# Associated Factors of Polypharmacy Among Elderly Patients Attended at Primary Care Setting.


## ABSTRACT

**Aims**: To determine the factors associated with polypharmacy in individuals aged 60 and over attending at a primary care unit.

**Methodology**: A case-control study was designed with the population served from January 2017 to December 2018 at the "Aragón" Family Medicine Clinic.

**Results**: A total population of 1,657 cases and 1,657 controls was included. The prevalence of excessive polypharmacy was significantly higher ($p < 0.001$) among patients seen in the MIDE module (n=203, 59.2%; 95% CI 54.2-65.0) and Dentistry (n=188, 48.1%; 95% CI 43.0-52.9). The most frequently prescribed and dispensed medications were nonsteroidal anti-inflammatory drugs, proton pump inhibitors, vitamins, statins, lipid-lowering agents, and non-insulin hypoglycemic agents. A significant association was observed between polypharmacy and the number of services used (OR=2.87; 95% CI 2.40-3.43, $p< 0.001$ for 2 services, and OR=11.21; 95% CI 6.28-20.03, $p< 0.001$ for 3 or more services), the presence of multiple morbidities (OR=5.65; 95% CI 4.73-6.76, $p< 0.001$), and the type of entitlement (OR=0.80; 95% CI 0.69-0.94, p=0.009; family members).

**Conclusions**: The risk factors associated with polypharmacy are linked to the clinical conditions of the patient and the medicalisation process of primary care.



*Keywords: polypharmacy; older adults; morbidity; primary health care; prevalence; odds ratio*


## 1. INTRODUCTION

Polypharmacy is a growing global public health problem present in all healthcare settings.[1-7] Reported prevalences range from 1-93%, depending on various factors: healthcare service delivery structures, health inequity, population characteristics, geographical region, and study inclusion criteria; it is especially prevalent in older adults (OA).[7-8] The prevalence of polypharmacy reaches 60% when defined as the unnecessary use of medications and 53.8% in institutionalised patients; it also accounts for 10% of emergency department visits and contributes to 10-17% of hospital admissions, of which 38% are potentially life-threatening.[7-8] This phenomenon is particularly common in OA with multiple morbidities, posing a significant challenge for primary care physicians as it diminishes patients' quality of life. When used appropriately, medications can extend life and help control symptoms of medical conditions, preventing excessive drug use. However, several factors contribute to the disproportionate use of medications: lack of knowledge about physiological changes associated with ageing, inability to discern between physiological and

pathological conditions, prescribing habits among physicians, and the relationship between potentially inappropriate medication prescribing (PIM) and polypharmacy. This detrimental vicious circle transcends the epidemiological transition in OA, as polypharmacy is, in turn, a risk factor for PIM and is linked to decreased functionality and autonomy in OA. The current healthcare system, designed to cure acute diseases rather than manage and minimise the consequences of chronic conditions prevalent in old age, favours polypharmacy.[9-12] In the current model of primary care medicalisation, work is compartmentalised, so addressing OA health conditions separately contributes to polypharmacy and lower quality care.[5, 8-9, 13] Factors associated with polypharmacy are divided into two categories: those related to the physician and the healthcare system, and those related to the patient. Among the former, polypharmacy is associated with the inability to identify new symptoms as adverse drug reactions rather than symptoms derived from a clinical condition that requires treatment, and poor medical advice, which can lead to improper or prolonged use of medications.

Currently, there is no definitive solution for managing chronic diseases (CD), and their therapeutic success is associated with the use of palliative treatments to maintain individuals in a functional state,[8, 14] perpetuating excessive medication use and deteriorating quality of life and functionality under the premise that increasing medication prescriptions will result in better control of CDs and new symptoms, thereby improving functional capacity; although this is not necessarily true. Additionally, demographic changes associated with ageing and the increase in CDs and their sequelae complicate their medical management and perpetuate the detrimental cycle affecting quality of life over the patient's lifespan. Polypharmacy is also clinically relevant due to its association with an increased risk of developing geriatric syndromes, loss of functionality and quality of life, more medication errors, and lower adherence to therapies.[15] It is also associated with the "prescribing cascade," where misinterpretation of adverse drug reactions leads to the prescription of more drugs.[15] This high rate of medication use is associated with a higher risk of negative outcomes in OA.[15] Prevalences of adverse drug reactions range from 5-78%, with significant negative outcomes such as hospitalisations, falls, loss of functionality, and increased mortality.[15] It is noted that 5-25% of hospitalisations related to OA are associated with adverse drug reactions, and 3-6% of these can be fatal or have serious consequences such as falls, cognitive decline, and institutionalization.[15] It has also been suggested that in some cases, polypharmacy is dependent on the healthcare system.[9] Among the latter, polypharmacy is attributed to gender (female), age (75 years or older), income,[16] treatments aimed at the presence of multiple morbidities, attitudinal behaviour, patient understanding of their treatment and medical condition, and lack of knowledge about medications. In this context, OA's ability to fully develop their autonomy is affected, and their dependency relationship increases.[8] Furthermore, it should be noted that almost 78% (95% CI 77-78.8) of our study population have polypharmacy. Therefore, our objective was to determine the factors associated with polypharmacy in OA in a primary care unit.

## 2. MATERIAL AND METHODS

### 2.1 Study Design, Population, and Sample Size

A case-control study was designed involving individuals aged 60 and over, entitled to ISSSTE, from the outpatient clinics of general and family medicine (GFMed), dentistry, gerontology, and the MIDE module (Comprehensive Diabetes Management by Stages) of the Family Medicine Clinic (FMC) "Aragón" in Mexico City. Data collection took place from January 2017 to December 2018. A census sample of 3,314 older individuals was included: 1,657 with polypharmacy and 1,657 without polypharmacy.

UNDER PEER REVIEW

## 2.2 Data Collection and Selection Criteria

The unit of analysis was the records from the "SIMEF" (Medical Financial System) and "SIAM" (Comprehensive Drug Supply System) databases. The "SIMEF" database was analysed to select records that met the inclusion criteria: individuals aged 60 and over, both genders, type of entitlement, ICD-10 diagnostic code, and consultation dates; with this information, the medication records provided at each consultation, the number of medications dispensed, the type of medication, and the presence or absence of polypharmacy per patient (from the "SIAM" database) were determined; polypharmacy was defined as the use of 5 or more medications (non-excessive polypharmacy= use of 5-9 medications and excessive polypharmacy= use of 10 or more). Subsequently, records that did not meet the inclusion criteria were eliminated. Records with incomplete information were excluded.

## 2.3 Statistical Analysis

Categorical variables are described as absolute frequency and percentage, and quantitative variables as mean, standard deviation (SD), and interquartile range (IQR). The former were compared using Pearson's chi-square (X2) test and McNemar's test, and Fisher's exact test, as appropriate. The latter were compared using the Mann-Whitney U test. The possible association between polypharmacy and various variables was assessed using univariate and multivariate logistic regression models, reporting the odds ratio (OR) and 95% confidence interval (95% CI). A p-value < 0.05 (two-tailed test) was considered significant.

## 2.4 Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and the Nuremberg Code. The protocol was approved by the Research and Ethics Committees of the FMC "Gustavo A. Madero" of ISSSTE. Patient identification data were treated confidentially, and an identification code was assigned.

# 3. RESULTS AND DISCUSSION

## 3.1 General Characteristics of the Study Population and Prevalence of Polypharmacy

The study population (n=3,314) was characterised by the following features: predominantly female (52.8%, 95% CI 51.1-54.5), pensioners (45.6%, 95% CI 42.7-48.3), individuals in their sixties (61.7%, 95% CI 60.0-63.4), attending the General and Family Medicine service (96.2%, 95.5-96.9), primarily in the morning shift (72.1%, 95% CI 70.6-73.7). Nearly 62% of the patients were under 70 years old. The average number of consultations attended over the two-year period was 7.59 (SD=7.86; IQR=2-11), and the average number of medications dispensed per month ranged from 3.89 to 4.52 per person. February 2018 (mean=4.516, SD=2.6516) had the highest average number of medications dispensed, while February 2017 (mean=3.887, SD=2.3395) had the lowest. The months with the lowest and highest consultation attendance were December 2018 and October 2018, respectively.

UNDER PEER REVIEW

When comparing the prevalence of polypharmacy, it was found to be higher ($p < 0.001$) among women, pensioners, individuals in their sixties, patients attended by the General and Family Medicine service, those who had five or more consultations, those using three or more services, and those with multimorbidity (Table 1).

**Table 1. Characteristics of study population.**

| Variables | Without polypharmacy n=1,657 (%, IC95%) | Polypharmacy n=1,657 (%, IC95%) |
|---|---|---|
| Sex – n (%) | | |
| Male | 782 (47.2, 44.8-49.4) | 782 (47.2, 44.8-49.4) |
| Female | 875 (52.8, 50.6-55.2) | 875 (52.8, 50.6-55.2) |
| Age | | |
| Mean (SD) | 69.14 (8.175) | 69.14 (8.175) |
| Distribution – n (%) | | |
| 60-69 | 1022 (61.7, 59.4-64.1) | 1022 (61.7, 59.4-64.1) |
| 70-79 | 412 (24.9, 22.8-26.9) | 412 (24.9, 22.8-26.9) |
| 80-89 | 180 (10.9, 9.4-12.3) | 180 (10.9, 9.4-12.3) |
| 90-99 | 42 (2.5, 1.8-3.3) | 42 (2.5, 1.8-3.3) |
| 100 and over | 1 (0.1) | 1 (0.1) |
| Type of entitlement – n (%) [a] | | |
| Pensioners | 690 (41.6, 39.2-44.1) | 781 (47.1, 44.7-49.4) |
| Workers | 383 (23.1, 21.1-25.3) | 344 (20.8, 18.8-22.8) |
| Relatives | 584 (35.2, 33.0-37.4) | 532 (32.1, 29.9-34.4) |
| Type of medical service – n (%) [a] | | |
| General Medicine | 1563 (94.3, 93.2-95.4) | 1626 (98.1, 97.5-98.7) |
| Dentistry | 131 (7.9, 6.6-9.4) | 260 (15.7, 14.0-17.6) |
| MIDE | 78 (4.7, 3.7-5.7) | 265 (16.0, 14.3-17.8) |
| Gerontology | 128 (7.7, 6.5-9.1) | 202 (12.2, 10.6-13.8) |
| Number of services used | | |
| Mean (DE) [a] | 1.15 (0.38) | 1.42 (0.63) |
| Distribution – n (%) [a] | | |
| 1 | 1427 (86.1, 84.4-87.7) | 1077 (65.0, 62.6-67.3) |
| 2 | 217 (13.1, 11.5-14.8) | 470 (28.4, 26.3-30.4) |
| 3 and over | 13 (0.8, 0.4-1.2) | 110 (6.6, 5.4-7.9) |
| Number of medical consultations | | |
| Mean (DE) [a] | 3.49 (3.75) | 11.69 (8.71) |
| Distribution – n (%) [a] | | |
| 1 | 539 (32.5, 30.2-34.8) | 88 (5.3, 4.3-6.4) |
| 2 a 4 | 744 (44.9, 42.5-47.2) | 294 (17.7, 15.9-19.6) |
| 5 and over | 374 (22.6, 20.6-24.6) | 1275 (76.9, 75.0-78.9) |
| Multiple morbidities – n (%) [a] | 947 (57.2, 54.9-59.6) | 1463 (88.3, 86.7-89.7) |

Source: Own elaboration with results from the SIMEF-SIAM database, 2017-2018. SD: standard deviation, MIDE: comprehensive diabetes management by stages. CI95% = 95% confidence interval. N = 3,314. Quantitative variables are expressed as mean and SD. Qualitative variables are expressed as frequency (%) and 95% confidence interval. [a] p-value < 0.01.

In the case group (polypharmacy), the prevalence of non-excessive and excessive polypharmacy was 18.7% and 31.3%, respectively. The prevalence of excessive polypharmacy was significantly higher ($p < 0.001$) among patients attending the MIDE module (n=203, 59.2%; 95% CI 54.2-65.0) and Dentistry (n=188, 48.1%; 95% CI 43.0-52.9), and lower among those attending Gerontology (n=143, 43.3%; 95% CI 37.6-49.1) and General and Family Medicine (n=1,030, 32.3%; 95% CI 30.5-34.0). The prevalence of non-

UNDER PEER REVIEW

excessive polypharmacy was similar across all services (MIDE: n=62, 18.1%; 95% CI 14.0-22.2; Dentistry: n=72, 18.4%; 95% CI 14.8-22.5; Gerontology: n=59, 17.9%; 95% CI 13.9-22.4; General and Family Medicine: n=596, 18.7%; 95% CI 17.4-20.2).

### 3.2 Main Medications Dispensed in the Study Population

The top ten medications dispensed fell into the categories of nonsteroidal anti-inflammatory drugs, proton pump inhibitors, vitamins, statins, lipid-lowering agents, non-insulin hypoglycaemic agents, and antiplatelet agents (Table 2). Among the control group, antihypertensives were also a significant category (Table 2).

**Table 2. Top 10 medications dispensed by the pharmacy area of the C.M.F. "Aragón" to people aged 60 and over.**

| Total population | | | Without polypharmacy | | | Polypharmacy | | |
|---|---|---|---|---|---|---|---|---|
| No. | Medication | N, %; IC95 % | No. | Medication | n, %; IC95 % | No. | Medication | n, %; IC95 % |
| 1 | Paracetamol | 1340, 40.43; 38.77-42 | 1 | Paracetamol | 355, 21.42; 19.43-23.36 | 1 | Paracetamol | 985, 59.44; 57.03-61.92 |
| 2 | Diclofenac | 976, 29.45; 27.88-30.96 | 2 | Diclofenac | 244, 14.73; 13.1-16.6 | 2 | Omeprazole | 751, 45.32; 42.91-47.74 |
| 3 | Omeprazole | 896, 27.04; 25.47-28.55 | 3 | Metformin | 184, 11.1; 9.66-12.67 | 3 | Diclofenac | 732, 44.18; 41.82-46.53 |
| 4 | Complex B | 891, 26.89; 25.47-28.39 | 4 | Atorvastatin | 182, 10.98; 9.47-12.55 | 4 | Complex B | 720, 43.45; 40.92-45.75 |
| 5 | Atorvastatin | 868, 26.19; 24.83-27.64 | 5 | Complex B | 171, 10.32; 8.69-11.77 | 5 | Atorvastatin | 686, 41.4; 39.05-43.63 |
| 6 | Bezafibrate | 810, 24.44; 23.05-25.98 | 6 | Bezafibrate | 169, 10.2; 8.75-11.71 | 6 | Bezafibrate | 641, 38.68; 36.27-40.98 |
| 7 | Metformin | 804, | 7 | Omeprazole | 145, | 7 | Metformin | 620, |

UNDER PEER REVIEW

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| | | 24.26; 22.84 - 25.74 | | | 8.75; 7.42-10.14 | | | 37.42; 35-39.83 |
| 8 | Naproxen | 652, 19.67; 18.32 - 20.97 | 8 | Enalapril | 137, 8.27; 7.0-9.6 | 8 | Naproxen | 528, 31.86; 29.51 - 34.04 |
| 9 | Hydroxocobalamin | 626, 18.89; 17.53 - 20.28 | 9 | Hydroxocobalamin | 130, 7.85; 6.58-9.17 | 9 | Hydroxocobalamin | 496, 29.93; 27.58 - 32.23 |
| 10 | ASA | 551, 16.63; 15.36 - 17.95 | 10 | Naproxen | 124, 7.48; 6.28-8.75 | 10 | ASA | 465, 28.06; 25.95 - 30.35 |

Source: Own elaboration with results from the SIMEF-SIAM database, 2017-2018. Omeprazole: includes Pantoprazole or Rabeprazole or Omeprazole.

Aspirin: acetylsalicylic acid. Enalapril: includes Enalapril or Lisinopril or Ramipril. N= 3,314. n=1,657. CI95%: 95% confidence interval.

In the polypharmacy group, the top four medication categories were primarily used to alleviate symptoms, particularly pain. The most frequently dispensed medication was paracetamol.

### 3.3 Main Reasons for Consultation in the Study Population

A total of 596 ICD-10 codes were recorded. The primary reasons for consultation included hypertension and type 2 diabetes, followed by acute upper respiratory infections, mixed hyperlipidaemia, dental caries, urinary tract infections, prostate disease, gonarthrosis, lower back pain, gastritis, peripheral venous insufficiency, hypothyroidism, chronic obstructive pulmonary disease, chronic ischaemic heart disease, and gastroenteritis and colitis of infectious origin. Gastritis, infectious gastroenteritis and colitis, metabolic disorders, and chronic ischaemic heart disease were observed only in patients with polypharmacy. Conversely, post-surgery convalescence, hypothyroidism, generalised primary osteoarthritis, and chronic obstructive pulmonary disease were observed only in patients without polypharmacy (Table 3).

**Table 3. Comparison of the top 15 reasons for consultation in older adults with and without polypharmacy.**

| No. | Polypharmacy | n, %; IC95% | Without polypharmacy | n, %; IC95% |
|---|---|---|---|---|
| 1 | Essential (Primary) Hypertension | 900, 54.32; 52.02-56.85 | Essential (Primary) Hypertension | 419, 25.29; 23.11-27.34 |
| 2 | NIDDM | 721, 43.51; 41.16-45.93 | NIDDM | 268, 16.17; 14.54-18.04 |
| 3 | AURTI | 574, 34.64; 32.05-36.87 | OEMC | 223, 13.46; 11.71-15.15 |
| 4 | Mixed Hyperlipidaemia | 308, 18.59; 16.72-20.58 | AURTI | 175, 10.56; 9.23-12.01 |

UNDER PEER REVIEW

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| 5 | OEMC | 293, 17.68; 16.05-19.49 | Mixed Hyperlipidaemia | 140, 8.45; 7.18-9.9 |
| 6 | UTI | 255, 15.39; 13.64-17.2 | Dental caries, unspecified | 124, 7.48; 6.22-8.69 |
| 7 | Dental caries, unspecified | 254, 15.33; 13.58-17.08 | UTI | 105, 6.34; 5.19-7.42 |
| 8 | OSDP | 175, 10.56; 9.11-12.19 | OSDP | 104, 6.28; 5.13-7.54 |
| 9 | Gonarthrosis, unspecified | 164, 9.9; 8.57-11.35 | Gonarthrosis, unspecified | 92, 5.55; 4.47-6.7 |
| 10 | Gastritis, unspecified | 155, 9.35; 7.91-10.8 | Lumbago, unspecified | 83, 5.01; 3.8-6.04 |
| 11 | Lumbago, unspecified | 131, 7.91; 6.64-9.23 | VIP | 62, 3.74; 2.78-4.71 |
| 12 | VIP | 124, 7.48; 6.22-8.69 | CFS | 60, 3.62; 2.72-4.59 |
| 13 | MD, unspecified | 118, 7.12; 5.97-8.39 | Hypothyroidism, unspecified | 52, 3.14; 2.29-3.98 |
| 14 | OIGIC | 111, 6.7; 5.49-7.91 | Generalised primary (osteo)arthritis | 49, 2.96; 2.17-3.8 |
| 15 | CIHD, unspecified | 105, 6.34; 5.25-7.42 | COPD | 48, 2.9; 2.11-3.86 |

Source: Own elaboration with the results from the SIMEF-SIAM database, 2017-2018. NIDDM: Non-insulin-dependent diabetes mellitus, without mention of complication. AURTI: Acute upper respiratory tract infection, unspecified. OEMC: Other specified medical care. UTI: Urinary tract infection, site not specified. OSDP: Other specified disorders of the prostate. VIP: (Chronic) venous insufficiency (peripheral). CFS: Convalescence following surgery. MD: Metabolic disorder. OIGIC: Other infectious gastroenteritis and colitis. CIHD: Chronic ischaemic heart disease. COPD: Chronic obstructive pulmonary disease, unspecified.

### 3.4 Factors Associated with Polypharmacy

Univariate regression models showed that age and gender were not associated with polypharmacy. However, type of entitlement was significant; compared to pensioners, workers and their family members had a lower probability of polypharmacy, with similar rates (47.3% and 42.3%, respectively). The probability of polypharmacy increased with the number of services used (from 43% for one service to 74.2% for two services and 91.8% for three or more services) and the number of consultations (starting from two or more), as well as with the presence of multimorbidities, which increased the probability by 85.0% (Table 4). The multivariate model indicated that the presence of multimorbidities increased the likelihood of polypharmacy by four times, and receiving consultations from three or more services increased it by seven times (Table 4).

**Table 4. Association between polypharmacy and sociodemographic variables in people aged 60 and over.**

| Variable | Crude OR (IC 95%) | *P*[a] | Adjusted OR (IC 95%) | *P*[b] |
|---|---|---|---|---|
| Sex | | | | |
| Male | 1 | | 1 | |
| Female | 1 (0.872-1.146) | 1.000 | 1.021 (0.88-1.19) | 0.789 |
| Age | | | | |
| Q1 (60-61) | 1 | | | |
| Q2 (62-65) | 1 (0.81-1.24) | 1.000 | 0.8 (0.63-1.01) | 0.064 |

UNDER PEER REVIEW

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|---|---|---|---|---|
| Q3 (66-70) | 1 (0.81-1.24) | 1.000 | 0.81 (0.64-1.02) | 0.075 |
| Q4 (71-76) | 1 (0.79-1.27) | 1.000 | 0.83 (0.64-1.08) | 0.174 |
| Q5 (≥77) | 1 (0.8-1.25) | 1.000 | 0.84 (0.66-1.09) | 0.188 |
| Type of entitlement | | | | |
| Pensioners | 1 | | | |
| Workers | 0.79 (0.66-0.95) | 0.011 | 0.87 (0.71-1.06) | 0.172 |
| Relatives | 0.8 (0.69-0.94) | 0.006 | 0.8 (0.67-0.94) | 0.009 |
| Number of services used | | | | |
| 1 | 1 | | | |
| 2 | 2.87 (2.4-3.43) | < 0.01 | 1.98 (1.64-2.39) | < 0.01 |
| 3 and over | 11.21 (6.28-20.03) | < 0.01 | 7.6 (4.23-13.67) | < 0.01 |
| Number of medical consultations | | | | |
| 1 | 1 | | | |
| 2 a 4 | 2.42 (1.86-3.15) | < 0.01 | | |
| 5 and over | 20.88 (16.21-26.89) | < 0.01 | | |
| Multiple morbidities | 5.654 (4.729-6.759) | < 0.01 | 4.66 (3.88-5.61) | < 0.01 |

Source: Own elaboration with the results from the SIMEF-SIAM database, 2017-2018. OR: odds ratio. The p-values were calculated using the chi-square Wald test. a p-value of the crude OR from the univariate logistic regression models. b p-value of the adjusted OR for the variables included in the multivariate logistic regression model. Variables included in the multivariate logistic regression model: Sex: male = 0, female = 1. Age: Q1 (60-61) = 0, Q2 (62-65) = 1, Q3 (66-70) = 2, Q4 (71-76) = 3, Q5 (≥77) = 4. Type of entitlement: pensioners = 0, workers = 1, relatives = 2. Number of services used: 1 = 0, 2 = 1, 3 and over = 2. Multiple morbidities: yes = 1, no = 0.

Older adults represent an increasingly significant proportion of the global population, particularly those in their eighties.[8] They often present with multiple chronic conditions (CCs), which favour the prescription of multiple medications (both prescribed and over-the-counter), thereby increasing the risk of polypharmacy, adverse drug reactions, drug interactions, and an unfavourable benefit-risk ratio depending on the setting and age. Older adults are typically prescribed between 3.7 and 6.9 medications (range= 0-16),[16-20] consistent with the findings of our study. The average number of medications was similar to those reported for populations in Germany (3.7), Tabasco (Mexico; 3.5), and Mexico City (3.9); lower than those reported for populations in Norway (6.9), Nuevo León (Mexico; 6.9), Canada (6.8), Tamaulipas (Mexico; 5.9), and Belgium (5); but higher than for the population in Valle del Mezquital, Hidalgo (Mexico; 2.8).[8,16-20] Moreover, depending on the study setting (hospitalised, rural, urban, from a care home, or primary care), between 14% and 93% of patients consume five or more different medications, and between 1.3% and 65% consume ten or more.[8, 18-19, 21-22]

The prevalence of polypharmacy observed in our study was higher than that reported for urban populations in the United States, Saudi Arabia, the United Kingdom, Chile, Colombia,

UNDER PEER REVIEW

Israel, Sweden, Canada, Ireland, the Netherlands, India, Finland, Singapore, Poland, New Zealand, Brazil, Turkey, Taiwan, and Tabasco, and for rural populations in Hidalgo, Nigeria, and the United States; it was lower than the prevalence observed for urban populations in Portugal, Malaysia, Australia, and for the beneficiaries of the Mexican Institute of Social Security (IMSS) in Mexico City, Tamaulipas, and Nuevo León, but similar to populations in Italy and Puebla.[7-8, 21-25] The prevalence of excessive polypharmacy was higher than reported for populations in the United States, Canada, the United Kingdom, India, New Zealand, the Czech Republic, Finland, France, Germany, Israel, Italy, the Netherlands, and Turkey, but lower than in Sweden, Australia, and Poland.[8, 21-22]

Only four studies have been conducted in primary care settings (three in Mexico and one in Brazil), and only two of these focused on patients with non-communicable diseases.[8] However, the prevalence of polypharmacy in those studies was higher than in our population. Only the study on patients with a history of traumatic hip fracture reported a prevalence of polypharmacy similar to our findings.[8] Consequently, the prevalence of polypharmacy varies between countries, regions, and settings, and according to the operational definitions used by the authors. In some cases, polypharmacy may be unavoidable. However, the medicalisation of primary care has perpetuated a vicious cycle that increases healthcare costs and often results in little to no improvement in disease management, leading to complications, more frequent doctor visits, new prescriptions (appropriate or inappropriate), and increased medication use in a population already identified as major consumers of drugs.[26-29] Additionally, the clinical, epidemiological, social, economic, and public health implications are significant, considering that polypharmacy leads to negative health outcomes for older adults, particularly the most vulnerable, with social determinants and life course factors associated with a higher likelihood of disease.[29-30] Age-related pharmacokinetic and pharmacodynamic changes increase the risk of adverse drug events, loss of autonomy, functional health status decline, cognitive impairment, higher fall risk, hospitalisations, and mortality, though not all studies report these associations.[29-30]

Adverse outcomes associated with medications increase with the number of prescribed drugs, and the complexity of prescriptions is linked to non-adherence and higher hospitalisation rates.[8] Our study showed that patients experienced at least three CCs, with three of the ten most common diseases being cardiovascular risk factors. This aligns with findings by Tsoi et al., who reported hypertension as the most prevalent condition (65%) among individuals aged 85 and older in Canada.[20] The prevalence of diseases in our population differed from the Canadian cohort, where osteoporosis, hypothyroidism, and gastroesophageal reflux disease were more common in women, and coronary artery disease was more prevalent in men.[20] We observed that the main categories of medications prescribed for both genders were anti-inflammatory and vitamin supplements; five of the ten main categories of medications were intended for symptom relief. Three of the remaining categories were prescribed for the management of CCs (diabetes and dyslipidaemia). Our data differ from the medications reported by Tsoi et al., who showed atorvastatin as the main medication prescribed for people aged 85 and over.[20] In contrast, in our population, metformin was one of the three most prescribed medications in the control group. The findings of this study demonstrate different patterns of disease prevalence and medication prescription compared to other populations.

The analysis of the main medications dispensed shows that most medical treatments were intended for symptom relief, a pattern similar to that reported by Tsoi et al.,[20] and that the most prescribed medications are affected by age-related pharmacokinetic and pharmacodynamic changes, highlighting that well-intentioned efforts to improve the health conditions of older adults can worsen their quality of life, autonomy, and cause harm, likely

UNDER PEER REVIEW

due to the presence of adverse drug effects, which are more probable in the context of polypharmacy.[9, 11, 15, 20, 31-32] The high prevalence of polypharmacy in our population, together with the presence of multimorbidities, creates a favourable environment for type C drug interactions (requiring dosage adjustments to avoid adverse effects), present in 90% of cases, and type D interactions (which should be avoided due to serious danger of adverse reaction or lack of therapeutic effect), observed in 10% of cases.[33] This also increases the risk of medication errors and drug-drug interactions,[26] which escalate with the number of medications consumed.[9, 34] According to observed data, for 78% of the population that has taken at least five medications, patients may experience at least ten possible drug-drug interactions, for 50% of patients who have taken at least ten medications, there will be 45 possible interactions, and for those who have taken at least fifteen medications, there will be almost 105 possible interactions,[9, 34] suggesting that a large percentage of the studied population is susceptible to adverse events secondary to polypharmacy. Furthermore, our data differ from the literature, which indicates that the number of medications taken increases with age.[35] Serra-Urra et al. indicate that 30% of people aged 75 years take more than three medications, which is lower than observed in our study population (78.3%).[35] Similarly, univariate and multivariate logistic regression models do not show an association between age and polypharmacy; instead, they revealed a confusing pattern. The univariate and multivariate regression models suggest that the risk of polypharmacy increases with the number of consultations, services used, and the presence of multimorbidities, similar to observations in the population of Valle del Mezquital, Hidalgo, but different from the SHELTER study, where the number of diseases was not associated with polypharmacy.[8] Protective factors included being employed and being affiliated as a family member. These data suggest that the probability of polypharmacy increases with the medicalisation process of primary care, and that disease-centred care rather than patient-centred care increases healthcare costs in primary care settings.

## 4. CONCLUSION

The data from this study provide epidemiological evidence demonstrating a high prevalence of polypharmacy and excessive polypharmacy. The main risk factors associated with polypharmacy are multimorbidities and the number of services used. Identifying these factors will help design interventions and programmes to ensure the appropriate and rational use of medications to improve the quality of life of older adults who reach advanced ages; through an early, timely, multidimensional, and intersectoral intervention approach, where prevention should begin from earlier ages, aiming to achieve changes in harmful lifestyle behaviours and causes of this behaviour, making older adults protagonists of their development and autonomy, and consequently, empowered agents of change in determinants that improve their health and quality of life.

UNDER PEER REVIEW

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declares that no generative AI technologies such as large language models (ChatGPT, Copilot, etc) and text-to-image generators have been used during writing or editing of manuscripts.

## CONSENT (NO APPLICABLE)

## ETHICAL APPROVAL

This study was conducted in accordance with good clinical practices as defined by Mexican legislation and the Declaration of Helsinki for research involving human subjects. The designed database utilized an assigned folio number to maintain patient confidentiality. The principles of the 1989 United Nations General Assembly were followed: the principle of lawfulness and loyalty (data were obtained legally), the principle of accuracy (data relevance was verified), the principle of purpose (the database was specific and legitimate before creation), the principle of non-discrimination, and the principle of security. The study was approved by the Local Research Committee and Local Research Ethics Committee of the Family Medicine Clinic 'Gustavo A. Madero'.

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