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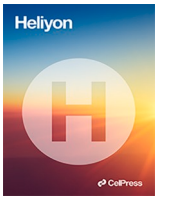

Review article

Enrollment and dropout rates of individuals with chronic obstructive pulmonary disease approached for telehealth interventions: A systematic review and meta-regression analysis

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ABSTRACT

Introduction: Telehealth interventions have the potential of improving health outcomes for individuals with chronic obstructive pulmonary disease (COPD). However, the precise impact of telehealth on exacerbation and hospital readmissions remains inconclusive. This lack of knowledge on the effectiveness of telehealth for COPD care might be due to lack of clarity regarding which variables are most strongly associated with enrolment and dropout rates.
Objectives: Among individuals with COPD in telehealth studies, we aimed to: (1) estimate the extent to which trial-related variables are associated with enrolment and dropout rates, and identify reasons for dropouts; (2) estimate the extent to which patients-related and intervention-related variables are associated with dropout rates; (3) estimate the effect of enrolment rate and dropout rate on effect size; (4) estimate the effect of trial-related, patient-related, and intervention-related variables on effect size.
Methods: A systematic literature search was conducted using four electronic databases. Two independent reviewers screened all retrieved titles, abstracts and full texts according to the inclusion criteria and extracted the data. A random-effect meta-regression analysis was conducted to estimate the overall enrolment and dropout rates, and estimated the different variables' effects on the enrolment rate, dropout rate, and effect sizes in the studies included in the review.
Results: A total of 56 studies comprising 7530 participants were identified. The estimated enrolment and dropout rates were 50.3 % and 14.9 %, respectively. Trial-related variables influence enrollment and dropout rates, including RCT designs and the recruitments. The patient-related variables, including age and severity of the disease, and intervention-related variables, including the components of the intervention and mode of delivery, influence dropout rates. Studies with low dropout rates had a bigger effect size by 0.23. The main reported reasons for

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dropping out of the intervention were related to death (21 %) followed by lost to follow-up (14 %).
Conclusion: Trial, patient, and intervention-related variables were found to influence the enrolment and dropout rates. This would help plan and develop a more appealing telehealth intervention that patients can easily accept and incorporate into their everyday lives.
Registration information: International Prospective Register of Systematic Reviews (PROSPERO); ID: CRD42017078541.

Abbreviations list

COPD	Chronic obstructive pulmonary disease
CONSORT	Consolidated Standards of Reporting Trials guidelines
CI	Confidence Interval
FEV1	Forced expiratory volume in the first second
GOLD	Global Initiative for Chronic Obstructive Lung Disease
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
RCT	Randomized controlled trials
SIGN	Scottish Intercollegiate Guidelines Network checklist

1. Introduction

Individuals with Chronic obstructive pulmonary disease (COPD) need appropriate management strategies (such as self-management) that require active participation by patients to minimize the likelihood of hospitalization and a further decline in their health status [1–3]. While the rationale for providing self-management interventions for individuals with COPD is apparent, current evidence regarding these interventions' effectiveness is limited and variable [1–3].

Telehealth refers to using electronic information and communication technologies to support distance healthcare, allowing clinicians and patients to exchange information and access healthcare services remotely [2,4–7]. Telehealth is used for remote monitoring of a patient's clinical data, such as their vital signs; this enables healthcare teams to promptly identify deterioration and deliver care [8]. Clinical trials have shown that individuals with COPD have positive attitudes towards participating in telehealth to promote patients' independence toward self-management [9,10]. However, telehealth precise impact on exacerbation and hospital readmissions remains inconclusive.

In any telehealth program, adherence is a key challenge and dropout rates for telehealth vary across clinical trials [9,11,12]. It is unclear which variables are most strongly associated with enrolment and dropout rates. Possible factors that may influence dropouts include patient characteristics, intervention features, and the context in which the intervention is delivered. Evaluating design elements that prevent individuals with COPD from enrolling and completing telehealth interventions may help clinicians appropriately tailor interventions to the individuals' needs and limit dropout rates.

Currently, there is little information on the enrolment and dropout rates of individuals with COPD in telehealth intervention trials. Thus, this study aimed to: (1) estimate the extent to which trial-related variables are associated with enrolment and dropout rates, and identify reasons for dropouts; (2) estimate the extent to which patients-related and intervention-related variables are associated with dropout rates; (3) estimate the effect of enrolment rate and dropout rate on effect size; (4) estimate the effect of trial-related, patient-related, and intervention-related variables on effect size.

2. Methods

Our published protocol details the methodology of this review [13].

2.1. Search strategy

A search of the literature was performed using electronic databases of Ovid MEDLINE, EMBASE, CINAHL and the Cochrane Database from inceptions to November 2018. The initial search strategy was constructed for Ovid MEDLINE (**Appendix 1**) and adapted to other databases. A combination of Medical Subject Headings (MeSH) terms, subject headings and/or key words was used. Searches were updated twice: in October 2019 (n = 44), and in October 2021 (n = 56).

2.2. Eligibility criteria

Inclusion criteria: trials with or without randomization and observational studies including individuals diagnosed with COPD ≥18

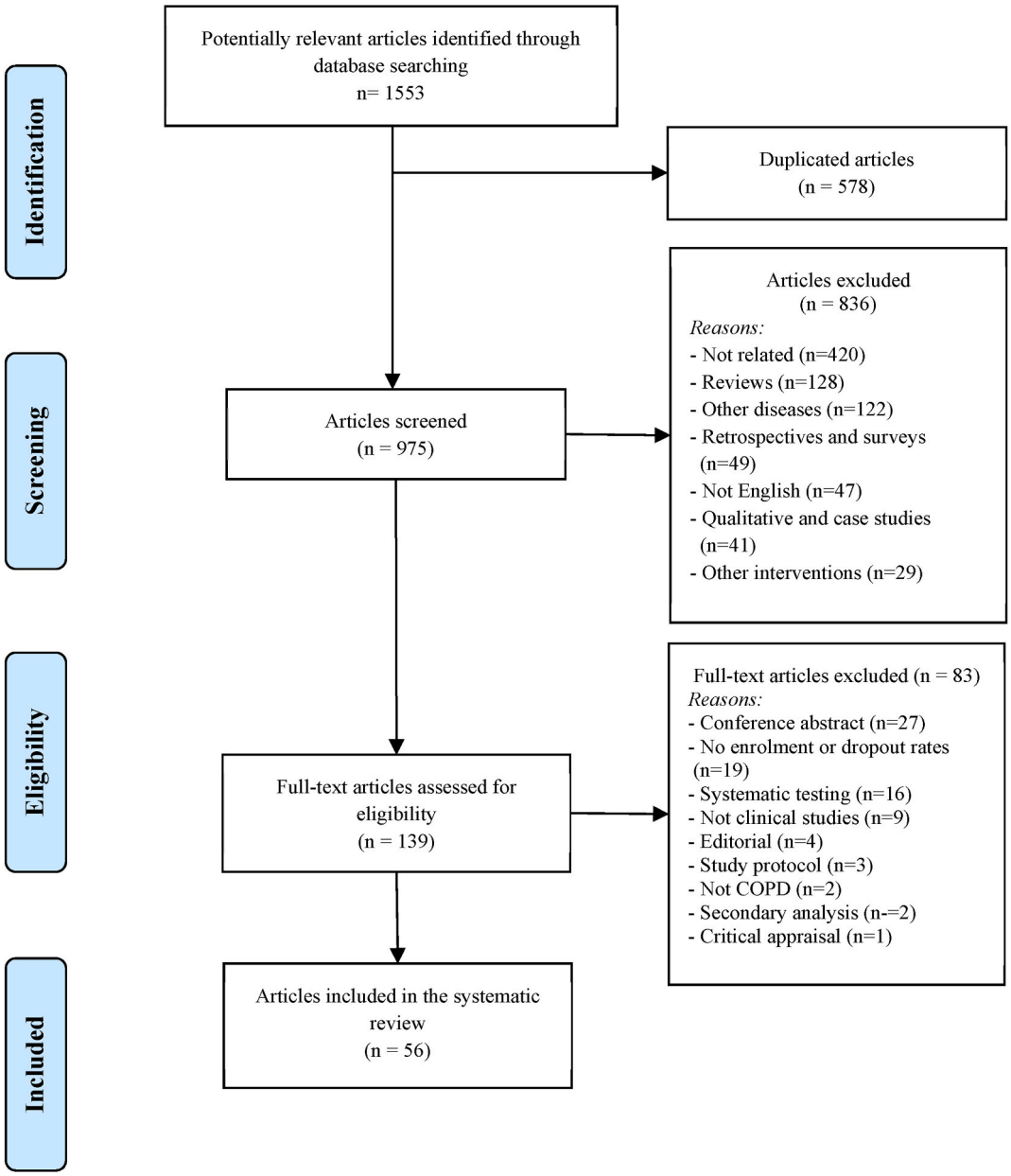

Fig. 1. PRISMA flowchart.

years; any information of technology tool designed for the clinical support of patients with COPD (see **Appendix 2** that presents various terms used to reference specific telehealth applications).

Exclusion criteria: articles published in languages other than English; studies that did not describe the telehealth interventions, and studies that did not report the number of patients who were approached for recruitment or the number of participants who dropped out.

2.3. Study selection

Two independent reviewers screened titles and abstracts, followed by retrieving full-text articles and evaluating for eligibility. Disagreements were resolved by discussion and consensus. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram [14] was used to guide the selection process.

Table 1
Characteristics of trial-related variables.

Author (year)	Study Place	Recruitment method	Sample Size	Intervention	Intervention Setting	Delivery Mode	Type of Control	Primary Outcome: (Effect Size)	Enrolment Rate/ Dropout Rate
Antoniades (2012) [11]	Australia	Outpatient settings	44	Tele-Monitoring	Patient's home	Laptop	Standard best practice care (SBP)	CRQ: (0.25)	9/18
Berkhof (2015) [12]	Netherland	Primary care clinic after regular visits	101	Tele-Medicine	Medical center to patient's home	Telephone	Usual care	CRQ: (0.81)	84/7
Calvo (2014) [22]	Spain	Outpatient settings	60	Tele-Health-Care	Patient's home	Internet	Usual care	emergency room visits: (.)	31/13
Cameron-Tucker (2016) [9]	Australia	Primary care clinic after regular visits	65	Tele-Rehabilitation	Medical center to patient's home	Telephone	Usual care	6MWT (meter): (0.07)	18/38
Chau (2012) [30]	Hong Kong	Primary care clinic after regular visits	45	Tele-Health-Care	Patient's home	Smartphone	Usual care	CRQ: (0.45)	73/27
Dale (2003) [64]	UK	Primary care clinic after regular visits	55	Tele-Monitoring	Patient's home	Telephone	No control	Hospital admission: (.)	100/20
De san Miguel (2013) [10]	Australia	Others (letters, homecare)	80	Tele-Health-Care	Patient's home	Telephone	Education	Ed visits: (0.12)	100/36
Dinesen (2012) [8]	Denmark	Primary care clinic after regular visits	111	Tele-Rehabilitation	Patient's home	Telephone	Home exercise	admission rate: (.)	91/5
Farmer (2017) [1]	UK	Primary care clinic after regular visits	166	Tele-Health-Care	Patient's home	Tablet	Usual care	SGRQ: (0.07)	81/13
Franke (2016) [56]	Germany	Primary care clinic after regular visits	44	Tele-Monitoring	Patient's home	Telephone	Usual care	daily training time (min): (0.19)	83/36
Halpin (2011) [31]	UK	Primary care clinic after regular visits	79	Tele-Health-Care	Patient's home	Smartphone	Usual care	E-RS: (1.2)	12/3
Ho (2016) [47]	Taiwan	Primary care clinic after regular visits	106	Tele-Monitoring	Patient's home	Laptop	Usual care	Hospital admission: (0.5)	33/0
Jakobsen (2015) [4]	Denmark	Primary care clinic after regular visits	57	Tele-Health-Care	Patient's home	Tablet	Phone call support	treatment failure: readmission due to COPD: (.)	9/26
Koff (2009) [28]	USA	Primary care clinic after regular visits	40	Tele-Medicine	Patient's home	Telephone	Usual care	SGRQ: (0.22)	100/5
Lewis (2011) [32]	UK	Others (letters, homecare)	40	Tele-Monitoring	Patient's home	Telephone	Usual care	SGRQ: (0.05)	40/0
Lilholt (2017) [5]	Denmark	Primary care clinic after regular visits	1225	Tele-Health-Care	Patient's home	Tablet	Usual care	SF-36 (physical): (0.01)	100/5
Marquis (2015) [57]	Canada	Community centre	22	Tele-Rehabilitation	Patient's home	Videoconferencing	No control	6MWT (meter): (0.68)	85/5
McDowell (2015) [41]	UK	Community centre	100	Tele-Health-Care	Patient's home	Telephone	Usual care	SGRQ: (0.36)	85/10
Nield (2012) [2]	UK	Outpatient settings	22	Tele-Health-Care	Patient's home	Laptop	Usual care	MOS: (0.83)	79/27
Pedone (2013) [29]	Italy	Outpatient settings	99	Tele-Monitoring	Patient's home	Cellular telephone	Usual care	incidence rate of exacerbations: (.)	57/11
Pinnock (2013) [42]	UK	Primary care clinic after regular visits	256	Tele-Monitoring	Patient's home	Internet	Self management education	SGRQ: (0.05)	61/1
Ringbaek (2015) [59]	Denmark	Outpatient settings	281	Tele-Health-Care	Patient's home	Internet	Usual care	Hospital admission: (0.02)	50/12
Ringbaek (2016) [33]	Denmark	Outpatient settings	115	Tele-Rehabilitation	Patient's home	Tablet	Usual care	ESWT (SEC): (0.01)	79/14
Rosenbek (2015) [51]	Denmark	Outpatient settings	37	Tele-Medicine	Patient's home	Internet	No control	TUG (sec): (0.56)	100/16
Schou (2013) [23]	Denmark	Outpatient settings	44	Tele-Medicine	Patient's home	Videoconferencing	Usual care	SGRQ: (0.52)	7/5

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Table 1 (*continued*)

Author (year)	Study Place	Recruitment method	Sample Size	Intervention	Intervention Setting	Delivery Mode	Type of Control	Primary Outcome: (Effect Size)	Enrolment Rate/ Dropout Rate
Shany (2017) [34]	Australia	Outpatient settings	42	Tele-Medicine	Patient's home	Telephone	RACS-Plus	Hospital admission: (0.37)	64/43
Sicotte (2011) [60]	Canada	Others (letters, homecare)	46	Tele-Monitoring	Patient's home	Internet	Usual care	SF-12 (physical): (0.55)	100/4
Stickland (2011) [71]	Canada	Outpatient/ hospital/primary physician	409	Tele-Health-Care	Medical center to patient's home	Videoconferencing	Standard pulmonary rehabilitation	SGRQ: (0.39)	100/12
Tabak (2014) [7]	Netherland	Outpatient settings	29	Tele-Health-Care	Patient's home	Smartphone	Usual care	6MWT (min): (0.2)	29/21
Trappenburg (2008) [61]	Netherland	Outpatient settings	115	Tele-Monitoring	Patient's home	Telephone	Usual care	CRQ: (0.26)	70/43
Tsai (2017) [43]	Australia	Outpatient settings	37	Tele-Rehabilitation	Patient's home	Laptop	Usual care	ISWT (m): (0.25)	29/3
Vianello (2016) [66]	Italy	Outpatient settings	334	Tele-Monitoring	Patient's home	Telephone	Usual care	SF-36 (physical): (0.07)	73/15
Bhatt (2019) [53]	USA	Outpatient settings	240	Tele-Rehabilitation	Patient's home	Smartphone	Standard pulmonary rehabilitation	30 day all cause readmission rate: (0.44)	100/6
Farias (2019) [54]	Canada	Outpatient settings	40	Tele-Health-Care	Patient's home	Smartphone	No control	Exacerbation recovery time: (0.27)	100/18
Farver-Vestergaard (2019) [55]	Denmark	Outpatient settings	8	Tele-Medicine	Patient's home	Tablet	No control	hospital anxiety and depression score: (0.19)	17/0
Kessler (2018) [40]	Canada	Outpatient settings	319	Tele-Health-Care	Patient's home	Tablet	Usual care	Annual unplanned all-cause hospitalization: (0.13)	92/17
Loeckx (2018) [49]	UK	Outpatient settings	159	Tele-Health-Care	Patient's home	Smartphone	No control	CAT: (0.72)	93/8
Miron (2018) [50]	Spain	Outpatient settings	26	Tele-Monitoring	Patient's home	Laptop	No control	CAT: (0.18)	93/8
Nyberg (2019) [3]	Sweden	Outpatient settings	83	Tele-Health-Care	Patient's home	Laptop	Usual care	CAT: (0.38)	45/10
Wu (2018) [52]	Canada	Outpatient settings	28	Tele-Health-Care	Patient's home	Smartphone	No control	Able to wear and maintain the smartwatch: (.)	16/43
Soriano (2018) [65]	Spain	Outpatient settings	229	Tele-Health-Care	Patient's home	Internet	Usual care	The number of exacerbations in the 12 month: (0.09)	97/26
Tupper (2018) [35]	Denmark	Outpatient settings	281	Tele-Monitoring	Patient's home	Tablet	Usual care	15-D score for HRQL: (0.28)	50/12
Walker (2018) [36]	Italy	Primary care clinic after regular visits	312	Tele-Monitoring	Patient's home	Telephone	Usual care	CAT: (0.05)	96/26
Rassouli (2018) [58]	Germany	Others (letters, homecare)	56	Tele-Rehabilitation	Patient's home	Smartphone	No control	CAT: (0.31)	16/68
Minguez Clement (2020) [26]	Spain	Outpatient/ hospital/primary physician	116	TeleMedicine	Patient's home	Internet	Usual care	number of home visits: (0.82)	94/11
Koff (2021) [39]	USA	Primary care clinic after regular visits	511	TeleHealthCare	Patient's home	Internet	Usual care	SGRQ: (0.54)	100/24
Galdiz (2021) [37]	Spain	Outpatient/ hospital/primary physician	94	TeleRehabilitation	Patient's home	Smartphone	Usual care	6MWD: (0.23)	70/9
Trosini-Desert (2020) [63]		Outpatient/ hospital/primary physician	42	TeleMedicine	Patient's home	Tablet		Number of errors made: (.)	84/19

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Table 1 (*continued*)

Author (year)	Study Place	Recruitment method	Sample Size	Intervention	Intervention Setting	Delivery Mode	Type of Control	Primary Outcome: (Effect Size)	Enrolment Rate/ Dropout Rate
Bentley (2020) [24]	UK	Outpatient/ hospital/primary physician	30	TeleHealthCare	Patient's home	Smartphone	Standard pulmonary rehabilitation (PR)	app used (no. of days): (.)	100/47
Jiang (2020) [38]		Community centre	106	TeleMedicine	Patient's home	Internet	Face to face PeR	CAT: (0.013)	52/11
Sink (2020) [27]	USA	Primary care clinic after regular visits	168	TeleMedicine	Medical center to patient's home	Automated phone call	Non-alerted Epharmix COPD system	time to COPD hospitilization: (.)	27/28
Stamenova (2020) [45]	Canada	Outpatient/ hospital/primary physician	81	TeleMedicine	Patient's home	Tablet	Usual care	PIH: (0.493)	10/15
Stamenova (2020) [45]	Canada	Outpatient/ hospital/primary physician	81	TeleMedicine	Patient's home	Tablet	Usual care	PIH: (0.235)	10/16
Holmner (2020) [62]	Sweden	Community centre	13	TeleHealthCare	Patient's home	Smartphone		FEV1%: (3.77)	52/15
Hansen (2020) [25]	Denmark	Outpatient/ hospital/primary physician	134	TeleRehabilitation	Patient's home	Videoconferencing	Standard pulmonary rehabilitation (PR)	6MWD (min): (.)	35/32
Duiverman (2020) [44]	Netherland	Outpatient/ hospital/primary physician	67	TeleMedicine	Patient's home	Internet	Initiation of NIV in hospital	PaCO2: (0.11)	57/27

SF-36: 36-Item Short Form Survey; SF-12: 12-Item Short Form Survey; 15D score for HRQL: 15-D score for health-related quality of life questionnaire; CRQ: Chronic respiratory questionnaire; SGRQ: St George's respiratory questionnaire; CAT: COPD assessment test; E-RS: EXACT-respiratory symptoms scale; MOS: MOS social support survey; 6MWT: 6 min walking test; ESWT: Endurance shuttle walking test; ISWT: Incremental shuttle walking test; TUG: timed up and go test; RCT: randomized clinical trials.

Table 2
Characteristics of patient-related variables.

Author (year)	Sample Size	Sample Size	Age Mean ± SD	Gender % of men	FEV1 % Moderate/ Severe[a]	Smoking Inter./ Ctrl	Patient's stability after discharge from hospital [b]	Dropout rate %
Antoniades (2012) [11]	44	22(I) 22(C)	69 ± 9	45	41/54	No/Yes	Stable	18
Bentley (2020) [24]	30	19(I) 11(C)	67±.	43	NR	NR	Stable	47
Berkhof (2015) [12]	101	52(I) 49(C)	68 ± 9	67	40/41	Yes/Yes	Not stable	7
Bhatt (2019) [53]	240	80(I) 160(C)	63.95 ± 10.95	84	45/49	Yes/Yes	Stable	6
Calvo (2014) [22]	60	30(I) 30(C)	73.5 ± 9.5	75	37/38	No/No	Stable	13
Cameron-Tucker (2016) [9]	65	35(I) 30(C)	69 ± 8.6	45	NR	Yes/Yes	Not stable	38
Chau (2012) [30]	45	22(I) 23(C)	72.93±.	98	34/44	NR	Stable	27
Dale (2003) [64]	55	55(I) 0(C)	. ±.	NR	NR	NR/Yes	Not stable	20
De san Miguel (2013) [10]	80	40(I) 40(C)	72±-.	46	NR	NR	Stable	36
Dinesen (2012) [8]	111	60(I) 51(C)	68±.	NR	40/43	NR	Stable	5
Duiverman (2020) [44]	67	33(I) 34(C)	63.35 ± 9	40	63/68	Yes/Yes	Stable	27
Farias (2019) [54]	40	40(I) 0(C)	69.8 ± 6.9	36	41/.	Yes/NR	Stable	18
Farmer (2017) [1]	166	110(I) 56(C)	69.8±.	61	47/50	Yes/Yes	Stable	13
Farver-Vestergaard (2019) [55]	8	8(I) 0(C)	72.6 ± 9.9	100	38/.	No/NR	Stable	0
Franke (2016) [56]	44	21(I) 23(C)	63.3±.	55	NR	NR	Stable	36
Galdiz (2021) [37]	94	46(I) 48(C)	62.65 ± 7.4	67	46/43	Yes/Yes	Stable	9
Halpin (2011) [31]	79	40(I) 39(C)	69.35±.	73	48/54	Yes/Yes	Stable	3
Hansen (2020) [25]	134	67(I) 67(C)	68.3 ± 9	45	33/34	Yes/Yes	Stable	32
Ho (2016) [47]	106	53(I) 53(C)	80.2 ± 8.7	76	62/62	Yes/Yes	Not stable	0
Holmner (2020) [62]	13	13(I) 0(C)	67±.	38	53/.	NR	Stable	15
Jakobsen (2015) [4]	57	29(I) 28(C)	75±.	38	44/42	Yes/Yes	Stable	26
Jiang (2020) [38]	106	53(I) 53(C)	71.36 ± 6.99	82	NR	Yes/Yes	Stable	11
Kessler (2018) [40]	319	157(I) 162(C)	66.9 ± 9.3	47	38/36	Yes/Yes	Stable	17
Koff (2009) [28]	40	20(I) 20(C)	65.8 ± 8.65	53	34/31	Yes/Yes	Stable	5
Koff (2021) [39]	511	352(I) 159(C)	68.35 ± 9.1	60.6	36/38	Yes/Yes	Stable	24
Lewis (2011) [32]	40	20(I) 20(C)	68.5 ± 9.5	50	38/40	Yes/Yes	Stable	0
Lilholt (2017) [5]	1225	578(I) 647(C)	69.95 ± 9.25	70	48/48	Yes/Yes	Stable	5
Loeckx (2018) [49]	159	159(I) 0(C)	66 ± 8	64	54/.	Yes/NR	Stable	8
Marquis (2015) [57]	22	22(I) 0(C)	65.2 ± 7.1	42	48/.	Yes/Yes	Stable	5
McDowell (2015) [41]	100	48(I) 52(C)	69.5 ± 7.25	80	46/43	Yes/Yes	Stable	10
Minguez Clement (2020) [26]	116	58(I) 58(C)	69 ± 8	70	50/52	Yes/Yes	Stable	11
Miron (2018) [50]	26	26(I) 0(C)	78 ± 7.9	93	51/.	Yes/NR	Stable	8
Nield (2012) [2]	22	11(I) 11(C)	65 ± 6.5	100	55/56	Yes/Yes	Stable	27

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Table 2 (*continued*)

Author (year)	Sample Size	Sample Size	Age Mean ± SD	Gender % of men	FEV1 % Moderate/ Severe[a]	Smoking Inter./ Ctrl	Patient's stability after discharge from hospital [b]	Dropout rate %
Nyberg (2019) [3]	83	43(I) 40(C)	70 ± 8	46	60/59	Yes/Yes	Stable	10
Pedone (2013) [29]	99	50(I) 49(C)	74.5 ± 6	73	53/55	Yes/Yes	Stable	11
Pinnock (2013) [42]	256	128(I) 128(C)	68.9 ± 8.6	44	44/40	Yes/Yes	Not stable	1
Rassouli (2018) [58]	56	56(I) 0(C)	57.5 ± 7.8	11	NR	Yes/NR	Not stable	68
Ringbaek (2015) [59]	281	141(I) 140(C)	69 ± 9.5	47	35/34	Yes/Yes	Not stable	12
Ringbaek (2016) [33]	115	46(I) 69(C)	68 ± 10	48	31/35	Yes/Yes	Stable	14
Rosenbek (2015) [51]	37	37(I) 0(C)	69.2 ± 8.8	14	27/.	NR	Stable	16
Schou (2013) [23]	44	22(I) 22(C)	70.5 ± 5.6	41	39/44	NR	Stable	5
Shany (2017) [34]	42	21(I) 21(C)	73 ± 8	46	NR	Yes/Yes	Not stable	43
Sicotte (2011) [60]	46	23(I) 23(C)	74 ± 9	57	NR	NR	Stable	4
Sink (2020) [27]	168	83(I) 85(C)	60.91 ± 1.08	36	65/63	Yes/Yes	Stable	28
Soriano (2018) [65]	229	115(I) 114(C)	71 ± 8	80	34/32	Yes/Yes	Stable	26
Stamenova (2020) [45]	81	41(I) 40(C)	72.17 ± 8.6	55	52/45	Yes/Yes	Stable	15
Stamenova (2020) [45]	81	41(I) 40(C)	72.17 ± 8.6	55	55/45	Yes/Yes	Stable	16
Stickland (2011) [71]	409	147(I) 262(C)	69.35 ± 9.15	50	48/49	Yes/Yes	Stable	12
Tabak (2014) [7]	29	15(I) 14(C)	63 ± 8	50	50/36	Yes/Yes	Stable	21
Trappenburg (2008) [61]	115	59(I) 56(C)	69.5 ± 9	53	42/39	Yes/Yes	Stable	43
Trosini-Desert (2020) [63]	42	42(I) 0(C)	. ±.	58	NR	Yes/NR	Stable	19
Tsai (2017) [43]	37	20(I) 17(C)	74 ± 8.5	50	60/68	Yes/Yes	Stable	3
Tupper (2018) [35]	281	141(I) 140(C)	69.6 ± 9.55	47	35/34	Yes/Yes	Stable	12
Vianello (2016) [66]	334	230(I) 104(C)	76 ± 6	72	42/42	Yes/Yes	Not stable	15
Walker (2018) [36]	312	154(I) 158(C)	71±.	66	49/50	Yes/Yes	Stable	26
Wu (2018) [52]	28	28(I) 0(C)	68.5±.	64	57/.	Yes/NR	Stable	43

I: intervention, C: control; NR: not reported.

[a] To note, the main criterion for COPD is a FEV1 ratio, sub-classification into mild (GOLD1: FEV1 $\geq$ 80 % predicted), moderate (GOLD2: 50 % $\leq$ FEV1 $<$ 80 % predicted), severe (GOLD3: 30 % $\leq$ FEV1 50 % predicted) and very severe (GOLD4: FEV1 $<$ 30 % predicted) disease is achieved by including various levels of FEV1 as percentage of predicted value.

[b] After an exacerbation is appropriately managed, a suitable discharge plan should be prepared. This will depend on the severity of the exacerbation, but should generally include reclassification of the patient according to the GOLD criteria, optimization of pharmacological therapy, management of comorbidities, patient (or home caregiver) education on the correct use of medications, referral to a Pulmonology Consultation if they are not already attending one, and a smoking cessation and pulmonary rehabilitation program.

2.4. Risk of bias assessment

Risk of bias of the quality of the included studies was assessed by two independent reviewers using the criteria list advised by the Cochrane Collaboration Risk of Bias criteria for randomized controlled trials (RCTs) [15] and the Scottish Intercollegiate Guidelines Network checklist (SIGN) for observational studies [16].

2.5. Data extraction

A data extraction form was created, which included information on enrolment and dropout rates as well as on variables (i.e. trials, patients, intervention) [13] that can influence by the enrolment and dropout rates.

Table 3
Characteristics of intervention-related variables.

Author (year)	Type of program	Classification	Mode of delivery	Professional guide	Parameters	Setting	Length (months)	Frequency
Antoniades (2012) [11]	Home support system	Self-management	Laptop	Nurse	8	Patient's home	12	Daily
Bentley (2020) [24]	Digital health system	Self-management and coping skills	Smartphone	RT	2	Patient's home	2	Daily
Berkhof (2015) [12]	Home support system	Self-management	Telephone	Nurse and pulmonologist	8	Medical center to patient's home	6	Others
Bhatt (2019) [53]	Home support system	Education and lifestyles changes	Smartphone	Telemonitoring team	3	Patient's home	3	Others
Calvo (2014) [22]	Home support system	Action plan	Internet	Pulmonologist and primary care physician	4	Patient's home	7	Daily
Cameron-Tucker (2016) [9]	Home support system	Action plan and lifestyles changes	Telephone	Nurse	3	Medical center to patient's home	2	Others
Chau (2012) [30]	Home support system	Self-management	Smartphone	Nurse	3	Patient's home	2	Daily
Dale (2003) [64]	Home support system	Self-management	Telephone	Nurse	3	Patient's home	3	Daily
De san Miguel (2013) [10]	Home support system	Self-management education	Telephone	Nurse	5	Patient's home	6	Daily
Dinesen (2012) [8]	Home support system	Action plan	Telephone	General practitioner	5	Patient's home	4	Daily
Duiverman (2020) [44]	Home support system	Self-management	Internet	Nurse	4	Patient's home	6	Others
Farias (2019) [54]	Home support system and Digital health system	Action plan and lifestyles changes	Smartphone	Nurse	1	Patient's home	12	Others
Farmer (2017) [1]	Digital health system	Self-management and coping skills	Tablet	Respiratory therapist	3	Patient's home	12	Daily
Farver-Vestergaard (2019) [55]	Home support system	Education	Tablet	Clinical psychologist	2	Patient's home	2	Others
Franke (2016) [56]	Home support system	Action plan	Telephone	Nurse	3	Patient's home	6	Daily
Galdiz (2021) [37]	Home support system	Self-management education, action planned	Smartphone	Pulmonologist and primary care physician	4	Patient's home	12	Others
Halpin (2011) [31]	Home support system	Action plan	Smartphone	Nurse	3	Patient's home	4	Daily
Hansen (2020) [25]	Home support system	Self-management education	Videoconferencing	PT	4	Patient's home	3	Others
Ho (2016) [47]	Home support system	Self-management	Laptop	Nurse and pulmonologist	3	Patient's home	2	Daily
Holmner (2020) [62]	Home support system	Self-management	Smartphone	Researcher	3	Patient's home	6	Others
Jakobsen (2015) [4]	Home support system	Self-management	Tablet	Nurse and pulmonologist	3	Patient's home	6	Daily
Jiang (2020) [38]	Home support system	Self-management education, action planned, coping skills	Internet	Nurse	3	Patient's home	6	Others
Kessler (2018) [40]	Home support system and Digital health system	Self-management and coping skills	Tablet	Telemonitoring team	3	Patient's home	24	Daily
Koff (2009) [28]	Home support system	Self-management education	Telephone	Respiratory therapist	2	Patient's home	3	Daily
Koff (2021) [39]	Digital health system	Self-management education, action planned	Internet	Researcher	2	Patient's home	9	Daily
Lewis (2011) [32]	Home support system	Self-management	Telephone	Nurse and pulmonologist	3	Patient's home	6	Daily
Lilholt (2017) [5]	Home support system	Self-management and coping skills	Tablet	Municipal healthcare worker	4	Patient's home	12	Daily
Loeckx (2018) [49]	Home support system and Digital health system	Education	Smartphone	COPD educator	1	Patient's home	3	Daily
Marquis (2015) [57]	Home support system	Self-management education	Videoconferencing	Nurse	3	Patient's home	2	Others
McDowell (2015) [41]	Home support system	Self-management education	Telephone	Nurse	3	Patient's home	6	Daily
Minguez Clement (2020) [26]	Home support system	Action planned	Internet	Nurse and pulmonologist	5	Patient's home	6	Others
Miron (2018) [50]	Home support system and Digital health system	Self-management	Laptop	Nurse	4	Patient's home	6	Daily

(*continued on next page*)

Table 3 (*continued*)

Author (year)	Type of program	Classification	Mode of delivery	Professional guide	Parameters	Setting	Length (months)	Frequency
Nield (2012) [2]	Home support system	Education	Laptop	COPD educator	1	Patient's home	1	Others
Nyberg (2019) [3]	Digital health system	Self-management	Laptop	Telemonitoring team	1	Patient's home	12	Daily
Pedone (2013) [29]	Digital health system	Self-management	Cellular telephone	Primary care physician	1	Patient's home	9	Daily
Pinnock (2013) [42]	Home support system	Self-management education	Internet	Respiratory therapist	1	Patient's home	12	Daily
Rassouli (2018) [58]	Digital health system	Education and lifestyles changes	Smartphone	Telemonitoring team	2	Patient's home	0.66	Daily
Ringbaek (2015) [59]	Home support system	Self-management consultation	Internet	Nurse	3	Patient's home	6	Others
Ringbaek (2016) [33]	Digital health system	Education and lifestyles changes	Tablet	Respiratory therapist	1	Patient's home	2	Others
Rosenbek (2015) [51]	Home support system	Self-management education	Internet	Telemonitoring team	2	Patient's home	1	Others
Schou (2013) [23]	Home support system	Self-management	Videoconferencing	Ward round ream	4	Patient's home	3	Daily
Shany (2017) [34]	Others (home support system and RACS-Plus)	Self-management education	Telephone	Nurse	7	Patient's home	12	Daily
Sicotte (2011) [60]	Home support system	Self-management	Internet	Nurse	3	Patient's home	3	Daily
Sink (2020) [27]	Home support system	Action planned	Automated phone call	Medical resident	3	Medical center to patient's home	8	Daily
Soriano (2018) [65]	Digital health system	Self-management	Internet	Nurse	4	Patient's home	12	Daily
Stamenova (2020) [45]	Digital health system	Action planned	Tablet	RT	5	Patient's home	6	Daily
Stamenova (2020) [45]	Digital health system	Action planned	Tablet	RT	6	Patient's home	7	Daily
Stickland (2011) [71]	Home support system	Self-management education	Videoconferencing	Respiratory therapist	3	Medical center to patient's home	2	Others
Tabak (2014) [7]	Home support system and Digital health system	Self-management, action plan and lifestyles changes	Smartphone	Physiotherapist	3	Patient's home	6	Daily
Trappenburg (2008) [61]	Digital health system	Self-management education	Telephone	Nurse	3	Patient's home	6	Daily
Trosini-Desert (2020) [63]	Home support system	Self-management education, action planned	Tablet	Physician, nurse, pharmacist, hospital person	2	Patient's home	0.25	Daily
Tsai (2017) [43]	Home support system	Action plan	Laptop	Physiotherapist	3	Patient's home	2	Others
Tupper (2018) [35]	Home support system	Self-management	Tablet	Nurse	3	Patient's home	6	Others
Vianello (2016) [66]	Home support system	Self-management	Telephone	Operator	3	Patient's home	12	Daily
Walker (2018) [36]	Digital health system	Self-management	Telephone	Telemonitoring team	5	Patient's home	9	Daily
Wu (2018) [52]	Digital health system	Action plan	Smartphone	Telemonitoring team	2	Patient's home	3	Daily

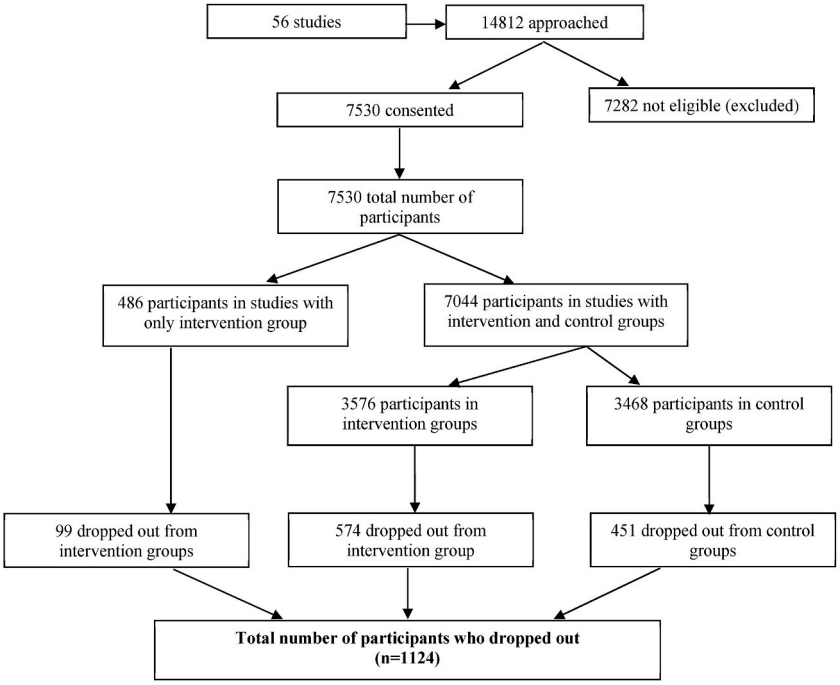

Fig. 2. Flowchart showing the numbers of participants from all included studies.

Table 4
Overall enrolment and dropout rates.

	Unweighted	Estimated (weighted)	SE	95 % CI
Enrollment rate (N = 56)	63 %	50.3 %	0.3	49.7 to 50.9
Dropout rate (N = 56)	18 %	14.9 %	0.1	14.7 to 15.2
Dropout rate in intervention groups (N = 56)	19 %	16.6 %	0.2	16.2 to 17.0
Dropout rate in control groups (N = 44)[a]	16 %	13.1 %	0.2	12.7 to 13.4

SE: standard error; CI: confidence intervals; N: number of studies.
[a] The number of studies with a control group was 36, as other studies were pre/post-intervention trials.

2.6. Statistical methods

Descriptive statistics were used to describe the characteristics of trials, patients, and interventions. Data were expressed as means ± standard deviation or as frequencies. The enrollment rate was defined as the proportion of individuals who consented to participate in the study out of the total number of eligible patients [13]. The dropout rate was defined as the proportion of participants who dropped out from the study (at the first evaluation point post-intervention) out of the number of participants who consented to participate in the study [13]. A random effect meta-regression analysis was used to estimate the overall enrolment and dropout rates of COPD telehealth interventions. This model accounted for the differential weights (due to different sample sizes) of each included study and estimated the different variables' effects on the enrolment rate, dropout rate, and effect size [17–19].

If studies had more than one outcome measure, the primary outcome's effect size was included in the analysis unless indicated otherwise. If the effect size was not reported in the study, it was calculated using Cohen *d* [20], taking the difference in the mean change in the primary outcome between the intervention and control groups and dividing it by the initial pooled standard deviation. For trials without a control group, the effect size was calculated by dividing the mean change in the outcome (pre and post-intervention) by the initial standard deviation. If the standard deviation was not reported in the study, it was estimated using the *p*-value or 95 % confidence intervals [21]. Where there was insufficient information to calculate the effect size, those studies were excluded from the effect size analysis.

The reasons for refusing to participate and dropping out of the telehealth interventions were listed by category in order of frequency. Recommendations provided by authors on ways to improve enrolment and dropout rates were summarized qualitatively. A *p*-value ≤ 0.05 was considered statistically significant. A dropout rate difference of 5 % was considered clinically significant. Statistical analyses were performed using the Statistical Analysis Systems (SAS version 9.4).

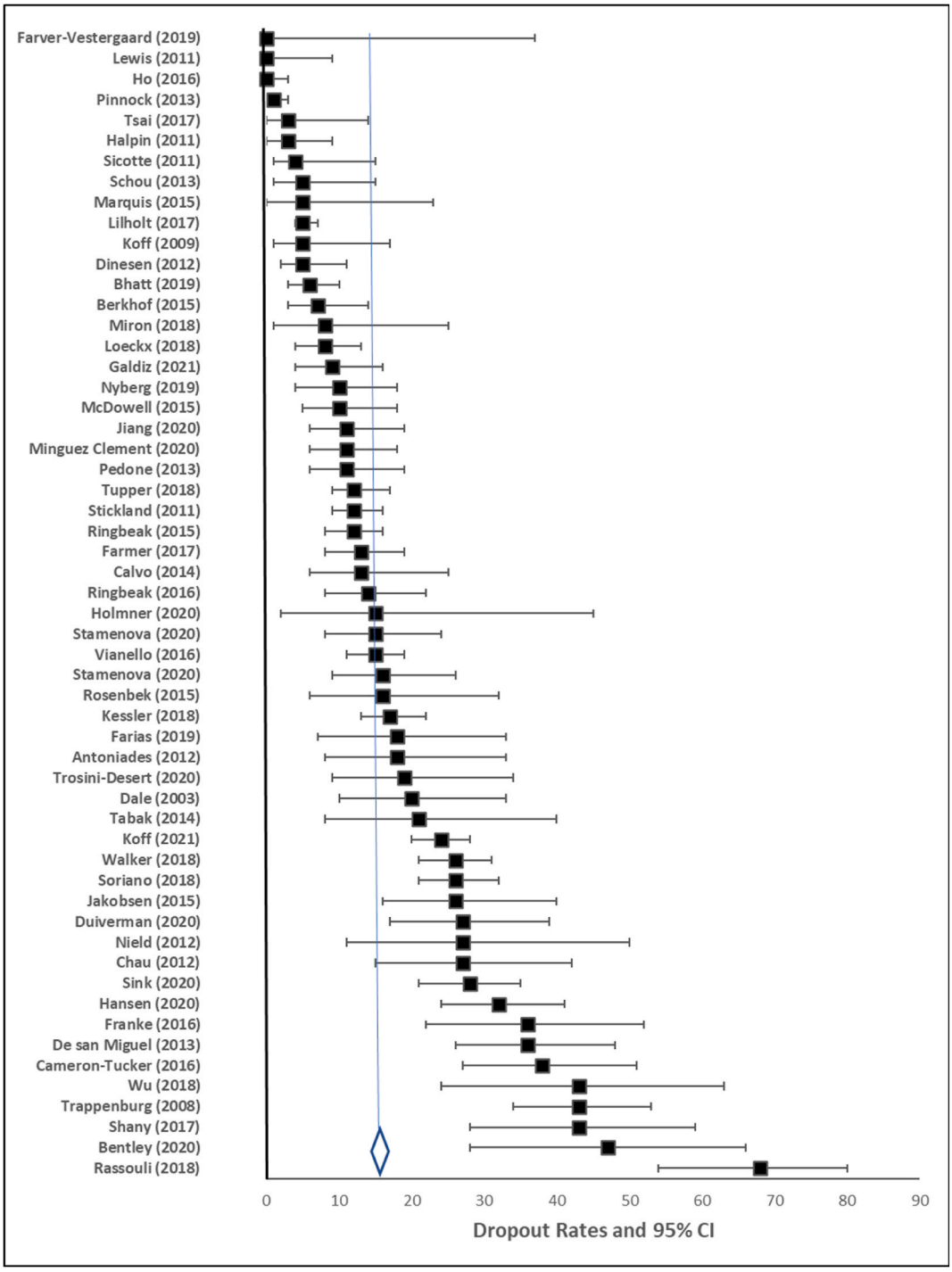

Fig. 3. Forest plot of dropout rates.

3. Results

3.1. Search results

Fig. 1 provides the details of the study selection process, and reasons for exclusion according to PRISMA flowchart [14]. The search strategy was updated in October 2021 and yielded a total of 56 articles.

Table 5
Effect of trial-related variables on enrollment rate.

Variables	N (%) of studies	N (%) of participants	Un-weighted Enrollment rate (%)				Estimated difference in enrollment rate in comparison to referent category			
			Mean (SD)	Median	Min	Max	Estimate	SE	95 % CI	p-value
Publication years										
2015–2021	38 (68 %)	5934 (79 %)	63.0 (32.4)	72	9	100	Reference	–	–	–
2010–2014	15 (27 %)	1386 (18 %)	58.3 (34.6)	61	7	100	−14.6	0.7	−16.0 to −13.3	<0.0001
2000–2009	3 (5 %)	210 (3 %)	90.0 (17.3)	100	70	100	30.1	1.1	28.0 to 32.2	<0.0001
Study place										
Denmark	10 (18 %)	2293 (30 %)	53.8 (36.9)	50	7	100	Reference	–	–	–
UK	9 (16 %)	907 (12 %)	72.3 (29.7)	81	12	100	−2.0	0.9	−3.9 to −0.2	0.0335
Australia	5 (9 %)	268 (4 %)	44.0 (37.6)	29	9	100	−28.7	0.9	−30.5 to −26.9	<0.0001
Others	32 (57 %)	4062 (54 %)	66.5 (31.1)	73	10	100	0.7	0.7	−0.7 to 2.0	0.3224
Study type										
RCT	39 (70 %)	6075 (81 %)	57.7 (32.2)	57	7	100	Reference	–	–	–
Others	17 (30 %)	1455 (19 %)	75.8 (31.2)	85	16	100	20.3	0.9	18.5 to 22.0	<0.0001
Recruitment method										
Outpatient settings	31 (55 %)	3643 (48 %)	61.2 (33.3)	70	7	100	Reference	–	–	–
Primary care clinic after regular visits	17 (30 %)	3424 (46 %)	65.4 (34.1)	81	9	100	12.6	0.6	11.4 to 13.9	<0.0001
Community center and Others (letters, homecare)	8 (14 %)	463 (6 %)	66.2 (30.7)	69	16	100	3.9	1.1	1.8 to 6.0	0.0003
Quality assessment										
Cochrane High	11 (20 %)	1286 (17 %)	58.2 (33.3)	61	7	100	Reference	–	–	–
Cochrane Fair	21 (37 %)	3988 (53 %)	56.3 (30.5)	57	9	100	8.6	0.7	7.2 to 9.9	<0.0001
SIGN Well covered	6 (11 %)	703 (9 %)	80.8 (32.4)	93	16	100	38.1	1.2	35.7 to 40.5	<0.0001
SIGN Adequate	10 (18 %)	697 (9 %)	70.3 (32.1)	82	16	100	12.2	1.3	9.8 to 14.7	<0.0001
Cochrane or SIGN Poor	8 (14 %)	856 (12 %)	66.1 (39.2)	86	9	100	3.5	1.0	1.5 to 5.4	0.0006

3.2. Risk of bias assessment

The overall assessment of the included RCTs based on the Cochrane Collaboration Risk of Bias criteria were judged as "High" in 11 (29 %) studies [2,3,7,22–29], "Fair" in 20 (53 %) studies [4,5,12,30–46], and "Low" in 7 (18 %) studies [1,8–11,47,48] (**Appendix 3**). The overall assessment of included observational studies based on SIGN was judged as "Well covered" in 5 (29 %) studies [6,49–52], "Adequately addressed" in 11 (65 %) studies [53–63], and "Poorly addressed" in one study (6 %) [64] (**Appendix 4**).

3.3. Characteristics of trial-related variables

A detailed description of each of the 56 articles included in this systematic review [1–12,22–45,47,49–66] is provided in Table 1. The majority of studies were RCTs (n = 38; 68 %; **Appendix 3**). Methods for recruiting patients varied, including: outpatient settings (41 %), primary care (29), and community (7 %).

3.4. Characteristics of patient-related variables

The total sample size was 7530, and the mean age of patients ranged from 57.5 to 80.2 years. The majority of studies included more men than women, and most patients were smokers. The severity of the disease ranged between moderate to severe (intervention group: FEV1% = 27%–65 %; control group: 31%–68 %), and 83 % of the patients were discharged from the hospital in stable condition (Table 2).

Table 6
Effect of trial-related variables on dropout rate.

Variables	N (%) of studies	N (%) of participants	Un-weighted Dropout rate (%)				Estimated difference in Dropout rate in comparison to referent category			
			Mean (SD)	Median	Min	Max	Estimate	SE	95 % CI	p-value
Publication years										
2015–2021	38 (68 %)	5934 (79 %)	19.3 (14.5)	15.2	0	68	Reference	–	–	–
2010–2014	15 (27 %)	1386 (18 %)	12.5 (11.0)	11	0	36	−5.0	0.3	−5.6 to −4.5	<0.0001
2000–2009	3 (5 %)	210 (3 %)	22.7 (19.1)	20	5	43	14.3	1.1	12.2 to 16.4	<0.0001
Study place										
Denmark	10 (18 %)	2293 (30 %)	12.7 (10.0)	12	0	32	Reference	–	–	–
UK	9 (16 %)	907 (12 %)	14.3 (15.0)	10	0	47	−0.6	0.3	−1.3 to 0.1	0.0897
Australia	5 (9 %)	268 (4 %)	27.6 (16.7)	36	3	43	20.6	0.8	19.0 to 22.3	<0.0001
Others	32 (57 %)	4062 (54 %)	18.6 (14.0)	15	0	68	8.9	0.2	8.5 to 9.4	<0.0001
Study type										
RCT	39 (70 %)	6075 (81 %)	16.8 (12.1)	13	0	47	Reference	–	–	–
Others	17 (30 %)	1455 (19 %)	19.7 (17.9)	15	0	68	2.6	0.4	1.7 to 3.4	<0.0001
Recruitment method										
Outpatient settings	31 (55 %)	3643 (48 %)	18.3 (12.3)	15	0	47	Reference	–	–	–
Primary care clinic after regular visits	17 (30 %)	3424 (46 %)	16.1 (12.7)	13	0	38	−3.3	0.2	−3.8 to −2.9	<0.0001
Community center	8 (14 %)	463 (6 %)	18.7 (22.8)	11	0	68	4.1	1.0	2.2 to 6.0	<0.0001
Quality assessment										
Cochrane High	11 (20 %)	1286 (17 %)	17.6 (14.2)	13	1	47	Reference	–	–	–
Cochrane Fair	21 (37 %)	3988 (53 %)	15.4 (10.4)	12	0	43	−2.4	0.3	−3.1 to −1.7	<0.0001
SIGN Well covered	6 (11 %)	703 (9 %)	20.5 (15.2)	14	8	43	−1.7	0.5	−2.6 to −0.8	0.0002
SIGN Adequate	10 (18 %)	697 (9 %)	19.2 (21.0)	15	0	68	4.2	0.8	2.6 to 15.8	<0.0001
Cochrane or SIGN Poor	8 (14 %)	856 (12 %)	19.5 (13.6)	19	0	38	3.0	0.5	2.0 to 4.0	<0.0001

3.5. Characteristics of intervention-related variables

The interventions provided in different studies were mostly home support system (66 %), aimed at delivering self-management support (32 %). The intervention setting was primarily patients' home (93 %), and the interventions were mostly web-based and provided through the internet, smartphone, tablet, and laptop (66 %). The control groups were mainly provided with usual care (57 %). The majority of studies (75 %) included guidance by a health professional. Most protocols required that patients monitor their parameter measurements daily (66 %) (Table 3).

3.6. Enrollment and dropout rates

Fig. 2 presents the flowchart of the numbers of participants from all included studies. A total of 14812 participants with COPD were approached, of whom 7530 consented to participate. The number of participants who dropped out from the intervention and control groups was 673 and 451 participants, respectively. This gave a total number of 1124 dropout participants across all the included studies. Using the random effects meta-regression model, the estimated enrollment rate and dropout rate of the included studies were 50.3 % (95 % CI 47.7 to 50.9) and 14.9 % (95 % CI 14.7 to 15.2); respectively (Table 4). The specific dropout rate of each study along with their 95 % CI is shown in Fig. 3.

The effects of trial-related variables on the enrollment rates indicated that studies using non-RCT designs had a higher enrollment rate by 20.3 % than studies which used RCT design. Compared with those studies recruiting from outpatient settings, the enrolment rate was higher by 12.6 % and 3.9 % in studies recruiting from primary care clinics, and community centers, respectively (Table 5). The effect of trial-related variables on dropout rates indicated that studies using other designs had a higher dropout rate by 2.6 % compared

Table 7
Effect of patient-related variables on dropout rate.

Variables	N (%) of studies	N (%) of participants	Un-weighted Dropout rate (%)				Estimated difference in Dropout rate in comparison to referent category			
			Mean (SD)	Median	Min	Max	Estimate	SE	95 % CI	p-value
Age										
60–69	35 (62 %)	5557 (74 %)	18.7 (15.4)	14	0	68	Reference	–	–	–
70 and over	19 (34 %)	1876 (25 %)	15.5 (12.1)	13	0	43	4.1	0.3	3.6 to 4.6	<0.0001
Not reported	2 (4 %)	97 (1 %)	19.5 (0.7)	20	19	20	5.8	0.2	5.5 to 6.1	<0.0001
Gender (% of men)										
<50 %	21 (37 %)	2234 (30 %)	23.2 (16.3)	18	1	68	Reference	–	–	–
50–64 %	15 (27 %)	1828 (24 %)	17.5 (13.9)	15	0	43	−1.0	0.4	−1.7 to −0.3	0.0080
≥65 %	18 (32 %)	3302 (44 %)	11.9 (9.0)	10.5	0	27	−8.0	0.3	−8.7 to −7.4	<0.0001
Not reported	2 (4 %)	166 (2 %)	12.5 (10.6)	12.5	5	20	−8.9	0.6	−10.1 to −7.7	<0.0001
Severity of disease (GOLD 3 or 4)										
≤50 %	10 (18 %)	1197 (16 %)	13.7 (11.5)	10.5	0	38	Reference	–	–	–
>50 %	25 (45 %)	4128 (55 %)	14.2 (12.2)	12	0	43	−4.1	0.3	−4.8 to −3.5	<0.0001
Missing	21 (37 %)	2205 (29 %)	23.7 (15.5)	20	0	68	7.1	0.4	6.4 to 7.9	<0.0001
FEV1 %										
≤38 %	13 (23 %)	2100 (28 %)	15.2 (10.1)	14	0	32	Reference	–	–	–
39%–44 %	9 (16 %)	1102 (15 %)	15.3 (13.1)	15	1	43	−5.3	0.4	−6.0 to −4.5	<0.0001
≥45 %	24 (43 %)	3762 (50 %)	13.8 (10.2)	11	0	43	−7.6	0.2	−8.0 to −7.2	<0.0001
Missing	10 (18 %)	566 (7 %)	32.2 (18.9)	36	4	68	11.9	0.8	10.4 to 13.4	<0.0001
Smoking (Intervention)										
Yes	43 (77 %)	6913 (92 %)	17.4 (14.1)	13	0	68	Reference	–	–	–
No	3 (5 %)	112 (1 %)	10.3 (9.3)	13	0	18	−0.5	0.5	−1.4 to 0.3	0.2334
Not reported	10 (18 %)	505 (7 %)	21.1 (14.9)	18	4	47	5.1	0.6	3.8 to 6.4	<0.0001
Patient's stability										
Stable after discharged	47 (84 %)	6234 (83 %)	16.7 (11.8)	14	0	47	Reference	–	–	–
Not stable after discharged	9 (16 %)	1296 (17 %)	22.7 (22.7)	15	0	68	−0.7	0.4	−1.6 to 0.1	0.0998

to studies that used RCT design. Compared with those studies recruiting from outpatient settings, the dropout rate was lower by 3.3 % in studies recruiting from primary care clinics, and higher by 4.1 % in studies recruiting from community centers (Table 6). Most trial-related variables had statistically significant effects on the estimated enrolment and dropout rates ($p < 0.0001$) (Tables 5 and 6).

The effect of patient-related variables on the dropout rate indicated that age, gender, and the severity of the disease were found to have the most effect on the dropout rate. Studies that included patients with a mean age of ≥70 years had a higher estimated dropout rate by 4.1 % than studies that included patients with a mean age of 60–69. Studies that consisted of 50%–64 % and ≥65 % of men had a lower dropout rate by 1 % and 8 %, respectively, compared to studies including <50 % of men. Studies with >50 % of patients with severe COPD (GOLD 3 or 4) had a lower dropout rate by 4.1 % than studies with ≤50 % of patients with severe COPD. Studies with FEV % ranged between 39% and 44 % or ≥45 % had a lower dropout rate by 5.3 % and 7.6 %, respectively, as compared to studies with FEV1 ≤38 %. Interestingly, studies that did not report or perhaps did not measure either GOLD or FEV1% had higher dropout rates by 7.1 % and 11.9 %, respectively (Table 7).

The effect of intervention-related variables on the dropout rate indicated that studies that delivered a digital health system had a higher estimated dropout rate by 12.8 % than a home support system (see **Appendix 2** for definitions). Compared to self-management consultation programs, self-management and coping skills had a lower dropout rate by 7.1, and higher by 0.4 % and 1.5 % for action plan and self-management education and lifestyle, respectively. Studies that had other modes of delivery had an estimated dropout rate lower by 7.7 % compared to using a telephone. Compared to interventions with durations of ≤ 3-month, the dropout rate was lower by 1.5 % for interventions lasting 7–24 months (Table 8). On examining the effect of patient-related variables (**Appendix 5**) and intervention-related variables (**Appendix 6**) on dropout rates within participants included in the intervention group only, some differences were noted in the magnitude of dropout rate estimates, but interpretations were the same. Most patient- and intervention-related variables had statistically significant effects on the estimated dropout rates ($p < 0.0001$).

Table 8
Effect of intervention related variables on dropout rate.

Variables	N (%) of studies	N (%) of participants	Un-weighted Dropout rate (%)				Estimated difference in Dropout rate in comparison to referent category			
			Mean (SD)	Median	Min	Max	Estimate	SE	95 % CI	p-value
Type of intervention										
Home support system	37 (66 %)	5009 (67 %)	14.0 (11.2)	12	0	38	Reference	–	–	–
Digital health system	13 (23 %)	1906 (25 %)	27.3 (17.7)	24	10	68	12.8	0.3	12.2 to 13.3	<0.0001
Others	6 (11 %)	615 (8 %)	19.2 (12.9)	18	8	43	5.1	0.4	4.4 to 5.8	<0.0001
Classification										
Self-management consultation	19 (34 %)	2263 (30 %)	14.2 (9.2)	12	0	27	Reference	–	–	–
Action plan	10 (18 %)	805 (11 %)	17.3 (13.9)	14	3	43	0.4	0.4	−0.5 to 1.2	0.3951
Self-management education and lifestyle changes	20 (36 %)	2588 (34 %)	19.4 (17.5)	13	0	68	1.5	0.3	0.9 to 2.1	<0.0001
Self-management and coping skills	4 (7 %)	1740 (23 %)	20.4 (18.2)	15	5	47	−7.1	0.2	−7.5 to −6.6	<0.0001
Others (self-management, education, action plan and lifestyle changes)	3 (5 %)	134 (2 %)	25.7 (10.8)	21	18	38	12.6	0.8	11.0 to 14.2	<0.0001
Mode of delivery										
Telephone	13 (23 %)	1439 (19 %)	21.8 (15.9)	20	0	43	Reference	–	–	–
Others	43 (77 %)	6091 (81 %)	16.4 (13.3)	13	0	68	−7.7	0.4	−8.4 to −7.0	<0.0001
Professional guide										
Nurse	19 (34 %)	1767 (23 %)	20.9 (13.4)	18	3	43	Reference	–	–	–
Nurse and Pulmonologist	5 (9 %)	420 (6 %)	8.8 (10.7)	7	0	26	−11.5	0.5	−12.4 to −10.5	<0.0001
Pulmonologist and primary care physician, GP, Primary care physician, Clinical psychologist, Medical resident	6 (11 %)	540 (7 %)	10.9 (9.5)	10	0	28	−5.1	0.5	−6.1 to −4.1	<0.0001
Respiratory therapist	8 (14 %)	1178 (16 %)	15.3 (13.7)	14	1	47	−8.7	0.4	−9.4 to −8.0	<0.0001
Others (Municipal healthcare worker, COPD educator, Operator, Researcher)	7 (13 %)	2306 (31 %)	16.2 (7.9)	15	5	27	−8.4	0.3	−9.1 to −7.8	<0.0001
Physiotherapist	3 (5 %)	200 (2 %)	18.7 (14.7)	21	3	32	5.3	0.8	3.7 to 7.0	<0.0001
Ward round team	8 (14 %)	1119 (15 %)	23.9 (21.7)	17	5	68	−0.5	0.5	−1.4 to 0.5	0.3751
Length of intervention										
≤3 months	21 (38 %)	1740 (23 %)	19.0 (18.1)	14	0	68	Reference	–	–	–
4–6 months	18 (32 %)	1727 (23 %)	16.6 (12.3)	12	0	43	−0.4	0.4	−1.3 to 0.5	0.3701
7–24 months	17 (30 %)	4063 (54 %)	17.2 (10.0)	16	1	43	−1.5	0.4	−2.3 to −0.8	<0.0001

Effect sizes were reported in 46 out of 56 studies among 6746 participants with COPD. The effect size ranged from 0.01 to 3.77 (Table 1). Results showed that studies with high (80%–100 %) enrolment rates had a smaller effect size by 0.04 compared to studies with low enrolment rates (7%–45 %). Studies with low dropout rates (6%–13 %) had a bigger effect size by 0.23 compared to studies with very low dropout rates (0%–5%) (Table 9). RCT Studies with quality assessment of Fair had a bigger effect size by 0.01 compared to RCT studies with High quality assessment (Table 10). Studies with 50%–64 % of men had a bigger effect size by 0.18 than studies including ≤50 % of men. Studies with >50 % of patients with severe COPD (GOLD 3 or 4) had a bigger effect size by 0.01 than studies with ≤50 % of patients with severe COPD. Studies with FEV1% ranged between 39% and 44 %, and ≥45 % had a lower effect size by 0.26 and 0.18, respectively, as compared to studies with FEV1 ≤38 % (Table 11). Studies that delivered the digital health system estimated a bigger effect size by 0.11 compared to the home support system. Compared to self-management consultation programs, action plan and self-management education and lifestyle changes had a bigger effect size by 0.29 and 0.09, respectively, and a smaller effect size by 0.23 for self-management and coping skills. Interventions of duration 4–6 months had an estimates of higher effect size by 0.24 compared to intervention of ≤3 months duration (Table 12).

Reasons for dropping out of the study were reported by 967 participants with COPD across 52 studies, as presented in **Appendix 7**. The main reasons for dropping out, at the patient level, were death (21 %), lost to follow-up (14 %), medical issues (11 %) and no interest in the intervention (8 %). Recommendations for improving enrolment rates and reducing dropout rates as suggested by authors

Table 9
Effect of enrolment rate and dropout rate on Effect size.

Variables	N (%) of studies	N (%) of participants	Un-weighted Effect size				Estimated difference in Effect size in comparison to referent category			
			Mean (SD)	Median	Min	Max	Estimate	SE	95 % CI	p-value
Enrollment rate										
7 %–45 % (low)	12 (28 %)	647 (10 %)	0.28 (0.26)	0.21	0.00	0.98	Reference	–	–	–
46 %–80 % (moderate)	13 (30 %)	1771 (28 %)	0.53 (1.04)	0.18	0.00	3.77	−0.15	0.01	−0.18 to −0.12	<0.0001
80 %–100 % (high)	18 (42 %)	3863 (62 %)	0.36 (0.39)	0.19	0.00	1.30	−0.04	0.01	−0.07 to −0.02	0.0017
Dropout rate										
0 %–5 % (very low)	9 (21 %)	1757 (28 %)	0.20 (0.30)	0.15	0.00	0.98	Reference	–	–	–
6 %–13 % (low)	13 (30 %)	2162 (34 %)	0.30 (0.37)	0.19	0.00	1.30	0.23	0.01	0.21 to 0.24	<0.0001
14 %–26 % (moderate)	12 (28 %)	1826 (29 %)	0.68 (1.02)	0.43	0.00	3.77	0.29	0.01	0.27 to 0.31	<0.0001
27 %–63 % (high)	9 (21 %)	536 (9 %)	0.33 (0.44)	0.18	0.03	1.43	0.14	0.01	0.12 to 0.17	<0.0001

*46 studies and 6746 participants.

of the included studies are presented in **Appendix 8**.

4. Discussion

This review reported results of the enrolment and dropout rates of telehealth interventions among individuals with COPD. The estimated enrollment and dropout rates across the included studies were 50.3 % and 14.9 %, respectively. To evaluate the potential benefit of a telehealth intervention in clinical care or a research context, individuals need to commit to enroll, adhere to the intervention protocol and recommendations, and complete the program.

The variables that were associated with enrollment and dropout rates rate were the trial-related variables including the RCT designs and the recruitments from outpatient clinics. The variables that associated with dropout rates were the patient-related variables including age, gender and severity of the disease, and intervention-related variables including the components of the intervention and mode of delivery. Effect size was influenced by trial, patient and intervention-related variables. A systematic review evaluated the overall attrition and dropout rates in telehealth interventions among individuals with COPD [67], resulting in an unweighted average of attrition (80 %) and dropout (19 %) rates. However, many limitations were raised from this study, including:

- The authors aimed to assess the overall attrition and dropout rates in telehealth interventions and to summarize the reasons for dropouts exploring the factors that impact overall attrition and dropout rates. Our review was more specific and aimed to: estimate the extent to which trial-related variables are associated with enrolment and dropout rates; estimate the extent to which patients-related and intervention-related variables are associated with dropout rates; estimate the effect of enrolment rate and dropout rate on effect size; and estimate the effect of trial-related, patient-related, and intervention-related variables on effect size.
- The authors claimed that they updated the review until April 2021 and included 27 studies, whereas the search should include more than 44 studies. We expanded the search to learn from all studies, including RCTs and observational studies. As we stated previously, this review was updated twice: one in October 2019, including 44 studies, and the other update was October 2021 and yielded a total of 56 articles.
- The authors claimed that they used only the Cochrane Risk of Bias to assess the bias of the included studies. This raises a question regarding how they assess the bias for non-RCT studies when Cochrane Risk of Bias is used to assess RCTs only.
- The authors used a meta-analysis to estimate the pooled difference in acceptance and dropout rates, including RCT and non-RCT studies, which raises another question about how they pooled the data from non-RCT studies.

Therefore, we cannot compare our results to this systematic review because of the trust issue of the published results.

One modifiable variable that can alter the enrolment rate is the recruitment method. We found that incorporating more than one recruitment method was found to increase the enrolment rate. The enrolment rate was lower in RCTs compared to other designs, perhaps because random assignment to a control group, perceived as less beneficial, might not have appealed to participants. However, the dropout rate was lower in RCTs compared to other designs. An explanation may be related to RCTs having stricter protocols for follow-up and retention of participants. Willingness to participate was associated with older age, having no children, and having already participated in clinical trials. Furthermore, multiple challenges were identified as impacting enrolment, including factors that affect access to tele-health, such as repeated hospitalization, medication management, and comorbidities [8,10,11,47,66].

Based on Cochrane systematic reviews, we can also highlight the lack of robust studies evaluating the effectiveness of the different technologies relating to telehealth interventions. Researchers should ensure that trials are adequately powered, developed with high

Table 10
Effect of trial-related variables on Effect size.

Variables	N (%) of studies	N (%) of participants	Un-weighted Effect size				Estimated difference in Effect size in comparison to referent category			
			Mean (SD)	Median	Min	Max	Estimate	SE	95 % CI	p-value
Publication years										
2015–2019	30 (70 %)	5050 (80 %)	0.41 (0.71)	0.19	0.00	3.77	Reference	–	–	–
2010–2014	12 (28 %)	1116 (18 %)	0.37 (0.42)	0.19	0.00	1.43	0.13	0.01	0.12 to 0.15	<0.0001
2000–2009	1 (2 %)	115 (2 %)	0.10 (NA)	0.10	0.10	0.10	−0.14	0.004	−0.15 to −0.14	<0.0001
Study place										
Denmark	7 (16 %)	1991 (32 %)	0.18 (0.17)	0.19	0.00	0.51	Reference	–	–	–
UK	7 (16 %)	822 (13 %)	0.42 (0.57)	0.10	0.00	1.43	0.34	0.01	0.32 to 0.36	<0.0001
Australia	5 (12 %)	268 (4 %)	0.16 (0.13)	0.18	0.03	0.36	0.08	0.005	0.07 to 0.09	<0.0001
Others	24 (56 %)	3200 (51 %)	0.49 (0.78)	0.23	0.01	3.77	0.21	0.005	0.20 to 0.22	<0.0001
Study type										
RCT	29 (67 %)	4951 (79 %)	0.31 (0.34)	0.19	0.00	1.43	Reference	–	–	–
Others	14 (33 %)	1330 (21 %)	0.56 (1.00)	0.17	0.00	3.77	−0.01	0.01	−0.03 to 0.02	0.6873
Recruitment method										
Outpatient settings	24 (56 %)	2931 (47 %)	0.38 (0.41)	0.21	0.00	1.43	Reference	–	–	–
Primary care clinic after regular visits	11 (25 %)	2887 (46 %)	0.25 (0.31)	0.10	0.01	0.98	−0.01	0.01	−0.02 to 0.00	0.1048
Community center	8 (19 %)	463 (7 %)	0.62 (1.28)	0.19	0.00	3.77	0.01	0.02	−0.03 to 0.05	0.5015
Quality assessment										
Cochrane High	6 (14 %)	575 (9 %)	0.49 (0.54)	0.28	0.06	1.43	Reference	–	–	–
Cochrane Fair	18 (42 %)	3792 (60 %)	0.25 (0.25)	0.21	0.00	0.98	0.04	0.01	0.02 to 0.05	<0.0001
SIGN Well covered	5 (11 %)	675 (11 %)	0.16 (0.21)	0.07	0.00	0.51	−0.17	0.01	−0.19 to −0.16	<0.0001
SIGN Adequate	9 (21 %)	655 (11 %)	0.77 (121)	0.18	0.00	3.77	0.19	0.02	0.15 to 0.24	<0.0001
Cochrane or SIGN Poor	5 (11 %)	584 (9 %)	0.30 (0.35)	0.19	0.03	0.87	0.06	0.01	0.04 to 0.08	<0.0001

*46 studies and 6746 participants.

methodological quality, and in compliance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines [68].

The effects of all patient-related variables on dropout rates were statistically significant, although not all were clinically significant. Age, gender and severity of the disease were found to have the most statistically significant effects on dropout rates. Although patient-related variables are not modifiable, interventions guided by healthcare professionals using strategies such as motivational messages tailored to individuals' profiles can reduce dropout rates and increase patients' engagement and motivation [69]. Using different strategies were highlighted by recommendations provided by researchers, which include providing incentives, encouragement, constant monitoring, structured support, and acknowledging the health literacy of participants to increase adherence to the interventions [42].

Regarding intervention-related variables, studies with a digital health system had a higher dropout rate compared to home support system. A possible explanation is that the majority of home support systems were guided by health professionals and peer-led health education and social support [8,10–12]. Online support groups can be asynchronous or synchronous, providing a range of therapeutic benefits that are similar to face-to-face support groups [4,47]. Most home support systems were provided through more convenient methods using videoconferencing [43,53], which saved time and made travelling to an intervention site unnecessary.

Moreover, results showed that studies with longer interventions (≥7-month) had lower dropout rates compared to shorter interventions (≤3-month). A possible reason could be that shorter interventions would not allow participants to master the required skills, increasing the dropout rate. However, in the case of longer interventions, participants may feel invested in these studies and hence feel more encouraged to continue. Another explanation is related to the complexity of the intervention, as short-term studies tend to examine interventions with many components, such as self-management education and lifestyle. This complexity may overwhelm the participants, which leads them to drop out from the study. A take-home note for health professionals is to provide telehealth interventions that aim at long-term goals with gradual addition of components adapted to accommodate the different challenges that

Table 11
Effect of patient-related variables on Effect size.

Variables	N (%) of studies	N (%) of participants	Un-weighted Effect size				Estimated difference in Effect size in comparison to referent category			
			Mean (SD)	Median	Min	Max	Estimate	SE	95 % CI	p-value
Age										
60–69	28 (65 %)	4727 (75 %)	0.48 (0.76)	0.23	0.00	3.77	Reference	–	–	–
70 and over	15 (35 %)	1554 (25 %)	0.23 (0.23)	0.18	0.01	0.87	−0.04	0.01	−0.05 to −0.02	0.0002
Not reported	0 (0 %)	0 (0 %)	NA	NA	NA	NA	NA	NA	NA	NA
Gender (% of men)										
<50 %	16 (37 %)	1526 (24 %)	0.27 (0.21)	0.27	0.01	0.68	Reference	–	–	–
50–64 %	12 (28 %)	1718 (27 %)	0.29 (0.21)	0.24	0.05	0.72	0.18	0.01	0.16 to 0.19	<0.0001
≥65 %	15 (35 %)	3037 (49 %)	0.40 (0.36)	0.36	0.01	1.20	0.00	0.01	−0.01 to 0.02	0.5990
Not reported	0 (0 %)	0 (0 %)	NA	NA	NA	NA	NA	NA	NA	NA
Severity of disease (GOLD 3 or 4)										
≤50 %	8 (19 %)	992 (16 %)	0.12 (0.11)	0.12	0.00	0.31	Reference	–	–	–
>50 %	20 (46 %)	3541 (56 %)	0.25 (0.30)	0.17	0.00	0.99	0.01	0.005	0.01 to 0.02	0.0021
Missing	15 (35 %)	1748 (28 %)	0.72 (0.94)	0.36	0.01	3.77	0.53	0.01	0.51 to 0.56	<0.0001
FEV1 %										
≤38 %	9 (21 %)	1547 (25 %)	0.33 (0.29)	0.22	0.00	0.87	Reference	–	–	–
39%–44 %	7 (16 %)	934 (15 %)	0.29 (0.33)	0.19	0.02	0.99	−0.26	0.01	−0.28 to −0.24	<0.0001
≥45 %	20 (47 %)	3361 (53 %)	0.54 (0.87)	0.21	0.00	3.77	−0.18	0.01	−0.20 to −0.16	<0.0001
Missing	7 (16 %)	439 (7 %)	0.14 (0.11)	0.15	0.01	0.32	−0.29	0.01	−0.30 to −0.27	<0.0001
Smoking (Intervention)										
Yes	34 (79 %)	5920 (94 %)	0.32 (0.39)	0.18	0.00	1.43	Reference	–	–	–
No	2 (5 %)	52 (1 %)	0.26 (0.14)	0.26	0.16	0.36	0.08	0.01	0.06 to 0.11	<0.0001
Not reported	7 (16 %)	309 (5 %)	0.77 (1.33)	0.19	0.07	3.77	0.16	0.04	0.08 to 0.24	0.0001
Patient's stability										
Stable after discharged	36 (84 %)	5146 (82 %)	0.43 (0.68)	0.19	0.00	3.77	Reference	–	–	–
Not stable after discharged	7 (16 %)	1135 (18 %)	0.16 (0.12)	0.18	0.02	0.32	−0.16	0.01	−0.17 to −0.14	<0.0001

*46 studies and 6746 participants.

are faced by patients in their everyday lives.

Acknowledging the identified variables in this study that influence the enrolment and dropout rates in telehealth interventions is important, as these variables have been found to influence the effect size of interventions. Our results indicating that a higher enrolment rate corresponded with a smaller effect size while a lower dropout rate was associated with a larger effect size. One explanation may relate to the combined effect of trial-related variables, patient-related variables, and intervention-related variables on the effect size. Such findings have been considered in a study indicating that participants who are benefitting less from the telehealth interventions are dropping out, enhancing the resultant effect of interventions and leading to biased parameter estimates [7]. This loss to follow-up would lead to overestimating treatment effectiveness [7]. Therefore, understanding the patterns and reasons for dropping out is very important, as they affect the validity and generalizability of studies.

The potential interest of telehealth interventions is to allow professionals to demonstrate and deliver exercise guidance virtually in real-time while participants complete the intervention from home [70]. Also, gaming approaches and guidance by a health professional can enhance engagements [69].

In this study we did not report on adherence, which for almost all studies is inadequately captured making it difficult to draw collective conclusions about adherence rates. Adherence is difficult to track, as it requires capturing participant's uptake of the defined protocol for the intervention. The challenge of measuring adherence influences the impact of interventions in a given study and the ability to compare results between studies that use different methods of study designs, recruitments and retention rates.

Table 12
Effect of intervention related variables on Effect size.

Variables	N (%) of studies	N (%) of participants	Un-weighted Effect size				Estimated difference in Effect size in comparison to referent category			
			Mean (SD)	Median	Min	Max	Estimate	SE	95 % CI	p-value
Type of intervention										
Home support system	28 (65 %)	4236 (67 %)	0.44 (0.75)	0.19	0.00	3.77	Reference	–	–	–
Digital health system	10 (23 %)	1749 (28 %)	0.28 (0.28)	0.20	0.00	0.87	0.11	0.01	0.09 to 0.13	<0.0001
Others	5 (12 %)	296 (5 %)	0.33 (0.38)	0.18	0.00	0.99	−0.02	0.02	−0.06 to 0.02	0.3988
Classification										
Self-management consultation	15 (35 %)	1946 (31 %)	0.47 (0.94)	0.19	0.00	3.77	Reference	–	–	–
Action plan	6 (14 %)	438 (7 %)	0.44 (0.39)	0.36	0.06	0.98	0.29	0.02	0.26 to 0.33	<0.0001
Self-management education and lifestyle changes	17 (39 %)	2372 (38 %)	0.33 (0.42)	0.18	0.00	1.43	0.09	0.01	0.07 to 0.11	<0.0001
Self-management and coping skills	2 (5 %)	1391 (22 %)	0.03 (0.02)	0.03	0.01	0.04	−0.23	0.01	−0.25 to −0.22	<0.0001
Others (self-management, education, action plan and lifestyle changes)	3 (7 %)	134 (2 %)	0.44 (0.49)	0.31	0.03	0.99	0.13	0.04	0.06 to 0.20	0.0004
Mode of delivery										
Telephone	10 (23 %)	1233 (20 %)	0.12 (0.13)	0.09	0.00	0.36	Reference	–	–	–
Others	33 (77 %)	5048 (80 %)	0.47 (0.70)	0.22	0.00	3.77	0.20	0.01	0.19 to 0.21	<0.0001
Professional guide										
Nurse	18 (41 %)	1712 (27 %)	0.32 (0.32)	0.19	0.01	0.99	Reference	–	–	–
Nurse and pulmonologist	3 (7 %)	257 (4 %)	0.37 (0.42)	0.29	0.00	0.82	0.15	0.02	0.11 to 0.19	<0.0001
Pulmonologist and primary care physician, GP, Primary care physician, Clinical psychologist, Medical resident	2 (5 %)	102 (2 %)	0.20 (0.05)	0.20	0.16	0.23	−0.11	0.01	−0.12 to −0.09	<0.0001
Respiratory therapist	6 (14 %)	1108 (18 %)	0.15 (0.19)	0.08	0.00	0.49	−0.23	0.01	−0.25 to −0.22	<0.0001
Others (Municipal healthcare worker, COPD educator, Operator, Researcher)	6 (14 %)	2264 (36 %)	0.96 (1.48)	0.28	0.00	3.77	−0.17	0.01	−0.19 to −0.15	<0.0001
Physiotherapist	2 (5 %)	66 (1 %)	0.19 (0.18)	0.19	0.06	0.31	−0.16	0.02	−0.20 to −0.13	<0.0001
Ward round team	6 (14 %)	772 (12 %)	0.42 (0.46)	0.26	0.01	1.30	0.15	0.02	0.11 to 0.19	<0.0001
Length of intervention										
≤3 months	14 (33 %)	1305 (21 %)	0.35 (0.46)	0.17	0.00	1.43	Reference	–	–	–
4–6 months	16 (37 %)	1559 (25 %)	0.51 (0.91)	0.21	0.00	3.77	0.24	0.01	0.23 to 0.26	<0.0001
7–24 months	13 (30 %)	3417 (54 %)	0.29 (0.32)	0.18	0.01	0.99	0.01	0.01	−0.001 to 0.02	0.0890

*46 studies and 6746 participants.

5. Strengths and limitations

Beneficial contribution of this review is due to: providing estimates of the enrolment and dropout rates of COPD telehealth interventions and their related variables; and identifying inputs from individuals with COPD regarding reasons for refusing or dropping out of these interventions. There are several limitations in this review that need to be addressed. This review excluded unpublished or grey literature and included only studies that were published in peer-reviewed journals. In this review, we did not evaluate the quality of the interventions using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, as the purpose was to explore possible variables that can influence enrolment and dropout rates. Moreover, other variables have been suggested as influencing the dropout rates, such as education and emotional status. This review could not include these variables in the analyses, as sufficient information was not provided in the included studies. In addition, we were unable to evaluate adherence as few studies measured and reported on adherence.

6. Conclusions

Trial, patient, and intervention-related variables were found to influence COPD telehealth interventions' enrolment and dropout rates. Tailoring interventions to best suit the needs, preferences, and lifestyles of individuals with COPD is crucial to help plan and develop a more appealing telehealth intervention that patients can easily accept and incorporate into their everyday lives. Furthermore, incorporating these findings into future clinical trials can enhance the enrolment rates and reduce the dropout rates, thus preventing biased estimates of studies outcomes and strengthening their generalizability.

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Ethics approval

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Consent to participate

Not applicable.

Consent for publication

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Data availability

Sharing research data helps other researchers evaluate your findings, build on your work and increase trust in your article. We encourage all our authors to make as much of their data publicly available as reasonably possible. Please note that your response to the following questions regarding the public data availability and the reasons for potentially not making data available will be available alongside your article upon publication.

CRediT authorship contribution statement

Rehab Alhasani: Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Tania Janaudis Ferreira:** Writing – review & editing, Validation, Methodology, Conceptualization. **Marie-France Valois:** Writing – review & editing, Validation, Software, Formal analysis. **Dharmender Singh:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Sara Ahmed:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

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Appendix A. Supplementary data

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