

Adherence To Respiratory And Nonrespiratory Medication In Patients With COPD: Results Of The German COSYCONET Cohort

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Background: Adherence to COPD medication is often considered to be lower than in other chronic diseases. In view of the frequent comorbidities of COPD, the economic impact of nonadherence and the potential for adverse effects, a direct comparison between the adherence to respiratory and nonrespiratory medication in the same patients seems of particular interest.

Objectives: We aimed to investigate the intake of respiratory and nonrespiratory medication in the same patients with COPD and frequent comorbidities.

Method: Within the COPD cohort COSYCONET, we contacted 1042 patients, mailing them a list with all medication regarding all their diseases, asking for regular, irregular and non-intake.

Results: Valid responses were obtained in 707 patients covering a wide spectrum of drugs. Intake of LABA, LAMA or ICS was regular in 91.9% of patients, even higher for cardiovascular and antidiabetes medication but lower for hyperlipidemia and depression/anxiety medication. Regular intake of respiratory medication did not depend on GOLD groups A-D or grades 1–4, was highest in patients with concomitant cardiovascular disorders and was lowest for concomitant asthma. It was slightly larger for LAMA and LABA administered via combined compared to single inhalers, and lower when similar compounds were prescribed twice. Most differences did not reach statistical significance owing to the overall high adherence.

Conclusion: Our results indicate a high adherence to respiratory medication in participants of a COPD cohort, especially in those with cardiovascular comorbidities. Compared to the lower adherence reported in the literature for COPD patients, our observations still suggest some room for improvement, possibly through disease management programs.

Keywords: COPD, treatment adherence, respiratory medication, nonrespiratory medication

Introduction

COPD is a prevalent disorder¹ associated with significant costs.² Of importance is not only the lung disease but also the high prevalence of, particularly cardiovascular, comorbidities.^{3,4} The comorbidities often result in a high number of prescribed medications, even in relatively mild stages of the lung disease, a fact which is of concern regarding multimедication⁵ but also raises the issue of medication adherence.

Several studies addressed this question via established questionnaires on medication intake and found associations between adherence to COPD medication and patients' characteristics such as quality of life and depression.^{6–8} A comparison of COPD with other chronic diseases is of particular interest^{9,10} to investigate factors

modulating adherence. For example, in insulin-dependent diabetes, adherence is likely to be higher than in disorders in which nonintake does not have immediate consequences; where COPD is located within this range is not known. A wide variety of inhaled single and combined formulations containing long-acting β -agonists (LABA), long-acting anticholinergics (LAMA), or inhaled corticosteroids (ICS) are prescribed across all COPD stages,¹¹ but most studies on adherence addressed the intake in a more general manner, for example via the Morisky Medication Adherence Scale (MMAS-8),^{12,13} and not on the level of each single prescribed drug.

In view of the frequent comorbidities of COPD, the economic impact of nonadherence¹⁴ and the potential for adverse effects,⁵ a direct comparison between the adherence to respiratory and nonrespiratory medication in the same patients seems of particular interest. For this purpose, a large cohort of well-characterized patients such as COSYCONET¹⁵ is well suited, although the adherence estimates in such a cohort may be higher than in clinical routine. The use of a longitudinal cohort not only has the advantage of clearly characterized patients but opens up the possibility to ask for the whole panel of respiratory and nonrespiratory medication in great detail. For this, we used a specially designed personal questionnaire, without using in parallel one of the conventional, validated tools, relying on the fact that medication prescription in COSYCONET is fairly constant over time.¹¹

Within the German COPD cohort COSYCONET (COPD and Systemic Consequences-Comorbidities Network),¹⁵ we designed a substudy addressing the intake of respiratory versus nonrespiratory medication and its dependence on patients' characteristics. For this purpose, we used a questionnaire in which for each patient all individual drugs were listed, with the possibility to add newly prescribed drugs. In the case of irregular or nonintake, the reasons for this were assessed. Patients were ensured by a personal letter that the information supplied would be available only to the coordinating center of COSYCONET in pseudonymized form.

Materials And Methods

Study Population

All patients from 23 study centers, who were participants of COSYCONET¹⁵ in the second half of 2017, were contacted per mail and asked for participation. From the patients' last visit within the follow-up, the latest information on medication was taken, and patients received a

detailed questionnaire in which their individual medication was listed together with questions regarding their adherence to each of the drugs (see [supplement](#)). The first questionnaires were sent out in September 2017 the last ones in March 2018. As the recruitment of COSYCONET was completed at the end of 2013,¹⁵ the last available follow-up visit of patients varied between visit 3 and visit 6. The questionnaire was accompanied by a letter, in which the patients were ensured that all information provided by them was collected in the coordinating center in Marburg and not available to the study nurses or treating doctors. We considered this as important based on the clinical experience that at least some patients might be reluctant to reveal their true adherence behavior to the medical staff. Ethical approval for the study was approved in addition to that for COSYCONET.

Characterization Of Patients

For the present analysis, data on medication, the presence of comorbidities, and the COPD categories according to GOLD grades 1–4¹ and GOLD groups A–D¹ were used. To get an overview, all respiratory medications were recorded ([Figure 1](#)), but in subsequent analyses, only LABA, LAMA and ICS were considered. The respective compounds and those referring to comorbidities are listed in [Table S1](#). The statistical evaluation was restricted to the analysis of contingency tables by chi-squared tests, in addition to descriptive figures and tables, assuming significance for $p < 0.05$. Details of the assessments and evaluations are given in the [supplement](#).

Results

Study Population

Overall, 1103 patients from 23 study centers were contacted. Data from 707 responders (64.1%) of GOLD grades 1–4 were analyzed, comprising 435/272 males/females, 65/327/244/72 patients of grades 1/2/3/4,¹ and 91/396/11/209 patients of the GOLD groups A/B/C/D.¹ Patients' characteristics and the distribution of major comorbidities are given in [Tables 1](#) and [2](#).

Patterns Of Adherence

Top 25 Of Respiratory Medication

As an overview of the specific compounds of respiratory medication including short-acting bronchodilators, [Figure 1](#) shows the top 25 prescribed medications, in terms of percentages of prescription, regular, irregular and nonintake. All

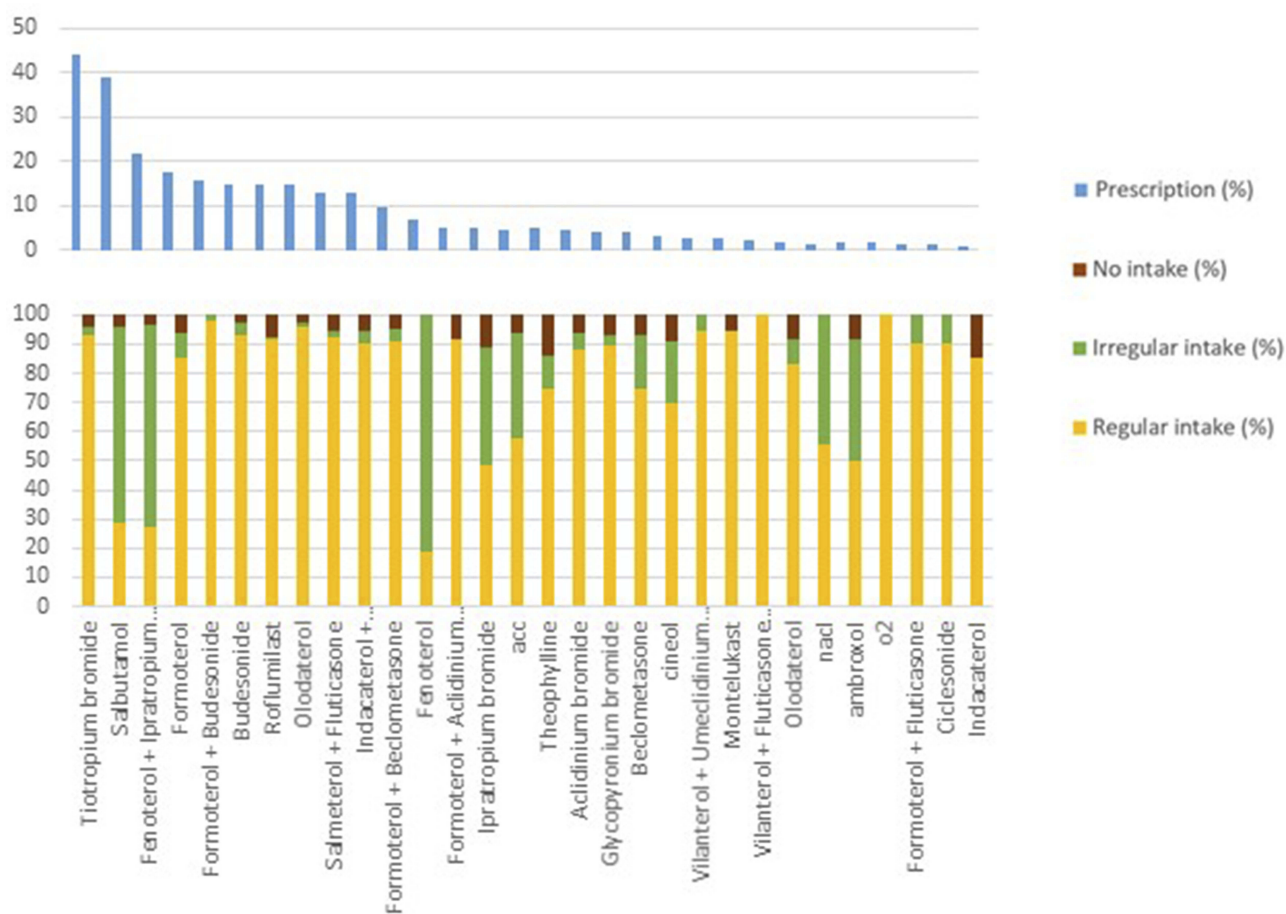


Figure 1 Top 25 respiratory medications prescribed. The figure shows the top 25 respiratory medications prescribed, most of them inhaled except for montelukast as oral medication, in terms of percentages of prescription, regular, irregular and non-intake. All percentages refer to patients in whom the respective medication was still prescribed.

percentages given below refer to patients in whom the respective medication was still prescribed. Tiotropiumbromide, a long-acting muscarinic agonist (LAMA), and salbutamol, a short-acting β -agonist (SABA), were the most prescribed drugs (44.3% and 38.9% of patients). Overall, LAMA was prescribed in 86.0% of patients, LABA in 89.5%, and ICS in 60.8%, irrespective of the formulation. Apparently, short-acting compounds were taken predominantly in a nonregular manner, whereas preparations based on long-acting compounds were taken more regularly. Overall, the reported rates of nonintake were low. Overall, the distribution of respiratory medication appeared to reflect the availability of well-introduced and more recent drugs at the time of the study; thus, the most recent triple formulation was found in only two patients.

Comparison Between Diseases

Figure 2A shows the percentages of prescription of medication for COPD and comorbidities, Figure 2B regular

intake, Figure 2C irregular intake and Figure 2D no intake; for numerical data see Table S2. In the definition of medication groups (Table S1), respiratory medication included LABA, LAMA and ICS only, excluding short-acting bronchodilators, theophylline and other oral drugs. Diabetes medication was divided into either insulin-type drugs or other antidiabetes drugs. Overall, adherences in terms of regular intake were high, especially for cardiovascular medication (94.6%), insulin-type drugs (100%) and antidiabetics excluding insulin-type drugs (93.6%). There was lower adherence (85.1%) for psychological medication which also showed a high percentage of non-intake, as well as hyperlipidemia (88.5%). None of these differences, however, achieved statistical significance.

Dependence On Gender, GOLD Grades And GOLD Groups

The adherence to respiratory medication comprising LABA, LAMA and ICS (see Table S1) showed slight differences

Table 1 Baseline Characteristics Of The Study Cohort (n=707) According To GOLD Groups A-D (Based On CAT) And GOLD Grades 1–4

Parameters	All n=707	GOLD A n=91	GOLD B n=396	GOLD C n=11	GOLD D n=209	GOLD I n=65	GOLD 2 n=327	GOLD3 n=243	GOLD 4 n=72
Gender m/f (%)	435/272 61.5/38.5	56/35 61.5/38.5	251/145 63.4/36.6	5/6 45.5/54.5	123/86 58.9/41.1	37/28 56.9/43.0	206/121 63.0/37.0	154/89 63.4/36.6	38/34 52.8/47.2
Age (years)	69.0 (±8.0)	68.6 (±9.0)	69.4 (±7.7)	67.6 (±9.5)	67.6 (±7.8)	70.2 (±8.5)	69.6 (±8.1)	68.5 (±7.4)	64.8 (±7.7)
BMI (kg/m ²)	26.7 (±5.2)	26.6 (±6.1)	26.8 (±4.9)	24.0 (±3.1)	26.5 (±5.3)	26.6 (±4.8)	27.9 (±5.4)	25.8 (±4.6)	24.0 (±4.6)
Smoking status									
Regular smoker	147	17	85	3	42	20	77	43	7
Occasional smoker	16	2	9	0	5	0	5	9	2
Ex-smoker	499	64	280	7	148	41	221	178	5
Never-smoker	45	8	22	1	14	4	24	13	4
FEV ₁ % predicted	53.7 (±18.7)	60.2 (±17.7)	55.2 (±18.4)	65.6 (±17.8)	47.5 (±17.8)	89.1 (±7.3)	63.0 (±8.4)	40.3 (±5.5)	25.2 (±4.1)
FEV ₁ /FVC	0.51 (±0.11)	0.54 (±0.11)	0.52 (±0.11)	0.56 (±0.07)	0.49 (±0.11)	0.63 (±0.05)	0.57 (±0.08)	0.45 (±0.09)	0.38 (±0.08)
FVC % predicted	79.8 (±19.2)	85.6 (±15.8)	80.7 (±19.1)	90.6 (±18.8)	74.9 (±19.7)	108.4 (±10.9)	86.4 (±13.2)	71.2 (±14.2)	53.1 (±12.5)

Note: The table shows mean values (± SD) for gender absolute numbers (percentages).

Abbreviations: BMI, body mass index; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; FEV₁/FVC, ratio of FEV₁ and FVC.

Table 2 Distribution Of Frequent Comorbidities Of The Study Cohort According To Gender

Comorbidities	All	Male	Female
Cardiovascular disorders (%)	60.0	64.8	52.2
Hyperlipidemia (%)	43.1	45.3	39.7
Diabetes (%)	11.0	13.8	6.6
Mental disorder (%)	25.0	20.7	32.0
Asthma (%)	20.7	15.9	28.3

Note: The table shows the percentages of the different comorbidities according to gender.

between men and women; in women, regular intake was 90.6% on average, in men, it was 92.8% ($p=0.025$). These data are also given in [Table S2](#), together with the corresponding data for nonrespiratory medication. We next addressed the question whether the GOLD grades or groups were associated with the adherence to respiratory medication. As illustrated in [Figure 3](#), there was only a tendency toward more regular intake in patients of higher GOLD grades. The difference between groups 1–4 was borderline nonsignificant ($p=0.050$). Regarding GOLD groups A-D, there was no significant dependence of regular intake on these ($p>0.05$), whereby it has to be kept in mind that the number of patients in GOLD group C was low ($n=11$) (see [Figure S1](#)).

Associations With Comorbidities And Quality Of Life

In the next step, the relationship between the intake of respiratory drugs and the presence of comorbidities was

assessed. In addition to the comorbidities such as cardiovascular disease, hyperlipidemia, diabetes and mental disorders, we included the diagnosis of asthma, which was similarly defined as the other comorbidities on the basis of patients' reports and/or disease-specific medication.¹⁶ [Figure 4](#) shows the intake of respiratory medication across comorbidities, illustrating that there were at most tendencies toward better adherence to respiratory medication in patients with cardiovascular diseases, while adherence was lower in patients with asthma or mental disorders. These differences were not statistically significant ($p>0.05$).

At all study visits of COSYCONET, the PhQ-9 test on depression was performed.¹⁵ When plotting the pattern of intake ([Table S1](#)) against the test results categorized according to standard criteria,¹⁷ there was no significant ($p>0.05$) shift toward reduced regular intake in patients with major depression syndrome in comparison with patients with no depression syndrome at all ([Figure S2](#)). Similarly, when using the VAS of the EQ-5D divided into four equal subranges, there was no significant ($p>0.05$) dependence on medication adherence from the quality of life ([Figure S3](#)). Education was divided into three categories: basic, secondary and higher education. We found no significantly ($p>0.05$) different rates of adherence to respiratory medication ([Table S1](#)) in patients with different education ([Figure S4](#)).

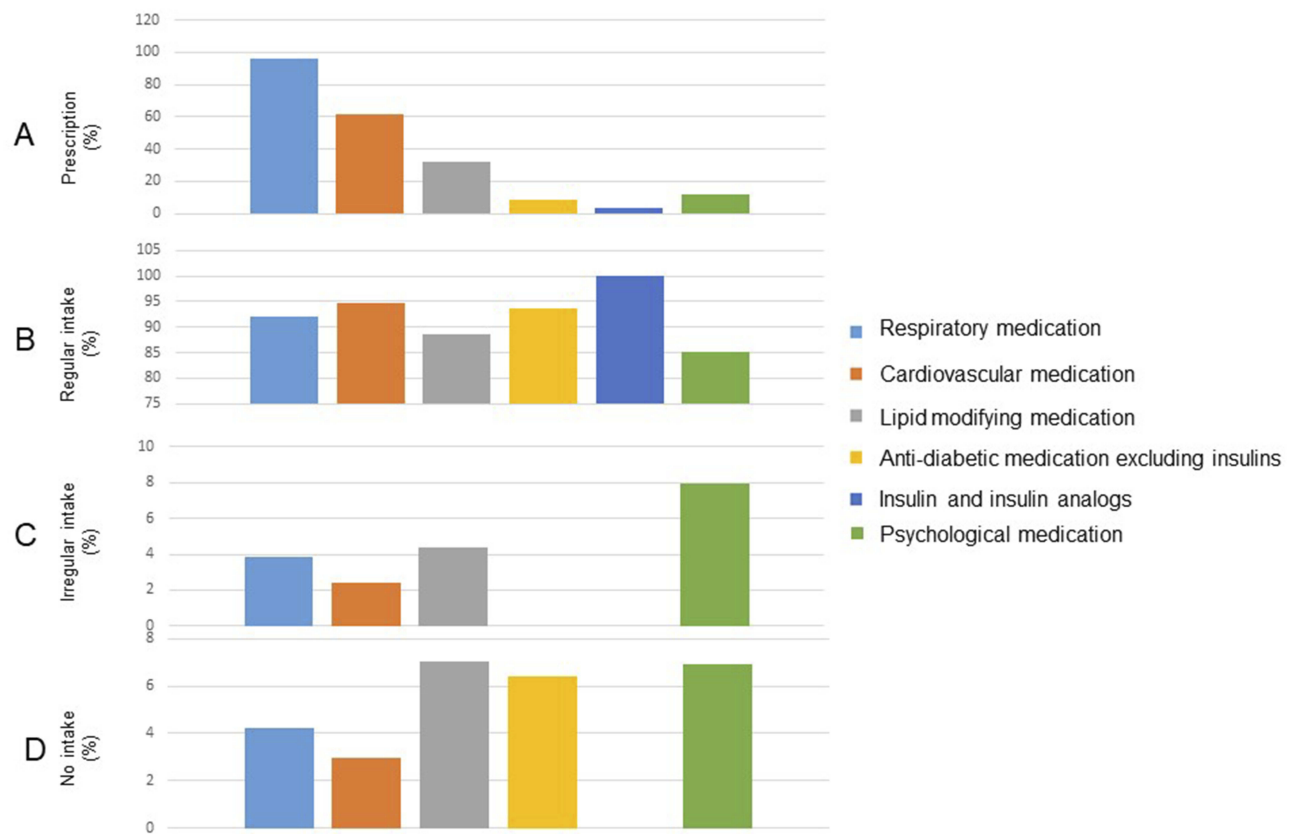


Figure 2 Treatment adherence to different medication groups. The figure shows the percentage of prescription in panel A (uppermost), regular intake in panel B, irregular intake in panel C and nonintake in panel D. Please note the different scales of the vertical axes, as the scaling has been chosen to provide maximal visual resolution. Medication is grouped into respiratory medication (leftmost), cardiovascular medication, hyperlipidemia-specific medication, antidiabetes medication excluding insulins, insulin-like antidiabetes medication and psychological medication, in that order. For all morbidities, the compounds that were defined as the corresponding medication are listed in [Table S1](#). In case of respiratory medication, this comprised only LAMA, LABA and ICS of any kind, excluding all short-acting bronchodilators and oral medication.

Respiratory Medication: Single Versus Combined Formulations

A question often discussed is the adherence to combined versus single preparations. To address this issue within our observational study, we selected all patients having both LABA and LAMA as medication and compared the adherence between the following conditions. a) intake of LABA and LAMA in combination, either dual or triple with ICS; b) intake of both LABA and LAMA, each as single formulation, regardless of a potential combination with ICS; we defined the intake of both as regular and the intake of none of both as non-intake; therefore, irregular intake means irregular or nonintake of one of both. Additionally, we analyzed the intake c) of LAMA and d) of LABA separately regardless of the number of formulations containing these drugs; this refers, for example, to patients having LABA+ICS and one LABA additionally. The results are given in [Figure 5](#). Regular intake was slightly higher for the combined formulation of LABA and LAMA, compared to the combination of their single

formulations, and was lowest if the condition was met that one or both of the compounds could be given twice, e.g. in combination with ICS. All differences were small and not statistically significant ($p > 0.05$).

When all of the previous analyses were performed including the former GOLD 0 patients¹⁸ ($n=102$, total $n=807$), there were only minor changes in the percentage values and virtually the same results were obtained.

Reasons For Nonregular Intake Of Respiratory Medication

Finally, we looked into the reasons for nonregular and nonintake of medication for all respiratory medication listed in [Table S1](#). “Irregular intake” was reported by 3.9% of all responders ($n=807$), whereby 3.0% reported “intake on demand”, while “intake forgotten” and “other reasons” ranged far below 1%. “No intake” was reported by 14.8% of patients, whereby 10.6% reported “no more prescribed”, 0.8% were “afraid of side effects”, 0.7% “do not experience effectiveness”, 0.3% reported “in my

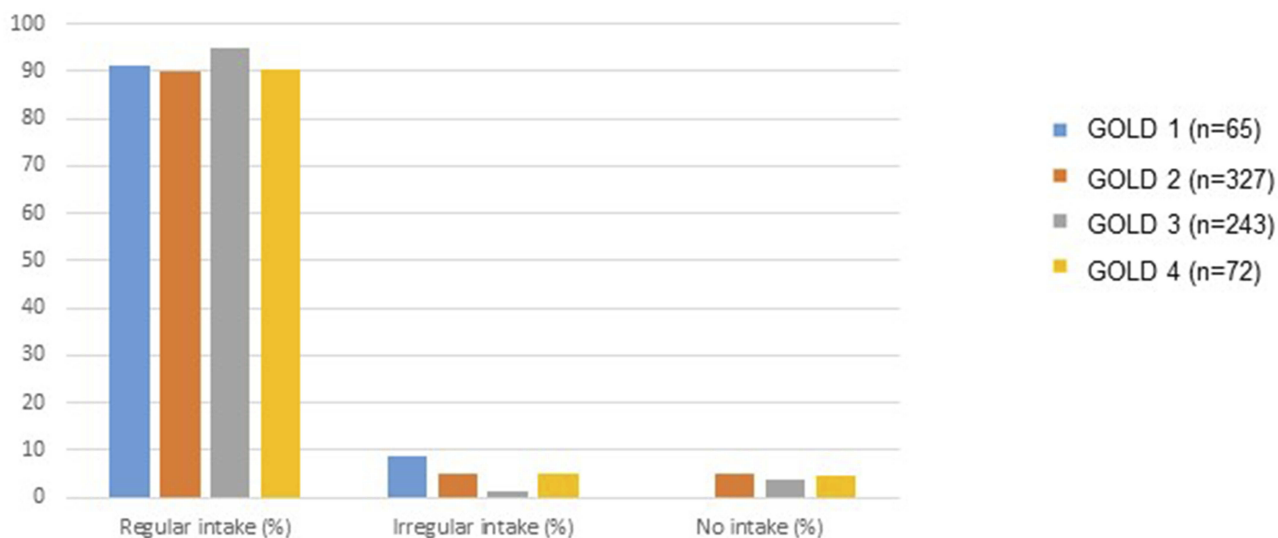


Figure 3 Adherence to respiratory medication according to GOLD grades 0–4. The figure shows the pattern of medication intake according to GOLD grades 0–4. The respiratory medication refers to the compounds described in [Table S1](#) (LAMA, LABA and ICS). GOLD grade 1/2/3/4 n=65/327/243/72. In this graph, regular, irregular and nonintake are arranged along the horizontal axis, and percentages are given on the vertical axis.

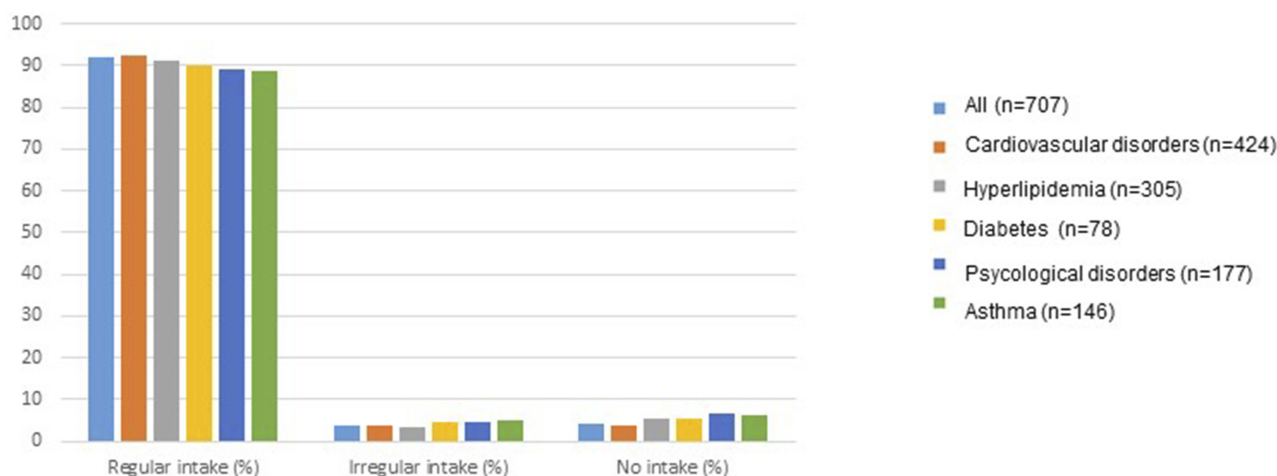


Figure 4 Adherence to respiratory medication in relation to comorbidities. The figure shows the adherence to respiratory medication (see [Table S1](#)) in analogy to [Figure 3](#) in relation to comorbidities as defined by patient reports and disease-specific medication (see “Methods”). The vertical axis shows the percentages of patients in the different adherence patterns stratified according to the presence of comorbidities. COPD n=707, cardiovascular disorders n=424, hyperlipidemia n=305, diabetes n=78, psychological disease n=177. Additionally, percentages are shown for patients with an additional diagnosis of asthma n=146.

opinion not necessary”, and in the remaining patients there was no information.

Discussion

The present study compared the adherence to COPD medication with that to medication for frequent comorbidities in the same patients of the German COPD cohort COSYCONET. Each patient was asked for each individual medication, and the mode of patients’ contact was aiming at a maximum rate of correct answers. The response rate was more than 75%, and reported adherences were very

high. About 92% of patients reported regular intake of long-acting bronchodilators. Regular intake of cardiovascular medication was reported by about 95% of patients, similar to that of antidiabetes drugs of both insulin- and noninsulin type. Regular intake was lowest for medication against hyperlipidemia or depression/anxiety and in the range of 85–89%, i.e. still high. The adherence to LABA and LAMA showed a tendency toward further improvement for combined formulations. Moreover, the adherence to LABA, LAMA and ICS increased with spirometric GOLD grades, whereas it was independent of GOLD

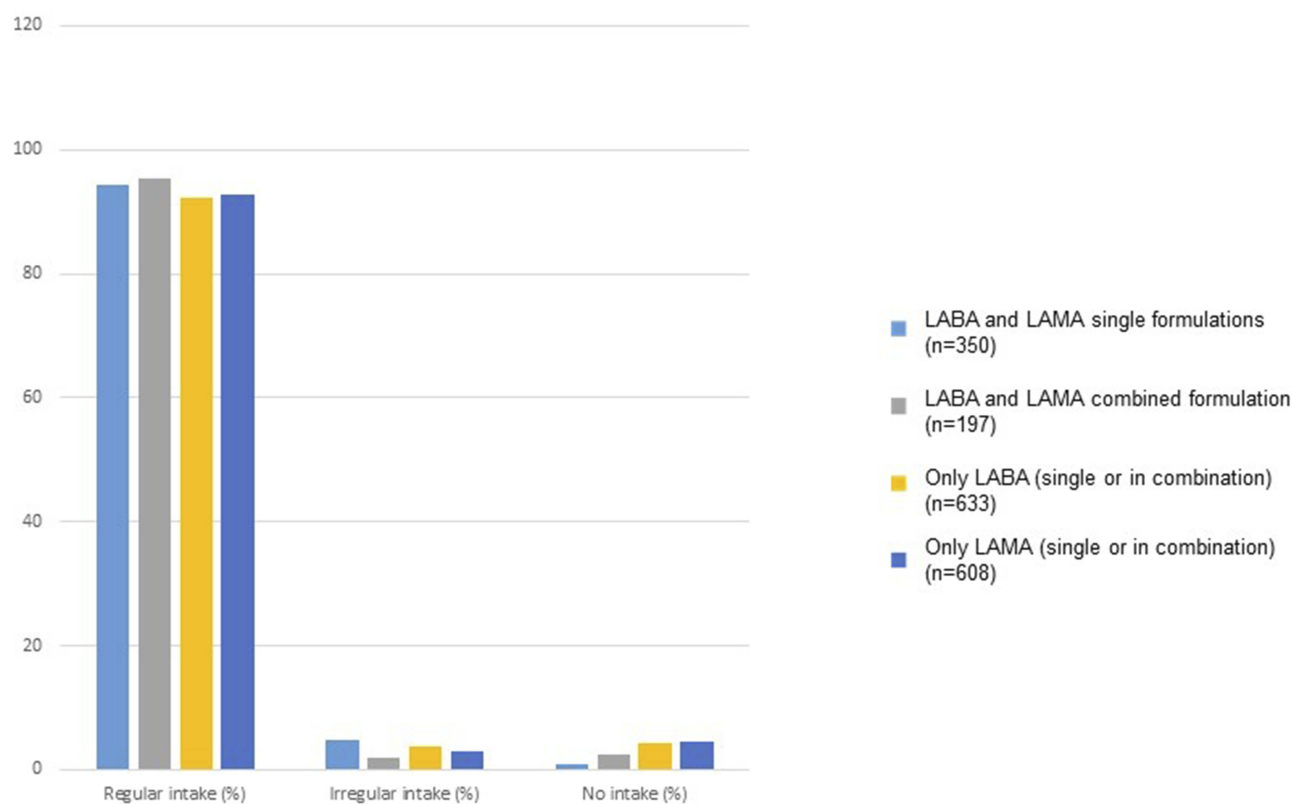


Figure 5 Adherence to respiratory medication: single versus combined formulations. The figure shows the pattern of intake of LABA and LAMA, again with adherence pattern along the horizontal axis. The first bar (blue) refers only to patients with exactly one LABA and one LAMA in separate formulations without any other LABA and LAMA. The second bar (gray) refers to patients with exactly one combined formulation of LABA and LAMA without any other prescription of LABA or LAMA. The third (yellow) and fourth bars (dark blue) refer to patients having prescribed any LABA or any LAMA, respectively, even if present in more than one inhaler containing each of these drugs.

groups A-D. There were tendencies toward associations with the level of education and generic quality of life. The fact that medication adherence was high probably resulted in a ceiling effect, which led to the abolishment of some of the influencing factors reported in the literature.

Our study population showed a wide spectrum of medication, particularly respiratory drugs. The spectrum of compounds and formulations as shown in Figure 1 probably reflected the prescription behavior in Germany within the study period of 6 months; thus, recently introduced drugs including inhaled triple formulations but also long-established drugs were present. For data evaluation, we restricted the panel of drugs to LABA, LAMA and ICS to avoid additional complexity from other, specifically oral drugs such as theophylline and to improve the comparability with the international prescription practice.

Previous studies regarding adherence to respiratory medication in COPD reported rates of regular intake between 29% and 58%.^{6,7,19} Compared to that, adherence to treatment appeared to be higher in patients with

cardiovascular diseases, ranging between 75% and 80%.²⁰ Greater variation of adherence was observed in diabetes, with values between 38% and 93%.^{21,22} In our analysis performed in the same patients, adherence to respiratory medication was markedly higher than previously reported^{6-8,23} but still lower than the adherence to cardiovascular medication, which was also high compared to literature data.

At the first view, the difference between respiratory and cardiovascular medication, although small, is surprising, because the intake of many cardiovascular drugs is associated with less immediate benefits, in contrast to respiratory medication. In case of diabetes, the high degree of adherence is probably related to immediate effects, and the fact that no patients reported no regular intake of insulin probably reflects intake on demand; correspondingly, the rate of nonintake was zero. To which extent the high intake of cardiovascular medication is due to the formulation as oral drug remains to be clarified. Another reason could be a higher intensity of educational programs

in cardiovascular diseases and diabetes. If this should be true, it would suggest further room for improvement in case of respiratory medication, despite the relatively high adherence in the study population. In accordance with this, patients with cardiovascular comorbidities showed a tendency toward a more regular intake of their respiratory medication.

A previous investigation showed an association between the treatment adherence to respiratory and nonrespiratory medication based on data regarding the type and time of prescription from the files.²⁴ Another approach is that followed by us, i.e. to compare the adherence to respiratory medication with that for frequent comorbidities in the same patients directly using a detailed personalized questionnaire, which included the reasons for non-adherence. We also addressed the frequently debated question of whether combined inhaler formulations ensure better adherence than single formulations given in parallel. Although a number of pharmacological studies were in favor of this assumption, sometimes the suspicion is raised that this could be partially due to the design of the interventional trials.^{25,26} In our observational study, we observed a similar difference, which was, however, very small due to the high overall adherence. Moreover, we observed a tendency that in case of compounds of the same kind given twice or more in different formulations, the average adherence slightly decreased, suggesting that patients did not appreciate this prescription.

The high degree of adherence to respiratory medication was probably a major reason why we did not observe associations with the diagnosis of depression⁸ or the PhQ score as a measure of depression. Interestingly, there was a slight dependence on the educational status, but different from that reported in the literature.¹⁹ Adherence tended to be lower in basic compared to secondary education, in accordance with data on the association with the socioeconomic status,^{8,19} but it was again lower in patients with higher education. This might reflect an attitude to manage part of their treatment on their own, depending on their daily clinical state. This interpretation is supported by the observation that the comorbidity of asthma tended to be associated with lower adherence; probably the variability of airway obstruction motivates patients to take part in their medication on demand. In accordance with this, patients of the former COPD grade 0 showed by far the lowest rate of regular intake of their respiratory medication, whereas with increasing obstruction the distribution of adherence was more or less flat. Surprisingly, there was

no association between the adherence to respiratory medication and the COPD groups A-D, i.e. the combination of exacerbation rate and symptoms. It has been argued that a higher cutoff value of the CAT score might be more appropriate,²⁷ but there was also no relationship to the redefined GOLD groups A-D. In a previous study,⁸ a relationship has been found for a higher cutoff value, but in this study adherence was only 49%, offering more room for variation in accordance with symptoms compared to our adherence of more than 90%.

Limitations

The study is limited by the fact that we relied on the patients' answers, which were not verified by direct observation of their drug intake. In the accompanying letter, each patient was granted that the whole effort depended on giving honest answers and that the answers would not be available to the treating physicians or study nurses, possibly compromising the patient's respect. The high response rate suggested a low bias from nonresponse, and the fact that all patients available at the time of data acquisition received the questionnaire reduced a bias arising from choosing a subpopulation. In addition, the rate of incomplete questionnaires was low, underlining the feasibility of our approach. It might be argued that the high percentage of reported adherence reflected a severe bias of our approach, particularly when comparing to other, much lower rates of adherence. We believe that patients participating in the cohort over at least four visits represented a positive selection, which would explain the high rate of adherence to respiratory medication. This probably did not affect the comparison between respiratory and nonrespiratory medication. In the questionnaire, this medication was listed in random order, thereby minimizing the likelihood of systematic carryover of positive or negative answers. In addition, evaluation of the DemTect questionnaire for the detection of cognitive impairment in the patients participating in this substudy indicated a very low rate of 1.2% of patients in which such an impairment could be suspected. The direct approach used by us allowed the rating of adherence whereby we took reference to the EMERGE-reporting checklist as far as possible.²⁸

It is possible that also for comorbidities a selection of closely monitored patients occurred, which again could explain the high rate of adherence to the respective medication. We do not know to which extent relative adherences for COPD and comorbidities were affected by this. Another limitation of our study is given by its cross-sectional

character, which did not allow us to assess whether adherence changed over time. Adherence might increase with increasing severity of the disease over time, although our cross-sectional findings regarding the association with GOLD grades and groups would not favor this.

Conclusion

The results of this analysis were obtained as a cross-sectional substudy of the COPD cohort COSYCONET, using specifically designed questionnaires that addressed each individual medication in each individual patient. Adherence to COPD medication was higher than previously reported, but that to cardiovascular medication was even slightly greater. It should be noted that patients participating in the cohort may represent a positive selection, which would explain the high rate of adherence. Accordingly, also the regular intake of inhaled respiratory medication tended to be highest in patients with cardiovascular comorbidities, while it was lowest in patients with concomitant asthma. It did not show marked relationships to GOLD grades 1–4 or groups A–D. The difference in adherence between respiratory and cardiovascular medication suggests considering improvements, for example by disease management programs for respiratory diseases, similar to the achievements in cardiovascular diseases.

Abbreviations

LABA, long-acting β -agonists; LAMA, long-acting anticholinergics; MMAS-8, Morisky Medication Adherence Scale; ICS, inhaled corticosteroids; SABA, short-acting β -agonist.

Statement Of Ethics

All assessments were approved by the central (Marburg [Ethikkommission FB Medizin Marburg]) and local (Bad Reichenhall [Ethikkommission bayerische Landesärztekammer]); Berlin (Ethikkommission Ärztekammer Berlin); Bochum (Ethikkommission Medizinische Fakultät der RUB); Borstel (Ethikkommission Universität Lübeck); Coswig (Ethikkommission TU Dresden); Donaustauf (Ethikkommission Universitätsklinikum Regensburg); Essen (Ethikkommission Medizinische Fakultät Duisburg-Essen); Gießen (Ethikkommission Fachbereich Medizin); Greifswald (Ethikkommission Universitätsmedizin Greifswald); Großhansdorf (Ethikkommission Ärztekammer Schleswig-Holstein); Hamburg (Ethikkommission Ärztekammer Hamburg); MHH Hannover/Coppenbrügge (MHH Ethikkommission);

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For further information see:

Karch A, Vogelmeier C, Welte T, Bals R, Kauczor HU, Biederer J, Heinrich J, Schulz H, Glaser S, Holle R et al: The German COPD cohort COSYCONET: Aims, methods and descriptive analysis of the study population at baseline. *Respir Med.* 2016;114:27-37.

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

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