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e-Monitoring of Asthma Therapy to Improve Compliance in children (e-MATIC): a randomised controlled trial

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ABSTRACT

Real-time medication monitoring (RTMM) is a promising tool for improving adherence to inhaled corticosteroids (ICS), but has not been sufficiently tested in children with asthma. We aimed to study the effects of RTMM with short message service (SMS) reminders on adherence to ICS, asthma control, asthma-specific quality of life and asthma exacerbation rate; and to study the associated cost-effectiveness.

In a multicentre, randomised controlled trial, children (aged 4–11 years) using ICS were recruited from five outpatient clinics and were given an RTMM device for 12 months. The intervention group also received tailored SMS reminders, sent only when a dose was at risk of omission. Outcome measures were adherence to ICS (RTMM data), asthma control (childhood asthma control test questionnaire), quality of life (paediatric asthma quality of life

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questionnaire) and asthma exacerbations. Costs were calculated from a healthcare and societal perspective.

We included 209 children. Mean adherence was higher in the intervention group: 69.3% versus57.3% (difference 12.0%, 95% CI 6.7%–17.7%). No differences were found for asthma control, quality of life or asthma exacerbations. Costs were higher in the intervention group, but this difference was not statistically significant.

RTMM with tailored SMS reminders improved adherence to ICS, but not asthma control, quality of life or exacerbations in children using ICS for asthma.

INTRODUCTION

Asthma is a serious global health problem and its prevalence is increasing in many countries, especially in children [1]. Asthma is associated with hospitalisations, decreased quality of life and a substantial economic burden [2, 3]. In a Dutch study [4], 55% of the children with doctor-diagnosed asthma had insufficient asthma control according to Global Initiative for Asthma (GINA) guidelines [5] in spite of the availability of effective maintenance therapy in the form of inhalation corticosteroids (ICS) [6]. This may be explained by poor adherence to ICS, which is on average ≤50% [7, 8].

Factors associated with nonadherence are broadly categorised into intentional and unintentional factors [9]. Intentional non-adherence may be due to limited illness perception, lack of confidence in the efficacy of treatment or perceived barriers, e.g. side-effects. Many educational and self-management interventions for improving intentional non-adherence have been studied, with limited effects [10]. In contrast, non-intentional non-adherence primarily associated with forgetfulness. To cope with this, interventions have been developed that focus on sending reminders to take the medicine. Systematic reviews have shown that sending short message service (SMS) reminders to patients can be effective in improving health outcomes [11] or in changing health behaviour [12].

A downside of the repetitive sending of SMS reminders at preset time intervals is that effects may wear off over time. This “alert fatigue” may be overcome by tailored SMS reminders that are sent only if a drug dose is at risk of omission. Tailoring SMS reminders requires the use of real-time medication monitoring (RTMM), which is an advanced version of the medication event monitoring system technology that has been proved to provide objective and reliable adherence data in various patient populations [13]. Three randomised controlled trials have evaluated the effect of RTMM with real-time patient feedback on adherence to ICS [14–16], one of which included children [14]. All studies reported higher adherence rates in patients receiving reminders: differences ranged from 18 to 54 percentage points. The study in children found that asthma control had improved as well, but only in the first 2 months after randomisation [14]. Moreover, the follow-up was limited to 6 months, so the persistence of the treatment effect was unclear. Furthermore, all studies used audiovisual reminders that were not available to parents, in real time, an essential consideration for improving adherence in children. In conclusion, our knowledge of the effect of RTMM with time-tailored SMS reminders is limited, especially in children with asthma, and no data exist on long-term use of RTMM.

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Therefore, we conducted the randomised controlled e-Monitoring of Asthma Therapy to Improve Compliance in children (e-MATIC) trial to compare the effects and cost-effectiveness of RTMM with tailored SMS reminders with RTMM alone, in children with asthma and their parents. We hypothesised that RTMM with SMS reminders would improve adherence to ICS and would subsequently improve asthma control, asthma-related quality of life and reduce asthma exacerbations.

METHODS

Study design

The e-MATIC study was a 1-year, multicentre, randomised controlled trial in children who use ICS for asthma. A comprehensive paper has been published on the e-MATIC study protocol [17]. All children received an RTMM device, which was connected to the pressurised metered-dose inhaler (pMDI) and recorded the time and date of administered ICS doses. Immediately after each actuation of the pMDI, data were sent to the study database through the mobile telephone network. In the intervention group only “time-tailored” SMS reminders were sent to the parents, and to the children, if they possessed a mobile phone, when a dose had not been recorded within 15 min of the planned time of administration.
Ethical approval was obtained from the medical ethics committee of the Erasmus Medical Center (Rotterdam, the Netherlands). Parents of all participants provided written informed consent. The e-MATIC study was registered with the Netherlands Trials Registry, number NTR2583 atwww.trialregister.nl.

Participants

Children were recruited from five outpatient clinics in the Netherlands. From the administration of each participating hospital, records were randomly selected of children aged 4–11 years who had doctor-diagnosed asthma for ≥6 months and who had visited the outpatient clinic in the past 12 months. After verifying the other inclusion criteria, the use of ICS (fluticasone, fluticasone/salmeterol or beclometasone) delivered via a pMDI for ≥3 months and having at least one parent/caregiver with a mobile phone, we contacted the parents and invited them to visit the paediatric outpatient department for an intake interview. A patient information leaflet was sent to the parents of the potential participants. If parents did not respond to our telephone calls, we retried three or four times before excluding the patient. Before patient inclusion, we obtained verbal and written informed consent from the parent or guardian.

Randomisation and masking

At registration at the RTMM software interface, children were automatically assigned to the intervention or control group. Computer-generated block randomisation was used per hospital with block size of 16 patients. Although physicians, researchers and patients were initially blinded for randomisation, patients were generally unblinded shortly after the start of the study period, when they found out whether they received SMS reminders or not.

Measurements and data collection

The primary outcome measure was timing adherence to ICS, defined as the proportion of all prescribed doses recorded by the RTMM device (E-haler/Adhaler;

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Evalan BV, Amsterdam, the Netherlands) within a 6-h time frame around the planned time of inhalation, i.e. from 3 h before to 3 h after.
Secondary outcome measures were asthma control, frequency of severe asthma exacerbations and asthma-specific quality of life. Asthma control was measured using the childhood asthma control test (c-ACT), which was completed each month of the follow-up period. The c-ACT is a seven-item questionnaire validated for detecting poorly controlled asthma in children aged 4–11 years [18]. In addition, the frequency of asthma exacerbations was collected as a measure of asthma control. Severe asthma exacerbations were defined as asthma-related hospitalisations, visits to the emergency department and/or episodes of systemic corticosteroid use [5, 19]. Hospital admissions and emergency department visits were collected from hospital records and oral corticosteroid burst therapy from dispensed-drug data of community pharmacies. Asthma-specific quality of life was assessed by completing the standardised paediatric asthma quality of life questionnaire (PAQLQ), at the beginning and end of the study period [20].
Patient characteristics were collected from medical records at the beginning and end of the study period. In addition, at the beginning and end of the study period, and each 3 months in between, parents were interviewed by research assistants about healthcare use, including contact with their general practitioner and school/work absence. Completed c-ACT and PAQLQ-questionnaires were collected. Research assistants were trained by the research team before interviewing patients.
Costs were calculated from a healthcare perspective and a societal perspective. The healthcare perspective included costs of outpatient hospital visits, hospital admissions, emergency room visits, general practitioner contacts and medication. For the societal perspective, parental production losses were also included for absence from paid work in order to care for their child. Resource use in hospitals was retrieved from hospital databases. For calculation of medication costs, lists of dispensed medication were obtained from community pharmacies. Costs (€, 2014) were calculated by multiplying the volume of resource use by cost per unit. Standard unit costs from the Dutch Manual for Costing Studies [21], adjusted for inflation, were used for all healthcare resource use (online supplementary table S1).
Medication prices were based on the official list prices of drugs published on the internet [22], including value added tax and increased by a standard prescription reimbursement for the pharmacist. The cost of production loss was calculated according to the friction cost approach [23].

Statistical analysis

Based on a power of 0.8 and a significance level of 0.05, a group size of 110 patients per arm was needed to detect an adherence difference of 15% between the intervention and control groups [17].
Data were analysed on an intention-to-treat basis. Patients with a follow-up of ≥7 days who actively used the RTMM device (adherence of ≥1.0%) were included in the data analysis. A per-protocol analysis was carried out including only patients with a minimum follow-up of 90, 180 and 270 days after randomisation.
Timing adherence was calculated per month; costs were calculated per 3-month period. Timing adherence, c-ACT, PAQLQ and costs were analysed in multilevel regression models for repeated measures (linear model with correlated errors and an exchangeable covariance matrix). For each outcome measure, the measurements at

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all moments in time were analysed simultaneously in a single regression model. Measurement (month) number and the interaction of measurement and treatment were used as explanatory variables. This made it possible to interpret the regression coefficients of the interaction terms as the effect estimates for the respective measurement times. The regression results were used to calculate adjusted means. Multilevel modelling exploits the fact that observations within patients are correlated. This allows the unbiased estimation of regression coefficients and to make optimal use of all the available data, even when some measurements are missing. This is achieved by adjusting the regression estimates for an optimal fit with the observed data as well as with the imposed correlation structure: all observations yield information on (the likelihood of) outcomes at all moments in time, even if these latter data are missing. This implies that all patients contributed to the estimates of the adjusted means in all intervals, although not everyone had measurements for all moments [24].
Adjusted exacerbation rates per treatment were calculated after applying negative binomial regression with treatment as explanatory variable, offset for time in study. Uncertainty around the point estimates was addressed using bootstrapping. Data were analysed in Stata 12.1 (StataCorp, College Station, TX, USA).

RESULTS

Participants

During the recruitment period (January 12, 2012 to December 7, 2012), out of the 563 children screened for eligibility, 219 were included in the study: 108 in the intervention group and 111 in the control group. 10 patients were excluded from the intention-to-treat analysis: seven in the intervention group and three in the control group (fig. 1). The baseline characteristics of the remaining 209 patients are presented in table 1. The groups were well balanced with regards to prognostic factors, notably asthma control, asthma-related quality of life, treatment location, type of RTMM device and medication belief. Mean±sd follow-up was 261.1±105.3 days in the control group and 251.2±123.4 days in the intervention group. This difference in follow-up was small and not statistically significant (hazard ratio for intervention versus control 1.08, p=0.569). Reasons why patients left the study prematurely were not systematically registered. No serious adverse events occurred during follow-up.

[FIGURE 1]

[TABLE 1]

Effect of SMS reminders on adherence to ICS

SMS reminders were sent about 56.8% of ICS doses in the intervention group. Approximately half of these reminders (53.3%) led to timely administration. Figure 2 shows the adjusted monthly adherence over the course of the study period. Especially during the first months of the study, patients in the intervention group were substantially more adherent than patients in the control group. In both treatment groups, adherence decreased steadily during the first 6

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months, after which it remained stable and statistically significant for most measurement times (fig. 2).

[FIGURE 2]

Over the full study period, adherence in the intervention group was 69.3% (95% CI 65.5–73.4%) and 57.3% (95% CI 52.8–61.7%) in the control group. The overall difference was statistically significant: 12.0% (95% CI 6.7–17.7%). The average estimated treatment effect over the first 6 months (15.0% (95% CI 9.3–20.7%)) was larger than in the second part of the year (9.0% (95% CI 2.4–16.3%)), but both were statistically significant (online supplementary table S2a). The results from the per-protocol analysis were comparable (online supplementary table S2b).
Results were similar when the analysis was restricted to patients with 6 or 9 months of follow-up (online supplementary table S2c and d).

Effect of SMS reminders on asthma control, quality of life and asthma exacerbations

The adjusted means of the c-ACT scores and PAQLQ scores at the end of follow-up and the frequency of asthma exacerbations were not different between the intervention and control groups (table 2). Mean c-ACT scores remained high and stable over time in both treatment groups (online supplementary figure S3).

[TABLE 2]

Costs

Total costs were higher in the intervention group, but the differences were not statistically significant: €731 versus €636 (difference €96, 95% CI €−55–271) from the healthcare perspective and €1043 versus €764 (difference €297 (95% CI €−13–437)) from a societal perspective (fig. 3, online supplementary table S5). Apart from the costs of the SMS intervention, only the costs for parental production losses due to absence from work were statistically significantly higher in the intervention group. When particularly high costs for one parent were excluded from the analysis, the difference in production losses decreased from €185 to €115 (95% CI €−55–271).

[FIGURE 3]

Discussion

The strength of the e-MATIC study was its prospective, randomised, controlled, multicentre design and, compared to other studies on medication adherence, a large study population and long follow-up period. Our study was the first to investigate RTMM with SMS reminders for 12 months in children with asthma. We found that the children receiving RTMM with time-tailored SMS reminders had higher timing adherence to ICS than the children with RTMM alone. The difference gradually declined during the first 6 months (adjusted mean 15.0%), but remained stable and statistically significant over the last 6 months (adjusted mean difference 9.0%).
The effect of RTMM with SMS reminders found in this study was larger than the estimates of treatment effects of most reported educational and self-management interventions aimed at improving adherence [10] and in the same range as that of periodical SMS reminders or telephone calls in patients with asthma [26]. The effect

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in our study (9% difference after 6–12 months) was smaller than in the only previous trial studying RTMM with real-time reminders in children with asthma (52% after 6 months) [14]. However, in that trial children were recruited from the emergency department after being diagnosed with an asthma exacerbation. The poor asthma control (mean c-ACT score <19) and low adherence (median 30%) at baseline may have contributed to the larger improvement in adherence than found in our population of clinically stable outpatients. In addition, the effect on adherence to ICS may have been overestimated by using a short follow-up period of 6 months, after which the effect is at risk of wearing off, as shown in our study.

No differences were found for asthma control (c-ACT score 21.1 versus 22.2), quality of life (mean PAQLQ score 6.2 versus 6.3) or asthma exacerbations (annual rate 0.23 versus 0.37). This disconnect between improved adherence but no improvement in health outcomes has been found in earlier studies on the effect of patient reminder systems in asthma patients [15, 26]. Interestingly, others have found an association between low adherence to ICS and higher risk of severe asthma exacerbations, but only in a limited number of high-quality studies [27]. Recently, Chan et al. [14] found a higher mean c-ACT score and a lower risk of exacerbations in children and adolescents with unstable asthma receiving RTMM with audiovisual reminders. However, this effect was absent after the first 2 months of follow-up.

The overall 12% improvement in adherence to ICS found in this study is not likely to be sufficient for clinically relevant improvement of asthma control. Parameters other than adherence, such as genetic factors [28] and environmental triggers [29] also contribute to asthma control. Klok et al. [30] hypothesised that asthma patients who have reached clinical remission and still receive treatment with ICS may maintain asthma control at a lower level of adherence than patients who have active asthma. This seems to apply to our study, since the majority of the population had good asthma control (c-ACT >19) despite suboptimal adherence rates. For example, in the control group, 63.5% of patients maintained good asthma control on an adherence level of 57.3%. This suggests that each patient has an individually defined critical ICS dose at which asthma control is only just maintained. As long as the ICS dose that is actually taken is higher than the critical ICS dose, asthma control does not deteriorate. Such overtreatment may explain the lack of effect on asthma control in our population. Another factor that might have contributed to our findings is the fact that c-ACT-based asthma control was reported to have <30% non-compatibility with GINA guideline base asthma control. Although the c-ACT is a validated questionnaire [18] and it is widely used for healthcare and research purposes, it seems to overestimate asthma control levels in children with poor asthma control or poor symptom perception [31, 32].

Apart from the costs of the SMS intervention itself, there was no statistically significant difference in costs between the intervention and control group, either from a healthcare perspective or from a societal perspective. The intervention costs were not outbalanced by a reduction in clinical costs for treating fewer asthma exacerbations in the intervention group.

RTMM is an objective and reliable method for measuring adherence [17]. Nevertheless, we may still have overestimated adherence. Being aware of the observations, children may have adhered to their medication regimens more than they would normally. Although too rare to introduce substantial errors, participants

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might even have fired their inhaler in order to fake the RTMM measurements [33]. In addition, ICS doses recorded may not have been inhaled using the correct inhalation technique. This could have interfered with the pharmacological action of ICS and therefore with patients' motivation to adhere to ICS therapy, and with the effect of ICS on asthma control and quality of life [34]. However, in this randomised trial, these phenomena are considered to be evenly distributed over both study arms.
During patient recruitment, 99 patients declined participation in the study. In addition, 110 patients did not respond to our telephone calls, despite the fact that we retried three or four times (fig. 1). If non-response to telephone calls or refusing to participate were associated with non-adherence to ICS-treatment, this may have caused pre-selection of patients with good adherence. This would have reduced the overall room for improvement of adherence, leading to an underestimation of the effect of the SMS intervention. However, we don't have any indication for the existence of such an association and it might well be that non-response is associated with better adherence rather than poorer adherence.
We found that patients in the control group had a longer follow-up period: mean±sd 261.1±105.3 days versus 251.2±123.4 days. This difference in follow-up was small and not statistically significant (hazard ratio for intervention versus control 1.08, p=0.569). Reasons why patients left the study prematurely were not systematically registered and could therefore not be analysed. We don't have any indications that dropping out of the study was associated with non-persistence with ICS, since the majority of the drop-out patients continued to use ICS after leaving the study. The difference in drop-out rate was addressed in the multilevel regression model, since it contained the treatment variable as a predictor of adherence.
Based on the RTMM data, no distinction could be made between intentional and unintentional non-adherence to ICS. Theoretically, SMS reminders are aimed at reducing the forgetting of ICS doses, which is a typical unintentional phenomenon. However, participating in a trial, and particularly receiving repetitive reminders may have raised awareness of the necessity of ICS treatment or of concerns about ICS treatment. Eventually, this may have reduced or stimulated intentional non-adherence to ICS.
A question that has yet to be answered is which children should receive an RTMM device with SMS reminders as investigated in this study. Explorative post hoc subgroup analyses indicated that the effect on adherence to ICS might have been higher in certain subgroups, including patients with good asthma control at baseline and patients who experienced a worsening of asthma control during the study. In clinical practice, the need for this intervention may be greatest in children who have poor asthma control despite prescription of ICS, and in children who are suspected of unintentional non-adherence. If motives for non-adherence are unclear, patients might also benefit from tailored SMS reminders combined with educational interventions, for example, which aim at intentional non-adherence. These hypotheses should be tested in future research. Users of RTMM should be aware that continuous full access to the mobile telephone network is required for sending real-time SMS reminders. We also recommend incorporating the measurement of inhalation technique into RTMM technology for asthma medication, since this is an important modifier of the association between adherence and asthma control [34].

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In recent years, the attention paid to asthma self-management has increased: children should be more involved in asthma treatment and are recommended to have an individual symptom-based action plan [5]. In our study, a part of the population has succeeded in maintaining asthma control at low levels of adherence to ICS. In fact, by deviating from the dosing instructions of the paediatrician and maintaining asthma control, they have already self-managed their asthma treatment. However, without proper guidance patients self-managing their asthma are at risk of relapsing into poor asthma control. Therefore, healthcare professionals should make sure the ICS dose is tailored to each patient's needs. Together with the patient, an individual symptom-based action plan should be written that covers not only adhering to the agreed ICS dosing schedule, but also self-monitoring of asthma symptoms, recognising and responding to worsening asthma and regular review of asthma control, treatment and skills by a healthcare provider [5]. Subsequently, patients should be supported to adhere to their written action plan. RTMM with SMS reminders may help children to manage their asthma symptoms independently. However, this approach requires a change of treatment aims: from maximising medication adherence to giving patients the means to manage and control their asthma symptoms themselves.

Conclusions

RTMM with SMS reminders effectively improved adherence to ICS in children with asthma. In our population, there was no evidence of better asthma control, improved asthma-specific quality of life or fewer asthma exacerbations due to the intervention. Apart from the costs of the SMS intervention, there was no difference in costs between the intervention and control groups.

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TABLES AND FIGURES

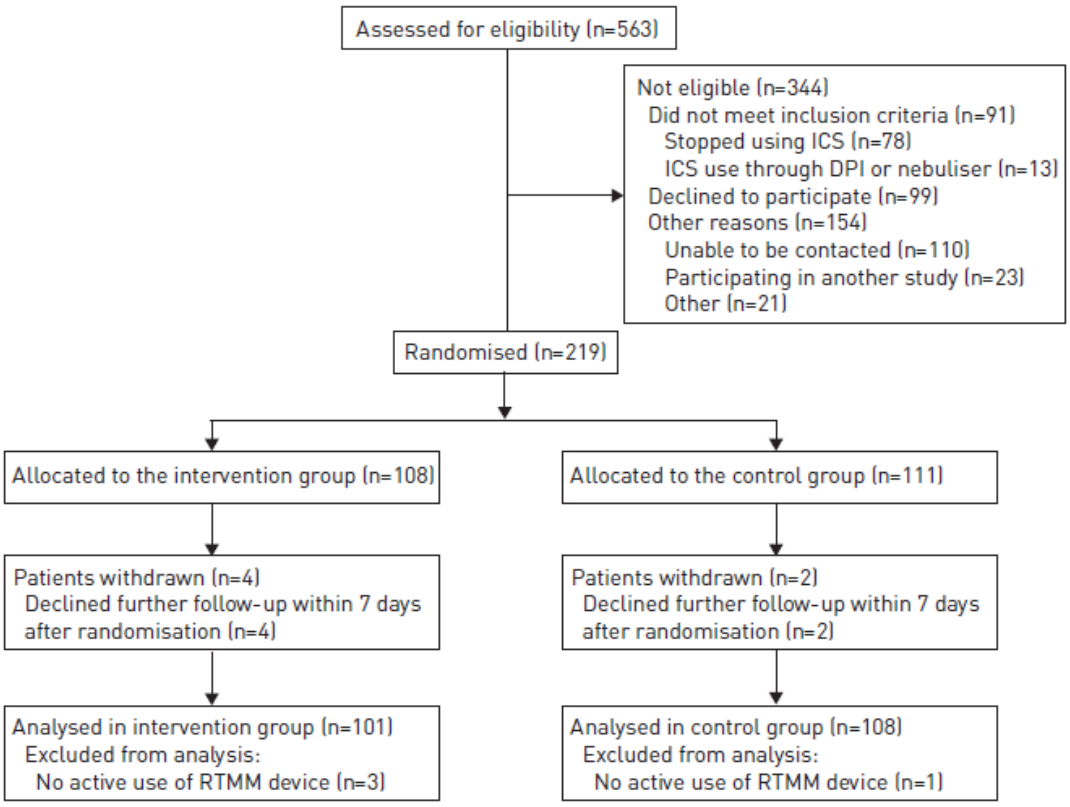

FIGURE 1 Patient flow chart. ICS: inhaled corticosteroid; DPI: dry powder inhaler; RTMM: real-time medication monitoring.

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TABLE 1 Patient characteristics

	Intervention	Control
Subjects n	101	108
Age at inclusion years	7.8±2.2	7.7±2.1
Male	59 (58.4)	72 (66.7)
Hospital		
AMC	9 (8.9)	9 (8.3)
EMC	21 (20.8)	22 (20.4)
GHZ	41 (40.6)	43 (39.8)
BovenIJ	18 (17.8)	18 (16.7)
SLAZ	12 (11.9)	16 (14.8)
Type of RTMM device		
E-haler (first generation)	26 (25.7)	26 (24.1)
Adhaler (second generation)	75 (74.3)	82 (75.9)
ICS type		
Fluticasone	23 (22.8)	16 (14.8)
Fluticasone/salmeterol	17 (16.8)	20 (18.5)
Beclometasone (extra fine particles)	61 (60.4)	72 (66.7)
ICS dosing frequency		
Once daily	13 (12.9)	10 (9.3)
Twice daily	88 (87.1)	98 (90.7)
ICS dose percentage of DDD	35.9±18.2	36.6±21.4
Family status		
Two-parent family	85 (84.2)	96 (88.9)
Single-parent family	16 (15.8)	12 (11.1)
Ethnicity		
Dutch	63 (62.4)	73 (67.6)
Non-Dutch	38 (37.6)	35 (32.4)
Parental level of education		
None/primary school	7 (3.5)	9 (4.2)
Secondary school	39 (19.3)	30 (13.9)
Intermediate vocational education	86 (42.6)	78 (36.1)
Higher vocational education	44 (21.8)	67 (31.0)
University	24 (11.9)	30 (13.9)
Unknown	2 (1.0)	2 (0.9)
Pet with fur or feathers	41 (40.6)	41 (38.0)
Quality of housing		
Poor	5 (5.0)	3 (2.8)
Insufficient	16 (15.8)	11 (10.2)
Sufficient	21 (20.8)	25 (23.1)
Good	59 (58.4)	67 (63.9)
Parental tobacco use		
Current smoker	34 (16.8)	45 (20.8)
Former smoker	50 (24.8)	61 (28.2)
Never-smoker	115 (56.9)	107 (49.5)
Unknown	3 (1.5)	3 (1.4)
Parental Dutch language skills		
Poor/moderate	13 (12.9)	17 (7.9)
Good	16 (7.9)	18 (8.3)
Excellent	169 (83.7)	178 (82.4)
Unknown	4 (2.0)	3 (1.4)
Parental employment		
Employed	157 (77.7)	170 (78.7)
Unemployed	41 (20.3)	42 (19.4)
Unknown	4 (2.0)	4 (1.9)
Family income (national average in 2012 was €2546 per month)		
<1 × average	27 (26.7)	26 (24.1)
1–2 × average	52 (51.5)	46 (42.6)
>2 × average	19 (18.8)	28 (25.9)
Unknown	3 (3.0)	8 (7.4)
Asthma control at inclusion total c-ACT[#] score	20.6±4.4	20.4±3.9
Poorly controlled asthma at inclusion total c-ACT[#] score ⩽19	39 (39.8)	38 (36.5)
Asthma-specific quality of life at inclusion PAQLQ[¶] score	6.1±0.8	5.9±0.8

Continued

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TABLE 1 Continued

	Intervention	Control
Medication beliefs at inclusion*		
BMQ* necessity score	19.3±3.7	18.6±3.5
BMQ* necessity score >15	83 (83.0)	92 (85.2)
BMQ* concerns score	12.9±3.1	12.5±3.2
BMQ* concern score >15	22 (22.0)	22 (20.4)

Data are presented as n, mean±SD or n (%). AMC: Academic Medical Center, Amsterdam, the Netherlands; EMC: Erasmus University Medical Center, Rotterdam, the Netherlands; GHZ: Groene Hart Ziekenhuis, Gouda, the Netherlands; BovenIJ: BovenIJ Hospital, Amsterdam; SLAZ: Sint Lucas Andreas Hospital, Amsterdam; RTMM: real-time medication monitoring; ICS: inhaled corticosteroid; DDD: defined daily dose, defined by the World Health Organization; c-ACT: childhood asthma control test; PAQLQ: paediatric asthma quality of life questionnaire; BMQ: beliefs about medicines questionnaire. #: seven-item questionnaire for detecting poorly controlled asthma in children aged 4–11 years [18]. Range: 0–27 points, cut-off score: 19 points (≤19 points: uncontrolled asthma, ≥20 points: controlled asthma). c-ACT questionnaires at baseline were completed by 98 patients in the intervention group and 104 in the control group. ¶: 23-item questionnaire [20]. Domains include activities, asthma symptoms and emotional function. Range: 1–7. PAQLQ questionnaires at baseline were completed by 100 patients in the intervention group and 108 in the control group. *: BMQ specific, which has one scale for beliefs in the necessity of ICS and one for concerns about long-term toxicity and disruptive effects of ICS. Both scales range from 5 to 25, with higher scores indicating stronger beliefs [25]. BMQ questionnaires at baseline were completed by 100 patients in the intervention group and 108 patients in the control group.

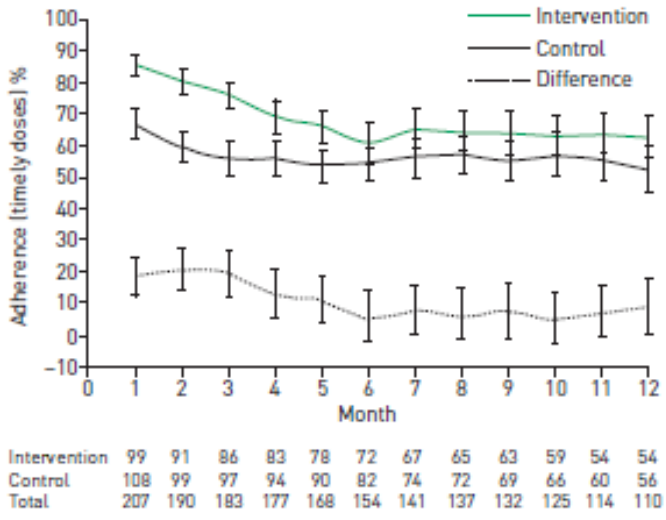

FIGURE 2 The effect of the text message intervention on adherence to inhaled corticosteroid treatment: adjusted mean adherence per treatment group, and the difference, over the course of the study period.

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TABLE 2 The effect of the text message intervention on asthma control and quality of life at the end of follow-up and on the frequency of asthma exacerbations

	Intervention	Control	Difference (95% CI)	p-value
Subjects	101	108		
c-ACT[#] score	21.10	22.17	−1.07 (−3.51–0.56)	0.203
PAQLQ[¶] score	6.19	6.25	−0.06 (−0.41–0.15)	0.659
Asthma exacerbations[+] per year	0.23	0.37	−0.14 (−0.61–0.25)	0.432

Data are presented as n, unless otherwise stated. The differences and p-values with regards to the childhood asthma control test (c-ACT) and paediatric asthma quality of life questionnaire (PAQLQ) presented in this table are the effect estimates and their p-values from the multilevel regression models for month 12. The confidence intervals were the results of bootstrapping procedures. [#]: seven-item questionnaire for detecting poorly controlled asthma in children aged 4–11 years [18]; range: 0–27 points; cut-off score: 19 points (⩽19 points: uncontrolled asthma, ⩾20 points: controlled asthma). [¶]: 23-item questionnaire [20]; domains include activities, asthma symptoms and emotional function; range: 1–7. [+]: defined as an asthma-related hospitalisation, a visit to the emergency department or an episode of systemic corticosteroid use [5]. The p-value was taken from the negative binomial regression model.

FIGURE 3 Mean adjusted costs per patient. Data are presented as n. GP: general practitioner; RTMM: real-time medication monitoring.

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