

## **Understanding Young People's Experiences of Anti-Obesity Drugs**

Billy White, Department of Population Health Sciences, UCL Institute of Child Health

Liz Jamieson, Department of Practice & Policy, UCL School of Pharmacy

Sarah Clifford, Oxford Outcomes (an ICON company), San Francisco, USA

Julian PH Shield, Bristol Biomedical Research Unit in Nutrition & School of Clinical Sciences,  
University of Bristol

Deborah Christie, Department of Child and Adolescent Psychological Services, University  
College London Hospital

Felicity Smith, Department of Practice & Policy, UCL School of Pharmacy

Ian C K Wong, Centre for Safe Medication Practice and Research, University of Hong Kong

Russell M Viner, Department of Population Health Sciences, UCL Institute of Child Health

**Keywords (3-6):** orlistat, metformin, adolescence, obesity, adherence, concordance

**Running Title:** Young People's Experiences of Anti-Obesity Drugs

### **Corresponding author:**

Dr Billy White

UCL Institute of Child Health,

6<sup>th</sup> Floor Paediatrics,

250 Euston Road,

London NW1 2PG

Email: [billy.white@ucl.ac.uk](mailto:billy.white@ucl.ac.uk)

**What is already known about this subject:**

- Only 2 anti-obesity medications are frequently used: orlistat and metformin
- Clinical trials of orlistat and metformin show small reductions in BMI; orlistat by 0.83 kg/m<sup>2</sup> and metformin by 1.4 kg/m<sup>2</sup>
- Pharmacoepidemiological studies show high rates of orlistat drug discontinuation

**What this study adds:**

- Doctors largely initiated anti-obesity drugs, with passive acceptance from young people
- Many had significant side-effects that were largely managed by families independent of clinicians using self-directed strategies and many received minimal support from health care professionals
- Patients terminated drugs independently of their doctors, largely related to inadequate benefit to justify the side-effects.

**Abstract**

**Background:** Only two anti-obesity drugs (AOD) are frequently prescribed in paediatric obesity, orlistat and metformin. Meta-analyses show modest benefit in clinical trials yet analyses of prescribing databases show high levels of discontinuation in routine clinical practice. Increased understanding of young people's experiences taking AOD could result in improved prescribing and outcomes. **Methods:** Semi-structured interviews with young people aged 13 to 18 years and their parents from 3 specialist obesity clinics, analysed using a general thematic coding methodology. **Results:** Theme saturation was achieved after interviews with 15 young people and 14 parents (13 parent-child dyads). Three models were

developed. Model 1 explored factors influencing commencement of AOD. Six themes emerged: medication as a way out of obesity, enthusiasm and relief at the prospect of pharmaceutical treatment, last ditch attempt for some but not all, passive acceptance of medication, fear as a motivating factor, and unique treatments needed for unique individuals. Model 2 described the inter-relationship between dosing and side-effects; side-effects were a significant experience for many young people and few adhered to prescribed regimens, independently changing lifestyle and dosage to tolerate medications. Model 3 described the patient-led decision process regarding drug continuation, influenced primarily by side-effects and efficacy.

**Conclusion:** Use of anti-obesity drugs is challenging for many adolescents. Multiple factors were identified that could be targeted to improve concordance and maximise efficacy.

Abstract: 221 words

## Introduction

The role of medications in the management of obesity in children and young people is unclear. In the UK, the National Institute of Health and Clinical Excellence (NICE) suggests anti-obesity drugs (AOD) may have a role in treatment of young people over 12 years of age with very high BMI or obesity comorbidities(1). Currently only one drug, orlistat, is licensed in the UK as an AOD in children. In addition, metformin is used off licence predominantly in obese subjects with insulin resistance (2). There are no current data to compare relative usage of these two drugs, however it is likely that metformin is more widely prescribed, especially by endocrinologists and gynaecologists in subjects with type 2 diabetes, insulin resistance and polycystic ovarian syndrome. Systematic reviews of metformin and orlistat, show small reductions in BMI; orlistat by 0.83kg/m<sup>2</sup> (3) and metformin by 1.4kg/m<sup>2</sup> (2). Whilst these clinical trials suggest the benefits of AOD may be very small, even small reductions in BMI can be important in growing children and adolescents. Primary care prescribing of these drugs has increased 15-fold in the UK between 1998 and 2007 (4).

Despite encouraging trial results which have evaluated the safety and efficacy of AODs, pharmacoepidemiological studies show that medication discontinuation rates outside the trial environment are very high in both children (4) and adults (5). Analysis of a national primary care prescribing database found 45% of orlistat prescriptions were discontinued after one month, and approximately 10% of children and young people remained on the drug for 6 months after initiation (4). The reasons for these high rates of discontinuation are unclear. Metformin and orlistat have high rates of gastrointestinal side-effects which may limit their use(7, 8). However there are no published data regarding patient experience of AODs in young people. Qualitative investigation of young people's experiences allows the generation of hypotheses regarding reasons for early discontinuation.

We undertook a qualitative investigation of experiences associated with AOD prescribing and use in adolescents in the UK in order to inform potential strategies to improve AOD use and therefore efficacy in young people.

### **Materials and methods**

We used a qualitative design utilising an in-depth, semi-structured interview schedule for young people and parent/carers developed by a multi-disciplinary team (two psychologists, two paediatricians, a pharmacist and a patient representative). The schedule contained questions regarding decision processes to take the AOD, expectations of AOD outcomes, experiences of AOD usage, understanding of mechanism of drug action, outcomes of AOD usage and suggestions for improved outcomes. The study was reviewed and approved by the NRES Committee London – Surrey Borders REC reference number 11/LO/1020.

Young people aged 12-18 years were eligible if they had BMI  $\geq$ 98<sup>th</sup> centile (9) and were prescribed orlistat or metformin for weight control within the last 3 years. Exclusion criteria were 1) use of metformin for management of diabetes, pre-diabetes or polycystic ovarian syndrome in non-obese young people 2) inability to participate in a face-to-face interview or 3) insufficient English to participate.

Young people were recruited from 3 paediatric obesity clinics in England (London, Bristol and Liverpool) through the Medicines for Children Research Network. We anticipated requiring approximately 10-20 families to achieve theme saturation (10). Based on our previous difficulties recruiting participants into obesity studies, all one hundred and nine subjects fulfilling eligibility criteria were invited by their hospital doctor to enroll in the study. Those consenting were invited to interview, together with one parent and each given a £10 gift voucher as participation compensation.

Face-to-face interviews were conducted in the participant's own home by one researcher (LJ) experienced in interviewing young people. Parent/young person dyads were independently interviewed unless either of the dyad opted out or wished to be interviewed together. Written assent for under 16 year olds and consent for those over 16 were obtained from both the young person and parent/carer. Interviews were audio recorded and field notes written immediately after the interview.

### ***Analysis***

Audio recordings from each interview were transcribed verbatim and anonymised by LJ. Transcripts and field notes were read and coded independently by LJ and a sample coded by BW using a general thematic coding methodology (11). Memos were written to summarise and synthesise emerging themes. This initial coding framework was used to code the subsequent transcripts and new codes were added as they emerged using a constant comparative technique to compare new and previously collected data to understand emerging themes. To ensure reliability, BW read all transcripts and reviewed the coding. BW and LJ developed models through an iterative process, in which the initial model was reviewed using constant comparison techniques (in which successive items of data are appraised and compared to ensure the code is reflective of all) and the models revised accordingly. The qualitative analysis was facilitated by the use of NVivo software - QSR International (UK) Limited, Southport, UK.

### **Results**

The interviews took place between January and May 2013; each lasted between 24 minutes and 1 hour 35 minutes. Theme saturation was reached after views from 16 families were collected. There were 13 parent and young person dyads, two young people without parents (one carer was not available and one did not speak English) and one parent alone (the young person did not wish to be interviewed). Four families (25%) were recruited from Bristol, 1 (6%) from Liverpool and 11 (69%) from London. Young people were aged 13 to 18

years, 12 (75%) were female, and 12 identified themselves as white British (the remaining identified themselves as White Jewish, Caribbean, British Bangladeshi, and British African). All carers interviewed were female. Ten participants (63%) were prescribed metformin only; 8 continue to take metformin. Four were prescribed (25%) orlistat only; none continue on the drug. Two were prescribed both (13%) both metformin and orlistat; two continue on metformin and one continues on orlistat. Self-reported weight change ranged from no change to 12.7kg loss. Participant-reported co-morbidities included insulin resistance, type 2 diabetes, asthma, hypothyroidism, epilepsy, androgen excess, obsessive-compulsive disorder, depression and hypertension. Participant demographics are summarised in table 1.

Three conceptual models were developed from the emerging themes and are summarised in figures 1-3. Models were a) the factors influencing the commencement of an AOD, b) the management of side effects, and c) decision to terminate the drug including balancing efficacy and side-effects. Below we relate the emergent themes within each model.

### **Model 1: Factors influencing why young people commenced on an AOD**

Six themes fed into the decision by young people to take the AOD: passive acceptance of the AOD, enthusiasm and relief at the prospect of a drug treatment, medication as a last resort, fear as a motivating factor, AOD as a way out of obesity and their own perceived uniqueness.

#### ***Theme 1: Passive acceptance of medication***

In all cases the doctor suggested an AOD to the young people. Young people's views were mixed; many had reservations about initiation and there was a general feeling that they should follow the doctor's advice. Passive acceptance was especially likely when the doctor medicalised obesity by highlighting the increased risk of co-morbidities such as type 2 diabetes, and where patients were younger.

“At the time I was thinking, well if it is stopping her from becoming totally diabetic, then the best thing for her to do is to take it, I suppose” (Parent 9)

“I remember them saying to me ‘you haven’t lost any weight, you have gone up, so let’s use this’ and I am like 12/13 years old, what am I supposed to do at this age?” (Young person 12, aged 16)

### ***Theme 2: Enthusiasm and relief at the prospect of a pharmaceutical treatment***

Many participants wanted a novel solution for obesity control and described the potential of a medicine helping them with weight control as “*awesome*” (Young person 12, aged 16 years) and “*exciting*” (Young person 8, aged 16 years). One participant described how the doctor “*made it sound like a miracle cure – he made it sound like it was going to fix all of my problems*” (Young person 9, aged 17 years). However, some young people felt disappointed that they were not able to lose the weight without medication.

“I felt incredibly relieved that there was something that could help her” (Parent 14)

### ***Theme 3: Medication as a last resort.***

Timing of drug initiation was an important factor, both in terms of timing in relation to other treatments, and in relation to readiness to controlling obesity. Many viewed an AOD as a “last resort” in obesity management. Some had tried all other treatment modalities with insufficient long lasting benefits, including changes in diet and exercise, partaking in programmes such as “Slimming World” and “Weight Watchers”, and “gastric band hypnotherapy” (Young person 5).

“I think I was at my wits end so anything was better than nothing” (Parent 13).

In contrast, others felt that they were put on the medication before they had had a chance to fully explore other treatment modalities, including management of eating disorders. One young woman said, “if I wasn’t binge eating I think there would have been an impact [on my weight]” (Young person 6, aged 14 years).

Families saw an AOD as an alternative to, rather than part of, a treatment package that included lifestyle changes.

“... and it was just about like, well okay then, if this is the last resort, but in some ways I don’t think it was” (Young person 12, aged 16 years).

The importance of controlling weight at the time of drug initiation was varied. This ranged from the belief that they would be able to control weight in the future without a drug to others wanting additional support immediately.

“if I was referred to it a year later or two years later I don’t think it would make too much difference” (Young person 15, aged 15).

#### ***Theme 4: Fear as a motivating factor***

Participants initiated AOD due to three types of health-related fears. Firstly, parents and young people were both concerned and confused by discussions with clinicians about diabetes; any mention of diabetes increased their acceptance of the AOD. Young people’s concerns were amplified if their parents or grand-parents had obesity-related conditions.

“It is because I am concerned that [my son] does not set up health problems for himself in later life and if we can avoid diabetes that to me seems a very good thing to do indeed while he is struggling to get his weight down, not only for

diabetes itself, but all the related things that come in its wake. So that seemed to be absolutely excellent.” (Parent 15)

“...I know that I have to get the weight off for health reasons, because like family members in the past have had lots of health things, especially on my Mum’s side and being overweight will affect those things and make them worse or make me more susceptible to them which I don’t want” (Young person 9, aged 17).

Secondly, some young people described feeling threatened by their doctor who told them that they would have to undergo bariatric surgery if weight loss was not achieved; they saw surgery as a “*last resort*” (Young person 6, aged 14 years) or “*final straw*” (Young person 9, aged 17 years) which they wished to avoid.

Thirdly, participants described a fear of being told off or patronised by clinicians, particularly dieticians, in regard to either continued weight gain, lack of exercise, or diet.

“I didn’t really find her [the dietician] very helpful. I think I need guidelines. And it was just oh, you need to eat healthily. I didn’t really find her useful..... [she] ask(ed) me what I eat and it made me feel guilty then. I know that that is kinda what the aim is but do that as well as help me. Not just make me feel bad.”  
(Young person 3, aged 16 years)

“For the first two years they wanted me to see the dietician and all you ever got were these really skinny bitches (mind my language) who just patronized you and said eat healthily and I am, like I have been coming here two years already, I already know what I am meant to do, and no matter how hard I try nothing is happening and you are not helping.” (Young person 9, aged 17 years)

### ***Theme 5: AOD as a way out of obesity***

For some young people, an AOD was seen as a ‘way out’ of obesity. Young people had their own personal reasons for wanting to lose weight. Some were emotional, and in these cases they saw the AOD as a way out of being bullied, feeling self-conscious or a way to alleviate their feeling of “desperation” (young person 9, aged 17 years). Others had lifestyle reasons for wanting to lose weight, which included improved fitness and ability to wear certain clothes.

“Just to help me lose weight because at the time I was feeling really self-conscious.” (Young person 13, aged 13 years)

“I want to just fit into a medium [sized clothes]”. (Young person 8, aged 16 years)

### ***Theme 6: Perceived uniqueness***

Some young people considered themselves to be “unique” either because they had a complex medical history or a genetic tendency to obesity and thus felt they needed specialised treatment to help them with their weight. Some believed that they were unlike other overweight young people, in that they did not have a sedate lifestyle or poor diet, but were incorrectly judged by others as doing so.

“It is not that I eat a lot, it is just because of my...I can’t remember what it is called, they think it has something to do with my complex medical issues ‘cos I don’t eat that much” (Young person 13, aged 13 years)

### **Model 2: Management of side effects**

Side effects from AODs were a key issue for many young people, although a minority did not experience any. Side effects of both metformin and orlistat were usually gastro-intestinal,

particularly abdominal cramps and diarrhea. For some, this involved spending “many, many hours on the loo” (Young person 15, aged 15 years, metformin), and “really weird, intense pain” (Young person 1, aged 18 years, metformin). Some were taken aback by the severity of the side effects; one young person reported “I have never seen diarrhea like it” (Young person 6, aged 14 years, orlistat), while another said “we were told that there could be mild stomach upsets or whatever but I didn’t expect it to be as uncomfortable as it was” (Young person 15, aged 15 years, metformin). A few young people attributed unusual symptoms to metformin, including hand tremor, headaches and change in moods.

Parents expressed concern about their children having to experience such unpleasant side effects. One mother felt that it was “*totally wrong*” for her daughter to have such side effects at her age (Parent 6 - Orlistat).

“It was awful and he would do it [faecal incontinence] in his trousers and he would phone me up and say Mum, I need to come home.” (Parent 5)

Nearly all young people were prepared to endure some side effects as their doctor had forewarned them. However, there was personal variation as to how much each individual tolerated these side effects; some continued taking the medication despite episodes of faecal incontinence while others stopped with much milder side effects. Some young people were more resilient than others in coping with side effects.

Some initiated self-devised lifestyle strategies or changes in drug regimen to minimise side effects; we identified a number of key likely mediators that influenced how these side effects were managed.

#### **a) Regimen change to minimize the side effects**

Regimen changes were devised and initiated by both doctors and families. Some young people used orlistat flexibly and omitted doses to minimize side-effects at pre-determined

important times. Firstly, this allowed them dietary freedom at special occasions such as birthdays and secondly, it minimized side-effects in certain environments or events, such as school-time or during exams.

“I stopped [the medication] because I didn’t want to take them during the exams in case I had a bad stomach it would take time off [the exam]” (Young person 2)

Doctors at times recommended changes in formulation, dosage and frequency to minimise side-effects.

“They [doctors] changed her metformin dose and changed it to slow release. Then after that they changed the time she was taking it. It would help her a bit more.” (Parent 1, metformin)

“With the higher [initial] dosage I was vomiting more..... by breaking it down to two in the morning and two in the evening, I think it [vomiting] is a lot better. “ (Young person 8, aged 16 years, metformin)

In contrast, some young people reported discussing side-effects with their doctors but were told that their symptoms would improve if they continued with the current regimen.

[I was] “...just told to take it and get on with it really” (Young person 5, aged 13 years).

#### ***b) Alternative self-initiated strategies to manage side effects***

Families reported a range of self-initiated strategies to cope with the side-effects, particularly diarrhea and faecal incontinence. These included taking spare clothes to school in case of incontinence, not leaving the house or taking additional medication to counteract the effects.

“...she would start taking loperamide [anti-diarrheal medication] to counteract the effects of it ... a few times because she was like, I have got to go to school,

I have got the runs and I can't keep going out of the lessons, so it was a bit difficult that one" (Parent 2, orlistat).

"I was asked to bring in spare things because she kept having accidents [faecal incontinence]. She had [already taken] a few herself which she had taken in her bag" (Parent 13, orlistat).

"It made me stop going out for a while as I was worried that it might come over me and I might have to dash off and it would be embarrassing." (Young person 4, aged 16, orlistat)

Only a minority of young people taking Orlistat recognized that the "side effects" they were experiencing were in relation to the fat they had consumed and changed their diet.

"I went back to the really healthy stuff" (Young person 13, aged 13, orlistat).

### **Mediators in dealing with side-effects**

Young people identified certain mediators which influenced how side-effects were managed.

#### **(a) Reluctance to discuss side-effects with clinicians**

Despite reporting trust in their doctors, some participants were disinclined to talk to them at planned appointments or initiate additional interim appointments. Some did not feel their GP had sufficient expertise to support AOD usage.

"I probably would have liked more support – however, my consultant is very good and I do prefer her to the local GP. She [consultant] sees loads of people with the same condition. Helping them to change their ways and this and that. But at the GPs they do loads of different things..." (Young person 10, aged 14 years)

Few turned to other healthcare professionals such as pharmacists for support, and sometimes these interactions heightened familial concerns, particularly if the professional questioned the appropriateness of the medication.

“... when I picked up his prescription the pharmacist said “the child is only 13” and I thought oh, is there a reason...He just thought it was unusual, it was normally for older people. He thought it was a bit odd and he said maybe you should ask that question. And he also said it would be helpful for me to give him some feedback after he takes them” (Parent 7)

**(b) *Understanding mechanism of action***

Understanding of food content, in particular fat content, was also variable and some young people reported not having received any dietetic advice prior to commencement of the AOD. This included patients prescribed orlistat. Many had familial experience of AOD usage that increased their own understanding; this was often grandparents taking Metformin for control of type 2 diabetes or mothers who had taken orlistat for weight control.

Some perceived their drug-related symptoms as “side effects” whilst others realized that they were a consequence of high fat intake. The majority of participants who correctly understood the mechanism modified either their diet or drug regimen.

“if I was eating the fat, I would have to go to the toilet” (Young person 3, aged 16, orlistat).

**(c) *Age***

Young people reported that if they had been early adolescents at the time the AOD was introduced, they did not listen to the information given by the Doctor, preferring to leave understanding to the parent.

“I was at that age where I don’t need to know” (Young person 6, aged 14 years).

**(d) *Concerns about safety***

A few had concerns about the safety of the medicine because of the side effects whilst others felt that the medicines must be safe because a doctor had prescribed them.

“I thought that it couldn’t be, like, safe if it was keeping me awake all night and making me like go a lot” (Young person 5, aged 13 years, metformin).

**(e) *Environmental influences***

Many had heightened awareness of toilet facilities, particularly their proximity and the impact of sharing toilets. This was driven by concerns about faecal urgency, risk of incontinence and the embarrassment related to the staining of toilets with oily faeces.

“She felt she couldn’t be comfortable taking them at school and college, because she just couldn’t rush out, and when she said she did, it was like an orangey/yellow oil that goes into the toilet and it doesn’t flush away. So that is very embarrassing if you are out somewhere.” (Parent 1, orlistat)

**Model 3: Drug continuation: efficacy versus side-effects**

Participants continued with the medication for between 1 month and 8 years. 9 of 12 prescribed metformin, and 1 of 6 participants prescribed orlistat continued beyond 6 months. 7 young people discontinued an AOD. The decision to either continue with, or stop, the AOD was frequently based on a decisional balance between the efficacy of the AOD and ongoing side effects. The decision to terminate treatment was frequently described as a balance between the perceived benefits of the AOD and its side effects. Various mediators influenced this decision, including perceived benefits and expectations, lack of support and understanding of drug action.

“I don’t want to take something that I don’t think was working and making me ill”

(Young person 6, aged 14 years)

“I just thought what is the point of taking it if it is not working and I am not eating the rubbish foods, there is no point as it weren’t really doing anything”. (Young

person 3, aged 16 years)

Participants described efficacy in terms of body weight, body shape and metabolic parameters. Individual goals varied from going down a clothes size, to weight stabilisation. Most young people had expectations of weight control that were aligned with published outcomes, although some hoped for outcomes that were faster, more extreme or more guaranteed. Weight stabilisation was acceptable for some, and they continued to take it fearing that it would increase faster if they stopped taking the medicine.

“He [clinician] said that they may help me lose weight and my mind crossed out the word ‘may’ and replaced it with the word ‘will’. (Young person 9, aged 17 years)

“ It is keeping her weight not going up.” (Parent 10)

There was significant variation in the understanding of drug action, in terms of mechanism and efficacy. Some perceived that the AOD required a restricted diet and increased exercise to be effective, whilst others believed that lifestyle changes were not necessary. These views seemed unrelated to the drug prescribed. Some described the futility of taking an AOD as they were unable to undertake healthy behaviours, and subsequently stopped the drug.

“..... they said this [the medicine] is not a miracle worker it doesn’t help you lose weight. You help yourself to lose weight and it just gives you a little pat on the back every so often to help you carry on what you need to do....” (Young person 10, aged 14 years)

“I don’t know whether the tablet actually makes you lose weight or just because it makes you stop eating, it makes you lose weight”. (Young person 2, aged 17 years)

Drug termination was an active decision by young people and their families, and not by their doctor. The decision was taken by the young person alone, or with the advice and support of their parent. Very few young people or parents reported adequate drug monitoring and support from the obesity specialist; this influenced their decision to independently stop the drug.

“She (Mum) advised me not to take them because it wasn’t very nice for me experiencing this” (Young person 6, aged 14 years)

“I just stopped taking them, went cold turkey”. Interviewer: “What put you off ringing up the clinic to discuss it?” Young person: “I just didn’t think it was important.” (Young person 15, aged 15 years)

Support was a theme that spanned across all 3 models. One mother described the period taking the AOD as a “*lonely*” time. Few reported adequate support from their obesity specialist, primary care physician or pharmacist. Two participants described disheartenment after being discharged from a specialist service due to inadequate progress, and reported subsequent weight gain. General practitioners mostly only issued repeat prescriptions. Many young people said that they would be happy to be monitored by their GP if they could not get an appointment at the specialist clinic, yet others felt that GPs had insufficient experience to support them. Emotional support mainly came from friends and family. Parental supervision, usually from a mother, ensured that younger adolescents took the medication. As young people matured, parents were more likely to step back and let the young person take responsibility for their medication.

“I think there were times when she tried skipping it, but she had a dragon as a mother. So as long as I am aware it happens, and what I do now is put it all out in individual pill boxes for the day.” (Parent 13)

## **Discussion**

These are the first published qualitative data on adolescent experiences of AOD use. In this sample, AOD prescriptions were uniformly suggested and initiated by specialist paediatricians, with passive acceptance by young people and families. After initiation, families mostly described receiving minimal support from the specialist prescriber as well as from local clinicians including GPs and pharmacists. There was a wide variation in the experience and tolerance of side effects, which were largely managed by families independently of clinicians using self-directed strategies. Although doctors made the decision to start the drug, we saw that patients decided to terminate the drug, usually because of insufficient benefit to justify the side-effects.

Participants had a range of co-morbidities, including depression and hypothyroidism, which may have impacted on their experience of AOD usage. Due to the wide range of co-morbidities and small numbers of each, it was not possible to explore more fully the interaction between these individual conditions and AOD usage.

Similar findings have been demonstrated in the adult studies exploring AOD usage. Qualitative study participants from three primary care practices reported that doctors initiated AOD, giving patients little choice in the decision and inadequate information about the drugs and related lifestyle changes (12). Similar patterns of use have been reported in adults. Two previous studies showed that side-effects were a major factor influencing adherence, and many adults report using the medication flexibly to fit in with their lifestyles, and minimize side-effects at inappropriate times (13, 14). The highly visual side effects also encouraged

some adults to consider their behaviour as a cause of their obesity and to adopt a healthier diet (13). Similar themes for drug discontinuation were reported in these previous studies; participants who benefitted from the drug continued with, or adapted the medication, and those who did not lose weight abandoned it (14). Similar themes have also been demonstrated in the adolescent adherence literature, with insufficient clinician support, embarrassment, insufficient belief in drug efficacy, interference with usual activities and side-effects all being reported as barriers to medication adherence in other chronic conditions (15).

Results from this study offer insight into the experiences of young people who are taking AODs, and offer potential targets for change that could potentially improve drug adherence and outcomes in this patient population. They suggest that more careful approaches are needed to improve drug initiation and ongoing support. Potential strategies are summarized in box 1.

Box 1. Potential strategies to improve AOD initiation and ongoing support.

- I. Ensure that families accept the need for medication, with alternative options discussed, and drug initiated only when it fits in with the families own treatment ladder.
- II. Initiate the medication at a time that is right for the family, with consideration of the school day, week and year, and avoidance of periods where side effects may be problematic (e.g. examinations).
- III. Ensure that those prescribed orlistat are fully informed and understand the difference between treatment effects and side effects. This could include dietetic input to enable its use as an educational tool to identify high fat foods, and subsequently enable a low fat diet.
- IV. Provide sufficient information about side-effects at initiation, with written advice related to side-effect management strategies
- V. Provide sufficient ongoing support from specialist services, particularly related to management of side effects. Active monitoring of non-weight related benefits, e.g. cardio-metabolic risk factors, may reduce drug cessation.

Obesity is likely to be a life long disease for this cohort, given that current treatments have modest efficacy. Long-term drug use is likely to be an integral treatment modality in addition to behavior modification strategies at both the individual and population level. Effective prescribing habits are needed to support both current and future generations of anti-obesity medications.

### **Limitations**

Participants were recruited from three hospital clinics in England, with the majority from one hospital in which two of the authors are clinicians. This has the potential of limiting generalisability and introducing bias. However AOD in young people are largely initiated in

specialist centres and those centres included in this study were amongst the largest of a very small number of specialist paediatric obesity clinics in the UK. To minimize bias, all data were collected by an independent researcher not part of any clinical team and responses were anonymised before analysis.

Delays in the study may have led to problems with recall for those patients who stopped the medication some time previously. As with all qualitative studies, the researcher's presence during interviews could have affected the subjects' responses; every effort was made to reassure the participants that the researcher was both non-judgmental and not part of the clinical team, and their responses would be fully anonymised prior to analysis by the team.

We aimed to include patients who were prescribed AOD, but never commenced it. However, no such young people responded to recruitment invitations. We are therefore unable to comment on those who were prescribed an AOD but who never initiated medication.

Only a small minority of eligible subjects enrolled in the study, despite thorough attempts to contact them using clinical research nurses. It is highly possible that those with negative experiences felt more motivated to participate in the study. Largely negative responses indicate that participants are likely to have felt reassured about their anonymity, and did not fear reprisal from their clinicians.

## **Conclusions**

Use of anti-obesity drugs is challenging and complex for many adolescents, and few young people in our study described positive experiences. Multiple factors were identified that could be targeted to improve medication concordance and maximise efficacy, including improved clinician-patient partnership in decision making, and better patient education and subsequent support. Many of these are not unique to the current generation of anti-obesity drugs, and are likely to be relevant to novel drugs.

Word count: 5122

### **Conflict of interest**

The authors declared no conflict of interest. This article presents independent research funded by the National Institute for Health Research (NIHR) in England under its Programme Grants for Applied Research programme (RP-PG-0608-10035). The views expressed in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, or the Department of Health. JPHS's work in the Biomedical Research Unit in Nutrition is supported by a grant from NIHR.

### **Acknowledgements**

BW, RV, IW, SC and DC conceived the study. LJ undertook the interviews. LJ and BW analysed the data, with support from FS, RV and SC. All authors were involved in writing the paper, and had final approval of the submitted and published versions.

With thanks to Sally Ayres, Karen Phelan, Louise Spencer, Jo Blair and Ruth Allen for recruiting participants.

### **References**

1. National Institute for Health and Care Excellence. Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children. NICE Clinical Guideline 43. London 2006.
2. Park MH, Kinra S, Ward KJ, White B, Viner RM. Metformin for obesity in children and adolescents: a systematic review. *Diabetes Care* 2009; 32:1743-5.
3. Viner RM, Hsia Y, Tomsic T, Wong ICK. Efficacy and safety of anti-obesity drugs in children and adolescents: systematic review and meta-analysis. *Obesity reviews* 2010; 11:593-602.
4. Viner RM, Hsia Y, Neubert A, Wong IC. Rise in antiobesity drug prescribing for children and adolescents in the UK: a population-based study. *Br J Clin Pharmacol* 2009; 68:844-51.
5. Padwal R, Kezouh A, Levine M, Etminan M. Long-term persistence with orlistat and sibutramine in a population-based cohort. *Int J Obes (Lond)* 2007; 31:1567-70.
6. Padwal R, Kezouh A, Levine M, Etminan M. Long-term persistence with orlistat and sibutramine in a population-based cohort. *International journal of obesity* 2007; 31:1567-70.

7. McDuffie JR, Calis KA, Uwaifo GI, et al. Three-Month Tolerability of Orlistat in Adolescents with Obesity-Related Comorbid Conditions. *Obesity Research* 2002; 10:642-50.
8. Today Study Group. A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes. *N Engl J Med* 2012; 366:2247-56.
9. Cole TJ, Freeman JV, Preece MA. Body mass index reference curves for the UK, 1990. *Arch Dis Child* 1995; 73:25-9.
10. Guest G. How Many Interviews Are Enough?: An Experiment with Data Saturation and Variability. *Field Methods* 2006; 18:59-82.
11. Braun V, Clarke V. Using thematic analysis in psychology. *Qualitative Research in Psychology* 2006; 3:77-101.
12. Psarou A, Brown I. Patients' experiences of prescribed anti-obesity drugs and perceptions of support from primary care: a qualitative study. *Primary Health Care Research & Development* 2010; 11:250-9.
13. Ogden J, Sidhu S. Adherence, behavior change, and visualization: a qualitative study of the experiences of taking an obesity medication. *J Psychosom Res* 2006; 61:545-52.
14. Hollywood A, Ogden J. Taking Orlistat: Predicting Weight Loss over 6 Months. *J Obes* 2011; 2011:806896.
15. Hanghøj S, Boisen KA. Self-Reported Barriers to Medication Adherence Among Chronically Ill Adolescents: A Systematic Review. *Journal of adolescent health* 2014; 54:121-38.