

Medication decision-making and adherence in lupus: Patient-physician discordance and the impact of previous 'Adverse Medical Experiences'

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Abstract

Objectives

Medication adherence is critical in the successful management of lupus. There is very limited existing literature on reasons why non-adherence is not reported. This study explores the impact of current and previous medical experiences on patient satisfaction, adherence and reporting of non-adherence.

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Methods

Mixed methodology involved thematic analysis of in-depth interviews (N=23) to further explore the statistically analysed quantitative survey findings (N=186).

Results

This study identified five themes: 1) physician-patient discordance and a 'hierarchy of evidence' in medication decisions, 2) the association of adherence with satisfaction with care, 3) the persisting impact of past Adverse Medical Experiences (AMEs), 4) the dynamic balance of patient-physician control, and 5) holistic care – beyond a purely medication- based focus. Improving quality of life (43% of participants) and a supportive medical relationship (24%) were the main reasons for adherence. Patient-priorities and self-reported symptoms were perceived as less important to physicians than organ-protection and blood results. Non-reporters of non-adherence, non-adherers and those with past AMEs (e.g. psychosomatic misdiagnoses) had statistically significant lower satisfaction with care. The importance of listening to patients was a key component of every theme, and associated with patient satisfaction and adherence. The mean rating for rheumatologist's listening skills was 2.88 for non-adherers compared to 3.53 for other participants (mean difference 0.65, P=0.003).

Conclusion

Patients would like more weight and discussion given to self-reported symptoms and quality of life in medication decisions. Greater understanding and interventions are required to alleviate the persisting impact of past AMEs on some patients' wellbeing, behaviour and current medical relationships.

Key messages

Many systemic lupus erythematosus/systemic autoimmune rheumatic disease patients prioritise current symptom improvement and quality of life over long-term considerations for medication decisions.

Non-adherers and non-reporters of non-adherence gave significantly lower ratings for physician listening skills

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4 Adverse medical experiences, particularly disbelief, psychosomatic-misdiagnoses and long diagnostic
5 journeys, can reduce longer-term patient satisfaction.
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8 Key words: SLE, Rheumatology, Medication adherence, patient-behaviour. Patient-physician
9 interactions
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11 12 **Introduction**

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16 Medication adherence can improve outcomes and reduce costs to health services¹. It is of particular
17 importance for systemic lupus erythematosus (SLE) and other systemic autoimmune rheumatic
18 disease (SARD) patients as these diseases remain incurable, necessitating lifelong medications in
19 those with moderate and severe disease². The timely use of appropriate medications in SLE/SARDs
20 can prevent or slow disease progression^{3,4}. Adverse drug reactions are more common in SLE
21 patients⁵, are often exacerbated by multimorbidity and polypharmacy, and can also reduce
22 adherence^{6,7}. Medication non-adherence is difficult to accurately quantify, with rates of 3% to 80%
23 previously reported in SLE patients^{8,9,10,11}.
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31 There are multiple models^{12, 13,14} relating to adherence and medical interactions, which provide
32 insights into patient beliefs and behaviours. Although the importance of the medical relationship in
33 promoting adherence has been researched, including in SLE⁸, the enduring impact of past medical
34 interactions has not been explored in-depth.
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40 We have used the concept of 'Adverse Medical Experiences' (AMEs) to encompass past experiences
41 which we identified in our previous research^{15,16} as having persisting negative psychological impacts.
42 AMEs include repeated physician dismissal and disbelief of patient-reported symptoms and/or a
43 feeling of being endangered by many physicians lacking the necessary knowledge to assist with
44 these potentially life-threatening diseases. We hypothesised that these AMEs may also negatively
45 impact medical relationships and medication adherence. We also explored the (greatly under-
46 researched) question of why patients do not inform their doctors when they have been non-
47 adherent. Previous studies showed that some SLE patients were not open about non-adherence,
48 even when measurements of serum concentrations of hydroxychloroquine (HCQ) and
49 mycophenolate mofetil (MMF) definitively demonstrated their non-adherence^{9,10,11}.
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58 We sought to gain insights into how clinician behaviour can positively or negatively influence patient
59 behaviour in order to improve medical relationships, adherence, and potentially reduce under or
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3 over-treatment.
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8 **Methods**

9 Data collection

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12 Inclusion criteria: age ≥ 18 years; reporting a diagnosis of lupus, undifferentiated connective tissue
13 disease, mixed connective tissue disease, Sjögrens, or overlap condition on their clinic letters.
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17 Ethical approval was obtained through the Cambridge Psychology Research Committee, and all
18 respondents gave informed written (electronic) consent.
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22 A questionnaire was made available online in December 2019, using Qualtrics, to LUPUS UK forum
23 members and an online Facebook lupus support group. Questions elicited quantitative (rated from
24 1-5), and qualitative responses, and included: perceptions of medical support, reasons for
25 adherence, non-adherence and non-reporting of non-adherence. Interviewees were purposively
26 selected from the questionnaires to ensure a range of socioeconomic and disease characteristics,
27 (including age, gender and severity of disease) adherence behaviours and views of medical support.
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29 The interview schedule was semi-structured and explored views of the relationship between
30 satisfaction with care and adherence. M.S, an experienced, qualitatively-trained researcher
31 conducted the interviews. They continued until thematic saturation was reached (no novel insights
32 arising from subsequent interviews). Interviews lasted for ≈ 1 h and were transcribed verbatim.
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39 Analysis

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42 Quantitative data were analysed using SPSS v.26, using comparison of means (t-tests) and
43 Spearman's rank correlations. Thematic analysis¹⁷ was used for the interviews and qualitative data
44 from the surveys to further explain quantitative findings. M.S. coded data using NVivo12, after
45 immersion in the transcripts. R.H. double coded 25% of interviews, and E.L reviewed all interview
46 extracts, to enhance agreement and reliability. Themes were discussed and agreed by the wider
47 team, including five patient representatives. Validity was strengthened by considering deviant
48 cases¹⁸, member checking¹⁹ and triangulating quantitative and qualitative results. Detailed methods,
49 the criteria for reporting qualitative research (COREQ) checklist²⁰, and the questionnaire are included
50 in the supplementary material, available at *Rheumatology* online.
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Results

Survey respondents were predominantly from the UK, white and female (>92%), and 83% had SLE (Table 1). The most prescribed medication amongst the 186 survey respondents was hydroxychloroquine, with 69% currently taking. Self-reported adherence rates (by asking if they always take/took as prescribed) were ascertained for each medication and ranged from 71% for HCQ to 86% for oral steroids. Reasons elicited for adherence and non-adherence were for any of their SLE/SARD-specific medications. Any percentages quoted within the text refer to survey data.

Position of Table 1- Participant characteristics

Themes

Five main themes were identified: 1) physician-patient discordance and a 'hierarchy of evidence' in medication decisions; 2) association of adherence with satisfaction with care; 3) the persisting impact of past adverse medical experiences (AMEs); 4) the dynamic balance of patient-physician control; and 5) holistic care – beyond a purely medication-based focus.

Theme 1: Physician-patient discordance and a 'hierarchy of evidence'

'They just tend to treat what they think you have rather than what you tell them that you've got' (Ppt Q, Male, 70s)

Many patients perceived that physicians prioritised blood results and their judgement over patient-reported symptoms and priorities. Examples of how this was considered to create a 'hierarchy of evidence' and generated barriers to being prescribed and/or adhering to an optimal medication regimen included the following.

Discordance between patient and physician priorities: Whilst physicians were perceived to be focused on preventing organ damage and death, less than 10% of respondents cited these long-term impacts as reasons for adherence. As Figure 1 shows, far more (43%) gave improving their immediate QoL/reducing symptoms as a reason for adherence:

I just want to maximise my quality of life now...I don't want [my children] to remember me being ill all the time and in bed constantly. (Ppt 94, Female, 40s)

Diagnostic delays/misdiagnoses: The lack of definitive diagnostic tests combined with the frequent dismissal of early patient-reported symptoms was felt to have led to misdiagnoses that delayed the correct diagnosis and relevant treatment (approx. 50% took >5 years to diagnosis). Patients reported enduring physical and psychological damage as a consequence (Table 2, quote 1).

Difficulties accepting disease and medications: The initial physician and societal disbelief of the often *'invisible'* symptoms could increase post-diagnosis self-doubt and delays in accepting the disease and medications (Table 2, quote 2).

Insufficiently accurate tests for diagnosis and monitoring: Blood tests were reported to often not correspond with how unwell participants felt yet were required as *'evidence'* for treatment initiation/continuation by some clinicians. This reliance on blood markers over patient-reported symptoms affected those at both extremes of the serological spectrum, leading to perceptions of under- and over-treatment (Table 2, quotes 3a,b,c).

Limited availability of evidence-based medications: Limited medication options and high costs were sometimes reported to have been given as reasons for not prescribing medications: *I said about the mycophenolate. 'I'm not prescribing an expensive drug like that' she [rheumatologist] said* (Ppt L, Female, 30s)

Position of Table 2- Barriers to being prescribed and/or taking appropriate medication

Theme 2: Association of adherence with satisfaction with care

'Supportive and empathetic...always makes time to listen' (Ppt F, Female, 40s)

Support, trust and feeling *'cared about'*

Almost a quarter (Figure 1a) of participants reported adhering due to a supportive medical relationship: *'I respect my rheumatologist, he's knowledgeable, up to date and I believe he has my best interests at heart'* (ppt 62, Female, 50s).

Trust in doctors was multi-faceted and discussed in interviews as being influenced by physicians listening, believing patient symptoms, being accessible in an emergency, sharing information, and

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3 showing that they care. Trust was correlated with multiple other measures of patient satisfaction
4 with care (Figure 2), and highly correlated with ratings of physicians' listening and knowledge ($r_s >$
5 0.8).
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10 Feeling 'cared about' by their clinicians was extremely important to patients, and reported by many
11 to improve their adherence, whilst perceptions of uncaring, inattentive doctors were reported to
12 have led to reduced adherence to medications and advice:
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16 *I feel that she [rheumatologist] doesn't care about me and so I no longer care about my lupus*
17 *treatment and medication either. The result is that I am a lot more patchy in taking my meds.* (Ppt D,
18 Female, 50s)
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23 Although only a minority directly reported on the survey that a negative or unsupportive medical
24 relationship was the cause of non-adherence (14%, Figure 1b), interviews revealed that non-
25 adherence involved complex inter-linked relationships between patient, system and physician
26 factors (Fig 3a). Most participants reported adhering in order to improve their condition, regardless
27 of the quality of the medical-relationship. Non-adherers had significantly lower levels of satisfaction
28 with care in most domains (Fig 3b). For example, the mean rating for listening skills of
29 rheumatologist was 2.88 for non-adherers compared to 3.53 for other participants (mean difference
30 (MD), 0.65, $P=0.003$).
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38 **Communication and information-sharing**

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42 Poor physician communication about medication risks/benefits, insufficient monitoring and not
43 sharing test results were widely reported, and contributed to non-adherence:
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47 *My appointments kept getting cancelled and I just stopped taking the meds, I thought I was falling*
48 *through the cracks, my bloods weren't getting done, no-one was telling me the results* (Ppt A, Female,
49 teens)
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53 This contrasted with other participants who reported feeling informed and reassured by being given
54 sufficient information on a new medication and the opportunity for discussion:
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58 *She [lupus nurse] was brilliant, she started me on [DMARD] and she went through*
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3 *absolutely everything with it...a leaflet, when to take it, these are the risks, the benefits...*
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5 *a time frame. (Ppt P, Male, 40s)*
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8 **Clinician impact on side-effects and non-intentional non-adherence**

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11 Although less explicitly identified by participants, non-adherence due to cognitive dysfunction and
12 side-effects could be reduced by clinicians' being supportive, non-judgemental, encouraging
13 discussion and offering advice.
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18 Reports of non-intentional non-adherence were almost wholly related to cognitive difficulties (35%
19 giving as a reason for non-adherence). Embarrassment was often expressed about memory
20 problems which reduced the likelihood of reporting their difficulties and accessing support:
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25 *Embarrassingly as I'm a nurse I regularly mis-dose myself, either forget or overdose due to my*
26 *memory problems. I still struggle with the idea of a Dosette box as I don't feel old (Ppt R, Female,*
27 *40s)*
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31 Discussions revealed that physicians could also reduce non-adherence arising from side effects
32 (which 44% gave as a reason for non-adherence). Many participants reported an unsympathetic
33 response to reports of side-effects, leading to patient-physician conflict and non-adherence:
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37 *I refused to take the medication that I was allergic to...Well it's your fault you're in pain because you*
38 *won't take the tablets...she [rheumatologist] said... didn't even listen...her own agenda (Ppt N,*
39 *Female, 50s)*
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42 **Impact of medical-relationships on openness in reporting non-adherence**

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45 Only 53% of respondents reported always informing their physician if they did not take their
46 medication as prescribed. An unsupportive or insecure medical relationship, including difficulty in
47 accessing support or fear of disapproval, was reported by over 50% of those specifying a reason for
48 non-reporting: *But I only see [rheumatologist] every 6 months and I've given up trying to talk to my*
49 *GP...not seen them in 3 years... so I'm on my own (Ppt 4, Female, 40s)*
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54 Those not informing physicians about non-adherence (excluding the 33% who gave the reason it was
55 too infrequent to mention) had a statistically significantly lower satisfaction with care in every
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3 domain (minimum $P=0.05$), with the exception of support with fatigue and mental-health (MH). The
4 difference was particularly pronounced in ratings of listening skills for GPs (Non-reporters = 2.5, all
5 other participants = 3.3, MD = 0.8, $P=0.016$) and rheumatologists (Non-reporters = 2.6 vs 3.3,
6 MD=0.7, $P=0.032$). This was explored further in interviews where multiple participants discussed
7 how their diagnostic difficulties and perceptions of poor physician listening skills led to non-
8 adherence and/or non-reporting of non- adherence:
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15 *Sometimes I feel it is pointless being honest as doctors never seem to listen properly and believe they*
16 *know best rather than listening to suggestions and how I feel... Doctors don't seem to care. (Ppt B,*
17 *Female, 20s)*
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21 Conversely, physicians who had built-up trust by being available and listening attentively were felt to
22 improve openness in reporting difficulties, including with medication:
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27 *We have a good relationship and he [GP] has an idea of who I am as a person and my health... even*
28 *the little things...I generally feel I can be very open with him (Ppt J, Male, 20s)*
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31 **Position of Figure 1- Main reasons given for adherence, non-adherence and non-reporting**

32 **Position of Figure 2 – Trust in doctors and medical support.**

33 **Theme 3: The persisting impact of past AMEs**

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37 *'Literally terrified...no confidence whatsoever' (Ppt S, Female, 30s)*
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41 Although the majority of interviewees reported current secure medical relationships, past 'Adverse
42 Medical Experiences' (AMEs) were found to have a persisting impact on medical security,
43 psychological wellbeing, trust (Fig 2b, column 2) and satisfaction with care, including in support in
44 managing medications/side effects.
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49 We defined AMEs as stressful healthcare-related experiences, including long diagnostic journeys (> 1
50 year) and previous MH or medically unexplained/'in your head' type misdiagnosis (MH/MUS) which
51 were commonly reported to have had persisting negative psychological impacts.
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56 **AMEs and satisfaction with care**

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3 Those whose diagnosis was delayed (using >1 year of symptom onset) gave statistically significantly
4 lower ratings in many areas of support including: support received at diagnosis (2.7 vs 3.18 for those
5 diagnosed <1 year, MD=0.48, P=0.031), support with managing flares (2.72 vs 3.31, MD=0.6,
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7 P=0.018) and support in overcoming psychological impact of delays/misdiagnoses (1.58 vs 2.13,
8 MD=0.54, P=0.019). The MH/MUS misdiagnosed gave significantly lower ratings for GP's listening
9 and knowledge (both Ps 0.037), likely because they were the physicians most frequently
10 misdiagnosing early SARD symptoms.
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16 **AMEs and adherence**

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20 There was no significant difference in adherence for AMEs categories despite lower satisfaction with
21 care. However, when looked at individually, some of the most traumatised by multiple AMEs, were
22 either highly avoidant: *I don't go to doctors or hospitals if I can avoid it, I've lost too much and feel*
23 *scared what will happen when I do'* (Ppt 95, Female, 50s) or highly adherent: *'I scored very high in*
24 *the PTSD [post-traumatic stress disorder] scale [from multiple AMEs]...spent too much of my life just*
25 *plain fighting to give in now...so I never take less than prescribed...greedily take whatever treatment I*
26 *can get'* (Ppt V, Female, 50s)
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33 **Position of Figure 3a - Inter-linking factors contributing to non-adherence and/or poor satisfaction** 34 **with care**

35 **Theme 4 – The dynamic balance of physician-patient level of control of medications**

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39 *'My body, my life, my illness'* (Ppt H, Male, 60s)

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43 Preferences for degree of control over medication decisions varied between participants. The vast
44 majority preferred a fully-informed collaborative approach, and felt it improved acceptance and
45 adherence:
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50 *Looked at all the pros and cons of a medication...before a final decision was reached. It felt like a kind*
51 *of joint brainstorming session and it meant that I felt entirely on board with the result* (Ppt T, Female,
52 50s)
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57 Many participants also strongly felt that they should be given more input into medication decisions
58 in order to improve, often very poor, QoL:
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3 *Surely the balance of risk should be discussed and assessed by both, and patients allowed an*
4 *informed opinion as to an acceptable level of risk... I'd risk a lot, almost anything, because this is no*
5 *life... few years of goodish life would be worth so much more than endless risk-free sofa years (Ppt E,*
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8 *Female, 60s)*
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10 11 **'Intelligent' non-adherence**

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14 Medical insecurity was frequently indicated to have resulted from doctors having insufficient
15 knowledge of lupus (Only 16% of participants rated GPs as having good/very good knowledge of
16 lupus). Patients therefore reported having to acquire knowledge and advocate for themselves:
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21 *I brought up that I needed an eye test, because I've been on Hydroxychloroquine for a long*
22 *time, and [GP] was like, 'Well, I've not heard of that, did you read it on the internet?'...they're out of*
23 *their depth (Ppt M, Female, 50s)*
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28 Some participants reported taking control and being 'intelligently' non-adherent for their own
29 safety:
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33 *I have no trust at all, particularly when I felt an interaction between HCQ and a GP-prescribed*
34 *medication but my GP dismissed it as all in my head...I found there is a potent interaction in some*
35 *patients that can cause heart standstill...won't be taking any medication on doctors' advice alone*
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38 *(Ppt G, Female, 50s)*
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42 Several patients discussed altering their dose themselves to improve QoL by balancing benefits with
43 reducing side effects:
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46 *"Well, if I'm going to only have another five years to go...I need quality of life...so I actually increased*
47 *my steroids...certainly made me a bit better....I just do it (Ppt Q, Male, 70s)*
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50 51 **More physician direction/information required at times**

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54 Many patients reported being given very little information, were often just handed leaflets, and felt
55 anxious and confused about the lack of physician direction in medication decisions, often then
56 seeking online advice from medically unqualified peers:
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3 *I find it really difficult that doctors do not give you their opinion any more. I appreciate the free*
4 *choice- but it is difficult to know what to do for the best...It seems like a pretty heavy duty drug [AZA]*
5 *to take if I don't really need it... would I be better off waiting until things get worse? Am I doing*
6 *myself harm by not taking it?* (Forum post, Female)
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11 Some participants preferred physicians taking a more decisive or directive approach at times,
12 especially when severely unwell. This could increase security and was reported to improve
13 adherence, especially within a trusting relationship. A very firm response from a trusted clinician to
14 non-adherence was also felt by some participants to ensure future adherence:
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20 *She very clearly, concisely & firmly told me 'never ever again change any medication dosage without*
21 *my approval'... my consultant's mode of communicating her point acted as very effective 'aversion*
22 *training'. I've never even been tempted to experiment with dosage since'* (Ppt K, Female, 60s)
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27 However, fear of physician displeasure was also a barrier to reporting non-adherence. Terminology
28 included 'embarrassment' and 'guilt,' and there was concern that reporting non-adherence could
29 lead to a withdrawal of support: 'they will give up on me'.
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33 **Theme 5: Holistic care – beyond a purely medication- based focus**

34 *'They're basically pill-centred...they're missing a trick'_(Ppt M, Female, 50s)*
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39 Rheumatologists were widely considered to be very focused on medications, with limited/no time
40 spent assisting patients with non-medication support to improve acceptance and self-management.
41 Physiotherapy, psychological support, diet and pacing advice were only occasionally provided (Table
42 3). Fatigue was reported as the most life-changing symptom, yet only 12% felt they were receiving
43 good/excellent support with fatigue and 41% reported no support at all.
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48 **Position of Table 3- Non-medication support**

49 **Discussion**

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52 To our knowledge, this mixed-methods study is the first to explore the enduring impact of past
53 medical interactions, particularly AMEs, on SLE/SARD patient behaviour. The potential comparison
54 with some aspects of adverse childhood experiences (ACEs)²¹ and other adverse life experiences²²
55 remains tentative, but highlights the severity of damage, and longer-term sequelae. Many
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3 participants reported repeated AMEs, particularly dismissal, psychosomatic misdiagnoses and lack of
4 physician knowledge, often on their arduous diagnostic journeys^{15,16,23}, but also post-diagnosis. An
5 unexpected finding in our study was that, although participants with AMEs had significantly lower
6 satisfaction with many aspects of medical care, the non-adherence rate for the AME group as a
7 whole was not significantly greater than the rate for the non-AME group. One theory, identified
8 through interviews, is that AMEs contributed to both extremes of adherence, thus balancing each
9 other out when combined quantitatively. In particular, some interviewees reported greater avoidance
10 of physicians, whilst others stated they were completely adherent due to the lengthy time
11 undiagnosed and untreated.
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20 Our findings are also in agreement with previous research identifying discordance between
21 SLE/SARD patient and physician priorities^{24,25,26,27} and the importance of medical-relationships in
22 medication adherence^{8,28}. Satisfaction with medical care was significantly lower for non-adherers
23 and those not reporting non-adherence to their physicians, particularly in relation to support,
24 information and listening skills. A key, previously unexplored, finding was that half of participants
25 who reported not telling their clinicians about non-adherence gave an unsupportive/unavailable
26 medical relationship as a reason. Supportiveness of the current medical-relationship was directly
27 cited by a quarter of participants as a reason for adhering, often with the use of the words 'trust'
28 and 'respect' when describing their current physician(s), particularly their rheumatologist. However,
29 many participants reported adhering to improve their QoL, regardless of the quality of their medical
30 relationships.
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40 Improving QoL was the most frequently cited reason for medication adherence whereas preventing
41 organ damage and/or death - which physicians were felt to be focused on - was only cited by <10%
42 of participants. Physicians have guidelines to follow²⁹ and clearly a responsibility for ensuring
43 medication choices prevent organ damage and reduce mortality. However, our findings suggest that
44 medication discussions may promote greater adherence if the physician elicits each patient's
45 priorities and presents the more immediate as well as long-term benefits. Although this study has
46 focused on intentional non-adherence, we found that clinicians could also influence the frequent
47 non-intentional non-adherence caused by the cognitive dysfunction common in many SARDs
48 patients. Participants' discussions of embarrassment and reticence to admit forgetting medication
49 suggests that non-judgemental raising of the topic and advice on memory-aids such as using Dosette
50 boxes, reminder apps and family support could be helpful.
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3 We identified a 'hierarchy of evidence' in both diagnosis and treatment decisions, perceived to be
4 dominated by a limited range of blood tests (especially with GPs and less experienced
5 rheumatologists) and clinician judgement. These were felt by patients to not always be reflective of
6 their actual condition, or in line with their often extensive knowledge of current research, thus
7 further reducing medical security. Whilst ANA is helpful (although not essential) in diagnosis, the
8 titre can vary over time independently of disease activity^{30,31,32}, and is therefore not recommended
9 for monitoring/ medication decisions²⁹. Although dsDNA and/or complement are accurate
10 biomarkers in some patients, that is not the case for all patients³³. This research builds on previous
11 reports²⁶ that greater prioritisation should be given to patient- reported symptoms. Patient self-
12 reported symptoms are often the least susceptible to external verification, yet can be the most life-
13 changing (fatigue, pain, neurological and cognitive difficulties)¹⁵. Currently, most studies only use
14 patient- reported outcomes (PROs) as secondary endpoints, if at all. This limited evidence-based
15 data likely influences many clinicians' preference (as perceived by these patients) for clinical or
16 laboratory evidence over PROs. However, with such a heterogenous disease and highly individual
17 responses/reactions to medications, our study participants expressed strong feelings that the
18 'evidence-based data' should also include evidence gained from actively listening to their symptoms.
19 Failure to listen to patients was commonly discussed as one of the main contributors to
20 misdiagnoses, damaging to the clinical relationship and potentially leading to sub-optimal
21 medication decisions. The key importance of listening in adherence was verified quantitatively by
22 ratings for clinicians' listening skills being significantly lower in non-adherers and non-reporters of
23 non-adherence. Rheumatologists were also viewed as medication-focused whilst patients wanted
24 greater support with non-pharmacological measures, such as physiotherapy and psychotherapy,
25 which have been found to improve QoL in previous studies^{34,35,36}.

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43 This study has a number of limitations, particularly in the self-reporting and self-selecting nature of
44 respondents to online surveys. Due to the exploratory nature of this study, reasons for adherence
45 were extracted from open-ended answers which can reduce reliability. In introducing the concept of
46 AMEs for these patients, we used proxy measures which were enlightening for initial exploration of
47 the concept yet cannot be assumed to be reliable. We will further explore the concept of AMEs, and
48 their enduring impact, in future studies. There was a low proportion of males and respondents from
49 minority ethnic groups leading to lower generalisability, although interviewees were selected
50 purposively to ensure more of a balance. Interviewees had a slightly longer than average¹⁵ length of
51 diagnostic journey, and we did not elicit quantitative measures of severity of physical and mental
52 health, both of which may have impacted views of care. Further details of the mixed methodology
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3 used, including strengths and limitations, are reported in the supplementary material, available at
4 *Rheumatology* online.
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8 We have extended the work of Náfrádi et al who identified the need for a flexible physician—patient
9 balance of control in medication decisions³⁷ with our findings that level of control desired differed
10 for each patient and varied over the disease course. We have also built on Smith’s discussions of
11 ‘institutional betrayal’³⁸ and how improved physician—patient concordance in decision-making can
12 ameliorate distrust from adverse medical events. Collaboration and concordance were
13 invariably preferred, although a more directive physician approach may be required/wanted more in
14 the early stages of diagnosis, when severely unwell or cognitively impaired. Although fear of
15 physician displeasure motivated adherence in some, it was also reported as a barrier to reporting
16 any non-adherence. Intelligent or creative non-adherence^{39,40} whereby knowledgeable patients
17 made rational decisions to self-adjust dosage or to not adhere was not infrequent, often
18 underpinned by distrust or inadequate access to support. As it was reported to have preferable
19 outcomes at times, patient-blaming⁴¹ and always viewing non-adherence as a negative patient
20 behaviour is not appropriate, especially in the context of many physicians being widely
21 perceived as lacking basic knowledge of SLE. This contributed to patient insecurity in the
22 appropriateness and safety of diagnostic, medication or monitoring decisions. With no clear
23 treatment pathways, and undiscovered or unclear biomarkers in some SARD patients,
24 there is an even greater requirement for improved physician-patient communication and shared
25 decision making, in addition to targeted, individualised tests and medication⁴².
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40 More physicians actively listening to patients, both in terms of symptom-reporting and ascertaining
41 individual treatment goals, would improve medical relationships, satisfaction, and potentially
42 medication adherence. Optimal medication prescribing and adherence, enabled by positive medical
43 relationships, not only improves disease outcomes but can also reduce the significant psychosocial
44 impact of SLE. Despite the many positive current medical relationships cited by most interviewees,
45 this study highlights the importance of clinicians being aware of the persisting impact on patient
46 wellbeing, behaviour and medical relationships of past adverse medical experiences (AMEs).
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53 **Ethical approval** - Ethical approval was obtained through the Cambridge Psychology Research Committee, and
54 informed consent was obtained from all respondents. This study complies with the Declaration of Helsinki.
55 PRE 2018–84: Approval for survey and interviews
56 PRE.2018.120: Approval for analysis and quoting from the LUPUS UK forum
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60

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Availability of data: Additional anonymised data may be made available on request

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NOTE: Physician influence on non-adherence relating to side-effects will be covered in more detail in a further paper.

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Figure 1- Main reasons given for adherence, non-adherence and non-reporting

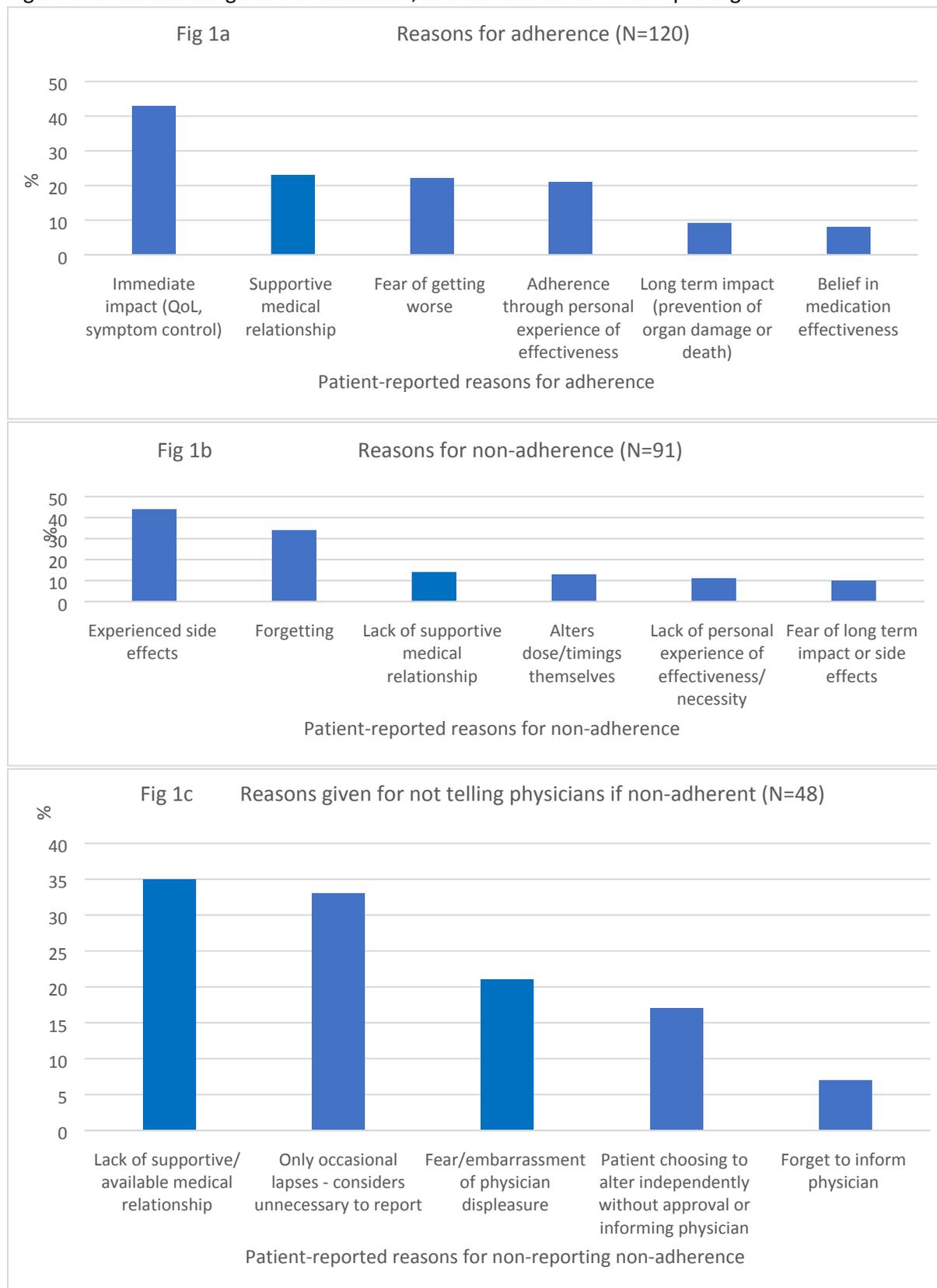


Figure 1 depicts the main reasons given by participants for medication adherence (Fig1a), non-adherence (Fig1b) and non-reporting of non-adherence to clinicians (Fig1c).

Note: These graphs were generated from responses to open-ended questions, e.g. *'Please give any reasons for taking your medication as prescribed'*. Some participants gave more than one reason. QoL: Quality of life

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Fig 2 – Trust in doctors and medical support.

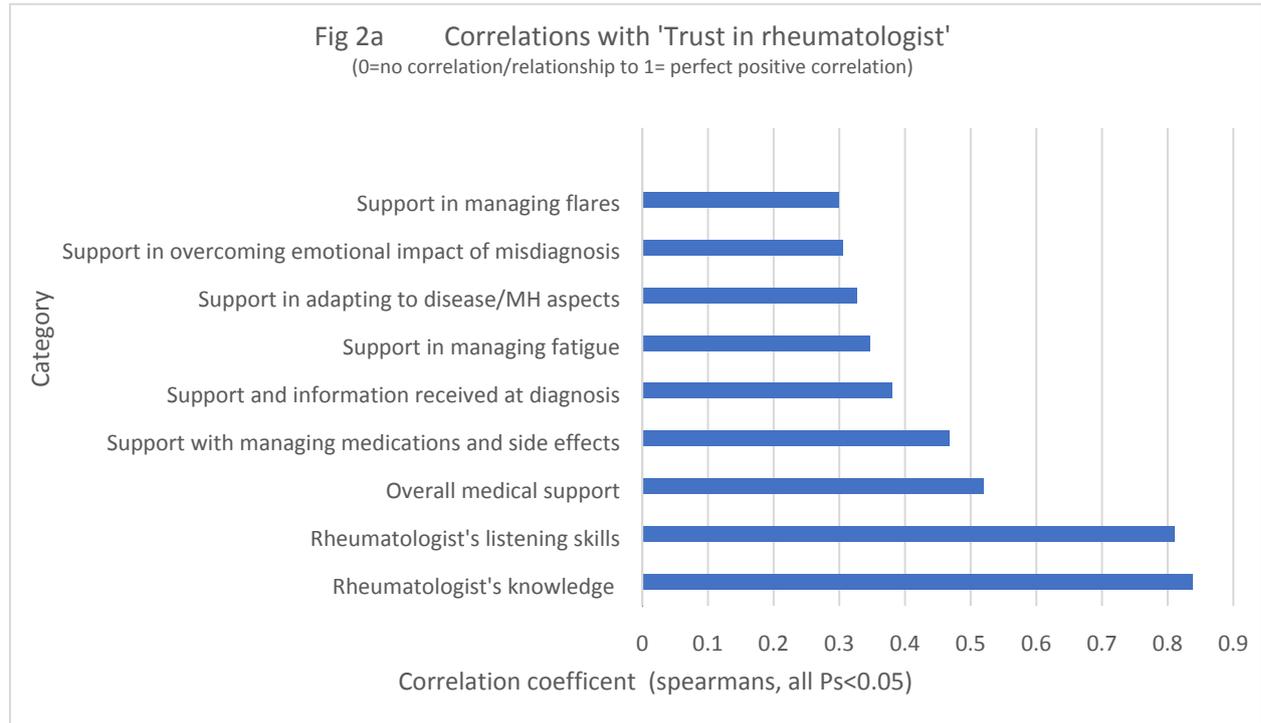


Fig 2b – Physician behaviours Influencing patient wellbeing and trust

| Positive Medical Experiences | Adverse Medical Experiences |
|---|---|
| <i>I have total trust in her diagnostic expertise & great respect for her instincts... during my first 5 or so years with her, she showed great caution in gradually designing the combined therapeutic meds (Ppt K, Female, 60s)</i> | <i>I suffered in silence and overwhelming fear for years without a diagnosis....cruel and uncaring experiences in hospital by doctors who are unrelated to my usual care, especially in A&E (Ppt 90, Female, 60s)</i> |
| <i>The relationship I had with [rheumatologist] was incredibly strong. This definitely impacted on my own approach to my medication and I always took all medication exactly as prescribed (Ppt D, Female, 50s)</i> | <i>Listen and do not presume that patients may have psychological symptoms. I was told for so many years that I did not fit the bill for the symptoms that I was describing. Shockingly, I began to doubt myself (Ppt 159, Female, 70s)</i> |
| <i>If there was a problem or emergency I can contact her team and she will be there for me. I enjoy her positive attitude and she reassures me...trust my rheumatologist...made real efforts to help me...her ability to reassure me by careful listening and going through the facts, tests, meds etc. is important (Ppt T, Female, 50s)</i> | <i>I have felt angry for the best years of my life, as too many Doctor's told me there was nothing wrong with me and 'go away and get on with my life'. People do not enjoy going to the doctor, so if you see a patient repeatedly, there is something going wrong in their body (Ppt 14, Female, 40s)</i> |

Figure 2a graphically presents correlations between 'Trust in rheumatologist' with other patient-reported measures of support and satisfaction with care. Figure 2b contains patient quotes relating to positive and adverse medical experiences that have altered trust.

Figure 3a - Inter-linking factors contributing to non-adherence and/or poor satisfaction with care

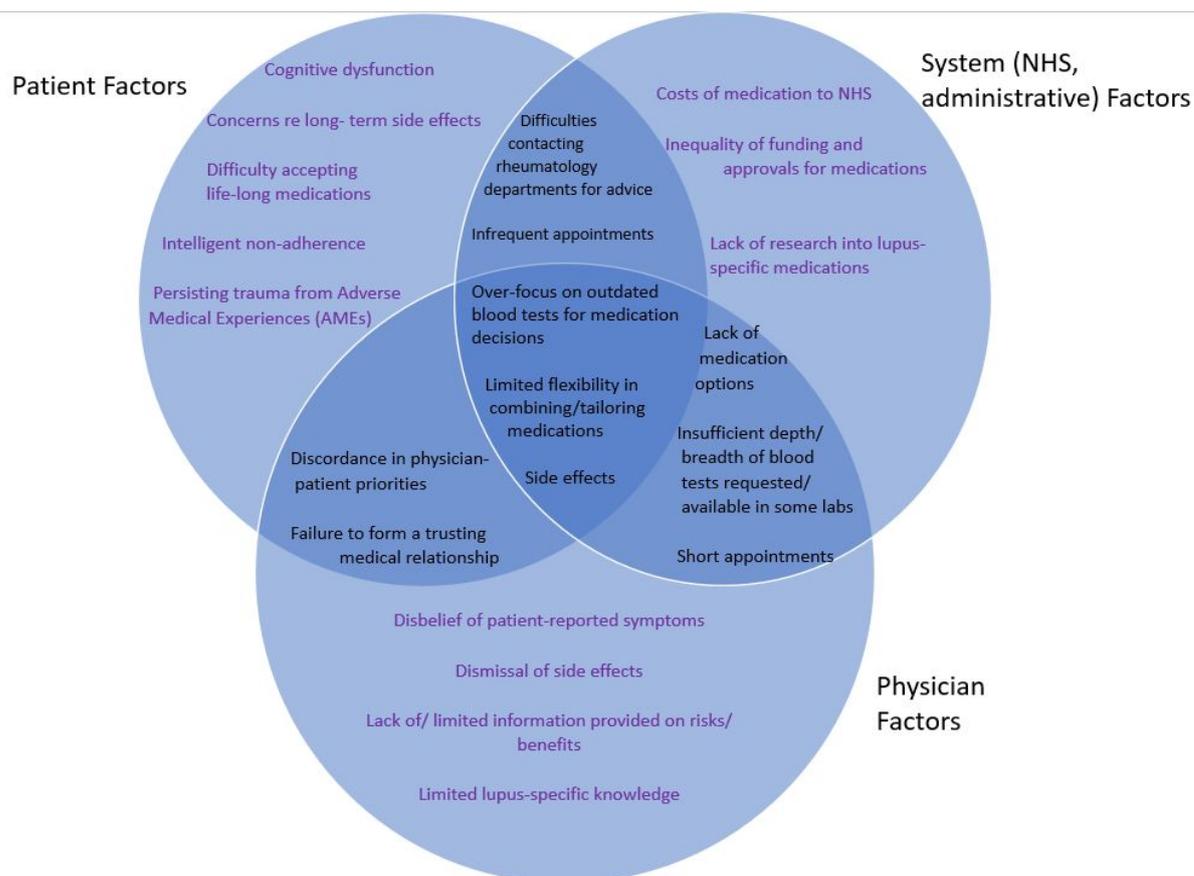


Fig 3b: Comparison (t-test) of satisfaction with care ratings between non-adherers and other Ppts

| | Non-adherers compared with all other Ppts (Total N=185) | | | |
|---|---|-------------------------|-----------------|----------|
| Satisfaction with care* | Mean for Ppts specifying non-adherence ** | Mean for all other Ppts | Mean Difference | P values |
| Support with managing medication/side effects | 2.7 | 3.4 | 0.71 | <0.001 |
| Support/information received at diagnosis | 2.47 | 3.15 | 0.68 | <0.001 |
| Listening skills of rheumatologist | 2.88 | 3.53 | 0.65 | 0.003 |
| Knowledge of rheumatologist | 3.4 | 3.94 | 0.54 | 0.007 |
| Overall level of medical support | 3.06 | 3.59 | 0.53 | 0.001 |
| Trust in GP | 2.87 | 3.33 | 0.46 | 0.022 |
| Trust in rheumatologist | 3.17 | 3.6 | 0.43 | 0.027 |
| Listening skills of GP | 2.94 | 3.37 | 0.42 | 0.035 |
| Support in overcoming psychological damage from misdiagnoses/delays | 1.51 | 1.92 | 0.4 | 0.019 |
| Knowledge of GP | 2.33 | 2.65 | 0.3 | NS*** |
| Support with MH and adapting | 1.79 | 2.05 | 0.26 | NS |
| Support with managing fatigue | 1.91 | 2.16 | 0.25 | NS |
| Support in managing flares | 2.75 | 2.91 | 0.16 | NS |

*Calculated from Ppt-reported ratings of satisfaction from 1=lowest rating to 5=highest rating.

**Includes all Ppts specifying a reason for non-adherence

*** NS=Statistically non-significant

Inter-linking factors contributing to non-adherence and/or poor satisfaction with care

Figure 3a shows Inter-linking factors contributing to non-adherence and/or poor satisfaction with care. Figure 3b statistically compares (t-test) mean satisfaction with care between those reporting non-adherence and other participants

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Table 1- Participant characteristics (Survey: N=186; Interview: N=23)

| Characteristic | Number (survey, N=186) | % (survey) | Number (interview, N=23) | % (interview) |
|---|---------------------------|------------|--------------------------------|---------------|
| Age Band (years) | | | | |
| 18-29 | 17 | 10 | 3 | 13 |
| 30-39 | 27 | 15 | 1 | 4 |
| 40-49 | 53 | 28 | 7 | 30 |
| 50-59 | 52 | 28 | 7 | 30 |
| 60-69 | 28 | 15 | 4 | 17 |
| 70+ | 5 | 3 | 1 | 4 |
| Diagnosis | | | | |
| SLE | 155 | 83 | 19 | 83 |
| UCTD/unspecified CTD | 12 | 6 | 4 | 17 |
| Sjögrens | 6 | 3 | 0 | 0 |
| MCTD | 4 | 2 | 0 | 0 |
| Cutaneous/discoid lupus | 4 | 2 | 0 | 0 |
| Overlap | 6 | 3 | 0 | 0 |
| Current Main Medications* | | | | |
| HCQ | 128 | 69 | 14 | 61 |
| Oral steroids | 61 | 33 | 13 | 57 |
| Steroid injections | 43 | 23 | 6 | 26 |
| MMF | 28 | 15 | 4 | 17 |
| MTX | 27 | 15 | 3 | 13 |
| AZA | 19 | 10 | 4 | 17 |
| Biologic | 12 | 7 | 2 | 9 |
| Cyclophosphamide | 6 | 3 | 0 | 0 |
| Frequency of reporting non-adherence to their doctor | | | | |
| Always | 78 | 53 | 10 | 59 |
| Usually | 19 | 13 | 2 | 12 |
| Sometimes | 15 | 10 | 2 | 12 |
| Occasionally | 10 | 7 | 0 | 0 |
| Never | 26 | 18 | 3 | 18 |
| Missing | 38 | | 5 | |
| Delays to diagnosis | | | | |
| < 1 year | 40 | 25 | 3 | 14 |
| 1-2 years | 23 | 14 | 4 | 18 |
| 3-5 years | 22 | 14 | 1 | 5 |
| 6-9 years | 18 | 11 | 6 | 27 |
| 10+ years | 57 | 36 | 8 | 36 |
| Missing/unsure or non-quantitative response given | 26 | | 1 | |

*Infusions/ injections were classified as 'current' if they were within the previous 12 months. SLE: systemic lupus erythematosus; UCTD: undifferentiated connective tissue disease; MCTD: mixed connective tissue disease; HCQ: hydroxychloroquine; MMF: Mycophenolate mofetil; MTX: Methotrexate; AZA: Azathioprine

Table 2: Barriers to being prescribed and/or taking appropriate medication

| Barriers | Illustrative patient quotes |
|--|--|
| Diagnostic delays/ Misdiagnoses <i>Quote 1</i> | <i>Very angry that I had been told it wasn't lupus all those years ago and that the rheumatologist diagnosed me within minutes...It ruined decades of my life and has had a lasting impact...also lost 6 babies...which I believe could have been prevented if I had been diagnosed and on treatment. (Ppt R, Female, 40s)</i> |
| Difficulties accepting disease and medications <i>Quote 2</i> | <i>They kept banging on take steroids, take steroids...I refused for a very long time...Because as a lupus patient, on the whole, you look fine, you know?...you don't have anything that people can see... I guess I doubted myself. Am I making this up? Is it in my head? (Ppt N, Female, 50s)</i> |
| Discordance in patient- physician views of disease severity and activity from blood test results <i>Quote 3a, 3b, 3c</i> | <p>Potential under-treatment- Quote 3a <i>I am told [only] hydroxychloroquine is a proportionate response...I feel once I have evidence of liver or kidney damage then someone will take it seriously but it will be a bit late then. I am still left with [multiple symptoms]...No actual interest at improving my quality of life...like the doctors don't care... I am sent away year after year to continue to suffer. (Ppt S, Female, 50s)</i></p> <p>Potential over-treatment – Quote 3b <i>[Rheumatologist] tried on two occasions to oblige me to take Aza because 'I'm nervous' he said. My dsDNA had increased...to 97, but I felt very well and had no symptoms...He would have prescribed what is a toxic drug without justification and then as my dsDNA went down, as it did, would have declared it was a success and kept me on it (Ppt G, Female, 50s)</i></p> <p>Misunderstandings of significance of blood test results – Quote 3c <i>[Local rheumatologist said] I'd not had a positive ANA since 2016, so my lupus wasn't active and therefore she'd be taking medications away... but [Lupus specialist] made it very clear that ANA is not a good indicator of lupus activity (Ppt C, Female, 40s)</i></p> |

Table 3- Patient quotes on receiving and/or the importance of non-medication support

| Non-medication options to improve quality of life | Patient quotes |
|---|---|
| Pacing and exercise | <i>One of the most useful things from a Doctor was my rheumatologist giving me a 30 minutes consultation once just to tell me to slow down, to take rest, pace myself etc. I didn't listen at the time, but it sank in and I now do it and it is the best advice and time spent by a Doctor ever. He also told me to take up Tai Chi to aid in pain relief and relaxation... massive positive impact on my lupus (Ppt R, Female, 40s)</i> |
| Psychological support | <i>I have become even more appalled at the lack of counselling support for patients of lupus and other chronic diseases. It would seem that you are expected 'to get on with it' (Ppt 159, Female, 70s)</i> |
| Alternatives offered to anti-depressants | <i>My GP has also always been very understanding and supportive...suggested last week that instead of going back on antidepressants straight away that he wants me to try holistic therapy first and see how that goes. I am very lucky to have such a sympathetic GP and I can message him any time if I need to. (Ppt F, Female, 40s)</i> |
| Fatigue management support | <i>I appreciate that they're doing all the stuff to do with heart and lungs as a priority...the fatigue is seen as a side effect, whereas I think it really is something that needs to be actually looked into...There must be chemical changes. There must be biology going on, and I just find it incredible that nobody seems to be able to say what that biology is (Ppt M, Female, 50s)</i> |
| Physiotherapy | <i>I've been waiting like 2 years, every time I go on about physio, to me this is a big deal like losing ability in hands and knees and stuff, whereas for her [rheumatologist] it seems like nothing but that's on my mind quite a lot...it's not on her agenda....Even to get some exercises I can do at home because I'll do it. Just get some advice (Ppt A, Female, teens)</i> |
| Holistic care | <i>My wonderful local nurses got me into a local hospice for extra support in the form of advice on pain management, reiki, reflexology and some counselling. I am eternally grateful...practical solutions, advice, reassurance and compassion (Ppt F, Female, 40s)</i> |
| Occupational therapy for cognitive dysfunction | <i>I didn't keep up with medication not because I chose not to, but often I would forget to take them, or I would forget to order new scripts in time. But now I have a monthly pill box, alarms, and working with OT for my dysfunction issues in general and that has made a big difference (Ppt J, Male, 20s)</i> |
| Diet advice | <i>Docs are terrible about issues of diet and lifestyle in the management of Lupus. I am on the autoimmune protocol and really notice a difference. When I eat something that doesn't agree with me I immediately fall into fatigue (Ppt 165, Female, 50s)</i> |