RESEARCH ARTICLE

Social support, social context and nonadherence to treatment in young senior patients with multimorbidity and polypharmacy followed-up in primary care. MULTIPAP Study

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Abstract

Objective

To estimate the prevalence of nonadherence to treatment and its relationship with social support and social context in patients with multimorbidity and polypharmacy followed-up in primary care.

Methods

This was an observational, descriptive, cross-sectional, multicenter study with an analytical approach. A total of 593 patients between 65–74 years of age with multimorbidity (≥3 diseases) and polypharmacy (≥5 drugs) during the last three months and agreed to participate in the MULTIPAP Study. The main variable was adherence (Morisky-Green). The predictors were social support (structural support and functional support (DUFSS)); sociodemographic variables; indicators of urban objective vulnerability; health-related quality of life (EQ-5D-5L- VAS & QALY); and clinical variables. Descriptive, bivariate and multivariate analyses with logistic regression models and robust estimators were performed.
Data Availability Statement: Regarding data exchange, the Aragon Ethics Committee approved this research without considering the option of data sharing. The data contains sensitive clinical information about the patient, so there are ethical and legal restrictions to sharing the data set. The data are part of the MULTIPAP study and can be requested by contacting the Aragon Ethics Committee at the email address ceica@aragon.es; for the request of data you can also contact the Primary Care Management of Madrid at the email address gap@salud.madrid.org; and by contacting the Technical Direction of Teaching and Research at the email address rtdei@salud.madrid.org. The MULTIPAP Group may establish future collaborations with other groups based on the same data. The main researchers of the project will be contacted (Alexandra Prados-Torres at sprados.ssipr@juntadeandalucia.es and Daniel Prados-Torres at uand.prados.sspan@juntadeandalucia.es and Isabel del Cura at isabel.cura@salud.madrid.org). However, each new project based on these data must be previously submitted to CEICA for approval.

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Results
Four out of ten patients were nonadherent, 47% had not completed primary education, 28.7% had an income ≤1050 €/month, 35% reported four or more IUVs, and the average perceived health-related quality of life (HRQOL) EQ-5D-5L-VAS was 65.5. The items that measure functional support, with significantly different means between nonadherent and adherent patients were receiving love and affection (-0.23; 95%CI: -0.40; -0.06), help when ill (-0.25; 95%CI: -0.42; -0.08), useful advice (-0.20; 95%CI: -0.37; -0.02), social invitations (-0.22; 95%CI: -0.44; -0.01), and recognition (-0.29; 95%CI: -0.50; -0.08). Factors associated with nonadherence were belonging to the medium vs. low tertile of functional support (0.62; 95%CI: 0.42; 0.94), reporting less than four IUVs (0.69; 95%CI: 0.46; 1.02) and higher HRQOL perception (0.98; 95%CI: 0.98; 0.99).

Conclusions
Among patients 65–74 years of age with multimorbidity and polypharmacy, lower functional support was related to nonadherence to treatment. The nonadherence decreased in those patients with higher functional support, lower urban vulnerability and higher perceived health status according to the visual analog scale of health-related quality of life.

Introduction
Population aging has led multimorbidity to be becoming increasingly prevalent in the adult population of most Western European countries [1]. Most studies define multimorbidity as the concurrent presence of two or more, or three or more chronic diseases; the latter definition is more suitable for the identification of patients with complex health needs [2]. It is estimated that the average number of chronic conditions in those over 75 years is 3.2, while that for the young seniors (65–74 years) is 2.8 [1–3]. Multimorbidity affects 81.5% of people older than 85 years, 62% of those 65–74 years old and 50% of those younger than 65 years old [4]. Multimorbidity is associated with polypharmacy, defined as the simultaneous consumption of five or more drugs [5]. Polypharmacy has undesirable consequences, such as increased risk of potentially inappropriate medication, misuse of doses, either by excess or by default of necessary treatments, nonadherence and increased risk of interactions and adverse drug reactions [6].

Studies on different population groups with respect to age and chronic condition showed an average of 50% adherence to long-term therapy. They found that about half of the chronic patients do not comply with their prescription or do so incorrectly, particularly with respect to time, dose, frequency and duration [7,8]. Nonadherence to prescribed treatment is a growing and complex problem for both patients and healthcare systems [9,10]. Haynes et al. [11] identified more than 250 factors that can influence drug adherence, among which being older and social isolation stood out as the most important ones [12]. Components of the social context are all those that encompass the individual’s living conditions: the physical environment in which they live, the socio-economic level, the level of education, work, income level, the social network and social support [13]. The challenge of improving adherence has traditionally focused on the individual characteristics of the patient, the complexity of the treatment, the type of information provided, health literacy, and the physician-patient relationship [14,15], with social factors being little explored [8,16]. Thus far, some studies have found a significant relationship between adherence and the social context, in terms of socioeconomic status [17].
and social support [18,19]. However, there are few studies exploring the impact of all these determinants together, which hinders the comprehensive approach necessary to study nonadherence to treatment [20].

The definition of social support includes whether the basic social needs of a person (affection, esteem, approval, belonging, identity and safety) are satisfied through the interaction with others [21]. It covers three areas: (1) structural, which assesses the number and pattern of direct and indirect bonds surrounding the individual; (2) functional, which corresponds to the different types of resources that flow through the bonds of the social network; and (3) informative, which reflects the knowledge provided to the individual through his or her social network [22,23]. Two meta-analyses have analyzed the relationship between social support and adherence to treatment, concluding that adherence improves more significantly with functional support than with structural support [20,24]. Having someone to talk to and have contact with, as well as someone who in turn provides emotional support, seem to play a prominent role in the association of functional support and adherence to treatment [18]. Moreover, the source of functional support and the type of help that is received also have a considerable influence on this association [19,24,25]. In this sense, jointly studying the different elements of the social context and exhaustively exploring the influence of functional support on nonadherence could be key to better understand this complex framework and the role that each factor plays in therapeutic adherence [19]. The main objective of this study is to estimate the prevalence of nonadherence to treatment and its relationship with social support and social context in patients with multimorbidity and polypharmacy followed-up in primary care.

Materials and methods

An observational, descriptive, cross-sectional study with an analytical approach was performed using baseline data from the MULTIPAP Study [26]. This study was a pragmatic group-controlled, randomized clinical trial with 12 months of follow-up conducted in 38 health centers in the regions of Andalucía, Aragon and Madrid (Spain) with the participation of 117 family physicians (GPs), each recruiting five patients. Patients aged 65–74 years with multimorbidity (≥3 chronic diseases) and polypharmacy (≥5 different drugs for at least the last three months) who visited their GP at least once in the last year and had given their written informed consent to participate in the MULTIPAP Study were included [26]. We excluded institutionalized patients with severe mental illness and those with a life expectancy of less than 12 months according to their physician. Patients were selected by random sampling among those who met the inclusion criteria. All the variables described below were collected by the GP through an interview during the consultation. The participating GPs were previously trained to conduct the interview through an electronic data collection notebook.

The main outcome variable was adherence to treatment (adherent/nonadherent), measured with the Morisky-Green test. The Morisky-Green questionnaire asks a series of closed questions to the patient: “do you ever forget to take the medicines to treat your illness; do you take the medicines at the indicated times; when you feel well, do you stop taking the medicine; if you ever feel bad, do you stop taking the medicine? Patients are considered adherent if they answer all four questions correctly and non-adherent if they answer three or fewer questions” [27]. The main independent variable was social support, measured in two ways: structural support (information about marital status and number of cohabitants in the home) and functional support. The latter was measured through the Duke UNC-11 Functional Social Support (DUFSS). This questionnaire offers a total score of functional support and two additional scores related to each of the domains revealed by its factor analysis: confidential and affective support [28]. The version used in this study was composed of 11 items. Each item uses a Likert-type
response scale from 1 (“Much less than I would like”) to 5 (“As much as I would like”) [29]. Since its creation to date, the instrument has been validated in very different populations, showing differences in the distribution of the items that make up each of the domains. Validation performed by Ayala et al. [30] was carried out in a noninstitutionalized Spanish population, with an average age of 72 years. As this is a population similar to ours, we have used the result of their factor analysis, in which confidential support is measured through seven items (4, 5, 6, 7, 8, 10 and 11), with a total score of 35, and affective support is measured through 4 items (1, 2, 3, and 9), with a total score of 20. The total score for social support was categorized in tertiles, being tertile 1 the lowest.

The following potential predictor variables were considered: a) sociodemographic variables such as age, sex, retirement status (retirement/no retirement), social class (collected through the 7 categories of the CNO-SEE12 instrument and subsequently grouped) [31], education level (primary education incomplete, primary education, secondary or higher education), and socioeconomic level (≤1050€/month, 1051–2250€/month and ≥2251€/month); b) indicators of subjective urban vulnerability (IUVs), based on those collected by the National Health Survey to explore participants’ neighborhood (noise level, odors, poor-quality drinking water, unclean streets, air pollution, lack of green areas, feral animals and crime) [32]; and c) clinical factors (number of chronic diseases and number of drugs consumed) and health-related quality of life (HRQOL) measured by the EQ-5D-5L [33]. The EQ-5D-5L determines the perceived general state of health measured by a visual analog scale (VAS) and utilities.

A descriptive analysis of the characteristics of the patients was performed, with frequencies and percentages for the qualitative variables and with means and standard deviations (SD) or medians and interquartile ranges (IQR) for the quantitative variables according to their distribution. The prevalence of nonadherence was estimated with the 95% confidence intervals (CI). The contrast of qualitative variables was performed with the Pearson Chi-squared test, and the contrast of normally distributed quantitative variables was performed with Student’s t-test. To study the association between functional support (independent variable) and nonadherence (dependent variable), a logistic regression model was fit with sequential forward fitting in three steps. Model 1 was adjusted for sociodemographic factors (age, sex, retirement status, social class, education level and socioeconomic status). Model 2 was adjusted additionally for IUVs (<4 vs. ≥4 indicators). A final model was constructed (model 3) adjusting additionally for clinical factors (number of diseases and number of drugs) and health-related quality of life. Considering that the patients were included in the study by cluster-sampling (each GP included five patients), robust estimators were obtained. The data analysis was performed with the statistical software STATA v14.

Ethical and legal aspects

The project was approved by the Clinical Research Ethics Committee of Aragon (CEICA) on September 30, 2015, with the reference number PI15/0217. And has been favorably evaluated by the Research Ethics Committee of the Province of Malaga on September 25, 2015, and by the Central Committee of Primary Care Research of the Community of Madrid.

Results

Of the 593 patients included in the study, a total of 40.8% (95% CI: 36.9%; -44.8%) were nonadherent. Table 1 shows the distribution of variables and the number of subjects (total population, nonadherent and adherent). More than half of the sample (56.3%) were women, and the mean age was 69.7 years (SD 2.7 years). Compared to adherent patients, those who were nonadherent reported a higher percentage of 4 or more IUVs (48.3% vs. 36.8%, p = 0.007) and had
|                       | Total n (%) | Adherent n (%) | Nonadherent n (%) | p-value |
|-----------------------|-------------|----------------|-------------------|---------|
| N                     | 593(100)    | 351(59.2)      | 242(40.8)         |         |
| Age *                 | 69.7(2.7)   | 69.8(2.7)      | 69.6(2.7)         | 0.55    |
| Sex                   |             |                |                   |         |
| Male                  | 259(43.7)   | 153(59.1)      | 106(40.9)         | 0.96    |
| Female                | 334(56.3)   | 198(59.3)      | 136(40.7)         |         |
| Retirement status     |             |                |                   |         |
| Retired               | 538(90.7)   | 321(59.7)      | 217(40.3)         | 0.46    |
| Nonretired            | 55(9.3)     | 30(54.6)       | 25(45.5)          |         |
| Social class          |             |                |                   |         |
| Mid-level supervisors and directors | 234(39.5) | 147(62.8) | 87(37.2) | 0.33 |
| Skilled primary sector | 217(36.6) | 125(57.6) | 92(42.4) |         |
| Unskilled             | 142(24)     | 79(55.6)       | 63(44.4)          |         |
| Education level       |             |                |                   |         |
| Primary education incomplete | 279(47.1) | 163(58.4) | 116(41.6) | 0.88 |
| Primary education     | 240(40.5)   | 145(60.4)      | 95(39.6)          |         |
| Socioeconomic level   |             |                |                   |         |
| ≥2251€/month          | 59(10)      | 37(62.7)       | 22(37.3)          |         |
| 1051–2250€/month      | 342(57.7)   | 199(58.2)      | 143(41.8)         | 0.45    |
| ≤1050€/month          | 170(28.7)   | 105(61.8)      | 65(38.2)          |         |
| NS/NC                 | 22(3.7)     | 10(45.5)       | 12(54.6)          |         |
| Urban vulnerability indicators |         |                |                   |         |
| <4 indicators         | 386(65.1)   | 244(63.2)      | 142(36.8)         | <0.01   |
| ≥4 indicators         | 207(34.9)   | 107(51.7)      | 100(48.3)         |         |
| Number of diseases**  | 6(4–7)      | 6(4–7)         | 5.5(4–7)          | 0.99    |
| Number of diseases*   | 6.1(2.5)    | 6.1(2.5)       | 6.1(2.4)          | 1.00    |
| Number of drugs**     | 7(5–9)      | 7(5–9)         | 7(6–9)            | 0.92    |
| Number of drugs*      | 7.4(2.4)    | 7.5(2.5)       | 7.4(2.2)          | 0.57    |
| HRQOL *               |             |                |                   |         |
| EQ-5D-5L-VAS          | 65.5(20.5)  | 68.3(19.7)     | 61.5(21.1)        | <0.01   |
| Utilities             | 0.77(0.2)   | 0.79(0.2)      | 0.75(0.2)         | 0.02    |
| Structural social support |         |                |                   |         |
| Cohabitation          |             |                |                   |         |
| Lives alone           | 106(17.9)   | 59(55.7)       | 47(44.3)          | 0.72    |
| Lives with 1 person   | 368(62.1)   | 221(60)        | 147(40)           |         |
| Lives with ≥2 people  | 119(20.1)   | 71(59.7)       | 48(40.3)          |         |
| Marital status        |             |                |                   |         |
| Single                | 23(3.9)     | 11(47.8)       | 12(52.2)          | 0.72    |
| Married or partner    | 447(75.4)   | 268(60)        | 179(40)           |         |
| Separated             | 29(4.9)     | 17(58.6)       | 12(41.4)          |         |
| Widow                 | 94(15.8)    | 55(58.5)       | 39(41.5)          |         |
| Functional social support (DUFSS) |         |                |                   |         |
| Total score*          | 43.7(8.8)   | 44.5(8.1)      | 42.7(9.6)         | 0.01    |
| 1st tertile (low)     | 190(32)     | 97(51.1)       | 93(49)            |         |
| 2nd tertile (medium)  | 191(32.2)   | 123(64.4)      | 68(35.6)          | 0.01    |
| 3rd tertile (high)    | 212(35.8)   | 131(61.8)      | 81(38.2)          |         |
| Confidential score*   | 29.5(5.9)   | 30(5.5)        | 28.8(6.4)         | 0.03    |

(Continued)
a lower EQ-5D-5L-VAS score (68.3 vs. 61.5, \( p < 0.01 \)) and utilities (0.79 vs. 0.75, \( p = 0.02 \)). There weren’t any statistically difference between adherent and nonadherent patients regarding number of diseases and drugs in our results.

Regarding structural support, neither number of cohabitants nor marital status were associated to treatment adherence. The mean score for functional support was 43.7 (SD 8.8) out of 55 points; for the confidential domain, 29.5 (SD 5.9) out of 35 points, and for the emotional domain, 14.2 (SD 3.7) out of 20 points. A statistically significant association was found between functional support and adherence, both for the total score and its domains (Table 1).

The detailed study of functional support showed significantly different means between adherent and nonadherent patients for the following items: receiving love and affection (-0.23; 95% CI: -0.40; -0.06), receiving help when sick in bed (-0.25; 95% CI: -0.42; -0.08), receiving useful advice about important events (-0.20; 95% CI: -0.37; -0.02), receiving social invitations (-0.22; 95% CI: -0.44; -0.01), and receiving praise and recognition at work (-0.29; 95% CI: -0.50; -0.08) (Table 2).

In the adjusted models, nonadherence was associated with having a medium vs. high functional support (OR 0.62; 95% CI 0.41–0.94), less than 4 IUVs (OR 0.66; 95% CI 0.44–1.99) and higher EQ-5D-5L-VAS score (OR 0.98; 95% CI 0.98–0.99) (Tables 3 & 4).

**Discussion**

**Main findings of the study**

In patients aged 65–74 years with multimorbidity and polypharmacy, nonadherence to treatment was moderate. Lower functional support was associated with treatment nonadherence in these patients, although this effect was not consistent across all levels of support. The specific

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Table 1. (Continued)

|                          | Total n (%) | Adherent n (%) | Nonadherent n (%) | p-value |
|--------------------------|-------------|----------------|-------------------|---------|
| **Affective score**      |             |                |                   |         |
| Affective score*         | 14.2(3.7)   | 14.5(3.4)      | 13.8(4)           | 0.02    |

*mean (SD)

**Table 2. Distribution of the DUFSS questionnaire items according to adherence.** Order of items following Ayala’s proposal.

| Confidential Domain Mean (SD) | Total       | Adherent    | Nonadherent | Difference of means | p-value |
|-------------------------------|-------------|-------------|-------------|--------------------|---------|
| **Item 7.** I have chances to talk to someone I trust about my personal and family problems | 4.2(1.1)    | 4.1(1.1)    | 4.2(1.1)    | -0.05 (-0.24–0.13) | 0.56    |
| **Item 8.** I have chances to talk to someone about money problems | 4.1(1.1)    | 4.1(1.2)    | 4.1(1.1)    | -0.11(-0.29–0.08) | 0.25    |
| **Item 6.** I have chances to talk to someone about problems at work or at home | 4.2(1.1)    | 4.1(1.2)    | 4.2(1.1)    | -0.13(-0.31–0.05) | 0.17    |
| **Item 5.** I receive love and affection | 4.3(1)      | 4.2(1.2)    | 4.4(0.9)    | -0.23(-0.40–0.06) | <0.01   |
| **Item 4.** I have people who care what happens to me | 4.4(1)      | 4.3(1.1)    | 4.4(0.9)    | -0.12(-0.28–0.05) | 0.16    |
| **Item 11.** I receive help when I am sick in bed | 4.3(1.1)    | 4.2(1.2)    | 4.4(0.9)    | -0.25(-0.42–0.08) | <0.01   |
| **Item 10.** I receive useful advice about important things in my life | 4(1.1)      | 3.9(1.1)    | 4.1(1)      | -0.20(-0.37–0.02) | 0.03    |

| Affective Domain Mean (SD) | Total       | Adherent    | Nonadherent | Difference of means | p-value |
|----------------------------|-------------|-------------|-------------|--------------------|---------|
| **Item 2.** I receive help in matters related to my home | 3.1(1.4)    | 3.1(1.4)    | 3.1(1.3)    | -0.05(-0.27–0.33) | 0.69    |
| **Item 1.** I get visits from friends and family | 3.6(1.3)    | 3.5(1.3)    | 3.7(1.3)    | -0.17(-0.38–0.04) | 0.12    |
| **Item 9.** I receive invitations to participate in activities and go out with other people | 3.8(1.3)    | 3.7(1.3)    | 3.9(1.2)    | -0.22(-0.44–0.01) | 0.04    |
| **Item 3.** I receive praise and recognition when I do my job well | 3.6(1.3)    | 3.5(1.3)    | 3.8(1.2)    | -0.29(-0.50–0.08) | <0.01   |

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Table 3. Factors associated with nonadherence to treatment in patients with multimorbidity and polypharmacy.

|                          | Model 0        |                     | Model 1        |                     | Model 2        |                     | Model 3        |                     |
|--------------------------|----------------|---------------------|----------------|---------------------|----------------|---------------------|----------------|---------------------|
|                          | OR (CI 95%)    | p-value             | OR (CI 95%)    | p-value             | OR (CI 95%)    | p-value             | OR (CI 95%)    | p-value             |
| Functional support       |                |                     |                |                     |                |                     |                |                     |
| 1st tertile (low)        | ref            |                     | ref            |                     | ref            |                     | ref            |                     |
| 2nd tertile (medium)     | 0.58(0.38–0.87)| <0.01              | 0.59(0.39–0.89)| 0.01                | 0.61(0.40–0.92)| 0.02                | 0.62(0.41–0.94)| 0.03                |
| 3rd tertile (high)       | 0.64(0.41–1.02)| .06                | 0.65(0.41–1.04)| 0.07                | 0.71(0.45–1.12)| 0.14                | 0.72(0.45–1.14)| 0.16                |
| Age                      |                |                     | 1.00(0.93–1.06)| 0.75                | 0.99(0.93–1.06)| 0.87                | 1.00(0.93–1.06)| 0.92                |
| Sex                      |                |                     |                |                     |                |                     |                |                     |
| Female                   | ref            |                     | ref            |                     | ref            |                     | ref            |                     |
| Male                     | 1.07(0.75–1.53)| 0.71                | 1.08(0.76–1.54)| 0.68                | 1.19(0.83–1.71)| 0.34                |
| Retirement status        |                |                     |                |                     |                |                     |                |                     |
| Retired                  | ref            |                     | ref            |                     | ref            |                     | ref            |                     |
| Nonretired               | 1.19(0.59–2.38)| 0.62                | 1.23(0.61–2.47)| 0.56                | 1.28(0.64–2.57)| 0.49                |
| Social class             |                |                     |                |                     |                |                     |                |                     |
| Unskilled                | ref            |                     | ref            |                     | ref            |                     | ref            |                     |
| Skilled primary sector   | 0.92(0.61–1.38)| 0.69                | 0.92(0.61–1.38)| 0.68                | 0.96(0.69–1.46)| 0.84                |
| Mid-level supervisors and directors | 0.72(0.44–1.18)| 0.20                | 0.71(0.43–1.18)| 0.18                | 0.77(0.46–1.29)| 0.31                |
| Education level          |                |                     |                |                     |                |                     |                |                     |
| Primary incomplete       | ref            |                     | ref            |                     | ref            |                     | ref            |                     |
| Primary education        | 0.99(0.66–1.47)| 0.95                | 0.98(0.66–1.45)| 0.91                | 1.03(0.69–1.53)| 0.90                |
| Secondary or higher education | 1.20(0.66–2.19)| 0.55                | 1.24(0.68–2.29)| 0.49                | 1.27(0.68–2.38)| 0.44                |
| Socioeconomic level      |                |                     |                |                     |                |                     |                |                     |
| ≤1050€/month             | ref            |                     | ref            |                     | ref            |                     | ref            |                     |
| 1051–2250€/month         | 1.26(0.84–1.87)| 0.26                | 1.24(0.83–1.84)| 0.30                | 1.18(0.79–1.77)| 0.41                |
| >2251€/month             | 1.12(0.58–2.13)| 0.74                | 1.10(0.57–2.11)| 0.77                | 1.08(0.56–2.09)| 0.82                |
| NS/NC                    | 1.96(0.77–4.98)| 0.16                | 2.12(0.83–5.45)| 0.12                | 1.80(0.73–4.44)| 0.20                |
| Urban vulnerability indicators |            |                     |                |                     |                |                     |                |                     |
| ≥4 indicators            | ref            |                     | ref            | 0.03                | ref            | 0.05                |
| <4 indicators            | 0.62(0.41–0.94)| 0.66(0.44–0.99)     |                |                     |                |                     |
| Number of diseases       |                |                     |                |                     |                |                     |                |                     |
| Number of drugs          |                |                     |                |                     |                |                     |                |                     |
| EQ-5D-5L-VAS             |                |                     |                |                     |                |                     |                |                     |
| Utilities                |                |                     |                |                     |                |                     |                |                     |
| Pseudo R²                | 0.0099         | 0.0168              | 0.0253         | 0.0418              |

Table 4. Factors associated with nonadherence to treatment in patients with multimorbidity and polypharmacy. Final model with those variables that were significantly associated in Table 3.

|                          | OR (CI 95%)    | p-value             |
|--------------------------|----------------|---------------------|
| Functional support       |                |                     |
| 1st tertile (low)        | ref            |                     |
| 2nd tertile (medium)     | 0.62(0.42–0.94)| 0.023              |
| 3rd tertile (high)       | 0.73(0.47–1.14)| 0.165              |
| EQ-5D-5L-VAS             | 0.98(0.98–0.99)| <0.01              |
| Urban vulnerability indicators |            |                     |
| ≥4 indicators            | ref            |                     |
| <4 indicators            | 0.69(0.46–1.02)| 0.061              |
| Number of drugs          | 0.94(0.88–1.01)| 0.085              |

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items associated with nonadherence were those related to affection, help in the disease, advice, social invitations and recognition. Nonadherence to treatment was associated with greater urban vulnerability and lower health-related quality of life.

**Strengths and comparison with other studies**

Among the strengths of our study, it is worth mentioning, on the one hand, the selected population, representative of the general population with these characteristics and hardly studied in previous research. The older youth with multi-morbidity and polypharmacy is a very frequent population among the adult population in most Western European countries, with a great potential for action in terms of optimizing adherence to treatment. On the other hand, the study of socioeconomic factors with nonadherence to treatment -with special emphasis on functional support-. Furthermore, the models were adjusted by a large number of clinical, sociodemographic and urban vulnerability variables, which favors a better understanding of the mechanisms underlying the associations found.

The nonadherence to treatment in our study is somewhat lower than that obtained in the meta-analysis conducted by Naderi et al. (43% in patients with an average age of 64 years), and another study by Alves et al. in which a prevalence of 50% was found in a population with multimorbidity and with a mean age of 56.5 years [34,35]. These differences can be explained by the age ranges included in each of the studies, where, as reported by Feehan et al., younger age is associated with lower levels of adherence [36].

In relation to the influence of functional support on treatment adherence, it is difficult to compare our results with those obtained in other studies because of differences in study populations, questionnaires and theoretical frameworks. A study conducted in the field of psychology concluded that there is an inverse association between social support and nonadherence, without obtaining a statistical significance. However, it excluded people over 65 years of age with multiple chronic diseases [7]. In a meta-analysis by Dimatteo et al., they found no statistical significance in the association between structural support and nonadherence to treatment, although they did find a significant association for functional support [19], as was the case in our study. A study by Mondesir et al., conducted in a population of chronic patients with a mean age of 66.2 years, found that having care support while having a disease or disability increased adherence to treatment [25], which coincides with the results obtained for item 11 of the DUFSS scale in our study.

An interpretative qualitative meta-analysis that had, among others, the objective of exploring the experiences lived by patients in the context of multimorbidity indicated that patients who have structural support may feel isolated if they believe that people in their environment do not want to understand their problems [37]. Additionally, another qualitative study on patients with chronic obstructive pulmonary disease concluded that this sense of incomprehension from their environment can lead people to passively cope with their disease [38]. Items that relate to the need to speak or receive support for aspects beyond the disease were not significantly associated with nonadherence in our study, but this may be due to the social needs and lifelong characteristics of the people who make up the sample. In young seniors individuals, their needs for social support could be more related to maintaining their affective, social and recognition relationships, requiring explicit help only for important events and situations of illness.

In the present study, indicators of subjective urban vulnerability were related to nonadherence. Two recent qualitative studies concluded that neighborhoods affect the health of residents by creating a social context that directly influences their beliefs and behaviors, such as adherence to prescribed treatment [39,40]. The fact that in our study nonadherence was associated with urban vulnerability and not with social class or income level could be because
people in this age range have more homogenous salaries coming from their pensions despite living in communities with varying social statuses. The urban vulnerability indicators may capture such heterogeneity in the socioeconomic and social class of the study patients throughout their working life. However, more studies are needed to delve into this relationship.

Regarding the state of perceived health according to the health-related quality of life VAS, the score obtained in our study is similar to that of another study performed in our country with people over 65 years of age who were not institutionalized, for whom a mean score of 66.6 (95% CI 65.3–68) was observed [41]. A worse perceived health-related quality of life has been previously associated with nonadherence to treatment. Alves et al. [35] found that nonadherence to treatment was associated with a poorer health-related quality of life in patients with chronic kidney disease. On the other hand, Mclane C. et al. found that patients with a better health-related quality of life had higher nonadherence rates, given that their health problem did not affect their daily routine [42].

Concerning the number of diseases and the number of drugs, which in other studies have been associated with adherence to treatment [39,43], these were not statistically significant in our case. This could be due to the fact that ours is a very homogeneous sample with respect to the clinical variables collected, since all of the patients presented multimorbidity and polypharmacy.

**Limitations**

Methods for measuring adherence to treatment based on self-reported information may have certain limitations due to recall bias, social desirability and faults in self-observation [44]. However, the Morisky-Green test has been validated and has high specificity, a high positive predictive value and is easy to perform [27]; therefore, it is widely used.

In relation to social support, there are different definitions and measurement instruments depending on the study discipline. Even studies carried out in the field of health that use the DUFSS questionnaire to measure functional support present important differences concerning the items included in the different domains and the reporting of results. This questionnaire has been validated in different population groups [45–49]. Among the Spanish validations, three of the studies were conducted in primary care. Among them, De la Revilla et al. and Bel-lón et al. validated it for socioeconomically disadvantaged women in the general population [28,50]. Cuellar-Flores et al. and Mas-Exposito et al. validated the instrument in caregivers and mental health patients [51,52]. In our study, we chose to use the most recent validation performed by Ayala et al. [30] in people 60 years or older who were not institutionalized given the similarities with our population. As for the interpretation of the results, there is also variability because authors can report their results either qualitative or quantitatively. In this study, we did not limit our exposure to the level of support, taking into account the subjectivity and variability of this interpretation depending on social, economic and cultural contexts [53].

Adherence is influenced by a large number of factors. Haynes estimated up to 250 factors [11], many of which have not been included in our study. This may explain why the relationship between nonadherence and social support does not hold up for higher levels of support.

The study of the social context implies the difficulty of studying strongly related multidimensional concepts. In order to study the social context, the present work collects the educational level, social class, educational level, physical environment through the indicators of subjective urban vulnerability and the monthly income of the family unit.

**Implications of the study findings**

By knowing the role that social support plays in relation to health behaviors and adherence, health professionals can anticipate a more effective approach, taking into account the
socioeconomic context of the patient, their health-related quality of life and preferences. The results of this study reveal that therapeutic nonadherence is not related to the quantification of the structural support of the person but, rather, to the importance that people confer to the support they receive and when they receive it. The perception of these patients concerning the environment in which they live and their health-related quality of life seems to explain this association too. Both urban vulnerability and health-related quality of life are complex and multidimensional concepts conditioned by the subjective perception of the person, reflecting aspects linked to both the physical and social environment, as well as individual-level life and health experiences. It is therefore essential to integrate these patient-reported outcomes in clinical practice to improve the care of older people with multimorbidity, enabling also to individualize their treatments and increase their involvement in self-care.

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