Factors Determining Efficacy with the Use of Pharmacotherapy
in Children with ASD and Other Disorders

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Abstract

A variety of medications is prescribed to treat the symptoms presented by individuals with ASD and any subsequent secondary diagnoses, although there is limited information providing sufficient proof of efficacy. Every person has potential to respond uniquely to any type of stimulus, including medications. It is important to consider the individual when prescribing treatments. A store of anecdotal information that represents the variety found in the population of those with ASD could make this more effective. This study seeks to answer: (a) What pharmaceutical treatments are physicians prescribing for children with ASD at different ages and with different secondary diagnoses? (b) Are parents satisfied with the benefits of each of their children’s medications? (c) Do parents feel the perceived benefits of pharmaceutical treatments supersede any side effects of the treatments? (d) At what ages are parents more likely to use pharmaceutical interventions for their child with ASD (pre-school, elementary school, high school, or older)? Data was gathered through an online survey and distributed through e-mail to parent support networks and through social media. Participants were parents of at least one child with ASD who could use a computer and speak English. Based on the results of this survey, it appears that pharmaceutical treatment for those with ASD often results in adverse side effects and unsatisfied parents. Additionally, those who have found pharmaceutical treatments to be beneficial for their children tend to keep them on the same treatment plan for ten or more
years. It was confirmed that while there are few proven treatments for ASD, parents will continue to search for a medication that helps their child uniquely, and are willing to risk the side effects in their search.

*Keywords: autism, medication, parent opinions*
Factors Determining Efficacy with the Use of Pharmacotherapy in Children with ASD and Other Disorders

There are many disorders and symptoms that occur with high frequency in individuals with ASD, including Attention Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), Obsessive Compulsive Disorder (OCD), and sensory disorders. Each case of ASD is unique with regard to the severity of each of the presented symptoms and diagnoses. There are also a number of medications and diets used to treat the presented symptoms. The variety of medications some children are prescribed, as well as the variability among children with similar diagnoses, is intriguing, as each affects individuals differently.

Self, Hale, and Crumrine presented a (2010) brief overview of the use of pharmaceutical drugs to alleviate symptoms of ASD in their 2010 article written specifically for speech-language pathologists. They confirmed that most of these drugs are not scientifically proven to help treat the specific symptoms they are targeting. According to these researchers, Ritalin and Risperdal are the only two medications that have been proven efficacious in accomplishing what they are created for, as well as being more beneficial than detrimental in relation to side effects.

The goal of this research will be to gather information from parents of individuals on the spectrum and to compare their use of pharmacologic treatments, in order to see if there is any trend towards certain treatments, in relation to child’s age, where they fall on
the spectrum, and secondary diagnoses, including their perceptions of each medication. The survey will be conducted with the intent of guiding future research with additional information regarding medication choices by collecting the personal opinions held by parents who see the effects of medication played out in their children's lives.

**A Review of the Literature**

ASD is a developmental disorder most commonly identified between 2-3 years of age, when a child's social and language skills are noticeably different from their peers (Lightdale, Hayer, Duer, Lind-White, Jenkins, Siegal, Elliott, & Heyman, 2001). ASD is diagnosed on a spectrum because there are many different behaviors and delays, ranging in severity levels that characterize individuals with autism, including self-stimulatory behaviors, whether through repetitive actions, words, phrases, and/or thoughts, inattention, mood disorders, and a wide range of language and speech delays (Self et. al., 2009, 367). Individuals with ASD often are reluctant to deviate from their favored routines and interests. Other external behaviors commonly identified in the majority of individuals with ASD that hinder their daily functioning are referred to as target symptoms. Nagaraj, Singhi, and Malhi (2006) listed the following behaviors that have a potential for improvement with appropriate pharmacotherapy: hyperactivity, temper tantrums, irritability, withdrawal, stereotypies, aggressiveness, self-injurious behavior, depression, anxiety, obsessive-compulsive behavior, inattention, tics, and sleep difficulties.

**Approaches to Intervention**
There are two main approaches to intervention for individuals with autism: behavioral and pharmacological. The most heavily researched behavioral intervention is applied behavioral analysis (ABA). There is a journal entirely dedicated to studies done using ABA, the *Journal of Applied Behavior Analysis*. This approach is used with children of all ages and is especially effective with young children. Based on Skinnerian theory, it uses reinforcement to shape behavior in contexts. The child is taught with skills in a one-on-one setting through repetition, such as naming objects or colors. When tasks are correctly accomplished, the clinician gives positive reinforcement. Other skills addressed include turn taking, imitation, and joint attention (Blane, 2011).

In order for behavioral intervention to be successful, the family must also provide consistent responses to re-enforce the behavior. Scholars of other approaches often criticize ABA for not teaching naturalistic skills, arguing that the work done in therapy is not easily generalized into social settings. Blane (2011) however, states that generalization into peer settings “can be achieved systematically by moving mastered skills into a small, supported play group with other children on the spectrum” (p. 7).

In theory, combining these approaches may be the most successful for some individuals, especially children who have more severe stereotyped behaviors that interfere with traditional language therapy. Certain pharmaceuticals can sharpen attention, assist with focus, decrease anti-social and compulsive behavior, and reduce anxiety. For example, DeLong, Teague, and Kamran (1998) showed language skill improvement in young children with ASD when fluoxetine was combined with behavioral therapy. Fluoxetine was
administered to 37 children who were evaluated before and after a prolonged treatment time. They also relied upon parental feedback to determine more functional effectiveness of the trial. DeLong et al. (1998) reported that eleven of the children “became animated and vivacious; their movements normalized; awareness of their surroundings and problem-solving and contextual cognitive functions improved, and they were able to attend school in regular classes successfully” (p. 552). They did, however, see negative results in approximately 40% of the 37 participants.

Motivations Behind the Use of Drug Therapy

Bodfish (2004) proposes that a “lack of satisfaction with either the existing treatment options or their availability” (p. 323) may be a factor in parents’ choice to use pharmacotherapy for their child. Because parents will pursue pharmaceutical treatments despite a lack of sufficient proof of efficacy, extensive research is necessary to determine what conditions are most advantageous for each drug, in order for physicians to be able to best advise their patients. Many factors can affect efficacy, such as child’s age when treatment begins, environmental conditions, dosage levels, child’s severity on the spectrum, and duration of treatment. Because many factors must be taken into account, it is hard to take results of research and generalize them to the population of those on the autism spectrum. Most importantly, the benefits of each treatment must outweigh the potential for unwanted side effects.

While many drugs have shown potential without proof, a few drugs have been able to consistently prove themselves as more beneficial across a wide usage range. In
particular, Nagaraj et al. (2006) found that Risperidone, the only FDA approved drug to treat the target symptoms of ASD, “significantly improved functioning in the domain of social responsiveness and nonverbal communications and decreased symptoms of hyperactivity and aggression and irritability” (p. 453). In addition, the “safe and effective short-term” use of Risperidone has shown “decreases in challenging behavior that were maintained over time as well as the likelihood of relapse upon withdrawal” (Floyd & McIntosh, 2009, p. 906). In other words, symptoms were alleviated soon after beginning treatment, reaching a steady level of improvement; after stopping treatment, the target behaviors came back, indicating the medication was the source of change. The old, or typical, antipsychotics were effective but also came with a very high risk of tardive dyskinesia, a neurological disorder that appears after prolonged high dosages of strong medicine resulting in uncontrollable tics and spastic muscle movements. All other drugs that have shown levels of efficacy that make them appealing to parents and doctors of children with ASD also come with risks that vary for each individual case. However, the effects these drugs have had in research settings are desirable and worth the risks to some parents.

Research of Effective Drugs

Drugs specific to behavior. As with all drugs, there are significant risks of adverse side effects, which can be influenced by other factors surrounding the individual at the time of use. Sometimes, pharmacotherapy can be useful for a period of time, and then the body becomes immune to desired effects; other times, one medication may work very well on
one individual, but quite adversely on another. In addition, some drugs work very well with adults, but lack evidence to advocate their use in children, such as selective serotonin reuptake inhibitors (SSRIs). Fluoxetine, mentioned under Approaches to Intervention, is an SSRI. More about the risks that go along with SSRIs will be discussed under Risks Inherent with Pharmacotherapy.

Drugs for comorbid conditions. As stated previously, ASD is often accompanied by multiple disorders and varying symptoms, therefore it is common that children with ASD are prescribed a wide array of medication for each. Doctors and researchers have observed that sometimes, medications created for one condition will affect untargeted behaviors in some subjects. Researchers who looked into the use of divalproex to treat other symptoms of ASD found in two studies a reduction in repetitive behaviors, instability, and aggression, with minimal side effects (Hollander, Dolgoff-Kaspar, Cartwright, Esposito, Rawitt, & Novotony, 2001; Hollander, Soorya, Wasserman, Esposito, Chaplin, & Anagnostou, 2006). Perhaps if researchers gather enough information from parents about specific effects they see in their children while on certain medications, they can begin to make correlations between medications and effects, shedding light on which combinations of chemicals may be responsible. There is evidence from a study by DeLong et al. (1998) of the potential of studying correlations in drug combinations. They found that divalproex and fluoxetine could “prevent early symptoms of activation or irritability” in children who were first treated with divalproex, then treated with fluoxetine. Fluoxetine has been previously found to also increase social functioning (Floyd & McIntosh, 2009, p. 907). While a few drugs have been proven efficacious in the treatment of some of the characteristics of autism, there are
other stereotypies left unaddressed. For example, SSRIs have been FDA approved for the treatment of depression and regulation of behaviors of OCD, but “their efficacy has not been confirmed” in the case of perseverative, obsessive, and repetitive behaviors of children with ASD (Self et al. 2010, p. 371).

One well-conducted, randomized study by Nagaraj et al. (2006) in Chandigarh, India studied children between the ages of two and nine with ASD referred from the city and nearby states, comparing the use of Risperidone to placebos in order to evaluate its improvements in functioning and its safety. They did not use participants who had severe mental retardation, malnutrition, or another significant disease in addition to their diagnosis of autism. They had 39 children complete the study, which lasted six months. After analyzing improvements in different areas, they found a 94% response rate in the 19 participants in the Risperidone group- only one reported as worsened, nine as “considerably improved” and the remaining nine as “improved to some extent.” However, it was later revealed that several of the children developed a mild dyskinesia, and one developed transient drooling, reminding researchers of the inherent risks for any drug treatment plan, regardless of potential or proven degree of improvement.

The effects of any medication, whether for symptoms of ASD or a mere headache, can plateau at a certain dosage, and the body can become desensitized to its’ effects after prolonged exposure. The timeframe and dosages at which this occurs differ for every medication and individuals unique body chemistry, prompting a need for research to assess how long to prescribe a medication for, and what the best dosage for each patient is.
In the case of Risperidone, despite it’s approval from the FDA as a treatment for target symptoms, none of the research conducted thus far has been able to “produce enough evidence or reliable conclusions regarding the optimum duration of treatment and the period up to which the beneficial effects of Risperidone can be sustained after discontinuation” (Nagaraj et al., 2006).

**Risks Inherent with Pharmacotherapy**

Despite a number of studies providing evidence of successful alleviation of behaviors associated with ASD through pharmacotherapy, there is a much larger number of studies proving many theoretical treatments ineffective, or as having too many adverse effects to be worth an insignificant beneficial improvement. In addition to drugs like Risperidone not addressing all the symptoms of autism, most pharmaceutics are “not typically impacting autism at a deep enough level to produce the kind of socially valid outcomes that are being tracked in these studies of adults outcomes in autism” (Bodfish, 2004, p. 322).

Some antidepressant SSRIs have been used to treat anxiety and repetitive behaviors but they have not been studied well enough to present any reliable data in order to generalize application of use. Several SSRIs even increase hyperactivity and irritability, which are already common characteristics of ASD. On the other hand, it may be a worthy risk if the child has a severe anxiety disorder. The quandary of treatment with potentially harmful drugs clearly indicates that more studies are needed to make progress in the guidelines for prescribing antidepressants and in predicting the level of adverse effects in
different individuals. Floyd and McIntosh (2009) boldly state that most physicians are merely making their “best guesses when choosing from the currently available range of options” for treating the different typical behaviors of ASDs (p. 908), a situation that may exist at the crossroads of medical knowledge and parent needs for solutions to the emotional cost of raising children with ASD.

**Are there better options?** It is important to note, however, that other therapy approaches have sufficient support to confidently employ various methods to reduce these characteristics. If behavioral therapy has research claiming success, why do parents and doctors still feel the need to possibly quicken their children’s improvement through the use of medications? If a more functional approach to therapy proves extremely effective for some individuals, why do parents and doctors feel the need to add medication to their child’s treatment? There are many ways to facilitate therapy within the different approach methods- taking the time to find which activities work best for each unique client is part of the job of the speech language pathologist, the occupational therapist, the physical therapist, and any other professionals involved in the treatment of the individual. Bodfish (2004) posits there are some benefits to adding pharmacological treatments, but when compared to the complex needs of children with ASD, they are seemingly quite insignificant in the long run. “Simply put: treatments may bring about less flapping, more words, and more interactions when flexibility, meaning, and friends are what is needed” (Bodfish, 2004, p. 323).
Even some medications that have a proven degree of efficacy still need to be weighed against the potentially greater efficacy of behavioral therapy, and the child’s individual needs and circumstances.

**Implications of These Studies**

After reviewing the literature regarding varying treatment options for autism, both conventional and pharmacological, it is clear that there is a great need for clarification and a deeper understanding of the effects each has on the target symptoms of ASD. How can parents and physicians be confident in their decisions to prescribe treatments that have not been proven to be efficacious? The questions this study presented in the form of a questionnaire investigated parent perspectives on intervention using medication, and collected data on the various factors surrounding their child’s treatment plan. Areas of interest included, but were not limited to: current diagnoses, past and present use of pharmaceutical interventions, outside influences, age of child, positive effects observed, and negative effects observed.

**Questions of the Study**

1. What pharmaceutical treatments are physicians prescribing for children with ASD at different ages and with different secondary diagnoses?

2. Are parents satisfied with the benefits of each of their children’s medications?

3. Do parents feel the perceived benefits of pharmaceutical treatments supersede any side effects of the treatments?
4. At what ages are parents more likely to use pharmaceutical interventions for their child with ASD (pre-school age, elementary school age, high school age, or older)?

Methodology

This study sought to gain answers to these questions through the use of an electronic survey, which was distributed through various parental support groups and ASD networks. The target participants were English-speaking parents of at least one child on the spectrum who are able to read and write, as well as use a computer, and are willing to share their open opinions of their child’s treatment plans. There was no control for the age, gender, or severity of the child’s diagnosis. A paper survey was available for parents who prefer to complete the survey on paper. Networks were e-mailed to seek participation; if they agreed to participate they received an introduction letter with a link to the survey. The groups then forwarded the information to their members, posted it on their website, or presented in their meeting, making it available for those who chose to participate. Included in the letter of introduction was a brief description of the four questions of the survey and contact information should they have any questions. Parents were also informed that they were under no obligation to complete the survey if at any time they did not feel comfortable answering and that there were no benefits or risk of harm in completing it.

Results

Participants were parents of at least one child with ASD who could use a computer and speak English, except for one adult who responded for herself. Fifty-one total participants took the survey, forty-four of which have pursued pharmaceutical treatments
and shared those experiences by answering each question on the survey. The remainder of respondents had chosen to pursue treatment through diet and supplement only, or had not pursued pharmaceutical treatment for various other reasons.

**Treatments, Age, and Secondary Diagnoses.** The age distribution of participants’ children is shown in Figure 1. It was observed that a large number of medication treatments are began during the 7-12 year age range. Most children had been prescribed more than one medication- 102 total medications were reported using the options listed. Medications reported in the open-response question that were not listed include, but are not limited to, Vyvanse, Prevacid, and Intuniv. The ages at which the 102 medications were prescribed were as follows: 1-3 years old (8), 4-6 (19), 7-9 (34), 10-12 (23), 12-15 (8), 16-18 (8) and 19-21 (1).

A pie chart illustrating the frequency of each secondary diagnosis is shown in Figure 2. Other diagnoses reported that were not listed were: depression, apraxia, mood disorder NOS, visual snow, cerebral palsy, cerebellar atrophy, delayed bone age growth, double vision/farsightedness/cataracts, and clinodactyly.

**Parent Satisfaction.** Knowing that there are very passionate opinions regarding the use of pharmaceuticals for individuals with autism, it is important to note that this study neither endorses nor advocates against the use of pharmaceutical treatments- it only seeks to assist those who choose to follow a medical route of treatment. In order to collect some of these opinions, the survey had an open-response question: “Are there any medications with which you have been extremely satisfied or dissatisfied?” Therefore, these results are
not statistical, but anecdotal. Each response gives insight into the lives led by the individuals behind the data, and the following paragraphs represent some of the most detailed and significant responses, along with the diagnoses of each child. By attaching every diagnosis with age and satisfaction, physicians and parents can add this information to their experience and knowledge of other cases of extreme satisfaction/dissatisfaction.

One parent was extremely pleased with Tenex (guanfacine) for their 10-12 year old with Asperger’s, ADHD/ADD, APD, anxiety disorder, enuresis, fine motor skills deficit, mixed receptive/expressive languages disorder, OCD, PDD, sensory integration and a tic/movement disorder: “Tenex really helped with his motor tics but we switched to the long acting one, Intuniv for better results.” However, the parent of a 19-21 year old with Asperger’s who attends college claimed that Tenex/Intuniv seemed to be a “gateway drug to acclimate parents to the notion of prescription treatment” and did not see any benefits of it, nor did they experience benefits that outweighed the emotional side effects of Ritalin/Concerta. For a 10-12 year old with Asperger’s, ADHD/ADD, anxiety disorder, OCD, PDD, and sensory integration disorder, Intuniv (guanfacine) has been his “miracle drug”.

Another parent of a 10-12 year old with Asperger’s, ADHD/ADD, APD, PDD, and sensory integration disorder reported that Vyvanse and Intuniv have worked the best for them, but they “had to advocate with the state for that medication mixture.” On the other hand, one 10-12 year old with high functioning autism, intermittent explosive disorder, PDD, and mood disorder NOS had hallucinations from Risperdol and Seroquel taken between ages 7-9, and “Haldol gave him such bad dystonia he had to go to the ER.” One parent of a boy with high functioning autism tried methylphenidate and amphetamine/dextroamphetamine at
7-9 years for her son, but stopped after only 0-3 months because “stimulant medications for my child totally changed what identified him, his smile, active personality to a child that laid still and didn’t move, smile or anything.”

**Do Benefits Outweigh Side Effects?** The most frequent durations of time reported were three years (15 times) and two years (14 times). Duration and satisfaction were compared and split into two charts. Figure 3 shows the most popular treatments. The criterion used to determine most popular treatments was frequency of use- eight was chosen as the cut off. Paroxetine was included in this chart because there were eight reported uses, even though one instance did not have duration information to chart. Similarly, Methylphenidate was reported twelve times, but one instance did not have duration information. Figure 4 shows those that appeared less than eight times.

**Discussion**

**Treatments, Age, and Secondary Diagnoses.** There was no significant trend observed correlating specific ages with specific medications. Looking at ages when treatment began for all medications listed (complete data listed under Results: **Treatments, Age, and Secondary Diagnoses**), the majority of respondents began to pursue pharmaceutical treatment for their children between the ages of 4-12. Within the 4-12 range, the majority of treatments began between 7-9, answering question four of the study “At what ages are parents more likely to use pharmaceutical interventions for their child with ASD?”. This is not surprising due to the increased academic demand on children in this stage of life.
**Parent Satisfaction.** Anecdotal responses spanned very positive to very extreme. Risperidone caused one 7-9 year old boy with Autism, sensory integration disorder, and epilepsy to develop breast milk; citalopram (Celexa) increased one 13-15 year old girl’s aggression to the point that 911 was called and her and her mother had to go to the ER. The same girl who also has anxiety disorder, expressive language disorder, and sensory integration disorder gained 100 pounds on Risperidone, but the effect on her behavior outweighed the weight gain. Conversely, several parents enthusiastically report Vyvanse (lisdexamphetamine), and Intuniv (guanfacine), as discussed earlier. From the responses in this study, only strongly negative anecdotal evidence was found; there were very few individuals that self-reported strongly positive anecdotal examples.

**Do Benefits Outweigh Side Effects?** If duration is an indication of satisfaction with the benefits, it is important to look closely at duration statistics. It would seem that it could be assumed that parents felt that the benefits were greater than any side effects experienced for those children who used their treatments for a more long-term use. However, eight of the two-year durations and four of the three-year durations had a neutral satisfaction ranking. In these instances, it is likely that parents allowed the treatment time to take effect, but never saw significant benefits.

For those medications that were taken for less than two years, it cannot be assumed that in each case the side effects far outweighed the benefits perceived- the survey did not require that information unless parents volunteered their reasoning for taking a child off a medication so quickly in the free response as a ‘highly unsatisfied’ medication. Six of the
medications used for less than two years were also reported as 'neutral' satisfaction, most likely meaning they parents felt that the while side effects were not significant, the benefits were also not significant enough to continue treatment. Due to their short durations, some of these treatments may not have had enough time to fully impact the individual in order for any benefits to be perceived, while others simply may not have been compatible with the individual’s specific body chemistry and that was noticed immediately.

Of the 71 satisfaction rankings of the most popular medications, there were 33 satisfactory results, 24 unsatisfactory, 12 neutral and 2 unnoticed. Of the 31 satisfaction rankings of the less popular medications, 13 were satisfactory, 11 unsatisfactory and 7 neutral. Also interesting to note is that very few of the participants has been on any pharmaceutical for more than two or three years. Preliminary predictions and explanations about the cause of such short durations are as follows: (1) they could be explained by those who are currently on a medication; for example, an individual might show as only being on a medication for 0-3 months, but if you look at the data closer, the age when treatment began is close to their current age- their response is not a true representation of the duration. Likewise, the satisfaction ranking will be somewhat skewed because they just began the treatment. (2) A number of them could be due to immediate adverse responses. Looking at durations that were reported as 10-13 months or less, it was observed that the majority of those who quit their treatment early due to adverse reactions were in the 4-9 year age range, while those who reported short durations as a result of currently being on that treatment plan were in the 10-12 year age range.
Limitations

The survey question regarding age when treatment began, duration, and satisfaction produced complex results that did not facilitate a simple comparison of data through a generated chart. The amount of negative anecdotal responses is possibly due to the openness of the free response question (“have there been any medications with which you have been extremely satisfied or dissatisfied?”) because often, negative experiences are more readily recalled than positive experiences. Key information this study lacked was the reasoning behind cessation of a treatment and a place to note that treatment was ongoing.

Future Studies

For future studies, the question regarding age when treatment began, duration, and satisfaction needs to be broken down into multiple questions and formatted in a way to make it easier to obtain more details and allow the responses to be easily converted into charts. While 33 satisfactory treatments compared to 38 unsatisfactory treatments is seemingly not a notable difference, it would be beneficial to make the same comparison in a larger study in which the data might represent a more diverse group of people. A larger amount of data would also be able to better predict age/medication correlates to find any trends connecting age of treatment with specific treatments levels of efficacy. To address the challenge in comparing so many cross points of data, there could be multiple studies that are age-controlled. Through increasing participant numbers and isolating age ranges perhaps correlations could be more readily found. In order to elicit positive anecdotal responses, it could be useful to ask one question about positive experiences, and another
about negative experiences. It could also be interesting to hear what a child’s opinion of their medication was- the adult female who answered for herself said that Concerta helped her do better in school. Would other individuals report the same satisfaction? Or would they dislike the way a medication affected their mood, appetite, etc.?

Conclusions

Overall, only 46 satisfaction responses would be considered positive (a 4-satisfied or 5-highly satisfied), while 56 satisfaction responses were less than satisfactory (a ranking of 3-neutral or below). While these statistics are quite similar, when one considers taking a less than 50% chance that their child will experience benefits by taking a new medication and a greater than 50% chance that they will experience very adverse side effects, it is still a frightening choice for parents to make. Based on the results of this survey, it appears that pharmaceutical treatment for those with ASD often results in adverse side effects and unsatisfied parents. Additionally, those who have found pharmaceutical treatments to be beneficial for their children tend to keep them on the same treatment plan for ten or more years.

Although the results were inconclusive with respect to any strong correlations for guiding physicians in prescribing treatments, they did provide useful information regarding the treatment of individuals with ASD.

It was confirmed that while there are few proven treatments for ASD, parents will continue to search for a medication that helps their child uniquely, and are willing to risk
the potential harmful side effects in their search to minimize the symptoms of ASD and other comorbid diagnoses.
References


Figure 1. Age distribution.
Figure 2. Secondary diagnoses.
Figure 3. Satisfaction and duration of the most popular medications.
Figure 4. Satisfaction and duration of the less popular medications.