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ORIGINAL ARTICLE

Anti-osteoporosis medication dispensing by clinical commissioning groups in England – an ecological study of variability in practice and of the effect of the Covid-19 pandemic

Sobia S. Janjua¹  | Helen F. Boardman¹  | Arvind Sami²  |
Antony Johansen^{3,4}  | Li Shean Toh¹  | Kassim M. Javaid^{2,4} 

¹Division of Pharmacy Practice and Policy, School of Pharmacy, University of Nottingham, Nottingham, UK

²Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, Botnar Research Centre, University of Oxford, Oxford, UK

³School of Medicine, University Hospital of Wales, Cardiff University, Wales, UK

⁴Falls and Fragility Audit Programme, Royal College of Physicians, London, UK

Correspondence

Li Shean Toh, Division of Pharmacy Practice and Policy, School of Pharmacy, University of Nottingham, University Park, Nottingham NG7 2RD, UK.

Email: lishean.toh@nottingham.ac.uk

Abstract

Purpose: To investigate whether the rate of Anti-Osteoporosis Medication (AOM) dispensing was related to prevalence of risk factors and hip fracture incidence in the local population.

Methods: The Open Prescribing database was used to analyse dispensed AOM at the level of Clinical Commissioning Groups (CCGs) in England. Male Healthy Life Expectancy (MHLE), Female Healthy Life Expectancy (FHLE), the prevalence of smoking and active adults, the incidence of hip fracture and of alcohol related hospital admissions, and local dispensing of a comparator drug (atorvastatin) were considered as predictor variables. Linear and multilinear regression were performed. Using atorvastatin as a comparator, AOM dispensing was compared after the start of the Covid-19 pandemic with the same quarter the previous year.

Results: Rates of AOM per 1000 people aged over 65 years in a CCG area varied between 379.2 and 1129.1, with a mean of 670.3. Population risk factors were individually related to the amount of AOM dispensed in an area. Collectively, local activity levels in adults ($p = 0.042$) and local hip fracture incidence ($p = 0.003$) were significantly negatively correlated with rates of AOM dispensed. Rates of alendronate dispensing fell significantly at the start of the Covid-19 pandemic ($p < 0.001$), whilst atorvastatin dispensing rates significantly increased ($p < 0.001$).

Conclusion: Lower rates of AOM dispensing were seen in areas with a higher proportion of active adults and higher incidence of hip fracture. Multidisciplinary services should be developed to address this care gap with consideration given to local population risk factors. Community pharmacists are ideally placed to play a vital role in osteoporosis management.

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KEYWORDS

bisphosphonates, community pharmacy, COVID-19, denosumab, osteoporosis medication, real-world data

Plain language summary

Osteoporosis leads to a “thinning” of the bones which makes them brittle and more likely to fracture. However, effective medications are available which prevent and treat the condition. Dispensing of medication for osteoporosis varies throughout England and fell during the first 3 months of the Covid-19 pandemic. Areas with higher hip fracture cases had lower rates of osteoporosis medication dispensed, indicating more people at risk need to start medication to prevent hip fractures occurring. Furthermore, areas where there were higher proportions of active adults had lower rates of osteoporosis medication dispensed, indicating a reduced need and highlighting the potential an active lifestyle could play in preventing osteoporosis.

Key Points

- Osteoporosis results in weaker bones, which increases risk of fracture, of which hip fractures are the most serious.
- The amount of anti-osteoporosis medication dispensed in England in 2019 was analysed against local population risk factors for the condition.
- The Covid-19 pandemic saw a significant decrease in the amount of alendronic acid dispensed during the first quarter after the national lockdown in England.
- Hip fracture incidence and adult activity levels were significantly negatively related to rates of anti-osteoporosis medication dispensed.
- Initiation of treatments to prevent hip fractures and promotion of active lifestyles may improve osteoporosis management and prevention in England.

1 | INTRODUCTION

Osteoporosis is a long-term condition characterised by weakened microarchitecture and strength of bones.¹ Its asymptomatic nature² means that it is often only diagnosed after a fragility fracture,³ which follows low level trauma such as a fall from a standing height. Hip fractures are one of the most severe outcomes of osteoporosis. They reduce mobility, quality of life⁴ and there is a three-fold increase in risk of death after a hip fracture.⁵ However, only one fifth of the deaths after a hip fracture can be explained by the fracture, with comorbidities accounting for the rest.⁶

Costs related to hip fracture have been reported as over £16 000 per patient, including hospital stay and two-year post fracture care.⁷ Risk factors for osteoporosis include history of fragility fracture, untreated premature menopause, low BMI (<18.5 kg/m²), smoking, alcohol intake (>14 units/week), family history of hip fracture and frequent use of glucocorticoids.⁸

Annual incidence for osteoporotic hip fractures has been predicted to affect 6.26 million people worldwide by 2050.⁹ Gender influences fracture rates and it has been estimated that 1 in 3 women¹⁰ and 1 in 5 men¹¹ will suffer a fragility fracture after the age of 50 years.¹² In the United Kingdom, osteoporosis affects over 3 million people. Annually, this results in more than half a million people receiving treatment in hospital for fragility fractures.¹² These

figures highlight osteoporosis as a significant health problem which needs to be addressed.

Fortunately, effective treatments are available which significantly reduce fracture risk evidenced by both randomised clinical trials¹³ and real-world evidence.¹⁴ In the United Kingdom, treatments for osteoporosis are listed in The British National Formulary (BNF)¹⁵ and recommended in National Institute of Clinical Excellence (NICE) guidance. These include bisphosphonates,¹⁶ denosumab,¹⁷ raloxifene,^{18,19} and parathyroid hormone analogues.¹⁹

Populations with higher prevalence of risk factors have more people appropriate for Anti-Osteoporosis Medication (AOM), and in a needs-based healthcare system capacity and capability should reflect this.²⁰ In England, social deprivation has been associated with higher hip fracture incidence.²¹ However, there is a lack of literature examining whether risk factors associated with osteoporosis and social deprivation, for example, healthy life expectancy, smoking, activity levels and excessive alcohol intake may be related to rates of AOM use. Furthermore, whether consequences such as hip fractures are related to AOM use.

We investigated the relationship between osteoporosis risk factors and incidence of hip fracture with the rate of AOM dispensing at the regional level in England.

The Covid-19 pandemic has affected fracture rates,²² and the management of osteoporosis, including bone health assessments²³ and the delivery of bone density scans,²⁴ so our study also considered

variation in AOM dispensing in England, both before and after the start of the pandemic.

2 | METHODS

2.1 | Study design and setting

This ecological study used the Open Prescribing database to analyse the number of products of AOM dispensed via community pharmacies in England in 2019.²⁵ The effect of the Covid-19 pandemic was investigated by comparing the first quarter after the national lockdown in England (April till June 2020) with the same quarter the previous year (April till June 2019).

2.2 | Participants and study size

Data were extracted for Clinical Commissioning Group (CCG) areas in England. A CCG covers a geographical area, where GPs and nurses have more input into services and allocation of costs.²⁶ Over time CCG areas have merged to provide improved healthcare to local populations. Dispensed AOM, risk factors and outcomes were obtained for 135 CCG areas in 2019.

2.3 | Data sources

2.3.1 | The open prescribing database

The Open Prescribing database²⁵ contains information from the NHS Business Service Authority's monthly published files. It lists the month, number of products, quantity of units and actual cost for individual medications dispensed via community pharmacies or personally administered by doctors in England from July 2015 until present. The database allows for analysis at the CCG level and allocates codes for individual medication products as listed in the BNF.¹⁵ We included medications listed in NICE guidance¹⁶⁻¹⁹ (see Supplementary Table 1). Monthly AOM items dispensed at the CCG level were added to obtain the annual items for each CCG in 2019.

2.3.2 | The Office for National Statistics

The Office for National Statistics (ONS) lists the number of people of every age at mid-year 2019 in a CCG area,²⁷ enabling calculation of the total number of people aged over 65 years. Product quantities and population numbers were used to calculate the outcome variable of AOM dispensed per 1000 people aged over 65 years.

England is also divided into Health Authority (HA) areas which administer the National Health Service. The ONS holds local population risk factor data for HA areas. Risk factors associated with osteoporosis were extracted and prevalence compared to dispensed AOM. Clinical Commissioning Group areas were mapped to Health Authority (HA) areas by population numbers from the ONS.²⁸

2.3.3 | The National Hip Fracture database

The number of people in a CCG area who sustained a hip fracture were extracted from the National Hip Fracture Database for 2019.²⁹

2.4 | Inclusion criteria

Osteoporosis medication items dispensed via community pharmacies in England and recommended in NICE guidance (bisphosphonates¹⁶: alendronate, risedronate, ibandronate, and non-bisphosphonates¹⁷⁻¹⁹: denosumab, raloxifene, teriparatide and strontium ranelate) were analysed. Where more than one indication existed for a drug, the dose specific preparation for osteoporosis was used. Raloxifene was considered an AOM since its other indication (breast cancer prevention) is not licensed in the United Kingdom.

2.5 | Exclusion criteria

Bone medications listed in the BNF section 6.6 which are not indicated for osteoporosis and not included in NICE guidance for osteoporosis were excluded, in addition to formulations / doses not used solely for osteoporosis. Zoledronic acid was excluded due to negligible dispensing via community pharmacy. Calcium and/or vitamin D were not included, since their effectiveness in this context is primarily as a co-prescription with the AOM listed above. Clinical Commissioning Group areas were excluded where there was a greater than 5% population difference with the corresponding HA. Also, if there was more than one CCG in an HA area and if population risk factors were not available at the CCG level.

2.6 | Variables

We examined the following ecological level osteoporosis risk factors from the ONS: Male Healthy Life Expectancy (MHLE), Female Healthy Life Expectancy (FHLE), percentage of people who smoke, percentage of active adults (at least 150 minutes of moderate intensity physical activity per week) and rate of alcohol related hospital admissions per 100 000 population.³⁰ Weighted averages were taken for HA areas

which had merged, with less than 5% population discrepancy with corresponding CCG area.

2.7 | Covid-19 pandemic

The most commonly dispensed oral and injectable AOMs were identified and compared to atorvastatin, the most commonly dispensed medication in England for hyperlipidaemia; another asymptomatic long-term condition whose prevalence increases with age (see Supplementary Table 2, for codes).³¹

Atorvastatin was therefore used as a comparator drug.

2.8 | Statistical methods

Data was analysed using IBM SPSS statistics V28.³² Outcomes and predictors were described using descriptive parametric and non-parametric statistics. Linear and multilinear regression methods were used to analyse population level osteoporosis risk factors on AOM dispensing rates per 1000 adults aged over 65 years in each region. Assumptions of a regression analysis model were checked by Cook's distance to confirm extreme outliers.

To investigate the early effect of the Covid-19 pandemic, the rates dispensed were compared for the first quarter (April – June 2020) after the national lockdown in England (23rd March 2020) to the same quarter the previous year (April – June 2019). Due to CCG mergers, mid-year population data for 2020 was presented for 106 CCGs,³³ therefore, to enable comparison, population data from 2019²⁸ was added for mergers.³⁴ Two-tailed p values <0.05 were considered significant.

3 | RESULTS

Some CCG areas had incomplete data (see Supplementary table 3 for exclusions and missing data). The characteristics for all CCGs and those with complete predictor data are compared in Table 1. The mean CCG population size was 416 940 and the mean proportion aged 65 years and over in a CCG area was 18.5% (range from 6.4% to 28.3%). The total AOM dispensed via community pharmacies in England in 2019 ranged from 10 257 to 221 398 products for individual CCG areas. For every 1000 people aged over 65 years, there were between 379 and 1129 AOM products dispensed at the CCG level.

3.1 | Linear regression

For CCGs with complete data (n = 94), simple linear regression showed there were significant relationships (p = <0.05) between MHLE, FHLE, percent smoked, percent active adults and alcohol related hospital admissions per 100 000 with the rate of AOM dispensed per 1000 people aged over 65 years.

TABLE 1 Characteristics of Clinical Commissioning Groups (CCGs) in 2019

Characteristic	All CCGS (n = 135)	CCGs with complete data (n = 94)
Total population ^a in England	56 286 961	42 354 674
Mean population ^a in CCG areas	416 940	450 582
Total population aged 65 years and over ^a in England	10 353 716	7 595 908
Mean population aged 65 years and over ^a in CCG areas	76 694	80 808
Mean proportion aged 65 years and over in CCG areas (%) ^a	18.5	17.7
Mean proportion female aged 65 years and over in CCG areas (%) ^a	10.1	9.6
Mean male healthy life expectancy ^a in CCG areas (years)	X	62.0
Mean female healthy life expectancy ^a in CCG areas (years)	X	62.5
Mean Smoked ^a in CCG areas (%)	X	18.0
Mean Active adults ^a in CCG areas (%)	X	56.0
Mean Alcohol-related hospitalisation admissions per 100000 ^a in CCG areas	X	672
Total AOM dispensed ^c in England	6 777 429	54 628
Mean AOM per 1000 aged over 65 years ^{a,c} in CCG areas	670	701
Hip fracture cases ^b in England	54 343	39467 ^d
Mean atorvastatin per 1000 ^c aged over 65 years ^{a,c} in CCG areas	4850.5	5246

^aOffice for National Statistics.

^bHip Fracture Database.

^cOpen Prescribing database.

^dn = 93 (missing data), X = excluded (See Supplementary Table 3 for exclusion details).

3.2 | Multilinear regression model

Due to exclusions (see Supplementary Table 3), 93 CCGs were included in the multilinear regression model (see Figure 1). The independent predictors of AOM rates per 1000 adults aged 65 years and over are shown in Table 2. Thirty one percent of the variation in AOM rate per 1000 aged over 65 years was explained by the population characteristics, predictors in the model (p ≤ 0.001, R² = 0.31). An increase of 100 hip fracture cases in a CCG area was significantly associated with a decrease of 22 items in the AOM dispensing rate. As the average population aged over 65 years in a CCG was 766,94, an increase in active adults by 1% significantly reduced the dispensing rate of AOM per 1000 aged over 65 years by an average of 77 per CCG area.

3.3 | Effect of Covid-19 pandemic on individual types of AOM dispensed

Pre-pandemic (2019), the most commonly dispensed oral AOM was Alendronate (5 912 234 products) and the most commonly dispensed injectable AOM was Denosumab (61 010 products). Excluding 3 CCGs with no community dispensing of Denosumab, the ratio of Denosumab versus Alendronate dispensed varied from 0.01% to 9.6% (median 0.5%). During the first quarter after the start of the pandemic (April to June 2020), rates dispensed of Alendronate per 1000 people aged over 65 years decreased across 89.6% ($n = 95$) of CCGs, when compared to the same quarter in 2019 ($p \leq 0.001$). Rates of Denosumab also decreased across

39.6% ($n = 42$) of CCGs but were the same for 9.4% ($n = 10$) of CCGs with no overall significant change ($p = 0.12$). In contrast, all CCG's in England had an increase in the dispensed rates of atorvastatin in the quarter April to June 2020 ($n = 106$), compared to the same quarter in 2019 ($p \leq 0.001$).

4 | DISCUSSION

Dispensed AOM rates varied across CCGs, indicating disparities in prescribing and subsequent dispensing behaviour. Much of this variation was not explained by ecological level predictors, and indeed ran counter to what these might suggest to be appropriate.

Improving effective osteoporosis management is a priority for the NHS, in both primary and secondary prevention settings.³⁵ Identification of populations with highest prevalence of risk factors for osteoporosis treatment would help to tailor interventions to local needs.

However, we have demonstrated counter-intuitive associations between rates of AOM amongst people aged over 65 years and both the local incidence of hip fracture and the local prevalence of adult activity. Accepting the limitation of ecological analyses this suggests a mismatch between local health-care need and delivery for osteoporosis.

4.1 | Local Hip fracture incidence

The introduction in 2005 of NICE guidelines on osteoporosis treatments to prevent fractures and the availability of generic alendronic acid has been associated with a significant increase in prescribing of osteoporosis medication and a reduction in hip fracture incidence.³⁶ Our study found that in 2019, hip fracture incidence was higher in areas with lower rates of AOM dispensed. This highlights the potential impact greater availability of osteoporosis treatments could have on prevention of hip fractures.

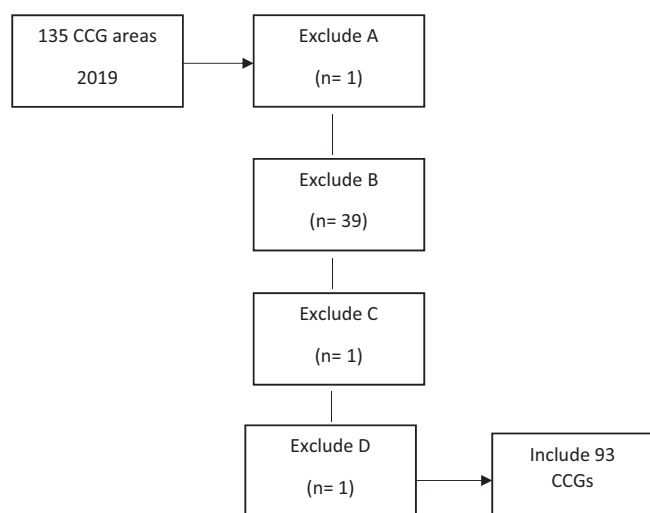


FIGURE 1 Selection of CCGs for multilinear regression. A = greater than 5% population difference in Clinical Commissioning Group (CCG) and corresponding Health Authority (HA) area. This includes single HA to a CCG area and where more than one HA covers a CCG area. B = More than one CCG in HA area. C = HA risk factor data exists for previous boundaries. D = Missing data.

TABLE 2 Univariate and multivariate regression showing the effect of a one unit increase in predictor (Unstandardised B) on the rate of Anti-Osteoporosis Medication (AOM) dispensed per 1000 people aged over 65 years

Predictor	n	Univariate		n	Multivariate	
		B	95% CI for B		B	95% CI for B
Male healthy life expectancy ^a (years)	94	-16.4	-25.0 to -7.9	93	7.5	-13.5 to 28.4
Female healthy life expectancy ^a (years)	94	-17.8	-25.8 to -9.8	93	-14.9	-34.1 to 4.2
Smoked ^a (%)	94	15.6	6.0 to 25.2	93	0.5	-13.7 to 14.7
Active adults ^a (%)	94	-11.4	-17.3 to -5.5	93	-7.2	-14.2 to -0.3
Alcohol-related hospital admissions per 100,000 ^a	94	0.3	0.1 to 0.5	93	0.1	-0.2 to 0.4
Hip fracture cases / 100 ^b	134	-4.1	-11.3 to 3.2	93	-21.6	-35.9 to -7.4
Total atorvastatin/1000 ^c	135	0.1	-0.3 to 0.2	93	0.4	0.2 to 0.6

^aOffice for National Statistics.

^bHip Fracture Database.

^cOpen Prescribing database (See Supplementary Table 3 for exclusion details), n = number of CCG areas.

4.2 | Local activity levels

Results of a systematic review found physical activity probably prevents osteoporosis in people aged 65 years and over.³⁷ Our study strengthens this finding as the percent of active adults in areas of England is both individually and collectively significantly related to lower rates of AOM dispensed, and therefore indicative of prevalence of osteoporosis in the local population. A 1% increase in active adults was associated with a reduction in approximately seven AOM items per 1000 people aged over 65 years. This was significant ($p = 0.042$) and highlights the importance of keeping active to prevent osteoporosis. However, other factors such as socioeconomic deprivation add to the complexity of the situation.

4.3 | Local socio-economic deprivation

The Index of deprivation for an area considers aspects such as employment, education levels, health and living conditions of the population.³⁸ Although our study did not specifically look at deprivation, our predictor variables have been linked to deprivation. Lifestyle risk factors such as smoking,³⁹ and alcohol consumption, in particular binge drinking⁴⁰ are more prevalent in deprived areas. Although, women are more likely to suffer from osteoporosis,¹⁰ those in the least deprived quartile of the population had significantly higher heel Bone Mineral Density (BMD) compared with the rest of the population.⁴¹ Women in this quartile were also significantly less likely to smoke, indicating a relationship between gender, smoking, deprivation and osteoporosis. Socioeconomic deprivation was also found to be a risk factor for osteoporosis in older adults.⁴² Our study did not include screening BMD and participants, however, the amount of medication dispensed in a CCG area was used as an indication of scale of occurrence of osteoporosis. Therefore, establishing the amount of medication people take in an area could be used to develop potential interventions to reduce disparities and improve lifestyles.

4.4 | Community pharmacy and the Covid-19 pandemic

Whilst rates of atorvastatin dispensing increased during the Covid-19 pandemic, there was a significant reduction in dispensing of alendronate and no change in that of denosumab.

The data presented in the Open Prescribing database contains the number of items of medication dispensed via community pharmacies in England. Analysis of the database highlights the variation and scope of interaction that people with osteoporosis have with the pharmacists and the potential for improve pharmacy-based osteoporosis services. This could include identification of people at risk for osteoporosis. Furthermore, the interaction at the pharmacy when collecting osteoporosis medication places the pharmacist in a unique position to deliver an intervention that may improve osteoporosis management. A continuous and tailored patient-centred education on

importance of keeping active or identification of any medication related concerns which prevent adherence is recommended. The impact of this interaction was highlighted during the Covid-19 pandemic when rates of the most commonly dispensed oral AOM, alendronate, was reduced. The picture was slightly different for denosumab with supplies not as affected. Denosumab is administered six monthly and NICE recommended treatment should not be postponed due to the Covid-19 pandemic.⁴³ Continued supply via community pharmacy enabled NICE guidelines to be met. This in part is due to their accessibility, as in England, 89% of the population live within a 20-minute walk of a community pharmacy, rising to 99% in deprived areas.⁴⁴

4.5 | Strengths and limitations

These analyses used real world data from across England to describe the pattern of AOM use at the regional level. However, the data sources; Open Prescribing database, National Hip Fracture Database and the Office for National Statistics are unlinked. Although being able to link the data would be helpful, this is not possible, therefore considered when making associations. The major limitation of this methodology is the lack of patient level information which precludes assumptions of causality.⁴⁵

The AOM data analysed was for 2019, but data sources of population risk factors were not all from the same calendar year. However, they are based on the latest Public Health England and the National Population Survey data available at the time of analysis for Health Authority areas in 2017.³⁰

Population discrepancies of up to 5% between CCG and HA were included, however, these could equate to large numbers. Dispensed item numbers do better reflect patient use of AOM than prescription data but do not confirm collection and ingestion of medication. Although a relatively small proportion is assumed, item numbers reported include those dispensed by doctors, resulting in an underestimation of AOM dispensed and this would apply to parental AOMs particularly. Furthermore, only the first quarter after the Covid-19 lockdown was compared to the same quarter the previous year. The use of segmented regression or ARIMA models to understand the impact of Covid-19 on subsequent quarterly time periods would have been useful.

4.6 | Future work

The ecological level observation that areas with higher prevalence of risk factors had lower rates of AOM dispensing requires confirmation using patient-level studies. These findings support research and clinical pathways that improve outcomes for osteoporosis patients, suggesting a scope for better integration of the community pharmacists in osteoporosis management. This is supported by the recommendation for research on continuity of care could promote multidisciplinary working as recommended by Royal Osteoporosis Society guidelines.⁴³

5 | CONCLUSION

The amount and type of AOM dispensed by community pharmacies varied considerably between CCGs. Populations with lower activity levels and/or a higher incidence of hip fracture should be targeted for services to address this gap in AOM provision. Community pharmacists are ideally placed to play this vital role in osteoporosis management, and further work is needed to optimise their support for effective and equitable osteoporosis management via multidisciplinary working.

AUTHOR CONTRIBUTIONS

S. S. Janjua: Conception and design, data acquisition, analysis and interpretation, writing original draft. H. F. Boardman: Data acquisition, data analysis, review and editing. A. Sami: Data analysis, review and editing. A. Johansen: Data acquisition, review and editing. L. S. Toh: Conception and design, review and editing. M. K. Javaid: Conception and design, data acquisition, analysis and interpretation, review and editing.

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CONFLICT OF INTEREST

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ORCID

Sobia S. Janjua  <https://orcid.org/0000-0002-4560-0208>

Helen F. Boardman  <https://orcid.org/0000-0002-5341-5619>

Arvind Sami  <https://orcid.org/0000-0003-2961-8579>

Antony Johansen  <https://orcid.org/0000-0003-4726-9106>

Li Shean Toh  <https://orcid.org/0000-0002-9228-6266>

Kassim M. Javaid  <https://orcid.org/0000-0001-7985-0048>

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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