

Prevalence of Polypharmacy in the Statutorily Insured German Population

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A substantial proportion of the insured German population is affected by polypharmacy, which is especially high in persons ≥ 65 years with cardiovascular comorbidities. In light of the significant burden of multi-medication, cases of polypharmacy should be monitored closely in clinical practice.

Background & Objective

Polypharmacy (PP) is defined as the concomitant use of multiple drugs and is especially common in older and multi-morbid patients¹. Still, a precise common definition of PP does not exist. PP has been shown to increase the risk for drug-drug interactions, prescription of potentially inappropriate medication (PIM), cardiovascular adverse events, and poor health outcomes²⁻⁵. Complex treatment regimens reduce adherence and, finally, treatment efficacy². So far, little is known about the actual extent of PP in the German population. Therefore, this study aimed to describe the prevalence and characteristics of patients experiencing PP in Germany.

Methods

The analysis was based on a subset (10%) of an anonymized German claims dataset representative of the statutorily insured German population concerning age and sex. (Excessive) polypharmacy (PP) was defined as the prescription of (≥ 10) ≥ 5 distinct drugs, identified via ATC code, in ≥ 2 quarters of 2019 (Figure 1). Moderate PP was defined as PP without excessive PP. Sensitivity definitions considered patients with the respective number of distinct drugs in ≥ 3 quarters of 2019. Topical preparations, vaccinations, diagnostics, and additives to intravenous solutions were excluded from the count of distinct drugs. The prevalence of PP, patient characteristics, and treatment use were assessed in 2019. Prevalence rates were additionally reported for subgroups of patients aged ≥ 65 years and patients ≥ 65 years old diagnosed with cardiovascular disease (CVD).

Note: The definition of PP was based on Bjerrum et al. 1997, who found the definition of PP as a purchase of ≥ 5 in the first 3 months of the year to be 80% predictive of 1 or more PP episodes in the respective year⁶, allowing for a definition of PP without considering the duration a patient was taking each identified drug.

| ↓ Number of distinct ATC codes ↓ | | | | PP ≥ 5 drugs in ≥ 2 Q | Exces- sive PP ≥ 10 drugs in ≥ 2 Q | Moderate PP PP but no exc. PP | PP sensi- tivity ≥ 5 drugs in ≥ 3 Q | Excessive PP sensitivity ≥ 10 drugs in ≥ 3 Q |
|----------------------------------|----|----|----|---------------------------------------|---|--|---|--|
| 2019 | | | | | | | | |
| Q1 | Q2 | Q3 | Q4 | | | | | |
| 1 | 0 | 1 | 2 | ☒ | ☒ | ☒ | ☒ | ☒ |
| 3 | 7 | 4 | 4 | ☒ | ☒ | ☒ | ☒ | ☒ |
| 5 | 3 | 2 | 6 | ☑ | ☒ | ☑ | ☒ | ☒ |
| 6 | 7 | 5 | 4 | ☑ | ☒ | ☑ | ☑ | ☒ |
| 3 | 4 | 11 | 10 | ☑ | ☑ | ☒ | ☒ | ☒ |
| 12 | 9 | 10 | 8 | ☑ | ☑ | ☒ | ☑ | ☒ |
| 9 | 11 | 13 | 12 | ☑ | ☑ | ☒ | ☑ | ☑ |

ATC, Anatomical Therapeutic Chemical Classification; PP, polypharmacy; Q, quarters

Figure 1. Algorithm to identify polypharmacy with example cases.

Results

SAMPLE SELECTION

The 10% subset of persons insured by the AOK PLUS who met the defined continuous insurance and being-alive selection criteria was comprised of 308,148 individuals (Figure 2). According to the main definition, PP was experienced by 39,190 individuals in 2019, of which 4,648 experienced excessive PP.

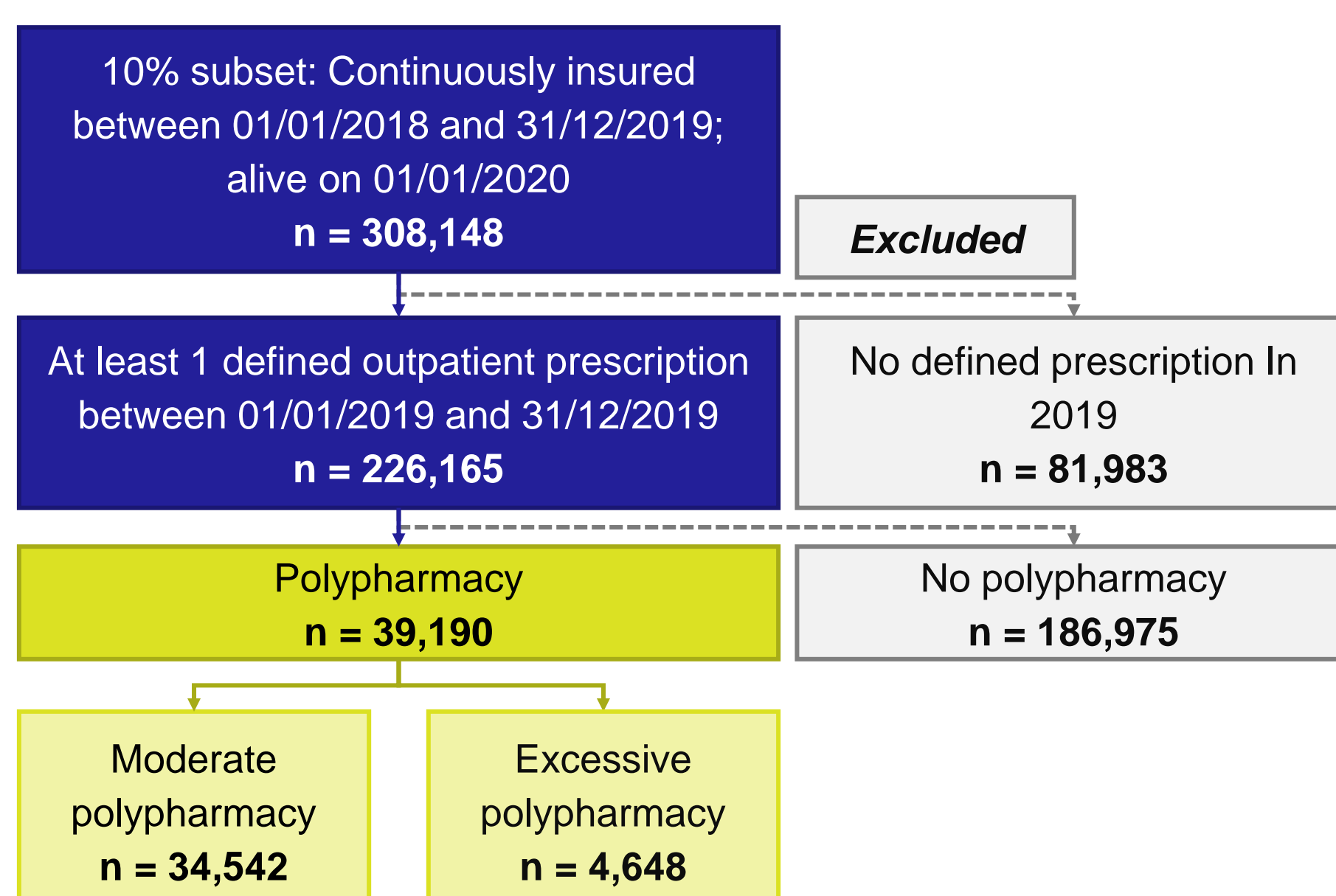


Figure 2. Attrition chart according to the main definition of polypharmacy.

PREVALENCE OF POLYPHARMACY

In the sample of 308,148 individuals analyzed, the prevalence of PP was found to be 127 per 1,000 persons in 2019 (12.7%), while 1.5% experienced excessive PP (Figure 3). Estimations using the sensitivity definition of PP were slightly lower, namely 9.3%/0.9% with PP/excessive PP, respectively. Among individuals aged ≥ 65 years and those aged ≥ 65 years with CVD, rates of (excessive) polypharmacy were considerably higher, with (5.1%) 40.0%/5.9% 45.3%. Among patients with PP in 2019, 78.0%/82.8% also indicated polypharmacy in 2018/2020.

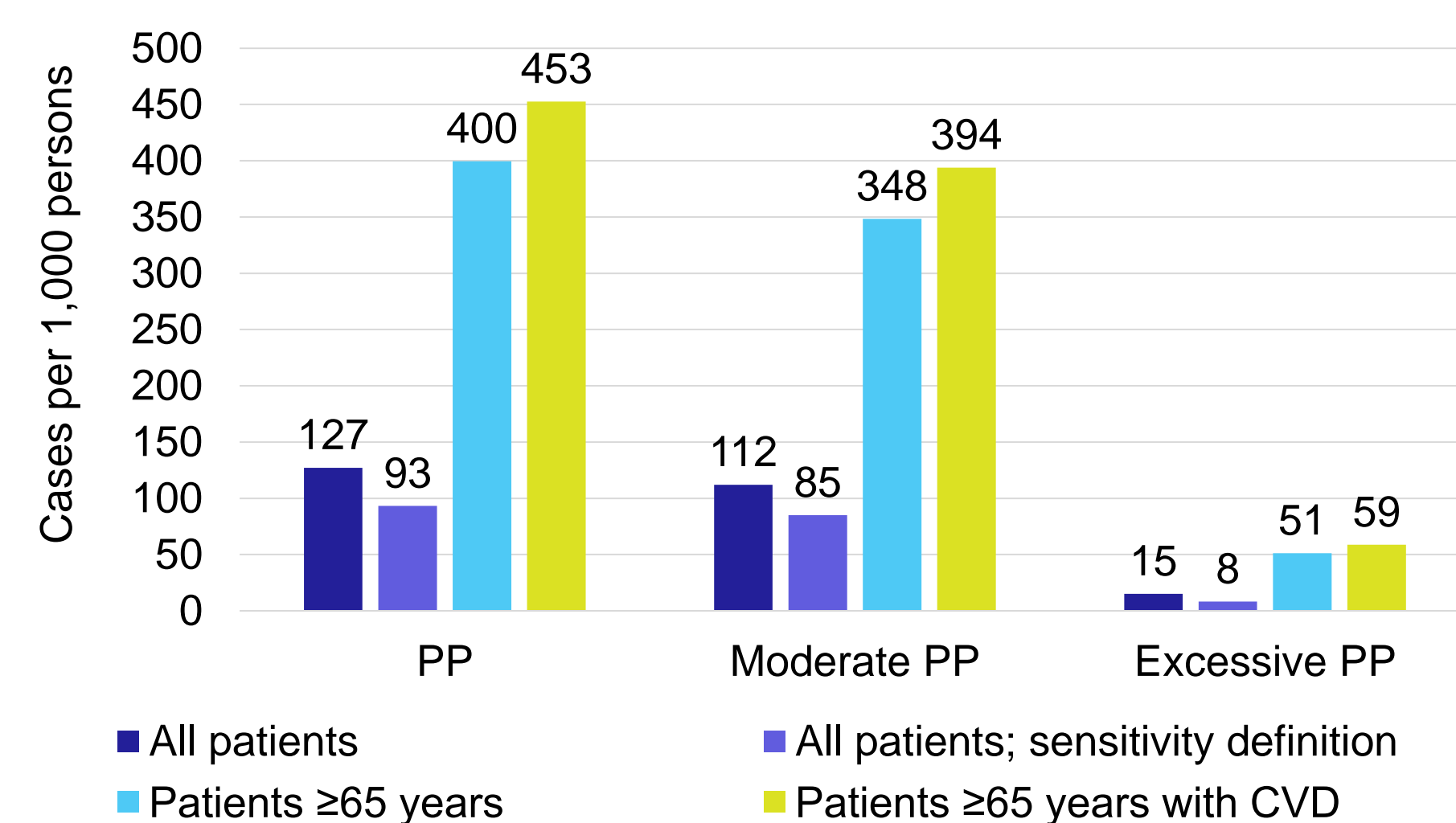


Figure 3. Prevalence of polypharmacy in 2019, expressed as number of cases per 1,000.

References

1. N. Masnoon, S. Shakib, L. Kalisch-Ellett, and G. E. Caughey, "What is polypharmacy? A systematic review of definitions", *BMC Geriatr*, vol. 17, no. 1, p. 230, Oct 10 2017. 2. N. Chen et al., "Polypharmacy, Adverse Outcomes, and Treatment Effectiveness in Patients ≥ 75 With Atrial Fibrillation", *J Am Heart Assoc*, vol. 9, no. 11, p. e015089, Jun 2 2020. 3. Thürmann, P., Mann, N.K., Zawinell, A., Niepraschk-von Dollen, K., Schröder, H. (2022). Potenziell inadäquate Medikation für ältere Menschen – PRISCUS 2.0. In: Schröder, H., Thürmann, P., Telschow, C., Schröder, M., Busse, R. *Arzneimittel-Kompass 2022*. Springer, Berlin, Heidelberg. 4. Y. A. Weng, C. Y. Deng, and C. Pu, "Targeting continuity of care and polypharmacy to reduce drug-drug interaction", *Sci Rep*, vol. 10, no. 1, p. 21279, Dec 4 2020. 5. L. Xue et al., "Persistent polypharmacy and fall injury risk: the Health, Aging and Body Composition Study", *BMC Geriatr*, vol. 21, no. 1, p. 710, Dec 15 2021. 6. L. Bjerrum, J. U. Rosholm, J. Hallas, and J. Kragstrup, "Methods for estimating the occurrence of polypharmacy by means of a prescription database", *Eur J Clin Pharmacol*, vol. 53, no. 1, pp. 7-11, 1997. 7. Chae, J.W., C.S. Song, H. Kim, K.B. Lee, B.S. Seo, D.I. Kim, Prediction of mortality in patients undergoing maintenance hemodialysis by Charlson Comorbidity Index using ICD-10 database. *Nephron Clin Pract*, 2011. 117(4): p. c379-84.

Disclosures

SJ is an employee of Cytel Inc. and has no conflicts of interest to declare. KW, PH and SM participated in this study as members of IPAM e.V. and have nothing to declare. AF works for a statutory insurance fund (AOK PLUS), which provided the data used in this study.

Table 1. Characteristics and treatment use in 2019 among cohorts without PP, with PP, and with excessive PP.

| | Variable | No PP in 2019 (n = 268,958) | PP in 2019 (n = 39,190) | Excessive PP in 2019 (n = 4,648) |
|-------------------------|--|--------------------------------|----------------------------|-------------------------------------|
| Character- istics | Age in years, mean (SD) median | 40.6 (22.2) 40 | 70.4 (15.0) 73 | 72.5 (11.9) 75 |
| | Age ≥ 65 years, n (%) | 40,962 (15.2%) | 27,267 (69.6%) | 3,497 (75.2%) |
| | Female sex, n (%) | 138,457 (51.5%) | 21,480 (54.8%) | 2,531 (54.5%) |
| | CCI, mean (SD) median | 0.6 (1.3) 0 | 4.0 (2.8) 4 | 6.1 (3.0) 6 |
| | CAD ₂ DS ₂ -VASc, mean (SD) median | 1.1 (1.3) 1 | 4.0 (1.8) 4 | 4.9 (1.7) 5 |
| | CVD, n (%) | 81,596 (30.3%) | 37,081 (94.6%) | 4,576 (98.5%) |
| Resource use | Hospitalization days, mean (SD) median | 1.2 (6.7) 0 | 6.5 (16.7) 0 | 12.9 (25.8) 4 |
| | Outpatient visits [†] , mean (SD) median | 9.4 (8.9) 7 | 26.3 (20.5) 23 | 41.2 (38.9) 32 |
| Treatment use | Prescriptions, mean (SD) median | 4.3 (5.3) 2 | 32.0 (14.4) 28 | 57.5 (17.2) 54 |
| | Distinct agents, mean (SD) median | 2.1 (2.2) 2 | 10.1 (3.7) 9 | 16.1 (3.9) 15 |
| | Distinct agent groups, mean (SD) median | 1.9 (1.9) 1 | 8.1 (2.5) 8 | 11.9 (2.5) 12 |
| Top-3 agents* | A02BC02 Pantoprazole, n (%) | N/A | 17,054 (43.5%) | 3,062 (65.9%) |
| | N02BB02 Metamizole sodium, n (%) | N/A | 14,768 (37.7%) | 2,737 (58.9%) |
| | C03CA04 Torasemide, n (%) | N/A | 13,499 (34.5%) | 2,795 (60.1%) |
| Top-3 agent classes* | C09 Agents acting on the renin-angiotensin system, n (%) | N/A | 31,228 (79.7%) | 3,970 (85.4%) |
| | C07 Beta-blocking agents, n (%) | N/A | 26,239 (67.0%) | 3,692 (79.4%) |
| | A02 Drugs for acid-related disorders, n (%) | N/A | 20,470 (52.2%) | 3,614 (77.8%) |

ATC, Anatomical Therapeutic Chemical Classification; CCI, Charlson Comorbidity Index based on Chae et al. 2013, not adjusted for age³. CVD, cardiovascular disease, defined as hypertension, heart failure, ischemic heart disease, arrhythmia, cerebrovascular disease, peripheral vascular disease, pulmonary circulation disorder, deep vein thrombosis, or cardiac arrest in 2019; N/A, not applicable; PP, polypharmacy

* Patients with at least 1 respective prescription in 2019. Agents based on distinct ATC codes. Agent classes defined by the first 3 ATC digits. † Outpatient visits approximated by the number of days with at least 1 invoiced outpatient procedure (EBM).

CHARACTERISTICS

The mean age of the identified individuals with PP was 70.4 years (median: 73), and 54.8% were female (Table 1). Patients with PP in 2019 were much older and more comorbid on average compared to those without PP and furthermore displayed higher resource use. Patients with excessive PP were slightly older and comorbid on average compared with the overall PP cohort. Among those with PP, the most common comorbidities were essential hypertension (89.6%), lipidemias (57.0%), and diabetes mellitus type 2 (52.5%).

TREATMENT USE

On average, individuals experiencing PP used 10.1 distinct drugs (median: 9) and redeemed a mean of 32.0 prescriptions (median: 28) in 2019. Half of the patients with PP received drugs of ≥ 8 different agent classes within one year. Among those with excessive PP, the mean number of prescriptions was 57.5 (median: 54), with an average of 16.1 (median: 15) distinct agents prescribed to these patients in 2019.

The most commonly prescribed medication classes among persons with PP were agents acting on the renin-angiotensin system (79.7% of patients), beta-blockers (67.0%), and drugs for acid-related disorders (52.2%). Agents most commonly used were pantoprazole (43.5%), metamizole sodium (37.7%), and torasemide (34.5%).

Conclusions

- In this study, we present a clear strategy to identify polypharmacy (PP), considering the number of distinct drugs received in consecutive quarters.
- A substantial proportion of the insured German population is affected by PP, which is especially high in persons ≥ 65 years with cardiovascular comorbidities. Considering the association of PP with PIM, drug-drug interactions, and decreased adherence, cases should be monitored closely in clinical practice.
- Apart from medications targeting the cardiovascular system, drugs for acid-related disorders, such as proton pump inhibitors, are among the most commonly used drugs in the German population.
- Further analysis of treatment adherence patterns, resource use, and survival of patients experiencing polypharmacy remains warranted.

LIMITATIONS

As the AOK PLUS insures about 3.5 million persons in the regions of Saxony/Thuringia, a regional bias cannot be ruled out. Characteristics and treatments are analyzed across a heterogeneous population and should be interpreted with care.

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