Supplementary

Appendix 1: PRISMA Checklist, The effect of monitoring adherence to regular inhaled corticosteroid (ICS) alone or in combination with a long-acting β2-agonist (LABA) using electronic methods on asthma outcomes: a narrative systematic review

		Reporting Item	Page Number
Title			
Title	#1	Identify the report as a systematic review	1
Abstract			
Abstract	#2	Report an abstract addressing each item in the PRISMA 2020 for Abstracts checklist	1
Introduction			
Background/rationale	#3	Describe the rationale for the review in the context of existing knowledge	2-3
Objectives	#4	Provide an explicit statement of the objective(s) or question(s) the review addresses	3
Methods			
Eligibility criteria	#5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses	4
Information sources	#6	Specify all databases, registers, websites, organisations, reference lists, and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted	6
Search strategy	#7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used	6
Selection process	#8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and, if applicable, details of automation tools used in the process	7
Data collection process	#9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and, if applicable, details of automation tools used in the process	7
Data items	#10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in	7

		each study were sought (for example, for all measures, time points, analyses), and, if not, the methods used to decide which results to collect	
Study risk of bias assessment	#11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and, if applicable, details of automation tools used in the process	7-8
Effect measures	#12	Specify for each outcome the effect measure(s) (such as risk ratio, mean difference) used in the synthesis or presentation of results	7
Synthesis methods	#13a	Describe the processes used to decide which studies were eligible for each synthesis (such as tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5))	8
Synthesis methods	#13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics or data conversions	7
Synthesis methods	#13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses	7
Synthesis methods	#13d	Describe any methods used to synthesise results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used	7
Synthesis methods	#13e	Describe any methods used to explore possible causes of heterogeneity among study results (such as subgroup analysis, meta-regression)	7
Synthesis methods	#13f	Describe any sensitivity analyses conducted to assess robustness of the synthesised results	7
Reporting bias assessment	#14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases)	7-8
Certainty assessment	#15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome	7-8
Data items	#10b	List and define all other variables for which data were sought (such as participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information	7

Results			
Study selection	#16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram (http://www.prisma-statement.org/PRISMAStatement/FlowDiagram)	8-9
Study selection	#16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded	8-9
Study characteristics	#17	Cite each included study and present its characteristics	10-12
Risk of bias in studies	#18	Present assessments of risk of bias for each included study	15-16
Results of individual studies	#19	For all outcomes, present for each study (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (such as confidence/credible interval), ideally using structured tables or plots	10-15
Results of syntheses	#20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies	N/A (narrative approach)
Results of syntheses	#20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (such as confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect	N/A (narrative approach)
Results of syntheses	#20c	Present results of all investigations of possible causes of heterogeneity among study results	N/A (narrative approach)
Results of syntheses	#20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesised results	N/A (narrative approach)
Risk of reporting biases in syntheses	#21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed	N/A (narrative approach)
Certainty of evidence	#22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed	N/A (narrative

			approach)
Discussion			
Results in context	#23a	Provide a general interpretation of the results in the context of other evidence	16
Limitations of included studies	#23b	Discuss any limitations of the evidence included in the review	18-19
Limitations of the review methods	#23c	Discuss any limitations of the review processes used	18-19
Implications	#23d	Discuss implications of the results for practice, policy, and future research	19
Other information			
Registration and protocol	#24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered	19
Registration and protocol	#24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared	19
Registration and protocol	#24c	Describe and explain any amendments to information provided at registration or in the protocol	19
Support	#25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review	19
Competing interests	#26	Declare any competing interests of review authors	19
Availability of data, code, and other materials	#27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review	n/a

Appendix 2: Draft electronic search strategy

Database	#	Index and keyword terms
Cochrane	#1	MeSH descriptor: [Asthma] explode all trees
	#2	(asthma* OR wheez* OR bronchospasm OR bronchoconstrict* OR "bronchial hypersensitiv*" OR "bronchial hyperreactiv*" OR "bronchial hyperresponsiv*" OR "bronchial allerg*" OR "bronchial constrict*" OR "respiratory hypersensitiv*" OR "respiratory hyperreactiv*" OR "respiratory hyperresponsiv*" OR "respiratory allerg*" OR "respiratory constrict*" OR "airway hypersensitiv*" OR "airway hyperreactiv*" OR "airway hyperresponsiv*" OR "airway allerg*" OR "airway constrict*"):ti,ab,kw
		#1 OR #2
	#3	MeSH descriptor: [Metered Dose Inhalers] this term only
	#4	MeSH descriptor: [Dry Powder Inhalers] this term only
	#5	(inhal* OR "inhaled corticosteroid*" OR "inhaled steroid*" OR "asthma* control*
	#6	medication*" OR "asthma* reliever medication*"):ti,ab,kw
		#4 OR #5 OR #6
	#7	(electronic OR digital OR technolog* OR device* OR audiovisual OR monitor* OR
	#8	emd* OR record* OR intervention* OR remind* OR "adherence digital monitor*" OR "adherence electronic monitor*" OR smart OR track* OR datalog* OR mdilog* OR "mdi chronology" OR propeller):ti,ab,kw
	#9	#7 AND #8
	#10	#3 AND #9
PubMed		((("Asthma"[Mesh]) OR ((asthma*[Title/Abstract] OR wheez*[Title/Abstract] OR bronchospasm[Title/Abstract] OR bronchoconstrict*[Title/Abstract] OR "bronchial hypersensitiv*"[Title/Abstract] OR "bronchial hyperreactiv*"[Title/Abstract] OR "bronchial hyperresponsiv*"[Title/Abstract] OR "bronchial allerg*"[Title/Abstract] OR "bronchial constrict*"[Title/Abstract] OR "respiratory hypersensitiv*"[Title/Abstract] OR "respiratory hyperreactiv*"[Title/Abstract] OR "respiratory hyperresponsiv*"[Title/Abstract] OR "respiratory allerg*"[Title/Abstract] OR "respiratory constrict*"[Title/Abstract] OR "airway hypersensitiv*"[Title/Abstract] OR "airway hyperreactiv*"[Title/Abstract] OR "airway hyperresponsiv*"[Title/Abstract] OR "airway allerg*"[Title/Abstract] OR "airway constrict*"[Title/Abstract])))) AND ((((("Metered Dose Inhalers"[Mesh] OR "Dry Powder Inhalers"[Mesh])) OR ((inhal*[Title/Abstract] OR "inhaled corticosteroid*"[Title/Abstract] OR "inhaled steroid*"[Title/Abstract] OR "asthma* control* medication*"[Title/Abstract] OR "asthma* reliever medication*"[Title/Abstract])))) AND ((electronic[Title/Abstract] OR digital[Title/Abstract] OR technolog*[Title/Abstract] OR device*[Title/Abstract] OR audiovisual[Title/Abstract] OR monitor*[Title/Abstract] OR emd*[Title/Abstract] OR record*[Title/Abstract] OR intervention*[Title/Abstract] OR remind*[Title/Abstract] OR "adherence digital monitor*"[Title/Abstract] OR "adherence electronic monitor*"[Title/Abstract] OR

		smart[Title/Abstract] OR track*[Title/Abstract] OR datalog*[Title/Abstract] OR mdilog*[Title/Abstract] OR “mdi chronology”[Title/Abstract] OR propeller[Title/Abstract])))
EMBASE	# 1 # 2 #3 #4 #5 #6 #7 #8 #9 #10 #11	'asthma'/exp asthma*:ti,ab OR wheez*:ti,ab OR bronchospasm:ti,ab OR bronchoconstrict*:ti,ab OR 'bronchial hypersensitiv*':ti,ab OR 'bronchial hyperreactiv*':ti,ab OR 'bronchial hyperresponsiv*':ti,ab OR 'bronchial allerg*':ti,ab OR 'bronchial constrict*':ti,ab OR 'respiratory hypersensitiv*':ti,ab OR 'respiratory hyperreactiv*':ti,ab OR 'respiratory hyperresponsiv*':ti,ab OR 'respiratory allerg*':ti,ab OR 'respiratory constric*':ti,ab OR 'airway hypersensitiv*':ti,ab OR 'airway hyperreactiv*':ti,ab OR 'airway hyperresponsiv*':ti,ab OR 'airway allerg*':ti,ab OR 'airway constrict*':ti,ab #1 OR #2 'inhaler'/exp inhal*:ti,ab OR 'inhaled corticosteroid*':ti,ab OR 'inhaled steroid*':ti,ab OR 'asthma* near/2 medication*':ti,ab #4 OR #5 electronic:ab,ti OR digital:ab,ti OR technolog*:ab,ti OR device*:ab,ti OR audiovisual:ab,ti OR monitor*:ab,ti OR emd*:ab,ti OR record*:ab,ti OR intervention*:ab,ti OR remind*:ab,ti OR 'adherence near/2 monitor*':ab,ti OR smart:ab,ti OR track*:ab,ti OR datalog*:ab,ti OR mdilog:ab,ti OR 'mdi chronolog':ab,ti OR propeller:ab,ti #6 AND #7 #3 AND #8 #9 AND #10
Web of Science	#1 #2 #3 #4 #5	TS= (asthma* OR wheez* OR bronchospasm OR bronchoconstrict* OR “bronchial hypersensitiv*” OR “bronchial hyperreactiv*” OR “bronchial hyperresponsiv*” OR “bronchial allerg*” OR “bronchial constrict*” OR “respiratory hypersensitiv*” OR “respiratory hyperreactiv*” OR “respiratory hyperresponsiv*” OR “respiratory allerg*” OR “respiratory constrict*” OR “airway hypersensitiv*” OR “airway hyperreactiv*” OR “airway hyperresponsiv*” OR “airway allerg*” OR “airway constrict*”) TS= (Inhal* OR “Inhaled corticosteroid*” OR “inhaled steroid*” OR “metered dose inhaler*” OR “dry powder inhaler*” OR “asthma* control* medication*” OR “asthma* reliever medication*”) TS= (electronic OR digital OR technolog* OR device* OR audiovisual OR monitor* OR EMD* OR record* OR intervention* OR remind* OR “adherence digital monitor*” OR “adherence electronic monitor*” OR smart OR track* OR datalog* OR MDIlog OR “MDI chronolog” OR propeller) #3 AND #2 #4 AND #1

Appendix 3: Data Extraction Sheet

Study	**Study design**	**No. of subjects**	**Population**	**Intervention**	**Comparative**	**Key Outcomes**	**Methods of adherence monitoring**	**Findings**
Berg 1998	RCT	55	Adult asthmatic patients	31 used MDI chronolog	24 used asthma diaries	Adherence score	MDI Chronotog	After a 6-week period, experimental group's adherence score increased and control group's adherence score decreased (U= 271, p=.043)
Boutopoulou 2018	SR	93	Severe outpatient asthmatic children	EMDs adherence interventions	Without adherence interventions	The influence of EMDs adherence interventions	EMDs	After six months of monitoring, baseline adherence rates 28% to 67% (control groups), after the intervention, rates increasing from 49 to 81%. Median adherence for whole population was 74%. Good adherence (≥80%) in 42% of patients, Suboptimal adherence (<80%) in 58% ($p < 0.0065$).
Jeminiwa 2019	SR & Meta-analysis	Total of 13,907 from 15 trials for qualitative synthesis and 12 trials for quantitative synthesis.	Children and adult asthmatic patients	eHealth	Usual care or without eHealth	• Effectiveness of eHealth on adherence to ICS • Types of eHealth in use	eHealth	eHealth adherence effect (SMD=0.41, 95%CI=0.02–0.79). Adherence effect in studies utilizing EMDs only as an adherence measure (SMD = 1.19, 95%CI = 0.49–1.89). MHealth adherence effect (SMD = 0.96, 95%CI = 0.28–1.64).

								MHealth adherence effect by utilizing EMDs (SMD = 1.28, 95%CI = 0.41–2.14). eHealth insignificant adherence effect in studies utilizing pharmacy refill data (SMD = −0.13, 95%CI = −0.70 – 0.44) or self-report (SMD = 0.25, 95%CI = −0.10 – 0.60), or social media, electronic health records, interactive voice response, telephone calls by health care providers (SMD = 0.20, 95%CI = −0.02 – 0.43).
Lee 2021	SR & Meta-analysis	Total of 1,123 from 10 trials	Children asthmatic patients	EMDs adherence interventions	Usual care, waitlist, or placebo	• Inhaler adherence • Clinical outcomes	EMDs	EMDs group was 1.50 times (RR = 1.50, 95% CI = 1.19–1.90) more likely to adhere to inhalers compared with the control (Z = 3.37, p < 0.001) with medium-to-large effect size (g = 0.64). C-ACT in the intervention group (Z = 2.42, p = 0.02) with a small effect size (g = 0.33). No significant differences in asthma exacerbation, lung function, or asthma control.
Chan 2022	Cochrane SR & Meta-analysis	Total of 15,207 from 30 studies	Children and adult asthmatic patients	Digital adherence intervention	Non-digital adherence intervention	• Adherence • Asthma Control • Exacerbation rate	Digital monitoring Vs. non digital monitoring	Adherence increase in poor baseline adherence patients (mean difference of 14.66

								percentage points, (95% CI 7.74 to 21.57). Asthma control increased by a small (SMD) 0.31 higher, (95% CI 0.17 to 0.44). Asthma exacerbations reduced (risk ratio 0.53, (95% CI 0.32 to 0.91). Quality increased (SMD) 0.26 higher, 95% CI 0.07 to 0.45). Adherence improved with EMDs (23 percentage points over control, 95% CI 10.84 to 34.16) Adherence improved with short message services (12 percentage points over control, (95% CI 6.22 to 18.03). No significant subgroup differences for in-person component Vs. fully electronic interventions, adherence feedback, one or multiple electronic components to the intervention, or participant age. No difference in lung function (forced expiratory volume in one second (FEV1) No data on cost-effectiveness or adverse events.

Pearce 2022	SR	Total of 3,913 from 15 trials	Children asthmatic patients	Adherence intervention to ICS with at least one outcome measure of adherence	Usual care or a basic education	adherence interventions aracteristics of successful herence interventions	Electronic adherence monitoring Vs. usual care	SmartTrack with audio-visual enabled Vs. with audio-visual disabled resulted in median adherence of 84% in the intervention group (10th percentile 54%, 90th percentile 96%), Vs. 30% in control group (8%, 68%) (p< .0001). Smartinhaler with feedback Vs. Smartinhaler alone, Smartinhaler with feedback (median adherence was 70% vs. 49% for control group) (p < .001), other study found mean percentage adherence intervention = 79% vs. control = 57.9% (p< .01). MHealth intervention Vs. control group (receiving only two reminders to sync their sensors). The unadjusted mean adherence: control = 40% vs. intervention = 34% (P = .56). A web-based interactive education and monitoring system Vs. education manual. Mean change since baseline for intervention= 11.2% increase vs. control= 4.4% decrease (p=.67).

Appendix 4: Data Extraction Sheet

Study Description	Search Strategy	Intervention	Comparator	Outcome Measures	Risk of bias	Study Findings	Electronic adherence Interventions	
							Pros (+)	Cons (-)
Impact of eHealth on medication adherence among patients with asthma: A systematic review and meta-analysis **(Jeminiwa et al., 2019a)**	A five databases search including PubMed, CINAHL, Academic Search Premier, PsycINFO, and International Pharmaceutical Abstracts (IPA) From inception until August 28, 2018	eHealth among children and adult asthmatic patients	Usual care or without eHealth intervention	• Effectiveness of eHealth on adherence to ICS • The types of eHealth in use	Clear quality appraisal of the studies	From a qualitative synthesis of 15 trials and quantitative synthesis of 12 trials, overall significant effect of eHealth interventions on adherence to ICS (SMD)=0.41, 95%CI = 0.02–0.79). Also, mHealth improved adherence VS. usual care in analysis of 4 trials (SMD=0.96, 95%CI=0.28–1.64).	**eHealth** A small effect (SMD=0.41,95%CI= 0.02–0.79) **MHealth** Effective and acceptable intervention in improving adherence in studies utilizing EMDs only as an adherence measure SMD = 1.19, 95% CI = 0.49–1.89).	**MHealth** Considered insignificant in pharmacy refill data or self-report as adherence measure. **eHealth** Insignificant effects include social media, electronic health records, interactive voice response, and healthcare telephone calls.

Interventions on Adherence to Treatment in Children with Severe Asthma: A Systematic Review **(Boutopoulou et al., 2018)**	A systematic search performed in MEDLINE, PubMed, Cochrane Library, and Scopus databases from January of 2012 to March of 2018	Children and/or adolescents with severe asthma and on medication adherence interventions.	Children and/or adolescents with severe asthma with usual care without adherence interventions	The influence of adherence intervention in improving adherence to controller inhaled medication in children with severe asthma.	No evidence of quality assessment.	One prospective observational cohort study evaluating the adherence rate of 93 severe outpatient asthmatic children for 6 months by EMDs, the baseline adherence rates ranged from 28% to 67%, after the EMDs, rates increasing from 49 to 81%.		**EMDs** After 6 months, Median adherence was 74%. Good adherence (≥80%) in 42% of patients, suboptimal adherence (<80%) in 58% ($p < 0.0065$).
Features of successful interventions to improve adherence to inhaled corticosteroids in children with asthma: A narrative systematic review **(Pearce et al., 2022)**	A systematic search performed in PubMed, Embase, Psych INFO, Medline, Web of Science, and Inter-national Pharmaceutical Abstracts databases from inception until October 3, 2020	Adherence intervention to ICS among asthmatic children.	Usual treatment or a basic education.	ICS adherence and the characteristics of successful adherence interventions.	Clear quality appraisal of the studies.	• 13 of the 25 identified studies were categorized as being highly reliable. • 9 of the 13 interventions were effective at increasing adherence. • 6 met the criteria for an adherence (the Perceptions and Practicalities Approach, PAPA) intervention.	**EMDs** • One study compared SmartTrack with audio-visual enabled Vs. audio-visual disabled with 84% median adherence in intervention group (10th percentile 54%, 90th percentile 96%), Vs. 30% in the control	**MHealth** One study compared MHealth intervention Vs. control group (receiving only two reminders to sync their sensors). The unadjusted mean adherence: control = 40% vs. intervention = 34% (P = .56). **eHealth**

						• 5 studies utilized electronic monitoring interventions: eHealth (n = 1) MHealth (n = 1) EMDs (n = 3)	group (8%, 68%) p< .0001. • Two studies compared EMDs with feedback Vs. EMDs alone, one study found increase in adherence by 21% in the EMDs with feedback group (median adherence was 70% vs. 49% (p < .001) and other study found mean adherence intervention = 79% vs. control = 57.9% (p< .01).	A study compared a web-based interactive education and monitoring system Vs. asthma education manual. Mean change since baseline for intervention= 11.2% increase vs. control= 4.4% decrease (p=.67).
Electronic adherence monitoring devices for	A systematic search using Cochrane Library,	Electronic adherence monitoring devices	Usual care, waitlist, or placebo group.	**Primary outcome** Inhaler adherence	Clear quality appraisal of the studies.	• 10 randomized controlled trials in 11 articles amongst 1123	**EMDs** Amongst 1,123 asthmatic children revealed that EMDs	

children with asthma: A systematic review and meta-analysis of randomized controlled trials **(Lee et al., 2021)**	PubMed, Embase, CINAHL, Web of Science, Scopus and ProQuest Dissertations and Theses from inception up to April 6, 2021.	attached to inhalers or built into the inhaler among asthmatic children.		**Secondary outcomes** Clinical outcomes including asthma exacerbation, lung function (FEV1), asthma control and acceptability.		participants were included in the meta-analysis. Meta-analysis revealed that the electronic adherence monitoring device group was 1.50 times more likely to adhere to inhalers compared with the control group with medium-to-large effect size (g = 0.64). • No significant subgroup differences were recognized among different parameters.	group was 1.50 times (RR = 1.50, 95% CI = 1.19–1.90) more likely to adhere to inhalers compared with the control (Z = 3.37, p < 0.001) with medium-to-large effect size (g = 0.64).	

Digital interventions to improve adherence to maintenance medication in asthma **(Chan et al., 2022)**	A search for clinical trials from the Cochrane Airways Trials Register The most recent searches on 1 June 2020, with no restrictions on language of publication.	Any digital adherence intervention among children and adult asthmatic patients	Any non-digital adherence intervention or usual care	**Primary outcomes** Adherence Asthma control Asthma exacerbations **Secondary outcomes** Unscheduled healthcare visits Time off school, work, or other commitments due to asthma Lung function Quality of life Cost-effectiveness Adverse events	Clear quality appraisal of the studies.	• 15% more people between 8% and 22% adherent by receiving digital technology Vs. without digital interventions. • Digital intervention group had better asthma control and half the risk of asthma attacks between 32% and 91%). • Quality of life and lung function, but the effect on lung function was small and may be of limited clinical relevance.	**Electronic interventions** Baseline adherence (mean difference 14.66 percentage points, 95% (CI) 7.74 to 21.57 **EMDs & MHealth** • EMDs adherence (23 percentage points over control, 95% CI 10.84 to 34.16 • MHealth adherence (12 percentage points over control, 95% CI 6.22 to 18.03; four studies) (P = 0.001). **Electronic interventions** • Asthma control Improve by (SMD) 0.31	**Electronic interventions** • Little or no difference in lung function (forced expiratory volume in one second (FEV1). • No data on cost-effectiveness or adverse events.

							higher, 95% CI 0.17 to 0.44. • Asthma exacerbations reduced (risk ratio 0.53, 95% CI 0.32 to 0.91. • Quality of life increased SMD 0.26 higher, 95% CI 0.07 to 0.45.	
Compliance with inhaled medications: The relationship between diary and electronic monitor **(Berg et al., 1998)**	A randomized, controlled study evaluating inhaler medication compliance, diary data to electronic monitoring	31 asthmatic patients were among electronic monitor using MDI Chronolog	24 asthmatic patients using daily asthma diary notes for six-week self-management program.	Adherence scores	No evidence of quality assessment.	Moderate correlations (r~ = -55, Mdnd = 95.8, Mdnc = 91.6) by comparing administrations by the Chronolog administrations reported in the subject's dairy.	**MDI Chronolog** The experimental group's adherence score increased while the control group's adherence score decreased (U= 271, p=.043).	**MDI Chronolog** Self-reported adherence was higher than monitored adherence.