

Supplementary material

Appendix 1 – Search strategy for electronic bibliography search

Search line	Search terms	Search field
1	exp compliance physical/ OR treatment compliance/ OR exp patient compliance/ OR persistence/	Subject heading
2	(treatment* OR therap* OR drug* OR medic*) ADJ2 (adher* OR complian* OR persist*)	.ti, ab, kw
3	1 AND 2	
4	exp questionnaire/ OR exp questionnaires/ OR exp "surveys and questionnaires"/ OR patient-reported outcome/ OR outcome assessment/ OR self report/	Subject heading
5	(develop* OR valid*)	.ti, ab, kw
6	4 AND 5	
7	3 AND 6	
8	exp qualitative research/ OR qualitative analysis/ OR exp interview/ OR exp interviews/ OR interviewers/ OR interviewing/ OR interviews as topic/ OR exp focus groups/ OR exp phenomenology/ OR ethnography/ OR grounded theory/ OR thematic analysis/	Subject heading
9	(review OR summar*)	.ti, ab, kw
10	8 AND 9	
11	3 AND 10	

12	7 OR 11	
13	Limit to past 5 years	
14	Limit to English language	
Ranking criteria	<ul style="list-style-type: none"> • Rank 1: Abstract is focused on development or validation of existing PRO adherence measures OR Abstract contains qualitative data from the patient perspective reporting concepts that impact on or drive patient adherence • Rank 2: Abstract reports data collected via PRO adherence assessments, but the measures are not the focus of the abstract OR Abstract does not contain qualitative data, but details concepts impacting patient adherence • Rank 3: Abstract reports quantitative adherence data, but does not specify measures used, may not be patient-reported • Excluded: Abstract does not report any quantitative adherence data or any concepts impacting patient adherence 	

Appendix 2 – Adherence concepts identified in ≥ 4 qualitative review articles

Concept	Description	Diseases concept reported in	Number of publications concept reported in (N=9)
Patient-related concepts			
Perceived treatment efficacy	The extent and speed at which treatment ameliorated symptoms influenced patient perceptions of efficacy. Patients were more likely to be adherent to treatment if they felt it was efficacious.	Osteoarthritis ¹ , asthma ² , inflammatory bowel disease (IBD) ² , cystic fibrosis ³ , (breast) cancer ^{4,5} , type II diabetes ⁶ , and renal transplant patients ⁷	n=7 ¹⁻⁷
Patient involvement in disease management	Patients who were involved in planning their treatment felt more autonomous and competent, which facilitated increased adherence.	Osteoarthritis ¹ , asthma ^{2,8} , type II diabetes ^{2,6} , breast cancer ⁵ , HIV ⁹ and liver ² and renal transplant patients ⁷	n=7 ^{1,2,5-9}

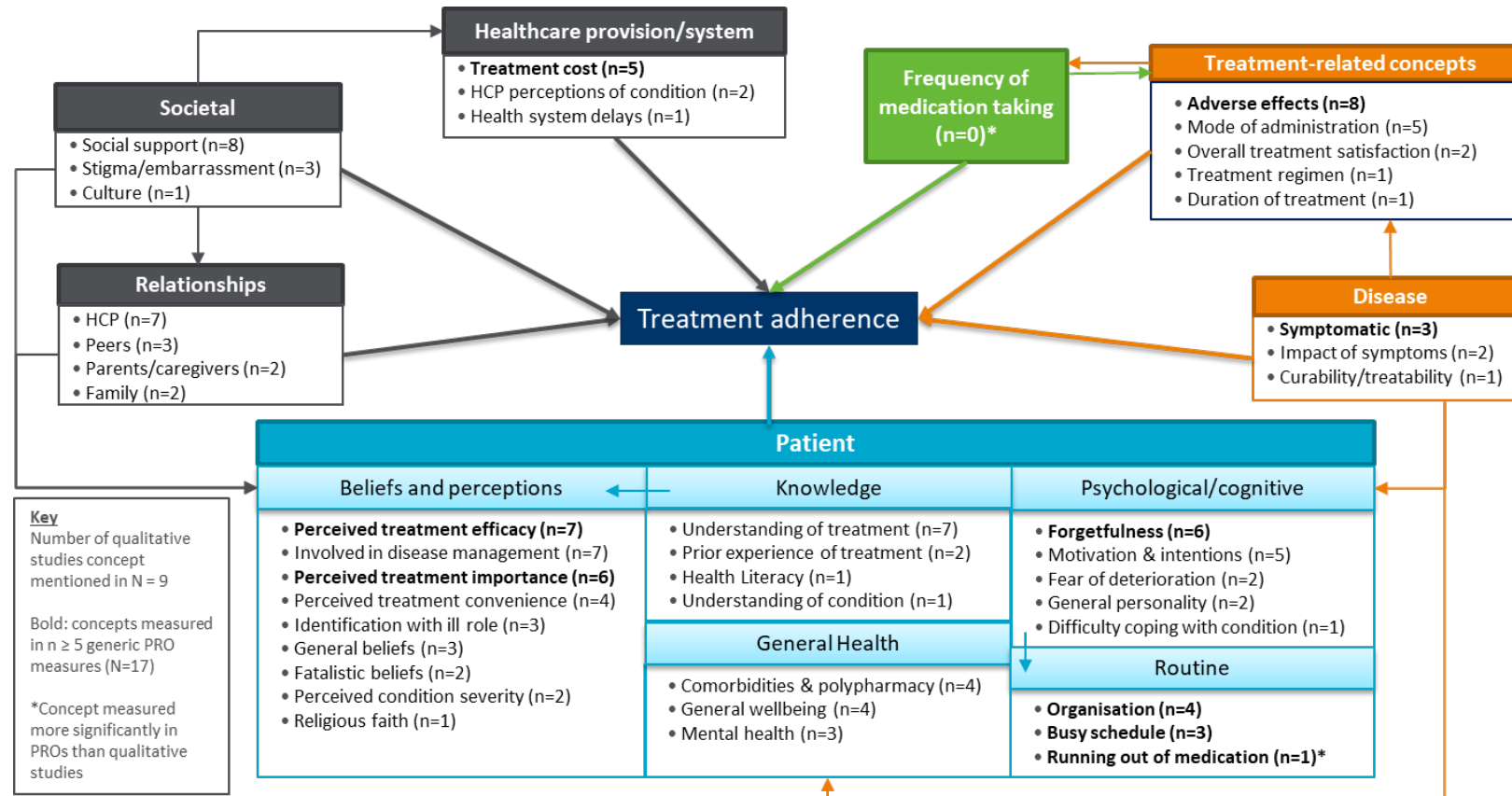
Concept	Description	Diseases concept reported in	Number of publications concept reported in (N=9)
Understanding of treatment	Patients who understood the purpose, mode of action, and mode of application of their treatment were more likely to be adherent.	Osteoarthritis ¹ , asthma ² , IBD ² , breast cancer ⁵ , type II diabetes ⁶ , HIV ⁹ , cystic fibrosis ³ , and renal transplant patients ⁷	n=7 ^{1-3,5-7,9}
Perceived treatment importance	Holding the beliefs that medication is unnatural or unnecessary for disease management was reported as a barrier to adherence.	Asthma ^{2,8} , IBD ² , haemophilia ² , (breast) cancer ^{4,5} , type II diabetes ⁶ , and cystic fibrosis ³	n=6 ^{2-6,8}
Patient forgetfulness	Unintentional nonadherence was regularly reported due to patients forgetting to take medication.	Asthma ^{2,8} , IBD ² , type II diabetes ^{2,6} , epilepsy ² , cancer ⁴ , cystic fibrosis ³ and liver ² and renal ⁷ transplant patients	n=6 ^{2-4,6-8}
Motivations and intentions	Patients who intended and felt obligated or otherwise motivated to take medication were more likely to be adherence. The desire for normalcy was a barrier to adherence where taking treatment was conspicuous, and	Osteoarthritis ¹ , asthma ² , kidney disease ² , type II diabetes ^{2,6} , sickle cell anaemia ² , rheumatoid arthritis ² , cystic fibrosis ³ , and liver ² and renal ⁷ transplant patients	n=5 ^{1-3,6,7}

Concept	Description	Diseases concept reported in	Number of publications concept reported in (N=9)
	a facilitator where treatment was discrete and reduced symptoms.		
Perceived treatment convenience	The perception that treatment disrupted daily activities was a barrier to adherence.	Osteoarthritis ¹ , asthma ² , kidney disease ² , cancer ² , HIV ⁹ , and cystic fibrosis ³	n=4 ^{1,3,9}
Organisation	Organisational barriers to adherence included forgetting to refill prescription medication, forgetting to take medication while travelling, and being unable to find medication.	Asthma ² , IBD ² , haemophilia ² , sickle cell anaemia ² , type II diabetes ⁶ , cystic fibrosis ³ , and renal disease ² and transplant patients ⁷	n=4 ^{2,3,6,7}
Comorbidities and polypharmacy	Patients with comorbidities or conditions requiring multiple medications were less likely to be adherent due to the perception that they were taking too many medications.	Osteoarthritis ¹ , asthma ² , IBD ² , type II diabetes ^{2,6} , and renal transplant patients ⁷	n=4 ^{1,2,6,7}

Concept	Description	Diseases concept reported in	Number of publications concept reported in (N=9)
General wellbeing	Patients reported a decrease in adherence to medications when feeling fatigued or unwell for reasons unrelated to their disease.	Osteoarthritis ¹ , asthma ² , IBD ² , breast cancer ⁵ , HIV ² , and cystic fibrosis ³	n=4 ^{1-3,5}
Non-patient related concepts			
Social support	Support in treatment management from friends, family, and health care professionals improved medication adherence; while perceived judgement from social networks was a barrier to adherence.	Osteoarthritis ¹ , asthma ^{2,8} , epilepsy ² , rheumatoid arthritis ² , type II diabetes ^{2,6} , breast cancer ⁵ , HIV ⁹ , cystic fibrosis ³ , and renal disease ² and transplant patients ⁷	n=8 ^{1-3,5-9}
Adverse effects	Both the occurrence of adverse events and side effects, and the fear of future adverse events or long-term side effects were reported as barriers to patient adherence.	Osteoarthritis ¹ , asthma ² , epilepsy ² , IBD ² , type II diabetes ⁶ , (breast) cancer ^{4,5} , HIV ⁹ , cystic fibrosis ^{2,3} , liver	n=8 ^{1-7,9}

Concept	Description	Diseases concept reported in	Number of publications concept reported in (N=9)
		transplant patients ² , renal disease ² and transplant patients ⁷	
Relationship with health care professionals	Patients reported that they were less likely to be adherent if their health care professional demonstrated poor quality communication, limited support, and decreased interest in adherent patients.	Asthma ^{2,8} , epilepsy ² , rheumatoid arthritis ² , type II diabetes ^{2,6} , breast cancer ⁵ , HIV ⁹ , cystic fibrosis ³ , and renal transplant patients ⁷	n=7 ^{2,3,5-9}
Treatment cost	Patients reported treatment costs and limited insurance coverage (in relevant countries) as barriers to adherence.	Osteoarthritis ¹ , asthma ² , IBD ² , type II diabetes ⁶ , HIV ⁹ , and cystic fibrosis ²	n=5 ^{1-3,6,9}
Mode of treatment administration	The complexity, comfort, and ease of treatment administration were reported to impact patient adherence.	Osteoarthritis ¹ , asthma ^{2,8} , IBD ² , HIV ⁹ , cystic fibrosis ^{2,3} , and renal disease ²	n=5 ^{1-3,8,9}

Appendix 3 – Preliminary conceptual model developed following literature review



Appendix 4 – Supporting quotes associated with forms and drivers of medication adherence

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
Forms of medication non-adherence				
Skipped dose: n=36/57; 63.2%	11/18; 61.1%	9/18; 50.0%	16/21; 76.3%	<p><i>“Yes but usually I remember it earlier. So when I wake up and see the box I go, ‘Oh, did I take it last night? No, I didn’t.’ But I don’t take it in the morning either. Instead I take the next one the next night, with the regular routine”</i> (German participant with hypertension)</p> <p><i>“At night I always take it, because if I don’t wake up at midnight, maybe a little fatigued and I have to use it as a rescue. So, I always take the night one. And in the morning, as maybe I get up very well, I breathe very well and I don’t notice anything, because there are times when I forget.”</i> (Spanish participant with asthma)</p> <p><i>“So sometimes, you know, at that point I go, you know what, I’ll just do it later, uh, or, you know, I, you know, skip to take it I suppose”</i> (USA participant with diabetes)</p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
<p>Taken later: n=29/57; 50.9%</p>	<p>11/18; 61.1%</p>	<p>5/18; 27.8%</p>	<p>13/21; 61.9%</p>	<p><i>“It did happen sometimes that I did not keep to the time and used it maybe a bit later because it was not fitting at the time”</i> (German participant with MS)</p> <p><i>“Yes I did. Uh... sometimes, it's because... if I work, for example, I take it before I go out to work. The day I wake up later, I take it later”</i> (Spanish participant with depression)</p> <p><i>“If I'm up, I'm watching TV, anything, or looking at something. I won't take it until I'm like through or whenever I get ready”</i> (USA participant with schizophrenia)</p>
<p>More medication: n=15/57; 26.3%</p>	<p>4/18; 22.2%</p>	<p>5/18; 27.8%</p>	<p>6/21; 28.6%</p>	<p><i>“Well, there are times when I proactively increase the 200 spray to three times a day”</i> (German participant with asthma)</p> <p><i>“Well, when I have the outbreaks, the crises, well, I usually increase the dose a little. I do it twice a day. Even up to 3 times a day”</i> (Spanish participant with psoriasis)</p> <p><i>“And the Klonopin would make me kind of—it would take the edge off me a lot to where I'd be more relaxed. Um, and so, um, I did take a little bit more of that”</i> (USA participant with schizophrenia)</p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
<p>Taken earlier: n=14/57; 24.6%</p>	<p>5/18; 27.8%</p>	<p>4/18; 22.2%</p>	<p>5/21; 23.8%</p>	<p><i>“When I go to bed at half past 10, I take it at 10 pm. When I go to bed at half past 9, then I take it at 9pm. But always in the evening”</i> (German participant with depression)</p> <p><i>“Let's see, for me the time interval is very wide. I mean, there are days I've taken it before”</i> (Spanish participant with hypertension)</p> <p><i>“I'm able to sleep and then take them too early in the morning. Um, or just, uh, because of fatigue, uh, fall asleep and not take them at all”</i> (USA participant with multiple sclerosis)</p>
<p>Less medication: n=13/57; 22.8%</p>	<p>8/18; 44.4%</p>	<p>1/18; 5.6%</p>	<p>4/21; 19.0%</p>	<p><i>“There I had a phase where I did not take it regularly and then had an attack again”</i> (German participant with multiple sclerosis)</p> <p><i>“Because with Pluralais, at the beginning, uh, I didn't stop suddenly but as I was forgetting pills and that's when I suddenly made the decision to, well, stop the medication”</i> (Spanish participant with asthma)</p> <p><i>“[If I] think I'm going to eat something bigger than I do and/or might give a little less when I think I'm not going to eat quite as much”</i> (USA participant with diabetes)</p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
Taken without food: n=2/57; 3.5%	0/18; 0%	0/18; 0%	2/21; 9.5%	<i>“Uh, I’ve done that sometimes, you know, if I’m in a hurry and I just have to get out. I will take—the pill is the most important thing to me. Eating is like secondary, but the pill, taking the pill is the most important thing to me”</i> (USA participant with hypertension)
Substituted other medication: n=2/57; 3.5%	0/18; 0%	1/18; 5.6%	1/21; 4.8%	<i>“But what I did was I just bought some over-the-counter one and just used a lot of that and mixed it with like the Aquaphor”</i> (US participant with psoriasis) <i>“Eh... yes, once I had a crisis and I didn't have the inhaler handy and instead of the Salbutamol they gave me... I mean, I had a friend who is also asthmatic and who uses Ventolin. And it's true that I took a shot of Ventolin”</i> (Spanish participant with asthma)
Not cleaning skin before use: n=1/57; 1.8%	0/18; 0%	1/18; 5.6%	1/21; 4.8%	<i>“INTERVIEWER: And do you always, um, adhere to this? Do you always apply it to clean skin? PARTICIPANT: Not always”</i> (USA participant with psoriasis)
Drivers of medication non-adherence*				

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
Forgetfulness: n=35/57; 61.4%	11/18; 61.1%	8/18; 44.4%	15/21; 71.4%	<p><i>“Yes, that I can tell you. 98% percent of the time, I always take my medication. In the early years, that was not always the case; I did forget them sometimes”</i> (German participant with depression)</p> <p><i>“And in the morning, as maybe I get up very well, I breathe very well and I don't notice anything, because there are times when I forget”</i> (Spanish participant with asthma)</p> <p><i>“Um, unless, you know, I forgot when I was at the office visit, uh, he said something and if it's not written on the prescription bottle then I could forget I guess”</i> (USA participant with diabetes)</p>
Not in usual routine: n=31/57; 54.4%	10/18; 55.6%	7/18; 28.9%	14/21; 66.7%	<p><i>“Well, like I said – normally, in my daily routine, I take them in the morning and the evening. But – like I said – if I go somewhere spontaneously, it happens that it is delayed”</i> (German participant with schizophrenia)</p> <p><i>“Okay... If I have gone out of my usual routine, in the case that I have gone out of my usual routine, I often forget”</i> (Spanish participant with hypertension)</p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
				<i>“Once it's not in my, my daily routine, it's—unless I'm experiencing symptoms—so, so like if I on a rare occasion where I'm transitioning from season to season but I don't experience symptoms, then I'm not really thinking of, you know, a flare-up or a reason to take the medication, so I don't”</i> (USA participant with asthma)
Busy: n=22/57; 38.6%	7/18; 38.9%	4/18; 22.2%	11/21; 52.4%	<i>“If I were out and about, maybe at a party, or if I were going somewhere and had forgotten to bring the medication: sure.”</i> (German participant with hypertension) <i>“Well, because I was busy with something else. I was immersed in another matter at the time of having to give me the dose, and... no... Maybe you mark what you have to inject and suddenly you start a conversation or some work or something. And all of a sudden, you forget”</i> (Spanish participant with hypertension) <i>“It's just too busy and I just didn't get around to it or sometimes the doctor's office don't call it in fast enough in a timely manner”</i> (USA participant with psoriasis)
Poor organization:	8/18; 44.4%	4/18; 22.2%	8/21; 38.1%	<i>“I slept over at a friend's once and forgot to bring it along”</i> (German participant with depression)

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
n=20/57; 35.1%				<p><i>“Well, because I went... uh... on a trip and forgot them at home”</i> (Spanish participant with multiple myeloma)</p> <p><i>“Uh, well we went on a trip, didn’t take it with me, a daytrip, that kind of stuff. Uh, if we’re going on an extended period, we, we remember to take it. Uh, an occasional daytrip, I may forget to take the stuff at nighttime”</i> (USA participant with diabetes)</p>
Running out of medication: n=16/57; 28.1%	4/18; 25.0%	5/18; 27.8%	7/21; 33.3%	<p><i>“It has happened to me. I looked into the package at night, oops, box empty. Yes, it has happened once”</i> (German participant with hypertension)</p> <p><i>“Because I remember once that I was not told at the pharmacy that it was the last month I had the prescription medication. And when I realized, I didn't have the medication”</i> (Spanish participant with depression)</p> <p><i>“The refills maybe later that day or the next day, um, sometimes I have not taken the full amount that I should have taken just because I wanted to last throughout that day or so before the refill happens on that”</i> (USA participant with diabetes)</p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
Experience of side effects: n=13/57; 22.8%	3/18; 16.7%	3/18; 16.7%	7/21; 33.3%	<p><i>“Well, I had quite a lot of different medications; and then you notice they do not agree with you, have side effects like strong feeling of hunger; and sometimes it also happened that they worsened the symptoms”</i> (German participant with schizophrenia)</p> <p><i>“I use this last one because it has fewer side effects and is easier to apply. And the other one was oral and had many more side effects”</i> (Spanish participant with psoriasis)</p> <p><i>“Um, but, uh, what happens is, is, um, um, those, um, uh—the, the pills that I take have become, um, uh, half like a personality and, uh, if I sometimes am agreeable with them and sometimes I’m not. When I’m agreeable, I am more compliant and usually follow—unfortunate—the rules”</i> (USA participant with multiple sclerosis)</p>
Low perceived necessity: n=12/57; 21.1%	3/18; 16.7%	4/18; 25.0%	5/21; 23.8%	<p><i>“It is a reason indeed because I’m a man. And men are strong and men don’t cry. And so I thought I could manage without”</i> (German participant with schizophrenia)</p> <p><i>“So of course, as I felt better and better, I’m not going to put drugs into my body, which I feel is neither good nor bad for me”</i> (Spanish participant with asthma)</p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
				<i>“Well I’m—well when I first started off, I just say I was a little lacking on it. But I found out how important. It’s very, you know, it’s very important that I take my medicine. I know for now to take it”</i> (USA participant with multiple myeloma)
Perceived side effects n=11/57; 19.3%	3/18; 16.7%	3/18; 16.7%	5/21; 23.8%	<p><i>“Yes, as I was saying: the side effects. I used to be afraid of them and I was also afraid I might not tolerate it because of some of the ingredients”</i> (German participant with psoriasis)</p> <p><i>“I’ve been avoiding side effects for a long time. Then, ‘Sometimes’ I stop it, but not completely; I reduce the applications, of course, because of side effects”</i> (Spanish participant with psoriasis)</p> <p><i>“And so sometimes I mean I have taken less of it because I thought I’m going to, you know, eat a good amount and then do a lot of activity and I don’t want my blood sugar levels to drop too low”</i> (USA participant with diabetes)</p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
Polypharmacy: n=10/57; 17.5%	5/18; 27.8%	0/18; 0%	5/21; 23.8%	<p><i>“What I do worry about is that I have to take far too many tablets in general”</i> (German participant with diabetes)</p> <p><i>“Because once upon a time I used to get the pre-pack, pill packs already packed. And my medicine sometimes was changing regular. So they couldn’t keep up with the, you know, pre-packed pills, so we had to go with pouring the—for me to pour my own meds”</i> (USA participant with multiple myeloma)</p>
Low perceived efficacy: n=9/57; 15.8%	1/18; 5.6%	2/18; 11.1%	6/21; 28.6%	<p><i>“Because on that day I was feeling more poorly than usual and I was thinking, “What am I doing this for”?”</i> (German participant with schizophrenia)</p> <p><i>“With the last (medication) I've had in the last few years, I didn't need it. But before I did; I used it more on demand because I felt bad”</i> (Spanish participant with asthma)</p> <p><i>“Of course sometimes I feel they're not doing anything and then they're just a waste of time and waste of money”</i> (USA participant with multiple sclerosis)</p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
No acceptance of sick role: n=8/57; 14.0%	2/18; 11.1%	2/18; 11.1%	4/21; 19.0%	<p><i>“Yes, it has happened: The sun was shining and I was thinking, “I’m not sick at all”. And I didn’t take them” (German participant with schizophrenia)</i></p> <p><i>“Uh... yeah. The Pluralais I am convinced that, for what I have, I do not need it (laughs)” (Spanish participant with asthma)</i></p> <p><i>“And I guess because it was new to me, so a couple days and then I was keeping an eye on my blood pressure and my blood pressure was fine when I didn’t take it and my blood pressure was fine” (USA participant with psoriasis)</i></p>
Low perceived importance: n=8/57; 14.0%	2/18; 11.1%	1/18; 5.6%	5/21; 23.8%	<p><i>“And one probably then tries to find out if it does not work also without them. But that is only possible ... when my condition is stable” (German participant with schizophrenia)</i></p> <p><i>“With the last (medication) I’ve had in the last few years, I didn’t need it. But before I did; I used it more on demand because I felt bad” (Spanish participant with asthma)</i></p> <p><i>“So the symptoms sort of remind me to take the medication. Whereas opposed to during the other seasons, out of sight, out of mind sort of thing” (USA participant with asthma)</i></p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
Stigma/embarrassment: n=7/57; 12.3%	2/18; 11.1%	0/18; 0%	5/21; 23.8%	<p><i>“But you do not want everybody to see it if you are maybe eating in a restaurant or are in the cinema or I don’t like to take them in public – I am sure there are people who don’t care about that, but I do not like it. And don’t like to be asked then ‘what kind of pills do you have to take?’ and I don’t like to tell people I have schizophrenia”</i> (German participant with schizophrenia)</p> <p><i>“I mean if I’m with a new group of friends or meeting, you know, somebody, I don’t want them to be embarrassed, but sort of embarrassed by it or don’t want to say, hey, oh my god, you know, guys, I got to do this for a minute”</i> (USA participant with diabetes)</p>
Cost: n=6/57; 10.5%	0/18; 0%	1/18; 5.6%	5/21; 23.8%	<p><i>“For the cost... years ago, yes. But not right now”</i> (Spanish participant with asthma)</p> <p><i>“I mean sometimes when I’ve had to pay out-of-pocket, um, you know, the cost of it is pretty extreme. And I haven’t had the full, the full amount to pay for it at that time and I had to sort of wait a little bit. So instead of taking the full amount just to make it last longer”</i> (USA participant with diabetes)</p>

Concept (n,%)	Germany (n,%)	Spain (n,%)	USA (n,%)	Supporting quotes
Feeling unwell: n=6/57; 10.5%	2/18; 11.1%	0/18; 0%	4/21; 19.0%	<p><i>“I think when I am ill. I remember a very bad stomach bug and I couldn’t keep any food inside. Of course I couldn’t keep any medication in me either”</i> (German participant with hypertension)</p> <p><i>“I would, I would say maybe once when I was sick or something because I, I do kind of— but then my daughter had brought it to me, which it's very rare that I miss a, a dose. I mean I really don’t miss it”</i> (USA participant with multiple myeloma)</p>

*Concepts reported by more than five participants are reported