1 A TELEPHONE SURVEY TO DETERMINE THE EXPERIENCES OF CHILDREN, AND

2 THEIR PARENTS/CARERS, FOLLOWING THE INITIATION OF A NEW MEDICINE

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- 36 Key Words
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- 38 Medication Therapy Management, Medication Adherence, Paediatrics, United Kingdom
- 3940 Word Count
- 41 Abstract = 228, manuscript = 2996
- 42 **ABSTRACT**

43 **Objective**

44 To determine what issues are experienced during the first few weeks of therapy by patients, and

45 their parents/carers, when a child/young person has been prescribed a new medicine.

46 Method

47 One-hundred patients aged \leq 18 years of age prescribed a new medicine for \geq 6 weeks were

48 recruited from a single United Kingdom National Health Service (NHS) specialist paediatric hospital

49 out-patient pharmacy. Six weeks after the first dispensing of their new medicine the patient or their

50 parent/carer received telephone follow-up by a researcher and verbally completed a questionnaire

51 containing both open and closed questions. Patient or parent/carer experiences were identified and

52 analysed using thematic analysis and descriptive statistics.

53 Results

- 54 Eighty-six participants were available for telephone follow-up. Six (7%) had not started their
- 55 medicine. Paediatric patients and their parents/carers experienced a range of issues during the
- 56 first few weeks after starting a new medicine. These included additional concerns/questions (24/80,
- 57 30%), administration issues (21/80, 26.3%), adverse effects (29/80, 36.3%) and obtaining repeat
- 58 supplies (12/80, 15%). The Morisky Medication Adherence Scale indicated that 34/78 (43.6%)
- 59 participants had a high adherence rating, 35/78 (44.9%) medium and 9/78 (11.5%) a low rating.

60 **Conclusion**

Paediatric patients and their parents/carers experience a range of issues during the first few weeks
after starting a new medicine. Further research is required to determine the type of interventions
that may further support medicines use in this group of patients.

64

65 Key Words

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67 Medication Therapy Management, Medication Adherence, Paediatrics, United Kingdom

69 Key Messages

70	What is already known on this subject:
71	• Little is known about the experiences of paediatric patients, and their parents/carers, during
72	the first few weeks after child has started a new medicine.
73	What this study adds:
74	• This study has shown that children, and their parents/carers, experience a range of issues
75	during the first 6 weeks after starting a new medicine.
76	• These issues include concerns/questions, information requirements, adverse effects,
77	arranging further supplies and adherence.
78	• Interventions to support medicine taking during this period may optimise medicines use in
79	this group of patients.
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87	INTRODUCTION
88	
89	People prescribed self-administered medicines typically take about half their doses.[1] Efforts to
90	assist patients with adherence might improve the benefits of prescribed medicines.

92 Medicines taking in children may be influenced by parents/carers beliefs about the condition,
93 treatment regimen, child resistance, relationships within families, desire to preserve normal life and
94 input from health professionals.[2]

95

96	A recent study of the experiences of medicine-related issues encountered by parents/care	rs of

97 paediatric liver transplant patients found they reported problems obtaining their medicine,

98 administering the medicines and side effects (including insufficient knowledge of side effect

99 management).[3]

100

A review of the medical notes of 11 – 18 year old patients with juvenile arthritis found that despite
 the increasing complexity of drug regimens major gaps existed in the documentation of knowledge
 and skills relevant to the self-management of such regimens by patients.[4]

104

105 Barber et al, in a study of adult patients started on chronic medicines, found they quickly became 106 non-adherent and identified a number of medicine related problems and information needs.[5] 107 These included side effects, concerns about taking a new medicine, swallowing difficulties and 108 remembering the regimen. In response to these issues the National Health Service (NHS) funded 109 New Medicines Service (NMS) was established in England in 2011.[6] This is a medication review 110 delivered through community pharmacists to support people with long-term conditions newly 111 prescribed a medicine. The NMS improves adherence by 10% and increases the number of 112 medicines problems identified and resolved.[7] Improved medication adherence has been shown to 113 improve disease outcomes in children with cystic fibrosis[8], asthma[9] and renal disease.[10] 114 However, the NMS may not be available to children and cannot be undertaken with a 115 parent/carer.[6]

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117	The rationale of medication review could apply to children with chronic diseases.[11] Issues such as
118	polypharmacy, wastage and medicine-related problems are likely to be similar to those in adults.
119	However, a literature review, using AMED, British Nursing Index, CINAHL, EMBASE, HMIC, MEDLINE,
120	PsycINFO and Health Business Elite, did not identify any studies of medication review specific to
121	children. Recently, the UK National Institute for Health and Care Excellence (NICE) recommended
122	further research concerning medication review in children, including minimising medicines related
123	problems.[12] Other initiatives that may optimise medicines use include better partnerships with
124	patients, telephone helplines, internet support websites and improving collaboration between
125	healthcare professionals.[13]
126	
127	The present study focused on the experiences of patients and their parents/carers during the first
128	few weeks after a paediatric patient began taking a new medicine.
129	
130	Aim
131	
132	To determine what medicine-related issues are experienced during the first few weeks of therapy by
100	
133	patients, and their parents/carers, when a child/young person has been prescribed a new medicine.
134	
135	Ethical Approval
136	
137	The study was approved by Yorkshire and Humber –Sheffield, UK, National Research Ethics Service
122	21/09/14 (REC reference $11/VH/1086$ IRAS project ID 148123)
100	24/03/14 (NEC reference 14/11/1000, INAS project id 140125).

140	METHOD
141	
142	Setting
143	
144	The study was undertaken at a specialist UK paediatric hospital (34 specialties, 361 beds, over
145	174,000 out-patient visits per year).[14]
146	
147	Participant Recruitment
148	
149	Potential participants were identified through presentation of a prescription to the out-patient
150	pharmacy which met the study inclusion criteria. Consent and recruitment were undertaken by
151	pharmacists based in the hospital's out-patient pharmacy whilst the participant waited for their
152	prescription. Written consent was taken from the patient's parent/carer if the child was under 16
153	years or the patient if 16 years or older. An assent form was used for patients aged $12 - 15$ years
154	and was signed by the patient alongside the parent/carer consent form. Age related participant
155	information leaflets were provided. To minimise impact on service delivery a convenience sample of
156	participants were recruited during the period February to July 2015. This study was exploratory and
157	the authors considered a recruitment number of 100 participants would provide sufficient range of
158	specialities and participants to identify important findings. There were no known published studies
159	to guide recruitment numbers.
160	
161	Inclusion Criteria
162	
163	Participant inclusion criteria were: ages 0-18 years; prescribed a new medicine to be taken for 6
164	weeks or longer; access to a telephone for follow-up; not receiving medication for a life-limiting

165	condition; could understand written and spoken English. The authors considered a period of 6
166	weeks to have provided the patient, and their parent/carer, sufficient experience of taking the new
167	medicine prior to follow-up.
168	
169	Data Collection
170	
171	Demographic information was recorded from the patient's prescription: medical/surgical clinic
172	attended, age/gender of the patient, medicine prescribed and therapeutic indication.
173	
174	A questionnaire containing both open and closed questions was used as the research instrument.
175	This was completed by telephone with direct support from the lead study researcher. Cognisant
176	testing of the questionnaire was assessed with a parent of a child taking long-term medicines and
177	piloted with 5 participants. Six weeks following the dispensing of their new medicine participants
178	received telephone follow-up by the study lead researcher. Participants were asked: whether they
179	had researched further information about the new medicine themselves and why, any
180	concerns/questions occurring over the previous 6 weeks, if they had experienced any problems
181	taking/administering the medicine, whether they had experienced adverse effects from their new
182	medicine and any problems arranging repeat supplies. Participants' adherence was assessed using
183	the Morisky Medication Adherence Scale (MMAS-8).[15]
184	
185	Responses were transcribed in real time by the researcher during the interview.
186	
187	Data Analysis
188	
189	Responses were analysed using thematic analysis. The responses were listed, grouped by
190	similar/related theme and coded. Collated responses were analysed using NVivo version 10.

- 191 Quantitative results were analysed using descriptive statistics using The Statistical Package for Social
- 192 Sciences (SPSS) version 22.

194 **RESULTS**

195

196 **Demographic Information**

197

- 198 One hundred participants were recruited to the study. Fifty-one patients were female and 49 male
- 199 with a mean age of 8 years (range 0.33 years 17 years). Patients were managed by one of 15
- 200 specialities (Table 1).
- 201

202 Table 1 Specialities

Speciality	Ν
General Paediatrics	23
Ear, Nose and Throat	14
Neurology	13
Dermatology	10
Urology	9
Respiratory	7
Rheumatology	5
Emergency Department	3
Gastroenterology	3
Hepatology	3
Nephrology	3
Ophthalmology	3
Cardiology	2
Inherited Metabolic Diseases	1
Plastics	1

203

204 In total 145 medicines were prescribed which patients had not previously received (Table 2).

205

206 Table 2 Medicines Prescribed for Study Participants

Therapeutic Use	Number of	Medicine (n)
-	Medicines (%)	
Eczema	27 (18.6%)	Topical corticosteroid (13)
		Emollient (7)
		Dressings (3)
		Hydroxyzine (2)
		Potassium Permanganate (1)
		Topical tacrolimus (1)
Asthma	17(11.7%)	Beclometasone (6)
		Montelukast (4)
		Fluticasone (2)
		Fluticasone/Salmeterol (2)
		Salbutamol (2)
		Ipratropium (1)
Allergy	14(9.7%)	Fluticasone (8)
		Cetirizine (2)
		Adrenaline (1)
		Chlorphenamine (1)
		Desloratadine (1)
		Nutramigen (1)
Urinary	14 (9.7%)	Desmopressin (6)
Frequency/Enuresis		Oxybutynin (6)
		Tolterodine (2)
Migraine/Headache	11(7.6%)	Pizotifen (6)
		Propranolol (2)
		Sumatriptan (2)
		Migraleve (1)
Gastro-Oesophageal	9 (6.2%)	Ranitidine (7)
Reflux		Lansoprazole (1)
		Omeprazole (1)
Epilepsy	8 (5.5%)	Levetiracetam(2)
		Acetazolamide (1)
		Carbamazepine (1)
		Lamotrigine (1)
		Sodium valproate (1)
		Stiripentol (1)
		Topiramate (1)

Therapeutic Use	Number of Medicines (%)	Medicine (N)
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Infection	8(5.5%)	Trimethoprim (3)
		Amoxicillin (1)
		Azithromycin (1)
		Co-trimoxazole (1)
		Erythromycin (1)
		Itraconazole (1)
Constipation	6 (4.1%)	Macrogols (5)
		Senna (1)
Vitamins	6 (4.1%)	Colecalciferol (2)
		Folic Acid (2)
		Alfacalcidol (1)
		Ergocalciferol (1)
Rheumatic diseases	5 (3.4%)	Nifedipine (2)
		Piroxicam (2)
		Hydroxychloroquine (1)
Immunosuppression	4 (2.8%)	Azathioprine (2)
		Ciclosporin (1)
		Methotrexate (1)
Cardiovascular	3 (2.1%)	Atorvastatin (1)
		Enalapril (1)
		Losartan (1)
Ophthalmic	3(2.1%)	Prednisolone (2)
		Fluorometholone (1)
Cholestasis	2 (1.4%)	Ursodeoxycholic acid (2)
Emesis	2 (1.4%)	Ondansetron (2)
Other	6 (4.1%)	Amitriptyline (1)
		Colestyramine (1)
		Dexamethasone/framycetin/gramicidin (1)
		Levomepromazine (1)
		Melatonin (1)
		Propranolol (1)

Eighty-six participants received telephone follow-up. Follow-up was undertaken with 83 (96.5%)

214 parents/carers and 3 (3.5%) young people (two aged 16 years and one 14 years following parental

215 consent). Fourteen participants were not contactable.

216

217 Adherence to the Prescribed Regimen

218

Telephone follow-up revealed that 6 (7%) patients had not taken their medicine. Two

220 parents/carers were concerned about side effects (macrogol and topical corticosteroid), 2 had not

221 required their medicine (chlorphenamine, pizotifen and sumatriptan), 1 patient refused to be

222	administered a macrogol suspension and 1 patient was concerned about how nifedipine would
223	interact with her other medicines.
224	
225	"I read the leaflet that it came with then decided to try naturally. I haven't started her on it yet.
226	They said that she wasn't drinking enough. I pushed the fluids, she's been better than she was. It
227	can cause diarrhoea and I didn't want to send her the other way" Parent of Patient 18 (macrogol)
228	
229	"I haven't been taking it because I couldn't find out if it was compatible with my other medicines. I'm
230	doing my exams at the moment, I didn't think it would be very smart to take them." Patient 46
231	(nifedipine)
232	
233	The MMAS-8 was used to determine self-reported adherence. Thirty-four (43.6%) scored zero
234	indicting high adherence, 35 (44.9%) scored 1-2 indicating medium adherence and 9 (11.5%) had a
235	score >2 indicating low adherence. Two participants were receiving medicine that was used on a
236	'when required' basis and thus were excluded from the analysis.
237	
238	Four (5%) participants had purchased medicine compliance aids.
239	
240	"We were advised to take it with or after food. If I'd forgotten I didn't know if I could then give it
241	and so I would miss the dose and give his next one." Patient 61 (ursodeoxycholic acid)
242	
243	"I don't find it difficult to stick to the plan because I know we have to stick to it because it's for his
244	eyes. A bit inconveniencedit blows his weekend out. We give it on a Saturday morning so we can
245	do something on a Friday night if we want to. I sometimes forget the folic acid as he has three days
246	off when he's on the methotrexate." Parent of Patient 20 (methotrexate)
247	

248	Eighteen (22.5%) participants intentionally omitted doses. These were due to adverse effects (5,
249	27.8%), concurrent acute illness (3, 16.7%), timing of administration (3, 16.7%), the desire to look up
250	more information before starting the medicines (2, 11.1%), incorrect use (2, 11.1%), child declining
251	to take (1, 5.6%), a mother not wanting their child to have the medicine as, although not used for
252	this indication, they were an antidepressant (1, 5.6%) and ran out of supplies (1, 5.6%).
253	
254	"He was poorly once and was taking Calpol, Nurofen and antibiotics. So I stopped giving it then as I
255	thought it was a bit much." Parent of Patient 100 (ranitidine)
256	
257	"Only the first night because of reading the side effects. My husband looked on the internet. Then
258	we read the information the doctor gave us and realised it was more related to children and my
259	husband was much happier so we gave it." Parent of Patient 56 (desmopressin)
260	
261	Seeking Further Information
262	
263	Twenty-six (30.2%) participants sought further information about their medicine. Twenty-two
264	participants (84.6%) searched the internet, 2 (7.7%) asked a friend/relative, 1 (3.8%) asked other
265	parents and 1 (3.8%) had looked in the British National Formulary.
266	
267	Participants sought further information to: find out about side effects (13, 50%), general interest (5,
268	19.2%), reassurance about the appropriateness of treatment (4, 15.4%), research a specific query (3,
269	11.5%) and check that there were no interactions with concomitant medicine(s) (3, 11.5%).
270	

271	"I'm giving something new. I want to know what side effects there are. [Patient 6] is on lots of
272	medicines, she's having seizures and I want to see how it interacts with the others, I don't want to
273	make these worse." Parent of Patient 6 (levomepromazine)
274	
275	"Basically, is that the right drug? Is it common to use it at this stage?" Parent of Patient 75
276	(azathioprine)
277	
278	Concerns and Further Questions
279	
280	Twenty-four (30%) participants who had taken/administered their medicine had some concerns.
281	These related to side effects (10, 41.7%), efficacy (6, 25%), administration (4, 16.7%) and other
282	concerns (4, 16.7%). Other concerns were the: perceived stigma of taking an antidepressant, impact
283	of a friend questioning the choice of therapy, anticipated repeat prescription problems through the
284	General Practitioner (GP) and advice provided by a pharmacist.
285	
286	"There was one thing. My friend works in a hospital, I'm not sure what she does, but when she saw
287	what [Patient 11] was on she said that they'd been told to stop using them. I don't know why that
288	is." Parent of Patient 11 (piroxicam)
289	
290	Administration Issues
291	
292	Issues regarding administration were experienced by 21 (26.3%) participants. These were issues
293	concerning: dislike of the taste/smell (11, 52.4%), timing of administration (3, 14.3%) and the impact
294	of autism/learning difficulties (2, 9.5%). Other (5, 23.8%) experiences included the: manipulation of

295	a tablet to obtain a part-dose, problems extracting a tablet from a blister pack, fear of an inhaled
296	spacer device, absence of a bottle adapter and swallowing difficulties.
297	
298	"It was difficult to find a suitable time as needed to be taken on an empty stomach an hour before
299	food. She took it at school as there's no afternoon break. In the morning she has breakfast, then
300	there's lunchtime. When she comes home she has an evening meal and then she's tired and it's time
301	for bed." Parent of Patient 23 (lansoprazole)
302	
303	"He's got a new spacer now as he couldn't cope with the big one. It scared him. He's got a smaller
304	one with bears on it now which is fine from the GP." Parent of Patient 33 (beclomethasone inhaler)
305	
306	Adverse Effects
307	
307 308	Whilst cause and effect was not established, adverse effects were reported by 29 (36.3%)
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307 308 309 310 311 312	Whilst cause and effect was not established, adverse effects were reported by 29 (36.3%) participants (Table 3). "Upper abdominal pain under her rib cage for three weeks, periodic headache, exhausted, very, very tired, her menstrual cycle has gone haywire. She's been off school for three weeks. I'm desperate to
307 308 309 310 311 312 313	Whilst cause and effect was not established, adverse effects were reported by 29 (36.3%) participants (Table 3). "Upper abdominal pain under her rib cage for three weeks, periodic headache, exhausted, very, very tired, her menstrual cycle has gone haywire. She's been off school for three weeks. I'm desperate to find out the cause to alleviate her symptoms. My head tells me it's the side effects from the drug"
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318 Table 3 Reported Adverse Effects

Therapeutic Use	Medicine	Number of Patients Reporting Effect	Reported Adverse Effect(s)
Eczema	Topical corticosteroid	1	Staining of clothing.
	Hydroxyzine	1	Drowsiness
Allergy	Fluticasone	2	Nose bleed, sore throat
Urinary	Oxybutinin	2	Drowsiness, dry mouth.
Frequency/Enuresis	Tolterodine	2	Drowsiness, dry mouth, constipation, abdominal pain.
Migraine/Headache	Pizotifen	3	Behavioural changes, constipation, increased appetite.
	Propranolol	1	Fatigue
Gastro-Oesophageal Reflux	Ranitidine	1	Vomiting
Epilepsy	Levetiracetam	2	Behavioural changes
	Acetazolamide	1	Behavioural changes
	Lamotrigine	1	Suicidal ideation
Constipation	Marogol	1	Diarrhoea
Rheumatic diseases	Nifedipine	1	Nausea, dizziness.
	Hydroxychloroquine	1	Abdominal pain.
Immunosuppression	Azathioprine	2	Blacking out/fainting, hairloss.
	Ciclosporin	1	Abdominal pain, headache, fatigued, changes to menstrual cycle.
	Methotrexate	1	Abdominal pain.
Other	Amitriptyline	1	Drowsiness
	Atorvastatin	1	Jaundice
	Enalapril	1	Dry cough
	Itraconazole	1	Abdominal pain.
	Propranolol	1	Coldness of the extremities

320 Further Supply Issues

- 321 Twelve (15%) participants experienced difficulties obtaining further supplies. Forty-seven
- 322 participants (58.8%) had sufficient supplies from the hospital and 21 (26.3%) obtained further
- 323 supplies from their GP. The problems experienced by participants included: delays in posting out
- 324 clinic letters to the GP (4, 33.3%), insufficient information on the letter for a repeat prescription (3,
- 325 25%), insufficient quantities prescribed by the GP (2, 16.7%), misreading of a letter by the GP (1,

326	8.3%), cancellation of a follow-up out-patient appointment where a repeat prescription was to be
327	provided (1, 8.3%) and confusion due to a therapy substitution by the hospital pharmacy which did
328	not then match the information in the clinic letter (1, 8.3%).

330 "Yes, there was some confusion between the doctors. The hospital hadn't written to the GP, the

331 letter hadn't been sent so I had to phone the consultant who organised the letter. Missed a week of

332 *the antibiotic."* Parent of Patient 26 (co-trimoxazole)

333

"Ran out of tablets. The doctor said to take the course and we'll see you back. Out-patient on 8th
June cancelled by the hospital and arranged for much later in August. Had to phone up and get it
brought forward. The doctor said to take it for 6 weeks. We only had a 4 week supply." Parent of
Patient 45 (amitriptyline)

338

339 **DISCUSSION**

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341 Patients have a right to decide not to take their medicine and may have different views about risks, 342 benefits and side effects.[16] In this current study, 6/86 (7%) participants had not started their 343 medicine and 18/80 (22.5%) participants had intentionally omitted some doses. Therefore some are 344 reviewing the initial therapy decision and others are making treatment changes without consulting a 345 healthcare professional. Shared decision making between clinicians and patients about treatment 346 choice is important.[17] Poor communication may lead patients to obtain information outside of a 347 consultation with a healthcare professional.[18] 348 349 Overall participant reported adherence in this study was comparable with that published in the

350 paediatric literature.[19, 20] Thirty-four (43.6%) participants exhibiting high adherence and 35

351 (44.9%) medium adherence. Four (5%) participants had purchased medicine compliance aids. Due

to a lack of beneficial outcomes with the use of compliance aids the UK Royal Pharmaceutical Society
 recommends original pack dispensing with appropriate pharmaceutical care including clinical
 medication review.[21]

355

356 A recent systematic review identified a number of findings that contribute to explaining treatment 357 adherence in paediatrics.[2] Including beliefs about the condition or treatment, treatment regimen 358 and child resistance. Findings from the present study were consistent with these. For example 3/86 359 (3.5%) participants decided against treatment, 21/80 (26.3%) experienced issues with administration 360 including the taste/smell of the medicine and timing of administration. Whilst the systematic review[2] focussed on long-term conditions it did not identify when during treatment these themes 361 362 occurred. This current study found that they can occur within the first six weeks after starting a new 363 medicine.

364

A study of adult patients prescribed a new long-term medicine found that once a patient has experienced their medicine, they gain some knowledge of what it does and new questions arise.[5] The current study has shown that children and their parents/carers have similar experiences after the first few weeks of therapy. This is illustrated by 26/86 (30.2%) participants researching further information about their new medicines, 24/80 (30%) having concerns or further questions and 29/80 (36.3%) possibly experiencing an adverse effect to treatment.

371

Twenty-one (26.3%) parents/carers had difficulties administering the medicine to their child. In
adults, oral solid dosage forms are mostly acceptable. However, potential paediatric patients may
include neonates, toddlers, young children and adolescents, and hence will have widely varying
needs.[22] A change in formulation is currently excluded from triggering a NMS consultation.[23]Any
future paediatric medication review should include changes in formulation as a trigger for a
medication review.

379

380 miscommunication and unintended changes to medicines is a significant problem.[24] This current 381 study suggests that this is an issue in paediatrics with 12 (15%) participants experiencing problems 382 arranging a repeat supply with 7 (58.3%) due to a miscommunication. 383 384 A systematic review of interventions to improve the safe and effective use of medicines by 385 consumers identified a scarcity of evidence in children/young people.[25] The benefits of a 386 medication review through the NMS have been appraised.[7] The NMS appraisal identified a variety 387 of factors impacting on adherence including forgetfulness, beliefs about treatment necessity, stigma, 388 lack of peer/family support, lack of knowledge, side effects, fear of dependency, regimen 389 complexity, inability to use the formulation and access to medicines. Each of these factors were 390 identified in this current study. The NMS applies a structured approach to identifying and resolving 391 these issues.[7, 23] However it may not be available to children and is not available to their 392 parents/carers.[6] 393

Current evidence suggests that when patients move between care providers the risk of

The results of this current study suggest that paediatric patients and their caregivers may benefit from some support initiative after the first few weeks of treatment with one option being an NMS type intervention. In addition to medication review a number of other initiatives may further support patients realising the benefits of their medicines. These include fostering better partnerships with patients, the use of telephone helplines for information on medicines, developing specific internet support websites, and improvements to how different healthcare professionals collaborate together.[13]

401

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404	The limitations of this study include sample size which was relatively small, specialist paediatric
405	centre setting which may limit how generalisable the results are and the restriction to English
406	language speakers.
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408	
409	
410	Conclusion
411	
412	Paediatric patients and their parents/carers experience a range of issues during the first six weeks
413	after starting a new medicine. Intervention at this stage may provide useful support to both the
414	patient and their parent/carer. Further research is required to determine the type of intervention
415	and how it could be integrated in to practice to optimise paediatric medicine use.
416	
417	Acknowledgments
418	
419	We are grateful to the support provided for the study by the staff of the Medicine Chest out-patient
420	pharmacy at Birmingham Children's Hospital NHS Foundation Trust, UK.
421	
422	Funding
423	
424	No funding was received for this study
425	
426	Conflicts of Interest

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428 Nil.

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