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# Diet and lupus: What do the patients think?

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Keyword:	Patient attitude to health, Diet therapy, Systematic lupus erythematosus, Attitude of health professionals, Primary care rheumatology, Cardiovascular Disease
Abstract:	Objectives Cardiovascular disease (CVD) is the leading cause of mortality in patients with systemic lupus erythematosus (lupus). Therefore, using diet to control blood lipid levels and modify CVD risk could be a promising therapeutic strategy to control disease symptoms. The primary objective of this study was to learn about lupus patient experiences with diet including their opinion on considering diet as a therapeutic option. The secondary objective was to obtain this information in a cost and time effective manner. Methods A lay summary and a 15 question diet-based online survey was publicly available for 3 weeks. Social media was used to promote the survey through relevant charities, hospitals and research groups. Results 300 responses were received, 284 of whom had lupus. Patients reported that there was a lack of clinical counselling regarding diet with only 24% of patients stating that their doctor had spoken to them about diet. Despite this, 100% of patients stated that they would change their diet if they knew it would help their symptoms and 83% would take part in a future diet-based clinical trial. Text analysis of patient research suggestions identified a particular interest in using diet to treat fatigue

and manage disease flares. Conclusions This project successfully gathered patient information regarding diet and lupus over a short timeframe using an anonymous social media platform The survey provided evidence that patients support further research and potential diet intervention studies investigating the effect of diet on the
symptoms of lupus.
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#### Diet and lupus: What do the patients think?

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22	Abbreviations:
23	APS: Antiphospholipid syndrome
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25	BRC: Biomedical Research Centres
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28	CRN: Clinical Research Network
29	CV/D: Cardiovasquiar diagona
30	CVD. Cardiovascular disease
31	NIHR: National Institute for Health Research
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33	PPIE: Public Involvement and Engagement
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#### Abstract

#### Objectives

Cardiovascular disease (CVD) is the leading cause of mortality in patients with systemic lupus erythematosus (lupus). Therefore, using diet to control blood lipid levels and modify CVD risk could be a promising therapeutic strategy to control disease symptoms. The primary objective of this study was to learn about lupus patient experiences with diet including their opinion on considering diet as a therapeutic option. The secondary objective was to obtain this information in a cost and time effective manner.

#### Methods

A lay summary and a 15 question diet-based online survey was publicly available for 3 weeks. Social media was used to promote the survey through relevant charities, hospitals and research groups.

#### Results

300 responses were received, 284 of whom had lupus. Patients reported that there was a lack of clinical counselling regarding diet with only 24% of patients stating that their doctor had spoken to them about diet. Despite this, 100% of patients stated that they would change their diet if they knew it would help their symptoms and 83% would take part in a future diet-based clinical trial. Text analysis of patient research suggestions identified a particular interest in using diet to treat fatigue and manage disease flares.

#### Conclusions

This project successfully gathered patient information regarding diet and lupus over a short timeframe using an anonymous social media platform. The survey provided evidence that patients support further research and potential diet intervention studies investigating the effect of diet on the symptoms of lupus.

#### Introduction

Systemic lupus erythematosus (lupus) is a complex autoimmune disorder characterised by chronic inflammation, multiple organ damage and increased risk of cardiovascular disease (CVD); CVD is the leading cause of mortality for patients (1-4). Our research and other published work has identified a therapeutic opportunity for the use of diet in controlling the symptoms of lupus and CVD risk through manipulation of serum blood lipid (fat) levels (5-8).

Involving patients and other stakeholders in clinical research through Patient and Public Involvement and Engagement (PPIE) strategies is an essential ethical mandate for clinical research (9-11). However, published data is difficult to find regarding patient opinion about basic science research. It is of huge importance to relate research to patient's experience; patients learn about the research being carried out regarding their disease and we as researchers learn how the work can impact the patient community (12, 13). In addition, patient engagement provides valuable insight into how patients view future therapeutic intervention ideas. A recent study by McDonnell et al. demonstrated a time and cost effective approach to PPIE that addressed these issues. Their online survey acquired 520 patient responses over a 3 week period through social media promotion to assess which research topics are of the most interest to patients with lupus and/or antiphospholipid syndrome (APS) (14). In this study an online survey approach was taken to gather opinion from patients with lupus about their experiences with diet and to ask them what were their priorities regarding research into lupus in general. A secondary objective was to validate the study carried out by McDonnell et al. showing that that PPIE using online platforms can be a simple, valuable and time and cost effective approach (14).

#### Methods

#### Study design

An anonymous survey was established consisting of a lay research summary and a brief description of the survey. The aim was to capture as many responses in the shortest time possible to facilitate a cost and time effective process. The survey consisted of 15 questions focused around diet in patients with lupus (Table 1). The questions were designed to gain as much information as possible without being too burdensome for patients to complete. A final question included a free text box for patients to share their ideas/preferences for research in this area. The UK Health Research Authority decision tool (https://www.hra.nhs.uk/approvals-amendments/) confirmed that ethical approval was not needed for this survey. The lay summary and questionnaire (Supplementary methods and Table 1) were reviewed by clinicians and basic science researchers at UCL, non-scientists and an expert patient to ensure it was clear and understandable.

#### **Response capture**

Survey monkey (www.surveymonkey.com) hosted the survey for three weeks during Lupus Awareness Month (May 2018) which also included World Lupus Day (May 10<sup>th</sup> 2018). Lupus UK, Verses Arthritis, Lupus Research Alliance, UCL Centre for Adolescent Rheumatology and UCL APS research and other lupus awareness groups helped to promote the survey on Twitter, Facebook and Instagram. An initial question asking patients to self-report that they had lupus was put in place to stratify responses. Multiple submissions from the same participant were prevented.

#### Analysis of responses

Analysis of the data extracted from survey monkey was carried out using Microsoft Excel 2010 and GraphPad Prism 6. 'Wordcloud' software (<u>https://www.wordclouds.com/</u>) was used to produce a wordmap from patient free text.

#### Results

# Online platforms provide substantial responses to PPIE surveys across multiple age ranges

A survey to obtain patient opinion on the use of diet as a therapy in lupus as well as information on patient experiences with diet and disease was established (Table 1). After 3 weeks of social media promotion by various charities 300 responses were received (Figure 1).

A gradual increase in survey responses was observed through the use of twitter to publicise the survey link across the lupus community. This was done through the aid of charities such as Arthritis Research UK and the Lupus Research Alliance (US-based association), awareness groups including Lupus Science & Medicine and Dr Rheum, and also university related groups such as UCL Faculty of Medical Science, APS research, young people united and UCLH/UCL NIHR BRC. An article was included on the NHS web page by NIHR CRN North Thames. This initial response of around 100 plateaued at the end of week 1 where a twitter post from Lupus UK (https://twitter.com/LUPUSUK/status/994647904907399172), containing our survey web link, boosted another 70-80 responses. Finally, Lupus UK posted the survey web link on their Facebook page and to their community forum which resulted in the biggest increase in responses to a total of 300 by the end of week 3.

Of the 300 respondents, 284 had a self-reported lupus diagnosis. Based on the style of responses from the other 16 it was possible that they had another autoimmune disease, however these were excluded from further analysis. The majority of respondents (98.59%) were female (Table 2). There was a fairly even spread of survey responses across age groups between the ages of 18 and 64 (Table 2). Fewer responses were obtained from patients younger than 24 and older than 65 while patients in the 45-54 age bracket provided most responses (30.63%).

#### Patients thought that diet could be important in controlling lupus symptoms

Patients considered that diet could be important in controlling symptoms of lupus (average score 5.88/10) (Figure 2A). Furthermore, respondents thought that it would be valuable to know how diet influences disease symptoms (average score 8.47/10) (Figure 2B). Despite this interest, only 24.11% of patients had ever discussed diet with their doctors in relation to their disease (Figure 2C). Almost all respondents (99.29%) felt that it was important for doctors to know whether diet could influence disease (Figure 2D). In addition, most patients revealed they would change their diet if they knew it would help their disease symptoms; 85.92% would alter their diet and a further 13.73% expressed they would alter their diet if recommended by their doctor (Figure 2E). Importantly, most patients surveyed (82.62%) would be interested in taking part in a diet trial in the future with the primary outcome to reduce disease symptoms (Figure 2F). Thus, patients were interested in finding out about how diet could influence their disease and would be willing to change their diet to help control their disease symptoms. No obvious difference in survey responses was seen across different age brackets apart from a possible increase in dietary counselling for younger patient ages 12-17 (Figure 2G).

#### Some lupus patients associated diet with improved disease symptoms

When asked whether they had tried dieting during the course of their disease, 35.82% of patients had not tried a diet at all (Figure 3A). Of those who had, the most popular diets were Slimming World, WeightWatchers, Paleo and Atkins. The majority of patients however selected 'other'; here the two most popular diets were gluten-free and low carbohydrate (Table S1). The most common reason for starting a diet was to lose weight (48.61%) followed by to improve their disease (26.53%) and to look good (9.80%). Notably, only 8.16% of patients started their diet due to doctor's recommendation (Figure 3B). The most popular free text response under the 'other' option was "to get healthier" and "for allergies" (Table S1). From those that had been on a diet, only 7.06% of patients said they did not benefit; whereas 43.87% lost weight

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and 22% considered their disease symptoms and mood had improved as a result of their diet. Vegan and low gluten and sugar diets provided the highest percentage of responses for improved disease symptoms (Figure 3D). Some respondents (21.19%) felt happier in their image and 14.5% had improved fitness (Figure 3C). Additional benefits stated under the "other" option were reduced fatigue and pain reported by 9% patients (Table S1). Of those that had been on a diet, only 27.24% of patients used an app to monitor it (Figure 3E).

As the management of lupus often involves prescribed dietary supplements, we asked about the supplements that these patients were taking. We found that 70.03% of these patients take dietary supplements (Figure 3F), the most popular being vitamin D (29%), iron (13%), multivitamins (12%) and fish oils (7%) (Table S1).

#### What should we be researching?

Finally, an optional free text opportunity was included where patients were asked to state research questions that they feel should be investigated with regard to diet in lupus. Almost half of the patients left a response to this question (125 out of the total 284, 44%). The analysis of these results was carried out using wordmap software to visualise the most commonly mentioned ideas (Figure 4). The top responses included diet, foods, symptoms, lupus, fatigue and flare ups and other responses such as supplements, gut microbiome, dairy, stress and oils were also stated (Table S2). Patients also expressed an interest in how therapeutics such as corticosteroids influenced their diet and weight (Table S3).

#### Discussion

 This survey revealed three key discoveries: First, patients thought it was important for themselves and their doctors to know how diet can influence lupus and that they would be interested in trying diet as a therapeutic option; despite this we found that very few doctors had discussed diet with their patients. Second, a large number of patients had never been on a diet; however, of those that had, many felt that it had improved their disease symptoms. Finally, this survey confirmed it is possible to obtain fast, cost effective patient opinion online through social media promotion and provided a template for future studies.

As expected, the majority of respondents were female reflecting the sex bias of the disease (15). However, the even spread of responses across the age groups between the ages of 18 and 64 was surprising considering social media is believed to be more popular amongst the younger age groups; in 2017 96% of people aged 16–24 used social media platforms whereas this was only 68% aged 45–54 years (www.ons.gov.uk). It was of little surprise that a lack of responses came from under 18's and over 64's as this is likely due to lack of access to or interest in social media as well as a known decrease in the incidence of lupus diagnosis in these age groups (16). Therefore, this social media-based approach for gaining public responses for research may not be as beneficial for diseases common in young children and older people.

Only 25% of patients who responded had discussed diet with their doctors, although most thought that diet could be important in their disease and 100% of patients said they would change their diet if they knew it would help their disease symptoms. This reflects a general interest of patients to engage with strategies where they have more control over the management of their disease (17). Furthermore, this positive attitude towards diet highlights the potential for recruiting and maintaining good compliance in any future trials focused in this area.

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Indeed, two thirds of respondents had undertaken a diet previously although only 22% of these patients reported notable improvement in disease symptoms. This observation could be confused by the wide range of diets attempted; WeightWatchers and Slimming World being the most popular. Interestingly, vegan and low gluten and sugar diets appeared to improve disease symptoms the most. In addition to diets, we inquired about dietary supplements. It was no surprise to see that 70% of patients were taking supplements as common symptoms on lupus include vitamin D and iron deficiency (18); however, only 7% of the patients taking supplements were taking fish oils, known to have health benefits (19), modify blood lipid profiles (20, 21) and reduce cardiovascular risk which is high in lupus patients (22).

The results of this survey show that patients with lupus are interested in research. Answers from the 'free text box' section of the survey revealed several common concerns, such as flare-ups and fatigue. Between 40% and 50% of adults with lupus are classified as obese (23-26) and patients with obesity have increased fatigue and disease activity (27). Davies et al conducted a diet trial in lupus comparing 23 patients on a low glycemic index diet to a low calorie diet for 6 weeks (28). Both diets were effective in reducing fatigue and helped patients to lose weight. In addition, both diets were well tolerated, with mild adverse effects including no increase in disease activity. This supports a role for diet in controlling disease symptoms and demonstrates how a research and patient driven idea can provide beneficial results. Importantly, patients raised concerns around the effects of current lupus therapeutics on diet and weight gain. This is particularly important for lipid metabolism as studies have highlighted how prolonged use of corticosteroids can cause dyslipidaemia, something that would need to be considered in a clinical trial related to using diet to modify lipid metabolism (29, 30).

PPIE can be a time-consuming and costly experience and studies have attempted to address this issue to improve and accelerate translational research (31, 32). For example, Elwyn et al. used postal distribution of a survey to 1146 participants with

 asthma, open to responses for 3 months, as well as a 3 week online post on a relevant charity website. A total of 370 responses were received with a cost of £29,000 (33). In contrast, we gathered 300 responses, with minimal cost (£35) from a 3 week online survey using the power of charity-based and individual social media pages for promotion.

There have been few previous attempts to use this approach for PPIE in basic science research. One example of its effectiveness however was demonstrated by McDonnell et al. where a similar number of responses were gathered over a 3 week period to assess topics that were of interest to a specific patient population (14).

12Limitations of this study include potential selection bias; survey responders may complete the survey based on a prior interest in the research topic. In addition, responses gathered through this type of survey can only be obtained from patients with access to social media and/or the internet. This could add bias towards responses from younger patients, although data obtained here suggests otherwise. One possibility is that the lay summary was too long and complicated for a younger audience and that the word 'Lupus' was not in the title; this could have accounted for the relatively lower than expected number of younger respondents. Future studies could benefit from feedback from a wider range of age groups. Another limitation to this approach is the language barrier; the lay summary and questions could however be translated in future. Finally, this approach leaves no opportunity for follow up questions as responses are anonymous.

In summary, this survey identified that patients with lupus are interested in finding out whether diet could influence their disease. We also identified that there is a lack of knowledge and education about diet in the responders and that most patients had not talked to their doctors about diet. Many patients had tried various diets but very few controlled trials have been performed to inform patient choices (34). This survey

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identified that patients would be enthusiastic to support research and diet intervention studies with close monitoring of disease symptoms and cardiovascular risk. Future, more focused face-to-face discussions with patients could help to optimise clinical trial design and determine feasibility of potential diet-focused therapeutic interventions. Thus, this survey provides evidence of patient support for further research into the effects of diet on the symptoms of lupus.

**Contributors:** Design of research study; GAR, TM, CW, LMG, CC, ITP, ECJ: Acquiring data; GAR, Analyzing data; GAR, AZK, CC, ITP, ECJ: Writing the manuscript; GAR, ECJ: Review of the manuscript; CC, LMG, TM, ITP, CW, JW,

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**Competing interests:** The authors have declared that no conflict of interest exists.

**Ethics approval:** The UK Health Research Authority decision tool (<u>https://www.hra.nhs.uk/approvals-amendments/</u>) confirmed that ethical approval was not needed for this survey.

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Number	Question
1	Do you have Systemic Lupus Erythematosus? (Yes/No)
2	Which gender are you? (Male/Female)
3	How old are you? (Tick box)
	How important do you think diet is in controlling symptoms for your lupus?
4	(1-10)
5	Has your doctor ever spoken to you about your diet? (Yes/No)
	Have you previously tried a particular diet? If yes please specify which
6	type? (Tick box and other response option)
7	Why did you begin the diet(s)? (Tick box and other response option)
	Did you benefit from the diet? If yes how? (Tick box and other response
8	option)
9	Did you use an App to monitor your diet? (Yes/No)
10	How valuable is it to you to know whether diet influences lupus? (1-10)
	Do you think it is important for doctors to know whether diet can influence
11	disease? (Yes/No)
	Would you change your diet if you thought it would help your lupus?
12	(Yes/No/Only if recommended by doctor)
	Do you take any regular dietary supplements? (Yes/No and text response
13	option)
	In the future would you consider taking part in a clinical study to
	investigate whether diet/dietary supplements can reduce disease
14	symptoms? (Yes/No)
	Optional: What research questions do you think we should investigate?
15	(Open text)

### Table 1: Online survey questionnaire

An anonymous online survey consisting of 15 questions asked lupus patients about their diet and disease experience as well as for feedback on what research topics patients were interested in. The response format given to survey responses is displayed in brackets.

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Demographic	Percentage (number)
Sex:	
Male	1.41 (4)
Female	98.59 (279)
Age:	
Under 12	0 (0)
12-17	0.70 (2)
18-24	7.04 (20)
25-34	14.44 (41)
35-44	22.89 (65)
45-54	30.63 (87)
55-64	18.31 (52)
65+	5.99 (17)

### Table 2: Demographic information of survey responders with lupus

Demographic table displaying the percentage (and number) of responders from the survey (survey monkey) (Table 1) that were male, female, and different age brackets.

Review



Figure 1: Cumulative response number over the 3 week survey period

Cumulative number of responses over the 3 weeks that the survey was publically accessible. Social media promotional help from various charities is highlighted with a particular acknowledgement to Lupus UK who helped greatly with survey distribution.

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Results from the 3 week anonymous survey (Survey Monkey). A-B) 0-10 graphs display the average response from rating scale questions. C-F) Pie charts display data

as percentages. G) Analysis of responses from 3 of the survey questions split by age. Data is displayed as percentage of total patients that responded 'yes' or rated 1-100%.

to per period

LUPUS



Figure 3: Survey responses regarding patient experiences with diet including reasons, types and outcomes

Results from the 3 week anonymous survey (Survey Monkey). A-C) Percentage of patients that responded with specific answers displayed. D) Percentage of patients (number displayed to the right of bars) that had improved disease symptoms as a result of specific diets. E-F) Pie charts display response data as percentages



#### Figure 4: Research questions important to lupus patients

Text cloud analysis, using 'wordcloud' software, of free text from an optional question in the survey asking for patient ideas for research. The size of the wording represents the frequency of times the word was found in the survey. See Table S2 and S3.

LUPUS

# Diet and lupus: What do the patients think?

## Supplementary data

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## Supplementary methods:

# Lay research summary and survey description given to patients

⁺UCL

## How you can help influence a new research proposal

We are a group of researchers at University College London (UK) studying patients with lupus. We want to increase our understanding of what causes the disease so that we can improve and develop new treatments for patients. We have a new and exciting idea that we believe could help to reduce disease severity. Before we start this project, we would like to find out from you whether you think this is an important area to investigate, and whether you have any experiences that could help us improve our research.

We are interested in how fats in the body influence the immune system (the body's natural defence system) in lupus. Fats in the blood can change the way the immune system works. We have found that blood fats and immune cell fats are altered in patients with lupus, and this is linked with disease flares. There are existing drugs that change fat production, which may be beneficial for patients with lupus; however, we would like to find out whether altering diet can have a similar beneficial effect on lupus. We hope this approach could reduce the dependence of patients on drugs.

We are particularly interested in measuring fats, such as cholesterol, that are transported in the blood. The liver plays an important role in producing and processing fats, which are either removed from the body or released into the blood. There are different types of blood fat transport; for example, 'bad' fat transport delivers these fats to the wall of blood vessels and can increase levels of harmful inflammation. 'Good' fat transport goes the opposite way and delivers fats from these areas back to the liver where they can be removed from the body; this also reduces inflammation.

We want to see if by making changes to diet or using diet supplements we can change the amount of fat in the body as well as reduce 'bad' fat transport and enhance the 'good' fat transport. Therefore, greater knowledge of how diet has affected patient experience with lupus would help us understand the potential of this new idea.

Before we begin this research, we would like to ask you some short questions to help us to focus on the areas that are most relevant to you as a patient. Your input is of huge value to our research. Please click 'Next' below to answer these questions.

All of us at the UCL Centre for Rheumatology Research would like to extend a grateful thank you for your time and support in answering these questions; it is only together that we can really make progress in understanding this disease. By completing this questionnaire, you are consenting to us sharing your responses. All of your answers will be completely anonymous.

# Supplementary Tables:

Question 6- Have you		Question 7- Why did		Question 8- Did you	
previously tried a		you begin the		benefit from the	
particular diet? If yes	%	diet(s)? (other):	%	diet? If yes how?	%
please specify which				(other):	
type? (other):					
Low/no gluten	20	Get healthier	16	Less fatigue	9
Low carbohydrate	13	Allergies	12	Reduced pain	9
General healthy eating	8	Gluten related	7	Less nausea	6
Vegan	8	Moral reasons	7	Reduced flares	6
5.2	7	For research	5	Lowered	3
5.2		i ol research		cholesterol	
Lactose free	6	High cholesterol	5		1
Calorie counting	4	Reduce fatigue	5		
Low fat	4	Improve nausea	2		
Vogotarian	1	Reduce blood	2		
vegetariari	-	pressure	2		
Autoimmune protocol	3			J	
Foodmap	3				
More fish	3				
No red meat	3				
Vitamin/mineral	2				
supplements	2				
Elimination diet	1				
Low salt	1				

# Table S 1: Free text (other) responses associated with questions 6-8

Tables displaying the percentage of the total responses that individual diets (left), reasons for starting the diet (middle) and benefits of the diet (right) were detected in the text analysis (survey monkey) of the free text (other) responses to question 6, 7 and 8 (Table 1).

Word	% of total responses	Number of times mentioned
Diet	30.4	38
Foods	25.6	32
Symptoms	20	25
SLE	12	15
Fatigue	8	10
Flare Ups	7.2	9
Affect Lupus	5.6	7
Dairy	4.8	6
Immune System	4	5
Cause Flares	4	5
Supplements	4	5
Vitamins	4	5
Help Reduce	4	5
Autoimmune Disease	3.2	4
Stress	3.2	4
Microbiome	2.4	3
Gut Bacteria	2.4	3
Long Term	2.4	3
Medical Profession	1.6	2
Medicine	1.6	2
Kidney	1.6	2
Note	1.6	2
Oils	1.6	2
Physical	1.6	2
React	1.6	2
Water	1.6	2
Vegan	1.6	2

# Table S 2: Text analysis of responses to question 15-What research questions do youthink we should investigate?

Table displaying the number of times and percentage of the total responses that individual words were detected in the text analysis (survey monkey) of responses to question 15- What research questions do you think we should investigate? (Figure 4) The top 27 words are displayed.

 Do you think your weight gain is related to drugs you take to control your lupus symptoms?

Would cholesterol reducing drugs reduce SLE flares? Do statins cause increased muscle pains in SLE patients? How does knowledge and education affect dietary compliance in chronic diseases such as SLE? Does glucose monitoring benefit SLE patient management? How do we minimise weight gain on high doses of steroids?

Types of fat relating to carbohydrates, dairy and also meat vs healthy natural fats with the understanding of the link to medication that lupus patients are on, like steroids and the difficulty that brings. For example I might feel slightly better with lupus on low carb, low fat diet, but then medication side effects especially stomach ones are worse, and medication side effects are better when stomach is lined with heavier carb type foods. Can you find a workable balance?!

Any supplements which might help reduce medications?

Supplements and vitamins

The role of pro-biotics and vitamins eg D

The use of oils in body? Do vitamins and minerals make any difference on modifying SLE?

The impact of UVA, UVB and infra-red rays upon SLE, the short/ long term effects. - Vitamin D deficiency prevalence in SLE - the time it take to diagnose lupus, why so lengthy and how to reduce this. - The impact of stress upon lupus - what advice do doctors provide lupus patient's which will be of benefit to their day to day functioning.

# Table S 3: Diet related open text responses associated with drug/corticosteroid and

#### supplement use

Table displaying the 'open text' responses from lupus patients regarding the use of corticosteroids and other therapeutics/supplements when considering diet in disease therapy. These responses were gathered from the text analysis (survey monkey) of responses to question 15- What research questions do you think we should investigate?