Comparison of Outcomes of Chronic Obstructive Pulmonary Disease Patients Hospitalized in Hospital-at-Home versus In-hospital Settings: A Systematic Review and Meta-analysis

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ABSTRACT Chronic obstructive pulmonary disease (COPD) is a disease state characterized by persistent respiratory symptoms and airflow obstruction determined by spirometry, including emphysema, chronic bronchitis, and small airway disease. Traditional treatment settings for COPD exacerbations typically involve in-hospital care. However, hospital-at-home (HaH) programs have emerged as an innovative model to provide hospital-level care at a patient's home. I synthesized available randomized controlled trials (RCTs) and compared the outcomes of COPD management in HaH and in-hospital settings. I searched for English language medical literature studies of COPD patients in HaH programs compared to in-hospital. Searches were performed in PubMed, EMBASE, Scopus, and CENTRAL. Outcomes were compared, meta-analyses were performed, and pooled odds ratios (ORs) and 95% confidence intervals (95%CIs) were calculated. Heterogeneity was evaluated and I^2 statistic was used to measure the proportion of inconsistency in individual studies. Potential publication bias was also calculated. Seven controlled studies representing 19 sub-studies (data sets) were selected according to the inclusion criteria. The OR of the HaH and in-hospital comparison was 0.542, 95%CI 0.379–0.774, P= 0.001. The different clinical outcomes of HaH were better or similar to those at regular hospitals, but with higher patient preference (OR 0.316, 95%CI 0.198–0.506). Heterogeneity and inconsistency were small, with no significant publication bias. HaH may be recommended for COPD patients' hospitalization when needed according to the specific indications and patients matching HaH criteria.

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KEY WORDS: chronic obstructive pulmonary disease (COPD), hospital-at-home (HaH), in-hospital hospitalization, meta-analysis, virtual medicine

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide, presenting significant healthcare challenges and resource utilization [1]. COPD is preventable and treatable, characterized by airway obstruction, persistent respiratory symptoms, and recurrent exacerbations, which lead to hospitalization. Exacerbations of COPD are frequent when maintenance therapy is neglected due to low compliance, as found in 71% of U.S. Medicare patients [2]. Unstable COPD characterized by frequent exacerbations and a decline in pulmonary function results in emergency department visits and hospitalizations [3]. Recovery time for symptoms and peak expiratory flow may be long and devastating [4]. The cost of exacerbation that requires hospitalization can range from US$7000 to US$39,200, with costs substantially elevated for patients who require mechanical ventilation [5].

Traditional treatment settings for COPD exacerbations typically involve in-hospital care. However, hospital-at-home (HaH) programs have emerged as an innovative model to provide hospital-level care at a patient's home. Such programs may benefit patient outcomes, increase satisfaction, and possibly lower healthcare costs. Despite growing interest, the comparative effectiveness of these models concerning traditional in-hospital care remains variable.

In this meta-analysis, I synthesized information from available controlled trials, compared the outcomes of COPD management between HaH and in-hospital settings, and provided a comprehensive view of efficacy across multiple outcome parameters.

METHODS

IDENTIFICATION OF STUDIES AND DATA EXTRACTION

PubMed, EMBASE, Scopus, and CENTRAL databases were searched until 30 April 2024 to identify controlled studies comparing hospitalization outcomes of patients with COPD exacerbation between HaH and in-hospital. All studies were written in English. The following search text and/or medical topic heading (MeSH) terms were used: *COPD AND Hospital-at-Home OR HaH [All Fields] AND "In-Hospital" [MeSH Terms].* To retrieve original studies, I conducted a manual search of all review articles and editorials. Hand searches included evaluation of bibliographies of articles. This meta-analysis used the PRISMA extension statement for interventions [6].

SELECTION CRITERIA: PRIMARY ENDPOINTS

Inclusion and exclusion criteria were decided before starting the study investigation. Appropriate articles included data that could be extracted, were written in English, and compared COPD hospitalization outcomes between HAH and In-hospital. Studies that did not meet these criteria were excluded. Included studies described patients with COPD exacerbations who needed hospitalization. COPD is a disease state characterized by persistent respiratory symptoms and airflow obstruction determined by spirometry, including emphysema, chronic bronchitis, and small airway disease. COPD was diagnosed according to accepted clinical signs and symptoms along with radiological criteria.

HETEROGENEITY, SENSITIVITY, AND PUBLICATION BIAS

The heterogeneity of the studies was calculated using the Cochran Q test and I^2 inconsistency index. It was considered to be present if the *Q*-test *P*-value was less than 0.10. The higher the I^2, the greater the heterogeneity [7]. The sensitivity testing was conducted by removing individual studies from the overall result. The publication bias was analyzed using a funnel plot complemented by Begg-Mazumdar and Egger statistics [8]. An adapted Slim et al. method (MINORS) for the evaluation of the quality of the study for meta-analysis was used [9].

STATISTICAL ANALYSIS

Analysis was performed with comprehensive meta-analysis software (Version 4, Biostat Inc., Englewood, NJ, USA). Pooled odds ratios (ORs) and 95% confidence intervals (95%CIs) were calculated to compare ORs of HaH and patient outcomes of in-hospital COPD using the random effects model. First, a meta-analysis calculation for all the studies was performed, and then a separate calculation was performed for four groups:

- Readmission
- Post-hospitalization admission to the emergency department (ED), General Practitioner (GP), secondary care physician (SCP), treatment failure (TF)
- Mortality
- Patient's subjective approach: satisfaction, preference, functional indexes, knowledge, self-management, not living at home, living in long-term residential care

To ensure unity in the direction of the meta-analysis calculation, only negative direction such as mortality (and not survival) and patients with low satisfaction were used. Non-inferiority was established when the 95%CIs were in the same range of true effect size.

RESULTS

A SYSTEMATIC REVIEW OF THE SELECTED STUDIES

Shepperd and colleagues (UK, 1998) [10]: Randomized patients with exacerbation of COPD, 15 HaH and 17 in-hospital patients. Readmission and mortality rates after 3 months were 8 and 6, 3 and 3, respectively.

- Davies et al. (UK, 2000) [11]: Randomized patients with exacerbations of COPD to HaH versus in-hospital care. Of 100 patients in HaH (45 men, average age 70 years) and 50 patients in in-hospital care (30 men, average age 70 years); 37 and 17 were readmitted, 9 and 4 died, after a follow-up of 3 months, respectively.
- Hernandez and co-authors (Spain, 2003) [12]: COPD patients, 121 HaH (117 men, mean age 71 years), 101 regular hospital care (98 men, mean age 71 years). Mortality 5 vs. 7, emergency room visits 16 vs. 31, better knowledge of the disease 70 vs. 27, and better self-management of their condition 98 vs. 48, respectively.
- Ricauda et al. (USA, 2008) [13]: Evaluated hospital readmission rates and mortality at 6-month follow-up in patients admitted to the hospital for acute exacerbation of COPD; 52 patients in HaH and 52 in a general medical ward. Readmission and mortality rates were 17 and 34, 9 and 12, respectively. In addition, very good/excellent satisfaction at discharge was 49 and 46, respectively.
- Leff and colleagues (USA, 2009) [14]: Randomized 214 patients aged 65 years and older, with exacerbation of COPD, congestive heart failure, pneumonia,

or cellulitis, who met previously validated HaH eligibility criteria, to HaH or in-hospital. Functional status was measured as five activities of daily living (eating, bathing, dressing, toileting, and transferring), and seven activities of instrumental activities of daily living (managing money, managing medications, preparing meals, shopping, engaging in light or heavy housework, using the telephone). In COPD patients better results were found for 44 and 25, and 46 and 17, of 72 (50 men, mean age 77 years) and 47 (35 men, mean age 76.9 years) patients, respectively.

- Utens et al. (Netherlands, 2013) [15]: Patients with COPD exacerbation were randomized to HaH and in-hospital care. Patient preference was higher in HaH than in-hospital, 60 of 70 and 29 of 69, respectively.
- Echevarria and co-authors (UK, 2018) [16]: Compared the outcomes of 60 COPD HaH patients with 58 COPD patients with the same disease severity allocated to in-hospital care. Death rates, readmission, one or more general practitioner attendances post-discharge, and one or more secondary care appointments at 90 days were 1 and 1, 22 and 23, 26 and 30, 48 and 41, respectively. The stated preference for HaH was 54 and 51, respectively.

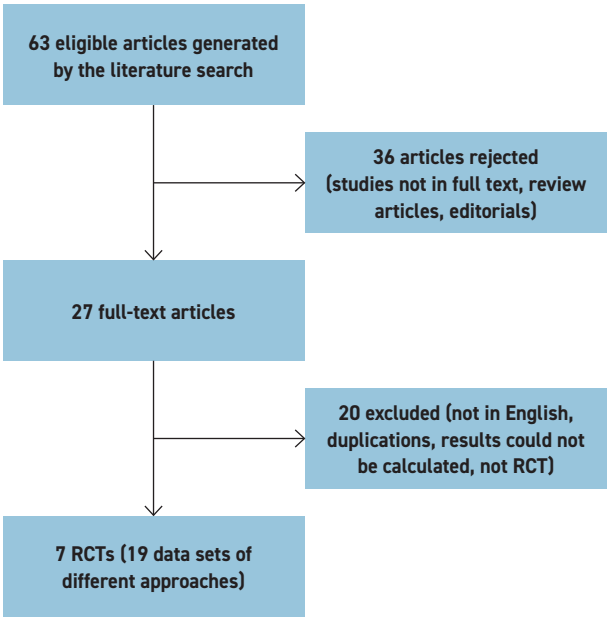
META-ANALYSIS RESULTS

The literature search revealed studies that compared COPD outcomes of HaH and in-hospital hospitalizations [Figure 1]. In total, 63 eligible studies were generated by the literature search; 36 were excluded due to incomplete articles, review articles, or editorials. Twenty additional studies were excluded due to being written in a language other than English, duplications, or not RCT. In addition, data from others were evaluated using average score and standard deviation for comparison of outcomes; thus, a meta-analysis could not be performed. Seven RCTs (19 datasets of different approaches) fulfilled the inclusion criteria, compared the outcomes, and were published before 30 April 2024. In total, there were 2531 patients, 1384 were randomized to HaH and 1147 to in-hospital hospitalizations in studies used for comparison of the different outcomes [Figure 2].

HOSPITAL-AT-HOME PROGRAMS HAVE EMERGED AS AN INNOVATIVE MODEL AIMING TO PROVIDE HOSPITAL-LEVEL CARE AT A PATIENT'S HOME.

The mean effect size of all the clinical outcomes was 0.542, 95% confidence interval (95%CI) 0.379–0.774, $P = 0.001$. Thus, outcomes were 46% better in HaH than in in-hospital hospitalizations. The Z-value tests the null hypothesis that the mean effect size was 1.000.

Figure 1. Flow chart of studies included in the meta-analysis
RCT = randomized controlled trial



The Z-value was -3.367 with $P = 0.001$. Using a criterion alpha of 0.050, this null hypothesis was rejected [Figure 2].

Separately measured meta-analyses of outcomes: readmission, admission to another facility, mortality, and patient preference revealed better or non-inferiority results favored HaH: OR 0.792, 95%CI 0.356–1.762, P = NS; OR 0.719, 95%CI 0.301–1.717, P = NS; OR 0.966, 95%CI 0.059–15.818, P = NS, and OR 0.316, 95%CI 0.198–0.506, $P < 0.0001$, respectively.

The relevant funnel plot [Figure 3] is symmetric and denies a significant publication bias. The Q-value is 53.823 with 18 degrees of freedom and $P < 0.001$. Using a criterion alpha of 0.100, we can reject the null hypothesis that the true effect size is the same in all these studies. The I^2 statistic is 67%, which is approximately 67% of the variance in observed effects that reflects variance in true effects rather than sampling error. Tau-squared, the variance of true effect sizes, is 0.382 in log units. Tau-squared, the standard deviation of true effect sizes, is 0.618 in log units. Assuming that the true effects are normally distributed (in log units), it could be estimated that the prediction interval is 0.139 to 2.109. The true effect size in 95% of all comparable populations falls in this interval.

Figure 2. Forest plot illustrating odds ratios and 95% confidence intervals for all outcomes of chronic obstructive pulmonary disease patients, comparing hospital-at-home and in-hospital results

Study name	Subgroup within study	Comparison	Time point	Statistics for each study					Odds ratio and 95% CI
				Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	
Shepperd S 1	COPD, readmission after 3m	UK	1998	2.095	0.506	8.674	1.020	0.308	
Shepperd S 2	COPD, mortality rate after 3m	UK	1998	1.167	0.197	6.893	0.170	0.865	
Davies L 1	COPD, readmission	UK	2000	1.140	0.559	2.324	0.361	0.718	
Davies L 2	COPD, 3m mortality	UK	2000	1.137	0.332	3.891	0.205	0.837	
Hernandez C 1	COPD, mortality	Spain	2003	0.579	0.178	1.883	-0.909	0.364	
Hernandez C 2	COPD, emergency room visits	Spain	2003	0.344	0.175	0.676	-3.098	0.002	
Hernandez C 3	COPD, "not better" knowledge of the disease	Spain	2003	0.266	0.150	0.470	-4.559	0.000	
Hernandez C 4	COPD, "not better" self management of the condition	Spain	2003	0.213	0.117	0.387	-5.068	0.000	
Ricauda NA 1	COPD, readmission at 6 months	USA	2008	0.257	0.114	0.580	-3.271	0.001	
Ricauda NA 2	COPD, mortality at 6 months	USA	2008	0.698	0.266	1.832	-0.731	0.465	
Ricauda NA 3	COPD, "not good/excellent satisfaction" at discahrge	USA	2008	0.394	0.096	1.615	-1.295	0.195	
Leff B 1	COPD, CHF, pneumonia or cellulitis, "lower functional status"	USA	2009	0.723	0.344	1.521	-0.855	0.393	
Leff B 2	COPD, CHF, pneumonia or cellulitis, "lower instrumental activity"	USA	2009	0.320	0.149	0.688	-2.917	0.004	
Utens CMA	COPD, patient preference "lower"	The Netherland	2013	0.121	0.053	0.275	-5.035	0.000	
Echevarria C 1	COPD, at 90 days, mortality	UK	2018	0.966	0.059	15.818	-0.024	0.981	
Echevarria C 2	COPD, at 90 days, readmission	UK	2018	0.881	0.419	1.853	-0.334	0.738	
Echevarria C 3	COPD, at 90 days, one or more general practitioner attendances	UK	2018	0.714	0.346	1.474	-0.911	0.362	
Echevarria C 4	COPD, at 90 days, one or more secondary care appointments	UK	2018	1.659	0.710	3.874	1.169	0.242	
Echevarria C 5	COPD, at 90 days, "not stated preference"	UK	2018	0.810	0.255	2.571	-0.358	0.720	
Pooled				0.542	0.379	0.774	-3.367	0.001	
Prediction Interval				0.542	0.139	2.109			

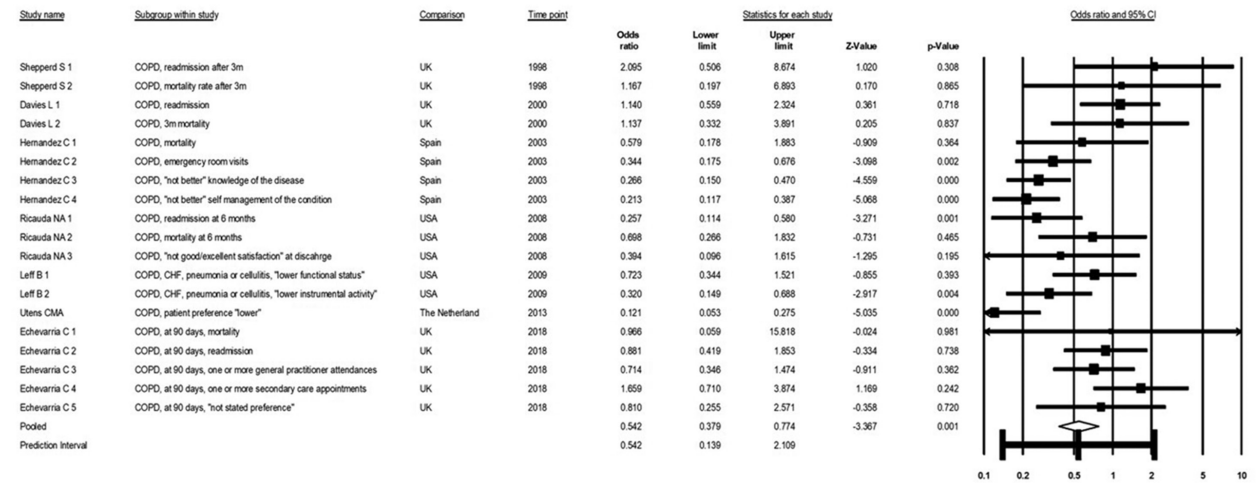
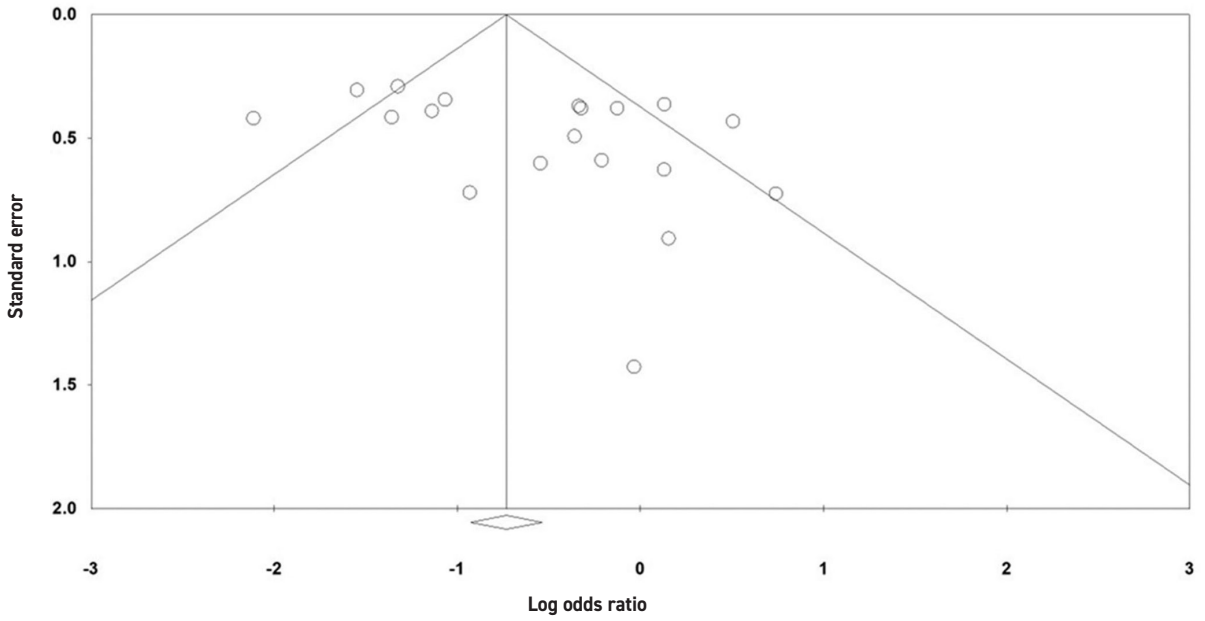


Figure 3. Funnel plot for publication bias



Sensitivity was measured by excluding individual studies and recalculating the overall meta-analysis outcome. This process was repeated for each of the studies. Deviations from the primary result were not significant with ORs varying between 0.121 (95%CI 0.053–0.275) and 2.095 (95%CI 0.506–8.674), the ranges of true effect were 0.212 to 0.388, and 0.139 to 2.109, respectively. In addition, the quality of the studies was measured using the MINORS method [Table 1]. Scores of 1.7 to 2.0 were found with a median of 2.0. Comparing studies with low MINORS scores of 1.7 to 1.8, and high of 2.0, we found OR 0.553 (95%CI 0.319–0.956), a range of true effect 0.121 to 2.095, and OR 0.536 (95%CI 0.327–0.878), a range of true effect 0.213 to 1.659, respectively.

DISCUSSION

Exacerbations of COPD are a major cause of healthcare resource use because they increase physician office visits, emergency department visits, and hospitalizations

Table 1. Evaluation of MINORS quality scores

Methodological items for non-randomized studies [reference number]	Shepperd [10]	Davies [11]	Hernandez [12]	Ricauda [13]	Leff [14]	Utens [15]	Echevarria [16]
Clearly stated aim: the question addressed is precise and relevant in the light of available literature	2	2	2	2	2	2	2
Inclusion of consecutive patients: all patients potentially fit for inclusion (satisfying the criteria for inclusion) were included in the study during the study period (no exclusion or details about the reasons for exclusion)	2	2	2	2	1	1	2
Prospective collection of data: data were collected according to a protocol established before the beginning of the study	2	2	2	2	2	2	2
Endpoints appropriate to the aim of the study: unambiguous explanation of the criteria used to evaluate the main outcome, which should be consistent with the question addressed by the study; the endpoints should be assessed on an intention-to-treat basis	2	2	2	1	2	1	2
Unbiased assessment of the study endpoint: blind evaluation of objective endpoints and double-blind evaluation of subjective endpoints; otherwise, the reasons for not blinding should be stated	2	2	2	1	2	1	2
Follow-up period appropriate to the aim of the study: the follow-up should be sufficiently long enough to allow the assessment of the main endpoint and possible adverse events	2	2	2	2	2	2	2
Loss to follow-up less than 5%: all patients should be included in the follow-up, or the proportion lost to follow-up should not exceed the proportion experiencing the major endpoint	1	2	2	2	2	2	2
Prospective calculation of the study size: information of the size of detectable difference of interest with a calculation of 95% confidence interval, according to the expected incidence of the outcome event, and information about the level for statistical significance and estimates of power when comparing the outcomes	2	2	2	2	2	2	2
Adequate control group: having a gold standard diagnostic test or therapeutic intervention recognized as the optimal intervention according to the available published data	1	2	2	2	1	2	2
Contemporary groups: control and studied group should be managed during the same time period (no historical comparison)	2	2	2	1	1	1	2
Baseline equivalence of groups: groups should be similar regarding the criteria other than the endpoints studied; absence of confounding factors that could bias the interpretation of the results	1	2	2	1	2	2	2
Adequate statistical analyses: whether the statistics were consistent with the type of study with calculation of confidence intervals or relative risk	1	2	2	2	2	2	2
Total	20	24	24	20	21	20	24
Average	1.7	2	2	1.7	1.8	1.7	2

The items are scored: 0 = not reported, 1 = reported but inadequate, or 2 = reported and adequate
The global ideal score was 16 for non-comparative studies and 24 for comparative studies

[3]. Between 37% and 71% of patients with COPD exacerbate annually [3,17]; 9–31% require an emergency department visit and 14–35% require hospitalization. Survival rates 5 years after a hospitalization for a COPD exacerbation are 45% [18].

The results from this meta-analysis indicated that HaH is a viable, non-inferior, and potentially superior alternative to traditional in-hospital care for managing patients with COPD. A significant finding from our analysis of 2531 patients across 7 RCTs was the overall effect size of 0.542, favoring HaH over in-hospital care with statistical significance ($P = 0.001$). This result suggests a meaningful improvement in outcomes that are not only statistically significant but also clinically relevant. Recently, a retrospective study compared clinical outcomes of acutely ill patients (both COVID-19 and non-COVID) admitted to either in-hospital or HaH [19] and found reduced hospitalization length and mortality rate in HaH.

HOSPITAL-AT-HOME MAY BE APPROPRIATE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENT HOSPITALIZATION WHEN NEEDED ACCORDING TO THE SPECIFIC INDICATIONS AND PATIENTS MATCHING HAH CRITERIA.

Separate analyses on individual outcomes such as readmission rates, admission to another facility, mortality, and patient preference consistently showed better or equivalent results for HaH. Notably, patient preference strongly favored HaH, as indicated by an OR of 0.316, which was highly significant ($P < 0.0001$). This preference might reflect the greater comfort and perceived quality of care in a home environment compared to hospital settings.

Analysis of publication bias and heterogeneity through the funnel plot symmetry, the I^2 statistic, and the Tau-squared value suggest robustness in our findings with moderate variability across studies likely reflecting true differences in effect sizes rather than mere sampling errors. High heterogeneity ($I^2 = 67\%$) indicated that while the overall trends were favorable toward HaH, individual study outcomes likely varied due to differences in program implementation, patient selection, and local healthcare system factors.

Our sensitivity analysis further supported the robustness of our conclusions, showing no significant deviations when individual studies were excluded and recalculated. This result confirms that no single study unduly influenced the overall meta-analysis outcome, underpinning the reliability of our conclusions. Furthermore, the quality assessment using the MINORS method showed consistently high scores (median of 2.0), and subgroup analysis comparing lower scores (1.7–1.8) to higher (2.0) revealed no substantial differences in effect sizes, suggesting that study quality did not skew results significantly.

The main limitation of our meta-analysis is the different outcomes that were chosen in each study. While some studies chose clinical outcomes such as readmission and mortality, others looked at patient preferences and satisfaction. The difference in clinical outcomes was not significantly better in HaH as in patient subjective preferences and satisfaction.

CONCLUSIONS

HaH programs for COPD not only provide a non-inferior alternative to in-hospital care but may enhance certain patient-related outcomes. These findings could have significant implications for healthcare systems globally, particularly where reducing hospital readmission and enhancing patient satisfaction are priorities. Future research could beneficially explore long-term outcomes, cost-effectiveness, and identification of patient populations that could benefit most from HaH programs.

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Capsule

Non-antibiotics disrupt colonization resistance against enteropathogens

Grießhammer and colleagues examined how non-antibiotics affect the ability of gut commensals to resist colonization by enteropathogens. The authors also developed an in vitro assay to assess enteropathogen growth in drug-perturbed microbial communities. Pathogenic Gammaproteobacteria were more resistant to non-antibiotics than commensals and their post-treatment expansion was potentiated. For 28% of the 53 drugs tested, the growth of *Salmonella enterica* subsp. *enterica* serovar Typhimurium (*S.* Tm) in synthetic and human stool-derived communities was increased, and similar effects were observed for other enteropathogens. Non-antibiotics promoted pathogen proliferation by inhibiting the growth of commensals, altering microbial interactions and enhancing the ability of *S.* Tm to exploit metabolic niches. Drugs that promoted pathogen expansion in vitro increased the intestinal *S.* Tm load in mice. For the antihistamine terfenadine, drug-induced disruption of colonization resistance accelerated disease onset and increased inflammation caused by *S.* Tm.

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Capsule

Humoral determinants of checkpoint immunotherapy

Dai et al. used rapid extracellular antigen profiling to map the autoantibody reactome within a cohort of 374 patients with cancer treated with checkpoint inhibitors (CPIs) and 131 healthy control participants for autoantibodies to 6172 extracellular and secreted proteins (the exoproteome). Globally, patients with cancer treated with CPIs had diverse autoreactivities that were elevated relative to control individuals but changed minimally with treatment. Autoantibody signatures in patients treated with CPI strikingly distinguished them from healthy individuals. Although associations of specific autoantibodies with immune-related adverse events were sparse, we detected numerous individual autoantibodies that were associated with greatly altered odds ratios for response to therapy. These included autoantibodies to immunomodulatory proteins, such as cytokines, growth factors and immunoreceptors, as well as tumor surface proteins. Functional evaluation of several autoantibody responses indicated that they neutralized the activity of their target proteins, which included type I interferons (IFN-I), IL-6, OSM, TL1A, and BMPR1A, and BMPR2. Modelling the effects of autoantibodies to IFN-I and TL1A in preclinical mouse tumor models resulted in enhanced CPI efficacy, consistent with their effects in patients.

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