patients were prescribed a mean of 7.4 distinct medications per prescription (SD: 3.4, range 1–23), of which a mean of 6.4 were dispensed into an MCA (SD: 2.8., Range 1–21). Only one medication was dispensed in an MCA for 2.3% (47) of the study group, while 25.1% (518) were prescribed 10 or more distinct medications. Almost half of the study group (47.9%, 988) had at least one medication concurrently dispensed outside of the MCA, of which 8.1% (80) were prescribed five or more medications outside of the MCA. Over a fifth of the study cohort (21.3%, 438) had at least a quarter of their total medications dispensed outside their MCA, and 4% (82) had more medications dispensed outside their MCA than within. The majority (72.1%, 1486) of patients had their MCA issued on a weekly basis with 0.5% (10) issued fortnightly and 27.3% (563) issued monthly. Only 13.9% (n = 286) of the study population collected their medications in person.

A total of 1977 PIMs were identified in the study group, with at least one PIM occurring in 57.8% (1190) of the cohort, two or more in 25.1% (518) and three or more in 7.5% (n = 154). The maximum number of individual PIM criteria for any one patient was five (10 patients) and the maximum total number of PIMs for a single patient was 21 attributable to 12 prescribed medications (one patient). The most frequent PIMs were potentially clinically significant DDIs (43.1%), 10 or more distinct medications (25.1%) and

medications with anticholinergic activity (16.6%). The frequency of PIMs according to the individual prescribing quality indicators are reported in Table 2.

The adjusted odds ratios for PIMs and prescribing quality indicators are reported in Table 3. After adjustment for age and Carstairs index score of social deprivation, PIMs were more frequently observed in females (OR 1.25, 1.04–1.51, $P < 0.05$) for all indicators of PIM, except polypharmacy (10 or more medicines). PIMs of any type were more frequently observed in patients aged <65 compared with those >80 years (OR 1.68, 1.27–2.20, $P < 0.001$). Specifically, those <65 years were 15 times more likely to be prescribed three or more psychotropic medications (OR 15.17, 7.80–29.46, $P < 0.001$) and four times more likely to be prescribed a long-acting benzodiazepine (OR 4.35, 2.49–7.60, $P < 0.001$) or anticholinergic drugs (OR 3.77, 2.79–5.10, $P < 0.001$). A similar pattern was observed for those aged 65–79 years with PIMs of any type being twice as likely to occur than in those over 80 years of age (OR 2.0, 1.6–2.53, $P < 0.001$). Specifically, those aged 65–79 years were significantly more likely to be prescribed three or more psychotropic medications (OR 5.88, 2.96–11.70, $P < 0.001$).

PIMs were significantly associated with low socioeconomic status, with those in Carstairs deciles 1–5 having a 30% increased risk of a PIM of any type (OR: 1.3, CI: 1.06–1.58). Specifically, polypharmacy (≥ 10 medicines; OR: 1.43, 95% CI: 1.16–1.78), and prescription for a long-acting benzodiazepine (OR: 1.84, CI: 1.14–2.98).

A total of 1359 potentially clinically significant DDIs were identified with 43.1% (887) MCA users having at least one DDI. Medications from 33 different drug groups were involved in potentially clinically significant DDIs. The maximum number of potentially clinically significant DDIs recorded for a single patient was 19 attributable to 12 prescribed medications. DDIs were more likely to occur in those with polypharmacy (>10 prescription medications in MCA; 3.95, 3.18–4.92, $P < 0.001$), women (1.29, 1.07–1.55, $P < 0.01$) and those aged 65–79 years (1.62, 1.31–2.02, $P < 0.001$). The 10 top drug groups accounting for 72.7% of DDIs were antidepressants (13.9%), calcium supplements (9.2%), statins (8.5%), antiplatelets (7.9%), proton-pump inhibitors (6.9%), anticonvulsants (6.1%), antihypertensive agents (6.0%). antipsychotics (5.6%), levothyroxine (5.0%) and neuropathic analgesics (3.6%).

Table 2

Prevalence of potentially inappropriate medicines associated with multicompartment compliance aid (n = 2060)

Prescribing quality indicators	Study population % (n)
≥10 distinct medicines	25.1 (518)
Long-acting benzodiazepines	3.7 (76)
Anticholinergic drugs	16.6 (342)
≥3 psychotropic drugs	4.3 (89)
Potential clinically significant drug–drug interaction	43.1 (887)
Any potentially inappropriate medicines use(any of the above)	57.8 (1190)

Discussion

This is the first study in the UK to report the prevalence of PIMs in a population of MCA users in the community. Over half of the patients issued with an MCA had at least one PIM and more than two fifths at least one potential clinically significant DDI. While previous studies have reported similar levels of PIM, the rate for potentially clinically

Table 3

Adjusted odds ratios for potentially inappropriate medicine use according to prescribing quality indicators, adjusted for age, sex, residence and Carstairs index score

	Prescribing quality indicators and adjusted OR (95% CI)					
	≥10 drugs	**Long-acting benzodiazepines**	**Anticholinergic drugs**	**≥3 psychotropic drugs**	**Potentially serious drug–drug interaction**	**Any PIM**
Female (ref: male)	NS	2.23 (1.31–3.78)**	1.35 (1.05–1.74)*	2.47 (1.49–4.08)***	1.29 (1.07–1.55)**	1.25 (1.04–1.51)*
Age (ref: ≥80 years)						
< 65	1.67 (1.24–2.24)**	4.35 (2.49–7.60)***	3.77 (2.79–5.10)***	15.17 (7.80–29.46)***	1.37 (1.05–1.78)*	1.68 (1.27–2.20)***
65–79	1.70 (1.34–2.17)***	1.57 (0.84–2.95)	2.27 (1.70–3.03)***	5.88 (2.96–11.70)***	1.62 (1.31–2.02)***	2.01 (1.60–2.53)***
Carstairs index 1–5 (ref: 6–10)	1.43 (1.16–1.78)**	1.84 (1.14–2.98)*	NS	NS	NS	1.30 (1.06–1.58)*

NS denotes variable-indicator combinations that were not significant in the multivariate analysis model. *$P < 0.05$ relative to reference group within variable category; **$P < 0.01$; *** $P < 0.001$. OR, odds ratio; CI, confidence interval; Any PIM, presence of at least one indicator for potentially inappropriate medicine; ref = reference variable; NS = not significant.

significant DDIs observed in our study are five-fold greater than the 8–9% reported for an older Swedish population [12, 13]. The reasons for the higher prevalence of DDIs in our population is unclear but it may be due to the wider use of psychotropic medications, which are particularly associated with DDIs in our relatively younger study population [12, 13].

The adjusted odds ratio for all the indicators for PIMs were increased in those under the age of 65 years compared to those aged ≥80 years, particularly for use of ≥ three psychotropic medications and long-acting benzodiazepines, possibly reflecting the nature of the disease burden (mental health issues) in the under 65 year age group necessitating MCA use. Of interest is the observed increase in the adjusted odds ratio for all but one of the indicators for PIMs in those aged 65–79 years relative to those ≥80 years. This observation, which has been previously reported by others, is believed to be due to the healthy survivor effect in those aged ≥80 years [12, 19]. Nonetheless, these findings indicate the need to focus particular attention on prescribing in MCA users <80 years.

The role of socioeconomic status and PIMs has not been previously reported. A significant relationship was observed between social deprivation and PIM occurrence in the lowest socioeconomic groups, in particular polypharmacy or a prescription for a long-acting benzodiazepine. It is well recognized that individuals of lower socioeconomic status tend to experience worse health and higher levels of anxiety and it is possible that these observations reflect an increased disease burden [20, 21].

A proportion of MCA users (almost half of our study population) required medications such as inhalers, which are not compatible with dispensing into an MCA. However, our finding that over a fifth of the study population had more than a quarter and almost one in 20 had more than half of their medications dispensed outside an MCA detracts from the simplicity of application and the goal of improved adherence, which MCAs are intended to achieve [15].

In this study population, only 14% of patients collected their prescriptions in person, therefore missing the opportunity for direct pharmacist–patient interaction, which has been associated with improved medication adherence [22]. Our finding that more than two fifths of subjects were exposed to a potential DDI further reinforces the importance for the pharmacist and prescribing physician to collaboratively assess both the MCA user and their prescription on a regular basis.

There are few data regarding the prevalence of MCA use in the UK; however, in 2001, Nunney *et al.* [23] estimated that there were 100 000 MCA users in the UK, equating to 170/100 000 of the population. Our data suggest that the prevalence of MCA use in 2015 was 900/100 000 of the population, representing a greater than five-fold increase over a 14-year period, which appears disproportionate to the 1.2-fold increase in the UK older population over the same period [24, 25].

Study strengths and weaknesses

Although this study provides insight into medication use by MCA users aged <65 years, the criteria used were originally validated in an older population (>65 years) and therefore may not be fully generalizable to all age groups [17]. However, it may be argued that the PIM criteria are equally applicable to all age groups and the presence of morbidity and comorbidity may be more relevant than age *per se*.

The finding that socioeconomic status appears to be independently associated with PIMs is significant; however, we were unable to account directly for patient disease burden, which is also directly associated with socioeconomic status [20]. Therefore, the observed relationship between socioeconomic status and PIM may be largely accounted for by disease burden. Patient socioeconomic status was determined from the supplying pharmacy postcode, thus assuming that both patient and pharmacy lay within the same geographical area. It has been reported that almost 90% of patients live within 1.6 km of their pharmacy, suggesting that this is a reasonable assumption to make [26]. The study population were exclusively residents of the north east of Scotland and hence findings may not be generalizable to the whole UK population and beyond.

The lack of clinical data prevented the use of more comprehensive screening tools for inappropriate medicine use such as the STOPP and START criteria, which prevented assessment of potential prescribing omissions and clinically relevant inappropriate medicine use. Therefore, our results are likely to be an underestimation of the actual PIM prevalence.

Conclusions

A significant proportion of MCA users in this study were prescribed PIMs including DDIs, with those younger than 80 years and those living in the poorest areas at greater risk. The simplification of medication consumption, which the MCA is designed to provide, appears to be confounded in a significant number of individuals by the concurrent supply of medications outside the MCA system. Our findings indicate a need for a more aggressive multidisciplinary approach (involving prescriber, dispensing pharmacist and patient) to the review of the medications prescribed to MCA users, which is particularly poignant given the apparent increase in MCA use in the UK.

Competing Interests

There are no competing interests to declare.

Contributors

D.C. designed the study, collected data, analyzed data and wrote the manuscript. J.M. collected data, analyzed data and wrote the manuscript. D.S. designed the study, analyzed data and wrote the manuscript. J.S.M. (Principal Investigator) designed the study, analyzed data and wrote the manuscript and acts as guarantor for the study.

References

1 Simpson SH, Eurich DT, Majumdar SR, Padwal RS, Tsuyuki RT, Varney J, *et al*. A meta-analysis of the association between adherence to drug therapy and mortality. BMJ 2006; 333: 15–20.

2 Office for National Statistics. Population Estimates for UK, England and Wales, Scotland and Northern Ireland, Mid 2014. Available at http://www.ons.gov.uk/ons/rel/popestimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/mid-2014/index.html (last accessed June 2016).

3 Mahtani KR, Heneghan C, Glasziou PP, Perera R. Reminder packaging for improving adherence to self-administered long-term medicines, The Cochrane Library. 2011.

4 Okuno J, Yanagi H, Tomura S, Oka M, Hara S, Hirano C. Compliance and medicine knowledge among elderly Japanese home-care recipients. Eur J Clin Pharmacol 1999; 55: 145–9.

5 Trevino J, Albright T, Wright F, Cigarroa L. Correlates of medicine knowledge and adherence: findings from the residency research network of south Texas. Fam Med 2005; 37: 712–8.

6 Kwint H, Stolk G, Faber A, Gussekloo J, Bouvy ML. Medicine adherence and knowledge of older patients with and without multi-dose drug dispensing. Age Ageing 2013; 42: 620–6.

7 Apoteket AB. Annual report (2010). Available at http://www.apoteket.se/globalassets/om-apoteket/media/pdfer/ekonomiska-rapporter/2010/apoteket_2010_en.pdf. Pg. 30. (last accessed June 2016).

8 Wekre LV, Spigset O, Sletvold O, Sund JK, Grimsmo A. Mulitdose drug dispensing and discrepancies between medicine records. Qual Saf Health Care 2010; 19: e42.

9 Sinnemaki J, Sihvo S, Isojarv J, Blom M, Airaksinen M, Mantyla A. Automated dose dispensing service for primary healthcare patients: a systematic review. Syst Rev 2013; 2: 1–7.

10 Royal Pharmaceutical Society (2013). Improving patient outcomes: The better use of multi-compartment compliance aids. [online] London: Royal Pharmaceutical Society. Available at www.rpharms.com/support-pdfs/rps-mca-july-2013.pdf (last accessed June 2016).

11 Carruthers A, Naughton K, Mallarkey G. Accuracy of packaging of dose administration aids in regional aged care facilities. Med J Aust 2008; 188: 280–2.

12 Johnell K, Fastbom J. Multi-dose drug dispensing and inappropriate drug use: a nationwide register-based study of over 700 000 elderly. Scand J Prim Health Care 2008; 26: 86–91.

13 Sjöberg C, Edward C, Fastbom J, Johnell K, Landahl S, Narbro K, *et al*. Association between multi-dose drug dispensing and quality of drug treatment – a register-based study. PLoS One 2011; 6: e26574.

14 Belfrage B, Koldestam A, Sjoberg C, Wallerstedt SM. Prevalence of suboptimal drug treatment in patients with and without multidose drug dispensing – a cross-sectional study. Eur J Clin Pharmacol 2014; 70: 867–72.

15 Wallerstedt SM, Fastbom J, Johnell K, Sjoberg C, Landahl S, Sundstrom A. Drug treatment in older people before and after the transition to a multi-dose dispensing system – a longitudinal analysis. PLoS One 2013; 8: e67088.

16 Carstairs V, Morris R. Deprivation and Health in Scotland. Health Bull (Edinb) 1991; 48: 162–75.

17 Fastbom J, Johnell K. National indicators for quality of drug therapy in older persons: the Swedish experience from the first 10 years. Drugs Ageing 2015; 32: 189–99.

18 Clinical Drug Information. Lexicomp® Online. Available at http://www.wolterskluwercdi.com/lexicomp-online/ (last accessed June 2016).

19 Bergman A, Olsson J, Carlsten A, Waern M, Fastbom J. Evaluation of the quality of drug therapy among elderly patients in nursing homes. Scand J Prim Health Care 2007; 25: 9–14.

20 Adler NE, Ostrove JM. Socioeconomic status and health: what we know and what we don't. Ann N Y Acad Sci 896: 3–15.

21 Lorant V, Deliège D, Eaton W, Robert A, Philippot P, Ansseau M. Socioeconomic inequalities in depression: a meta-analysis. Am J Epidemiol 2003; 157: 98–112.

22 Murray MD, Young J, Hoke S, Tu W, Weiner M, Morrow D, *et al*. Pharmacist intervention to improve medicine adherence: a radomised trial. Ann Intern Med 2007; 146: 714–25.

23 Nunney JM, Raynor DKT. How are multi-compartment compliance aids used in primary care? Pharm J 2001; 267: 784–9.

24 Office for National Statistics. Population estimates for UK, England and Wales, Scotland and Northern Ireland, Mid 2014. Available at http://www.ons.gov.uk/ons/rel/popestimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/mid-2014/index.html (last accessed June 2016).

25 Aberdeen City Council 2014 Mid-Year Population Estimates – Aberdeen City. Available at http://wwwaberdeencitygovuk/tourism_visitor_attractions/tourists_visitors/statistics/2014_Pop_Est_Aberdeen_Cityasp (last accessed May 2016).

26 Todd A, Copeland A, Husband A, Kasim A, Bambra C. The positive pharmacy care law: an area-level analysis of the relationship between community pharmacy distribution, urbanity and social deprivation in England. BMJ Open 2014; 4: e005764.