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Family Planning and Pregnancy Issues for Women with Systemic Inflammatory Diseases: Patient and Physician Perspectives

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Author Contributions

EC: substantial contribution to conception and design, interpretation of data, drafting and critical revision of the manuscript, and final approval of the manuscript for submission.

MEBC: substantial contribution to conception and design, interpretation of data, drafting and critical revision of the manuscript, and final approval of the manuscript for submission.

DSP: substantial contribution to conception and design, interpretation of data, drafting and critical revision of the manuscript, and final approval of the manuscript for submission.

SM: substantial contribution to conception and design, acquisition, analysis and interpretation of data, critical revision of the manuscript, and final approval of the manuscript for submission.

CG: substantial contribution to conception and design, interpretation of data, drafting and critical revision of the manuscript, and final approval of the manuscript for submission.

Abstract

Objectives: To identify family planning and pregnancy (FPP) issues for female patients of child-bearing age living with a chronic inflammatory disease and to assess whether current clinical practice routinely provides adequate support to alleviate these concerns.

Setting: Multinational survey and an analysis of online patient activity.

Participants: Premenopausal women (aged 20-45 years of age; N=969) were surveyed in USA, UK, Germany, France, Italy and Spain. Rheumatologists were surveyed in Germany (N=50), France (N=50), Italy (N=50) and the USA (N=100) and gastroenterologists were also surveyed in the USA (N=100).

Primary and Secondary Outcome Measures: Two online surveys were undertaken to identify FPP issues for both physicians and patients. The surveys examined the frequency of dialogue on these topics between physicians and patients, alongside assessment of patient satisfaction regarding these conversations. Online analysis identified key themes for patient discussion outside their doctors' office/clinic/surgery.

Results: 32-56% of physicians spontaneously reported having talked about FPP with their female patients of child-bearing age. When prompted, the majority of rheumatologists (74-92%) and gastroenterologists (74%) reported having discussed conception/pregnancy with female patients; however, less than half reported consulting their patient's treating GP/gynaecologist about these topics.

The majority of patients reported their FPP-related concerns are not adequately addressed/settled during their medical appointments. Furthermore, only 30-40% of patients considered advice/information to be consistent across multiple healthcare professionals.

Key online FPP-related patient discussions included: disease state, adverse effects, treatment, switch behaviour and wash-out requirements.

Conclusions: Female patients who live with chronic inflammatory disease have important FPP concerns. The majority of patients, however, do not feel that their FPP concerns are adequately addressed in current clinical practice and report that they receive inconsistent advice from the various healthcare professionals who manage different aspects of their care. There is a clear need for provision of up-to-date and consistent information/support to female patients.

Article Summary

Article Focus:

- To identify key family planning and pregnancy (FPP) issues for female patients of child-bearing age who live with a chronic inflammatory disease and to assess whether current clinical practice routinely provides adequate support to alleviate these concerns.

Key Messages:

- Female patients of child-bearing years wish to discuss FFP issues in relation to their disease with their physicians but the majority of female patients who live with chronic inflammatory disease feel that their concerns are not adequately addressed.
- Physicians should initiate discussion of FPP issues with their female patients, particularly those receiving immunosuppressive treatment up to the ages of 50, and establish their expectations and concerns.
- Treating physicians should work to maintain this dialogue, at least once per year or when treatment changes, and align the advice offered to their female patients of child-bearing age with that from other physicians involved in their care.

Strengths and Limitations:

- Strengths: investigation of both patient and physician perspectives, involvement of specialists from different areas of interest and cross-cultural investigation.
- Limitations: absence of formal survey validation, reliance upon patient self-reporting, complications associated with delivery of the survey in local languages and possible bias in netnography research due to regional differences in language usage.

Introduction

Autoimmune and inflammatory diseases often affect women of reproductive age. Although RA becomes more common as patients age,[1] women are increasingly choosing to start their family later in life and treatments to control RA are now often started at a younger age. Moreover, even though only a minority proportion of RA patients are women of child-bearing age,[2] the high prevalence of the disease means that it does impact a significant number of young women. Many other inflammatory diseases, including ankylosing spondylitis (AS),[3 4] Crohn's disease (CD),[5 6] inflammatory bowel disease (IBD)[7] and systemic lupus erythematosus (SLE),[8] also affect a younger population and thus have a direct effect on women of child-bearing age.

Pregnancy and child rearing are important facets of life for most women. Now that improved therapies for inflammatory diseases have enabled better physical function and quality of life, many women who previously would have felt too ill to consider child-bearing are now better able to fulfil desires for family life. Family planning and pregnancy (FPP) are also important issues for this patient population as multiple studies have linked these disease states to a decreased chance of conceiving,[9] carrying to full term[10] and increasing the risk of other potential complications.[11-13] Due to this impact on pregnancy outcomes, expert advice is to achieve and maintain stable low disease activity prior to conception and throughout pregnancy.[14-16] Some anti-inflammatory treatment options can be potentially hazardous for pregnant women to take as drugs can pass across the placenta and may affect the foetus.[17] Methotrexate, a common RA treatment, can be damaging to foetal development (at least at high doses)[18 19] whilst other disease-modifying anti-rheumatic drugs such as leflunomide have been shown to cause malformations in animal studies.[20]

However, use of medications during pregnancy is not always contraindicated and an individual risk-benefit discussion should be undertaken between the patient and expert physician to provide the best management of both the disease and the pregnancy.[21] Inadequate dissemination of appropriate advice describing which drugs may be continued can lead to women unnecessarily forgoing potentially helpful medications and thus suffering throughout pregnancy, with the increased risk of further complications to both mother and child due to the effects of active disease.[22] Furthermore, patients are increasingly seeking additional information on the internet,[23] while a recent analysis of information regarding medication safety on active internet sites has noted an inadequate evidence base for the advice often provided and inconsistent guidance.[24] It is clear that communication of reliable and consistent information is required to enable the correct treatment of these women before and during pregnancy, and while breast-feeding. Education and information should be shared by healthcare professionals dealing with these diseases, medications and situations on a daily basis. Accurate, consistent information must be communicated to women considering or entering pregnancy in order to support patients through this delicate journey.

Two surveys were undertaken to investigate some of these issues, one of physicians and another of female patients, to identify the key concerns of both groups related to the topics of FPP in inflammatory disease. The surveys were designed to gauge whether there is a gap in the communication between what healthcare professionals provide in terms of information/support and what patients feel that they receive. The patient survey also investigated where patients go to seek additional information. Two key objectives of the study were to examine the proportion of physicians who discuss FPP issues with their female patients of child-bearing age and the proportion of patients who have discussed these topics, in the context of their condition, with their healthcare professional. The survey also

assessed the proportion of patients who feel that their concerns on this topic have been satisfactorily addressed by these discussions. Here we aim to communicate the insights gained from this investigation to clinicians treating women of child-bearing age, who live with chronic inflammatory conditions, in order to provide advice on how best to support these patients.

Methods

Physician Survey

The online physician questionnaire was delivered in two phases, the first phase (baseline) was distributed in July 2012 (Europe) and September 2012 (USA), and the second phase was distributed in November 2012 in both Europe and USA. The survey was delivered in the local language and translations were checked for consistency against the original in English by native speakers with fluency in both languages (the complete Physician Questionnaire can be found online in Appendix 1). The questionnaire was designed to elicit both spontaneous (open-ended question) and prompted (closed question in which FPP topics were an option among other answering categories) responses. Participants were recruited from the WorldOne Physician Panel. Rheumatologists were surveyed in four countries: Germany (N=50), France (N=50), Italy (N=50) and the USA (N=100). Gastroenterologists were surveyed in the USA (N=100). Responses were compared between phases using two-sided z-tests with significance level 0.05, which corresponds to a confidence interval of 95%.

Participating physicians had to meet the following criteria: 3 to 30 years of experience, ≥50% patient-facing time, had not participated in medical research within their specialist area in the past month, were not currently a clinical investigator for a pharmaceutical manufacturer and were not currently active in medical research or advertising. Physicians with Rheumatology as their primary specialty had to meet the following additional criteria:

treat ≥20 RA patients per month and have ≥10 patients on biologics per month. Physicians with Gastroenterology as their primary specialty had to meet the following additional criteria: treat ≥8 CD patients per month and have ≥2 patients on biologics per month.

Patient Survey

The online patient questionnaire was designed according to standard market research survey methodology, including scaling questions and avoiding skewed questions. The questionnaire was delivered in the local language and translations were checked for consistency against the original in English by native speakers with fluency in both languages (the complete Patient Questionnaire can be found online in Appendix 2). The questionnaire was targeted at premenopausal women (age was self-declared and the survey excluded women under 20 and over 45 years of age; see Question 3 Patient Survey). A professional recruitment agency was used to recruit patients.

The patient questionnaire was delivered in two phases and was distributed in six countries (USA, UK, Germany, France, Italy and Spain). The first phase (baseline) consisted of 16 questions and was disseminated to patients between 17th July and 15th August 2012. There were 1,069 respondents to the first phase which covered patients with RA, SLE, CD and ulcerative colitis (UC). The second phase consisted of the original 16 questions from the first phase plus an additional 8 questions included in order to avoid so-called 'false positives' (i.e. covered topics included in other questions to test consistency of response) and to provide greater insight into patients' experience in terms of medical care and needs. The second phase elicited 969 responses and was distributed between 13th October and 16th November 2012 to patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA), in addition to RA, SLE, CD and UC patients. All responses were anonymous. The patients who were invited to participate in the two survey phases were not identical, although there may have

been some overlap (responses were anonymous therefore the extent of overlap could not be determined).

Netnography Research

Online discussions (English language only) relating to FPP issues were investigated using two approaches: social media monitoring, and search engine landscape/content analysis (SELA).

Social media monitoring was undertaken by identifying categories of interest (defined as: 'ulcerative colitis', 'systemic lupus erythematosus', 'rheumatoid arthritis', 'colitis ulcerosa', 'lupus', 'regional enteritis', 'Crohn's disease') and keywords of interest (defined as: 'pregnancy', 'miscarriage', 'birth control', 'miscarriages', 'fertile', 'family planning', 'gestation', 'pregnant', 'fertility', 'pregnancy disease evolution', 'disease transfer to baby', 'breastfeeding', 'breast feeding', 'conception', 'conceived' and 'placental transfer'), and then combining keywords together with the categories of interest to ensure coverage of all topics of interest.

SELA methodology involved identification of keywords (including generic keywords/keyword phrases and specific keywords/keyword phrases), assessment of keyword search volume and ranking of individual sites in search engine results. The 'click through rate' was combined with the 'monthly search volume' to estimate the 'share of attention index'. The final keyword pool included the categories 'colitis ulcerosa', 'ulcerative colitis', 'Crohn's disease', 'lupus', 'rheumatoid arthritis', 'regional enteritis' and 'systemic lupus erythematosus', and the following FPP-related keywords 'gestation', 'birth control', 'pregnancy', 'fertility', 'miscarriage' and 'family planning'.

Results

Physician Survey

Many rheumatologists and gastroenterologists spontaneously reported having discussed FPP-related topics with their female patients of child-bearing age; reports were consistent across all countries studied (Figure 1A). Interestingly, the number of US gastroenterologists who discussed these topics with their female patients increased significantly between the first and second Phases of the survey (Figure 1A). This was particularly true for fertility, pregnancy and/or family planning issues specifically, in which the percentage of US gastroenterologists discussing these topics increased from 67% to 79% between the two Phases (significant difference, 95% confidence level; N=100 for both survey phases); however there was no difference in European practice, with levels remaining at 60%.

When prompted, the majority of rheumatologists (74-92%) and gastroenterologists (74%) reported having discussed conception/pregnancy with female patients of child-bearing age. However, less than half of these physicians discussed FPP related issues with their patient's treating GP (i.e. primary care physician) or gynaecologist (Figure 1B and Figure 1C; survey Phase 2 data shown; see Questions 20 and 21 Physician Survey Appendix 1).

When seeking additional information regarding FPP, community rheumatologists and gastroenterologists reported currently relying on presentations and educational events at congresses, other healthcare professionals and key opinion leaders as their preferred sources of information.

Patient Survey and Netnography Analysis

Patients reported that the frequency of FPP-related conversations during their medical appointments was lower than their discussions about emotional well-being and employment (Figure 2A), although most female patients of child-bearing age (up to 85%) reported discussing these issues at some point during their care pathway (Figure 2B).

Patients currently on medication for the treatment of their condition reported being more concerned about FPP issues than those not receiving medication, with 63% of those on medication reporting that pregnancy was a concern compared to only 32% of patients not receiving medication. In addition, the female age group with most concerns related to FPP was between the ages of 30 and 34, with >60% of these patients reporting concerns (Figure 2C; survey Phase 2 data shown, similar trend observed in Phase 1). Concern was high between the ages of 25 and 39 (57-63%) but decreased to 44% in patients aged between 40 and 45.

Patients were asked when they would prefer to discuss the topics of FPP. The survey revealed that approximately 35% of patients prefer to discuss these issues in the context of their disease and treatment whenever a decision is made that could have an impact on their family planning or ability to become pregnant (Figure 3A). Approximately a quarter feel that one conversation with their healthcare professional on this topic is enough, although approximately 17% would like to discuss these topics at every visit. Furthermore, approximately a third of patients prefer to initiate conversations on this topic themselves (30-40% patients) or to obtain information from their healthcare professional when appropriate to their individual situation (15-35% patients).

Patients gave a range of reasons for not discussing FPP concerns with their healthcare provider, with the most common reason being that they forgot to mention it (Figure 3B). Other important reasons identified as barriers for discussing FPP was the impression that the healthcare professional either did not have time for discussions or that they were not the correct physician to provide advice on these topics. Importantly, some patients also reported that they choose to not discuss FPP issues as they were reluctant to change medication. Very few patients felt that their healthcare professional was reluctant to discuss these topics. Over a quarter of respondents indicated that they had 'other' reasons for not discussing these issues with their doctor (Figure 3B). A higher proportion (39%) of patients aged 40-45 years recorded 'other' reasons for not discussing FPP issues with their doctor, compared to younger patients ('other' was recorded by 21.7% of 20-24 year olds, 18.3% of 25-29 year olds, 18.7% of 30-34 year olds and 25.6% 35-39 year olds).

Patients report a preference for seeking information regarding FPP from their gynaecologist (Figure 4A), whereas disease specialists (e.g. rheumatologist or gastroenterologist) are their key contact point for management of their chronic condition (Figure 4B). GPs/primary care physicians were also identified by patients as central to their discussions of both FPP and their chronic condition (Figure 4A-B). It should be noted, however, that patient reports of a preference for one specialist over another regarding FPP discussions could be expected to vary by country given differences in treatment practices. For example, in the USA patients may commonly visit a gynaecologist/obstetrician for all pregnancy care whereas in the UK the patient's GP and local midwife may oversee most of their pregnancy planning and management. In addition, when responding to the survey some, but not all, patients may have regarded the terms 'obstetrician' and 'gynaecologist' as interchangeable based on their own experience.

Other than their doctors' office/clinic/surgery, patients reported researching and discussing information regarding FPP through multiple channels (Figure 4C): predominantly on disease-related websites and with family and friends. In addition, patients reported that specific condition-related forums/patient organisations did not play a prominent part in their search for online information on these topics. A number of key themes, such as discussions around disease state, adverse effects, treatment, switch behaviour and wash-out requirements, emerged after following online patient activity. Other themes noted were patient emotions and feelings, interactions with healthcare professionals, how best to identify the correct healthcare professional for their treatment, concerns about inconsistent advice, infertility, sexuality and conception, disease carry-over to the baby, placental transfer of treatments and breastfeeding.

Importantly, approximately 30-55% of female patients reported that their concerns relating to FPP are not adequately addressed or settled during their medical appointments (data from patient survey Phase 2). Some variability in this response was observed across countries, with 30% of patients from the USA, 34% from Italy, 35% from Spain, 39% from the UK, 43% from France and 54% from Germany reporting their concerns were not settled (data from patient survey Phase 2). Patients also reported that consistency of advice and information given by multiple healthcare professionals, including nurses, was low with only about 30-40% of patients reporting consistent advice. Again, responses to this question varied across countries with 33% of patients reporting consistent advice from Spain and the UK, 36% from Germany and Italy, 40% from the USA and 41% from France (data from patient survey Phase 2). Inconsistent advice was reported by about 30-50% of patients overall: 27% from Italy, 32% from Spain, 38% from France, 41% from the USA, 44% from Germany and 49% from the UK (remaining patients selected a neutral response to this question; data from patient survey Phase 2).

Discussion

The investigation described here was carried out to illuminate some of the issues surrounding FPP for female patients of child-bearing age who live with chronic inflammatory diseases. Recently it was reported that almost half of female IBD patients feel their disease and/or treatment influences their decisions about FPP but despite this about two thirds had not discussed these issues with their doctor.[25] The results from the current study confirmed that FPP are considered important issues by this group of female patients and that there are key gaps in communication which result in inconsistent advice and subsequent patient concern/confusion. Importantly, the majority of female patients of child-bearing age reported that current clinical practice does not adequately address their concerns related to FPP in inflammatory disease.

Some clinical recommendations for the management of inflammatory disease during pregnancy have been published[14-16 21 26] and advise that clinical remission/stable low disease activity be achieved prior to conception and maintained throughout pregnancy using appropriate therapy as needed. However, in the current study few patients reported discussing FPP at the point their condition was stable enough to become pregnant, suggesting a gap in necessary communication from physicians to patients regarding the need to control disease activity prior to conception, the impact of disease activity on pregnancy outcomes and the need to adjust medications during pregnancy. Indeed, a general lack of patient knowledge regarding continued use of medication during pregnancy was highlighted recently by a survey of female IBD patients which revealed a widespread, but inaccurate, belief that all medications needed to be stopped during pregnancy.[25] Respondents to the current patient survey also reported that inconsistencies in advice regarding the use of anti-inflammatory and immunosuppressive medications during

pregnancy are common. Together, these results suggest a need for continuing education of all specialists involved in the care of women with inflammatory disease in order to ensure women understand the implications of their condition and treatment on FPP. Timely discussion of FPP issues is also an important consideration given a high percentage of pregnancies are unplanned.[27] Congress presentations and associated education events were identified by physicians, specifically rheumatologists and gastroenterologists, as their currently preferred source of information and continuing education – which may also be applicable to other specialists. As such, these events should be actively targeted to maximise and improve continued education.

GPs/primary care physicians and gynaecologists were identified by patients as frequently central to their discussions on FPP issues, although research has previously shown that 41% of GPs do not initiate discussion of FPP with female patients affected by IBD.[25] Importantly a gap in communication was identified between these physicians and the specialists who treat chronic inflammatory diseases. As such, improved cross-specialty communication should be strongly encouraged, particularly for discussions regarding planning and treatment guidelines. A recent survey of GPs in Ireland did show that the majority of GPs report seeking additional advice on FPP issues, in relation to their female IBD patients, from tertiary specialists[25] so improved education for all specialties and fostering communication should assist dissemination of information and consistent advice for patients. Furthermore, all of those involved in the care of female patients of child-bearing age who live with chronic inflammatory disease, not only the immunological disease specialists, should be exposed to continued education on this topic.

In order to improve the dissemination of information regarding FPP to patients, it is important to identify when patients prefer to receive such information and also why this

information may not be adequately communicated. Patient preference regarding timing of discussions about FPP varied. This variability may be due to the personal nature of this topic, differences in retention of information and differences in healthcare services/societal norms across different countries. Patients did, however, generally report that they wished to discuss FPP-related issues with their specialist physician (i.e. rheumatologist or gastroenterologist) every time a decision was made that could impact upon their FPP. As such, healthcare professionals should routinely consider any issues that affect fertility or pregnancy and offer to have a conversation with their patient regarding these issues at every clinic visit, unless it is known not to be relevant. It may also be useful to clarify patient expectations for support and advice during these discussions. Patients on medication were more concerned about FPP issues than those not receiving medication, as were female patients between the ages of approximately 25 and 40. The high level of concern in both of these groups highlights these patients as key populations requiring additional consideration, although it could be argued that all women of child-bearing age should be targeted for such communications.

The most common reason patients offered to explain why they did not raise FPP with their healthcare provider was that they forgot to mention it during their consultation. Many also stated they avoided such discussion as they did not want to change their medication, implying that a fear of destabilising their disease could influence the preparedness of patients to discuss FPP topics. Other key reasons identified were the impression that their physician did not have time for the discussion or that they felt their treating physician was not the correct physician to consult on these topics. Consequently, physicians should consider periodically raising the issue themselves, particularly when treatment decisions or disease activity could impact FPP plans. Notably over a quarter of respondents indicated that they had 'other' reasons for not discussing these issues with their doctor. It is possible that

this high response was due to patient demographics (e.g. age, social background or current use of contraception) and patients considering their family already complete. Indeed, a higher proportion of older patients recorded 'other' reasons for not discussing FPP issues with their doctor compared to younger patients. Patient emotions was an important theme identified for online discussions, perhaps particularly relevant for those with a history of miscarriage/stillbirth or infertility problems, and it should also be considered that such associations could be a factor underlying why some patients reported that they did not discuss FPP with their physician for 'other' reasons.

Of key importance, many female patients of child-bearing age reported that they did not feel that their concerns relating to FPP in the context of their disease were adequately addressed during their medical appointments. There was some variability in patient response across countries to this question, suggesting that cultural differences and differences in healthcare system structure may contribute to the variability in patient satisfaction. However, it is clear that there can be a definite improvement in the response to these issues and all healthcare professionals should consider how they could increase such communication and support to their patients. This could include provision of better patient educational material and advice on reliable and up-to-date websites containing FPP-related information. Indeed, patients reported that they frequently sought information online, although specific condition-related forums/patient organisations did not appear to be common sources of this information. Furthermore, the online landscape was fragmented by disease area, with no specific resource (beyond "Motherisk"; www.motherisk.org) that provides FPP guidance on common autoimmune conditions and medication use affecting women in the reproductive age group. As such, development of a single site with consistent up-to-date guidance covering topics identified by patients as key interests would probably be of great value. Alternatively patient and/or physician organisations could incorporate more detailed information and advice on

their websites to offer improved support to concerned patients and the various physicians involved in their care during pregnancy. Another key improvement would be increased dialogue, by telephone, letters or e-mail, between the varied physicians involved in an individual patient's care in order to provide coordinated advice and support. Together these measures would aim to improve patient support and satisfaction.

It should be noted that this study does have some limitations. Two important limitations of the patient survey were an absence of formal survey validation and the reliance upon self-reporting of diagnosis by patients. Furthermore, even though the surveys were translated into local languages, differences in terminology and healthcare system structure exist across countries which could impact pooling of results; for example, the terms obstetrician and gynaecologist could be understood as being interchangeable in some countries but distinctly different specialties in others meaning patient interpretation of the survey could vary. The physician survey may also suffer related issues. In addition, the physician survey was only delivered to gastroenterologists in the USA and did not investigate the activities of these physicians in other countries. Furthermore, the netnography research may have been limited by use of keywords common to one country/region but different in others (e.g. 'fertility' vs 'infertility') which could have restricted comprehensive analysis of the online landscape and patient discussions. Finally, this study did not investigate the related concerns of men suffering from inflammatory disease who may be using chronic medication and also considering a family; indeed this population is often understudied and may need improved support.

In summary, FPP are extremely important issues for female patients of child-bearing age who live with chronic inflammatory disease. A summary of key considerations, highlighted by the results from the current study, for all physicians involved in the treatment of this

often neglected group of patients is presented in Figure 5. It is clear that female patients of child-bearing age do wish to discuss these issues with their physicians although expectations regarding frequency of discussion and their preferred physician for advice vary considerably. Currently it appears that more can be done to provide these patients with consistent and co-ordinated information regarding their disease and how it, and associated treatments, could affect conception or pregnancy. Results from this study suggest physicians should regularly initiate discussion of these topics with their female patients of child-bearing age, particularly those on chronic medication or when changes to the treatment plan could impact pregnancy outcome, in order to improve patient support. In addition, greater cross-speciality communication between physicians involved in different aspects of the patient's care, from gastroenterologists and rheumatologists to gynaecologists/obstetricians and GPs, is needed to improve the consistency of advice offered to this often overlooked patient population.

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Figure 1. Frequency of physician-initiated discussions regarding FPP issues with female patients and their GPs or gynaecologists (survey Phase 2 data shown in B and C)

Abbreviations: Ga = gastroenterologist; Rh = rheumatologist. *p<0.05 compared to Phase 1 (two-sided z-test with significance level 0.05)

Figure 2. Patient reported (patient survey) topics of discussion with specialist physicians, the frequency of patient-initiated FPP discussion and the importance of FPP issues stratified by patient age (data from survey Phase 2 shown in C)

Figure 3. Patient preference for frequency of discussions relating to FPP issues and identification of issues that prevented discussion (data from patient survey Phase 2 shown)

Figure 4. Patient preference for choice of healthcare provider for discussions of their condition and FPP issues, and their preferred source of additional information (outside doctors' office/clinic/surgery) relating to both their condition and FPP issues (data from patient survey Phase 2 shown)

Figure 5. FPP-related considerations for practicing physicians treating female patients of child-bearing age who live with chronic inflammatory disease: key messages from the survey of current clinical practice and patient perceptions.

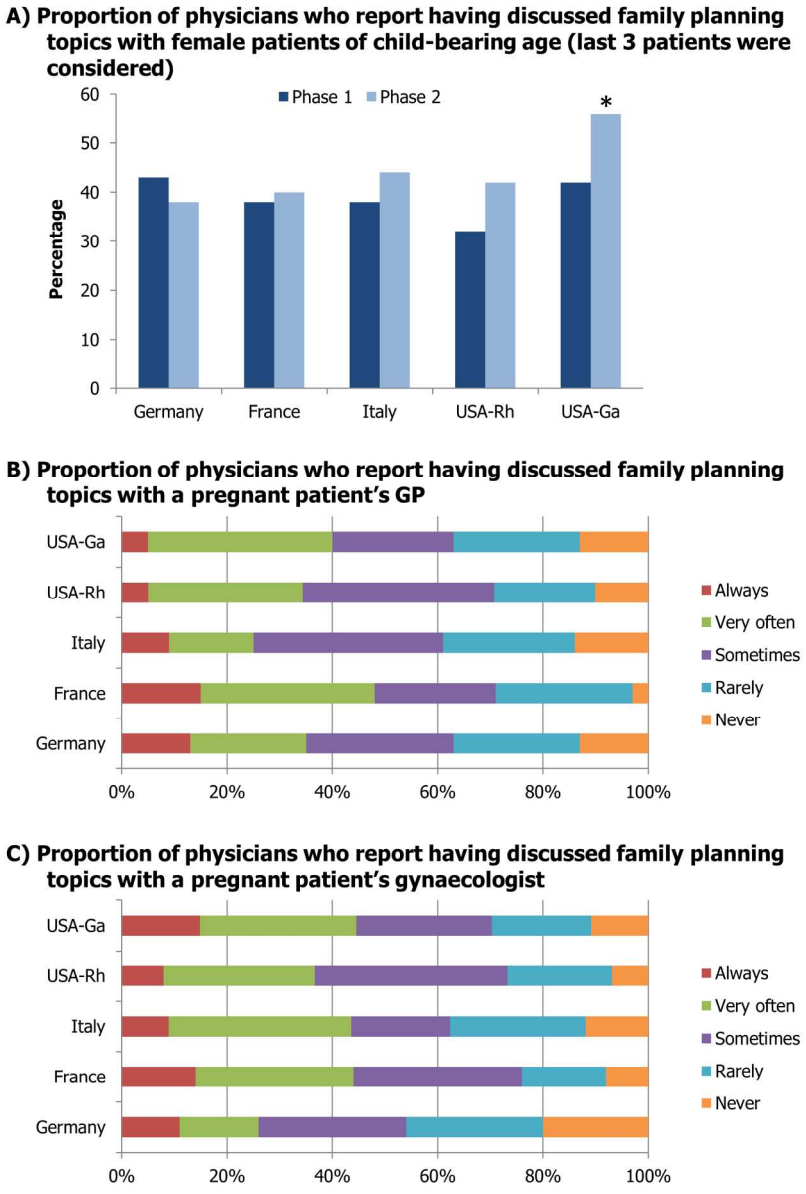

Figure 1. Frequency of physician-initiated discussions regarding FPP issues with female patients and their GPs or gynaecologists (survey Phase 2 data shown in B and C). Abbreviations: Ga = gastroenterologist; Rh = rheumatologist. *p<0.05 compared to Phase 1 (two-sided z-test with significance level 0.05).
180x253mm (300 x 300 DPI)

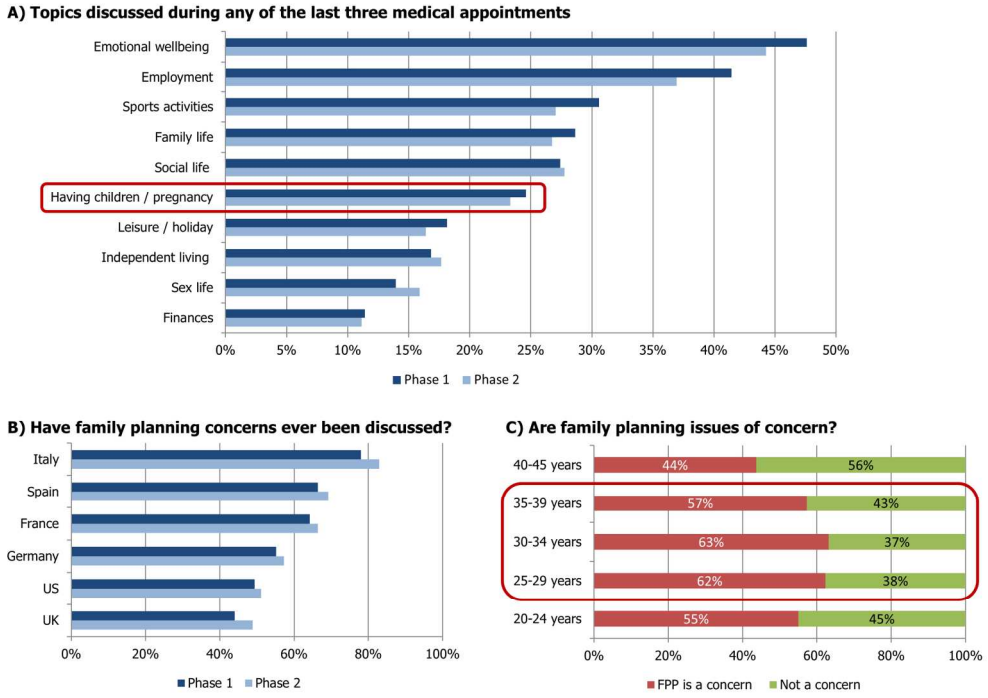

Figure 2. Patient reported (patient survey) topics of discussion with specialist physicians, the frequency of patient-initiated FPP discussion and the importance of FPP issues stratified by patient age (data from survey Phase 2 shown in C).
180x128mm (300 x 300 DPI)

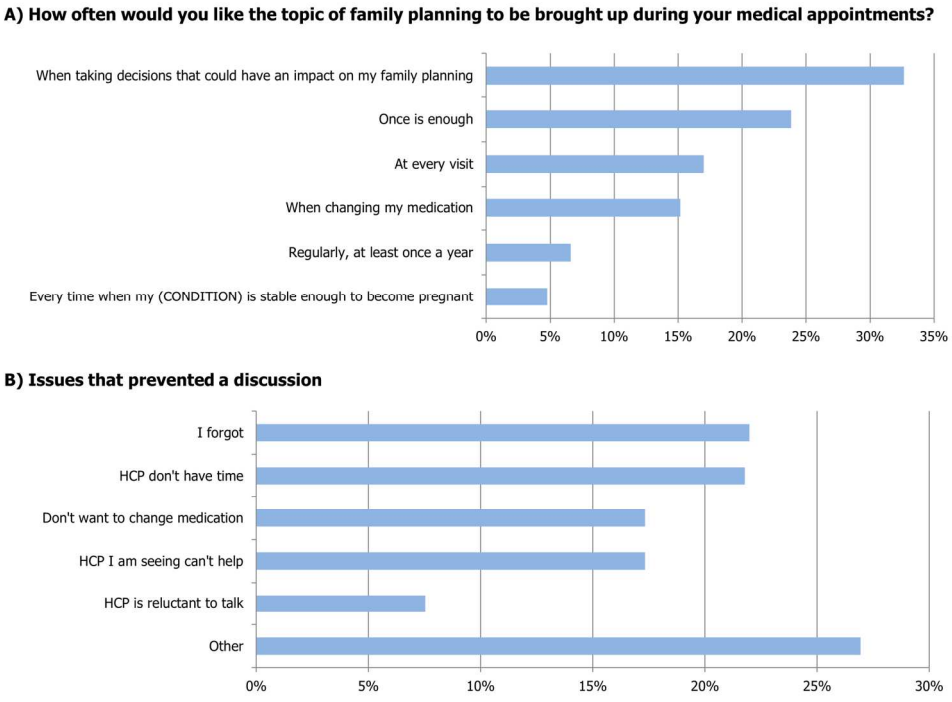

Figure 3. Patient preference for frequency of discussions relating to FPP issues and identification of issues that prevented discussion (data from patient survey Phase 2 shown).
180x126mm (300 x 300 DPI)

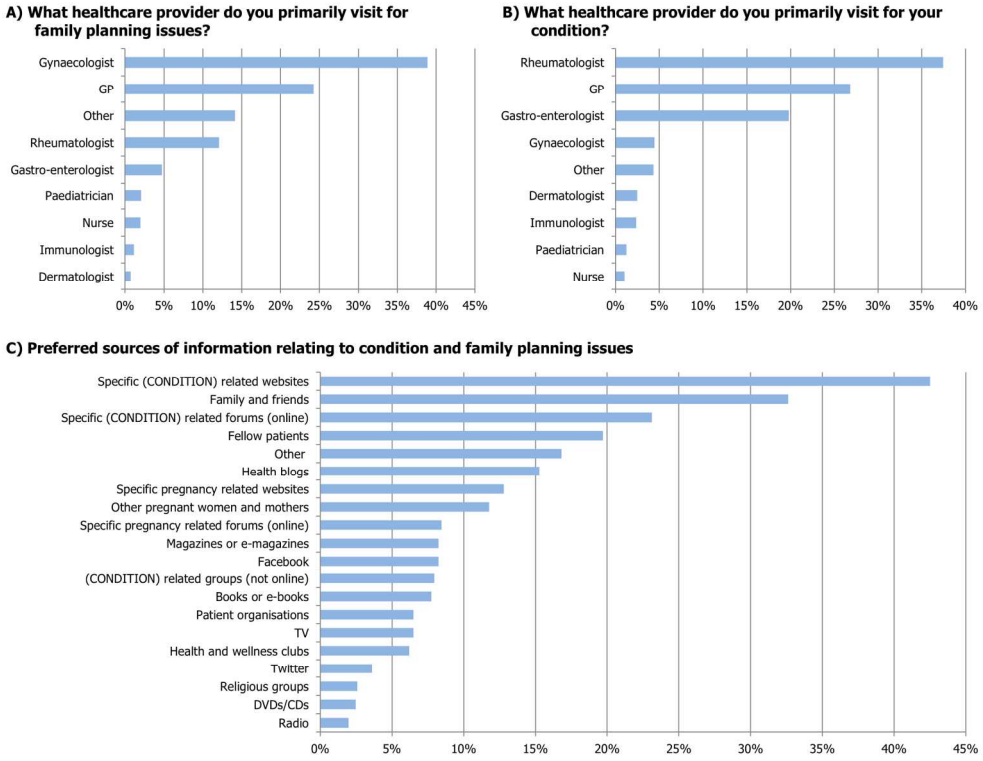

Figure 4. Patient preference for choice of healthcare provider for discussions of their condition and FPP issues, and their preferred source of additional information (outside doctors' office/clinic/surgery) relating to both their condition and FPP issues (data from patient survey Phase 2 shown).
180x138mm (300 x 300 DPI)

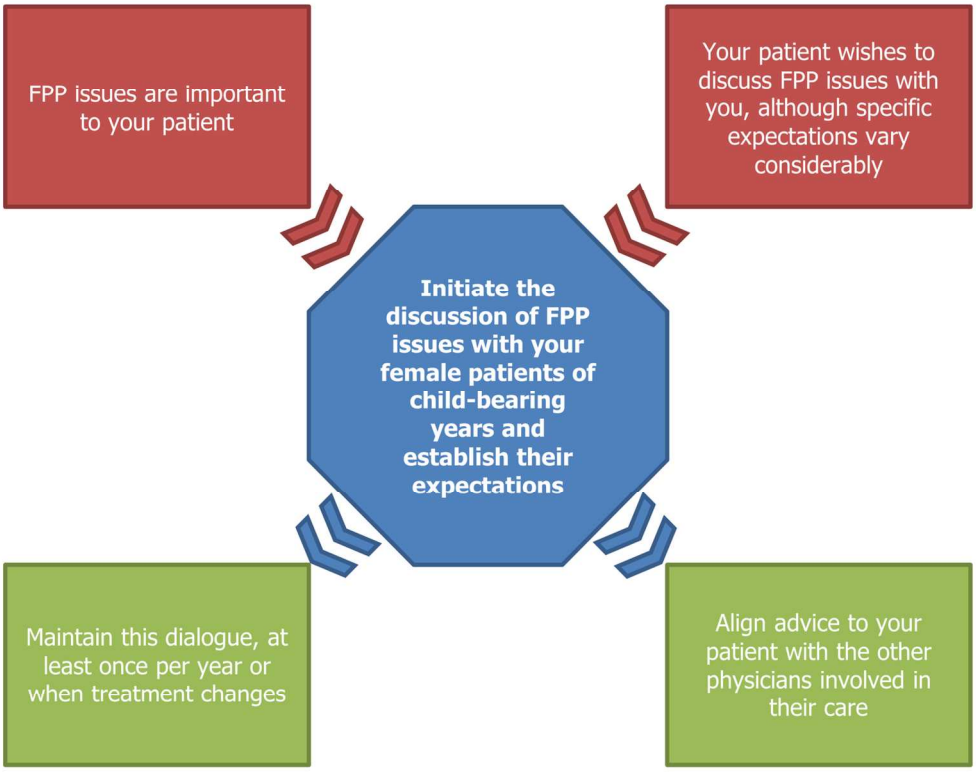

Figure 5. FPP-related considerations for practicing physicians treating female patients of child-bearing age who live with chronic inflammatory disease: key messages from the survey of current clinical practice and patient perceptions.
145x117mm (300 x 300 DPI)

Appendix 1

Physician Survey Questionnaire

Overview – survey flow

1. Participant profiling and screening
2. Implicit measurement of impact FPP
3. Communication testing
4. Explicit measurement of FPP related conversations

Thank you for your interest in our study. Before we begin, we would like to assure you that we act in accordance with the ESOMAR, EphMRA, ABPI, MRS and BHBIA codes of conduct regarding anonymity and confidentiality.

Any information you disclose will be treated in the strictest confidence and the results are pooled so none of the answers are attributable to individual respondents.

First we would like to ask you a few qualifying questions. This will take less than 1 minute. The questionnaire takes some 20 minutes to complete and covers the domain of Rheumatoid Arthritis/Crohn's Disease.

The market research is being conducted on behalf of a pharmaceutical company. The market research study itself is strictly non-promotional. The company commissioning this research has no access whatsoever to information regarding respondents.

If you have any problems or questions filling out this questionnaire, please feel free to contact us at support@leadphysician.com.

- ❑ I hereby agree to proceed with the questionnaire on this basis. **STOP if not selected**

The participant should agree to treat with the utmost confidentiality all data and information to which he is made privy in light of and/or as a result of his participation in this study.

The participant expressly guarantees that he will not divulge said information or data, nor will third parties be granted access. He will not publish or reproduce the information, nor will he exploit it in any other way.

Only public information or information that the participant may also obtain via other legitimate means than through participation in this study are not subject to this obligation of confidentiality.

This obligation is irrevocable and remains in effect as long as the information is to be considered confidential and has, therefore, not been made public by the authorized party or parties.

- ❑ Yes, I expressly and unconditionally accept the above obligation of confidentiality. **STOP if not selected**

ADVERSE EVENT REPORTING: We have been asked to provide our client with details of adverse events divulged during the course of this market research. Although this is an online survey and the information you provide will of course be treated in confidence, we are still under an obligation to report any information on adverse events in specific patients, even if you have already reported said event to the company or the regulatory authorities. In this case you will be contacted with a request to waive the confidentiality provided under the market research codes of conduct specifically for this particular adverse event. All other information you provide during the course of the survey will remain confidential.

- ❑ I hereby confirm to have been informed that the organiser of the survey is under the obligation to collect and report all information on adverse events linked to the client's product as recorded by me during the course of this research. **STOP if not selected**

[Parameters to be recorded from panel database:

- *Age*
- *Gender*
- *Region*
- *No Clinical investigation or pharmaco/biotech manufacturer (not in US)]*

PARTICIPANT PROFILING AND SCREENING

1. What is your primary specialty?

Question type: Single response

- ❑ Gastroenterology (US only) =GASTROENTEROLOGIST
- ❑ Rheumatology = RHEUMATOLOGIST
- ❑ Internal medicine specialized in rheumatology (Germany only) = RHEUMATOLOGIST
- ❑ Internal medicine not specialized in rheumatology (Germany only) **STOP**
- ❑ Other specialty **STOP**

[Gastroenterologists get questions personalized to Crohn's Disease, Rheumatologists to Rheumatoid Arthritis.]

2. How long have you been IN PRACTICE since qualifying as a specialist?

[Question type: Open comment - numeric

Max score allowed: 50 ("Years" - next to box)]

[ ]

[If < 3 or > 30 => STOP]

3. What percent of your working time is dedicated to treating patients?

[Question type: Open comment - numeric

0 to 100%]

☐ % is dedicated to treating patients **[STOP if less than 50%]**

4. In an average month, approximately how many different patients do you see for <u>all disorders and conditions</u> and for whom you are personally involved in making treatment decisions? Please count each patient once, not the number of visits.

[Question type: Open comment - numeric

Max score allowed: 1000]

[STOP if <20]

☐

5. In an average month, approximately how many different patients do you see for <u>Rheumatoid Arthritis</u> (for Rheumatologists)/ <u>Crohn's Disease</u> (for Gastroenterologists) and for whom you are personally involved in making treatment decisions? Please count each patient once, not the number of visits.

[Question type: Open comment - numeric

Max score allowed: number at S4

Number needs to be lower or equal than in previous question.]

[STOP if < 20 RA patients or < 8 CD patients]

☐

6. In an average month, approximately how many different patients with Rheumatoid Arthritis (for Rheumatologists)/ Crohn's Disease (for Gastroenterologists) do you see that are on biologic treatment?

[Question type: Open comment - numeric

Max score allowed: Number in S5

Number needs to be lower or equal than in previous question]

[STOP if < 10 RA patients or < 2 CD patients]

7. What type of practice do you have? (tick only one)

[Question type: Single response]

- ❑ Office only *[STOP in France]*
- ❑ Hospital only
- ❑ Office and hospital *[(don't show in Germany)]*

8. What is the size of hospital where you carry out your regular practice?

[Question type: Single response]

[Show only if 'hospital' or 'office and hospital' was selected in q0]

- ❑ More than 700 beds
- ❑ 400 to 700 beds
- ❑ Less than 400 beds

9. Have you taken part in a market research study in the area of Rheumatoid Arthritis (for Rheumatologists)/ Crohn's Disease (for Gastroenterologists) in the last month?

[Question type: Single response]

- ❑ Yes ***[STOP]***
- ❑ No

10. What percentage of your Rheumatoid Arthritis/Crohn's Disease patient base can be attributed to the following categories?

[Question type: Open comment - numeric

Should add up to 100%]

Male younger than 45 years old	%
Male 45 years or older	%
Female younger than 45 years old	%
Female 45 years or older	%

IMPLICIT MEASUREMENT OF IMPACT FPP

In the following questions we would like to talk about the topics you discussed with your moderate to severe Rheumatoid Arthritis/Crohn's Disease patients.

Obviously, most of the conversations are about clinical topics, but from now on we would like you to think about **non clinical nor treatment related topics**.

11. Please think back about your last 6 *[3: IF Q10_1 OR Q10_2=0]* male patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease that were initiated on treatment by you. Which topics did you discuss with these patients?

Please bear in mind to mention non clinical and non-treatment related topics.

[Question type: Open comment – text]

	Last 3 patients younger than 45 years old *[only show if Q10 "Male younger than 45 years old" > 0]*	Last 3 patients of 45 years or older *[only show if Q10 "Male 45 years or older" > 0]*
Male patient 1		
Male patient 2		
Male patient 3		

12. Please think back about your last 6 *[3: IF Q10_3 OR Q10_4=0]* female patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease that were initiated on treatment by you. Which topics did you discuss with these patients?

Please bear in mind to mention non clinical and non-treatment related topics.

[Question type: Open comment – text]

	Last 3 patients younger than 45 years old *[only show if Q10 "Female younger than 45 years old" > 0]*	Last 3 patients of 45 years or older *[only show if Q10 "Female 45 years or older" > 0]*
Female patient 1		
Female patient 2		
Female patient 3		

13. Please think back about your last male patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease that were initiated on treatment by you.

Other than disease related topics, which of the following topics did you discuss with these patients?.

[Question type: Multiple response]

[Randomisation: Yes]

LAST 3 MALE PATIENTS YOUNGER THAN 45 YEARS *[only show if Q10 "Male younger than 45 years old" > 0]*

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)
- ❑ None of the above

LAST 3 MALE PATIENTS OF 45 YEARS OR OLDER *[only show if Q10 "Male 45 years or older" > 0]*

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)
- ❑ None of the above

14. Below, we have listed the topics you discussed with your last male patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease.

Please select the 5 topics you spent most time on, and rank them by attributing a score between 1 and 5, where 1 indicates the topic you spent most time on.

[PN: Show text before each part of question and adjust number of topics selected when less than 5]

[Question type: ranking (top 5)

Randomisation: Yes]
[Filter: only show options selected in Q13]

LAST 3 MALE PATIENTS YOUNGER THAN 45 YEARS (max 5)

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)

LAST 3 MALE PATIENTS OF 45 YEARS OR OLDER (max 5)

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)

15. Please think of your last male patient with whom you discussed conception / having children.

Who initiated this discussion on conception / having children?

[Question type: Single response]

[Filter: only show if "Conception / having children" is selected in Q0]

- ❑ I initiated this discussion
- ❑ The patient initiated this discussion
- ❑ I don't remember who initiated this discussion

16. Please think back about your last female patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease that were initiated on treatment by you.

Other than disease related topics, which of the following topics did you discuss with these patients?

[Question type: Multiple response]

[Randomisation: Yes]

LAST 3 FEMALE PATIENTS YOUNGER THAN 45 YEARS *[only show if Q10 "Female younger than 45 years old" > 0]*

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)
- ❑ None of the above

LAST 3 FEMALE PATIENTS OF 45 YEARS OR OLDER *[only show if Q10 "Female 45 years or older" > 0]*

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)
- ❑ None of the above

17. Below, we have listed the topics you discussed with your last female patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease.

Please select the 5 topics you spent most time on, and rank them by attributing a score between 1 and 5, where 1 indicates the topic you spent most time on.

[PN: Show text before each part of question and adjust number of topics selected when less than 5]

[Question type: ranking (top 5)]

[Randomisation: Yes]
[Filter: only show options selected in Q16]

LAST 3 FEMALE PATIENTS YOUNGER THAN 45 YEARS (max 5)

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)

LAST 3 PATIENTS OF 45 YEARS OR OLDER (max 5)

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)

18. Please think of your last female patient with whom you discussed conception / having children.

Who initiated this discussion on conception / having children?

[Question type: Single response]

[Filter: only show if "Conception / having children" is selected in Q6]

- ❑ I initiated this discussion
- ❑ The patient initiated this discussion
- ❑ I don't remember who initiated this discussion

QUESTIONS REGARDING FPP MANAGEMENT

In the next chapter, we would like to ask you some questions regarding the Family Planning and Pregnancy management of your patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease.

19. How often do you consult the following channel(s) in order to look for extra information regarding Family Planning and Pregnancy issues?

[Question type: Single response]

[Randomise options]

	Always	Very often	Sometimes	Rarely	Never
Congresses/meetings	❑	❑	❑	❑	❑
Medical Science Liaison (MSL)	❑	❑	❑	❑	❑
Sales representative	❑	❑	❑	❑	❑
Industry-sponsored symposia or meetings	❑	❑	❑	❑	❑
Company websites with disease management education	❑	❑	❑	❑	❑
Social media (e.g. Facebook, LinkedIn, Twitter) for your profession (please specify):	❑	❑	❑	❑	❑
Other healthcare professionals (peers)	❑	❑	❑	❑	❑
Expert opinion blogs (please specify):	❑	❑	❑	❑	❑
Physician communities (please specify):	❑	❑	❑	❑	❑
KOLs (Key Opinion Leaders)	❑	❑	❑	❑	❑
Online consultation	❑	❑	❑	❑	❑
Other (please specify):	❑	❑	❑	❑	❑

The family planning and/or pregnancy related issues, questions… your patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease could have, might also be relevant for their other treating physicians.

[Filter: only show if "Conception / having children" is selected in Q0 or Q0]

20. To what extent do you discuss these questions, issues… with the patient's GP?

[Question type: Single response]

[Filter: only show if "Conception / having children" is selected in Q0 or Q0]

1 Never discuss with patient's GP	2	3	4	5 Always discuss with patient's GP
❑	❑	❑	❑	❑

21. To what extent do you discuss these questions, issues… with the patient's gynaecologist?

[Question type: Single response]

[Filter: only show if "Conception / having children" is selected in Q0]

1 Never discuss with patient's gynaecologist	2	3	4	5 Always discuss with patient's gynaecologist
❑	❑	❑	❑	❑

Appendix 2

Patient Survey Questionnaire

1. Please specify the country where you live:
    - United States
    - United Kingdom
    - France
    - Italy
    - Germany
    - Spain
    - Other (OUT)
2. Please specify your gender:
    - Male (OUT)
    - Female
3. Please specify your age:
    - Under 20 years (OUT)
    - 20-24 years
    - 25-29 years
    - 30-34 years
    - 35-39 years
    - 40-45 years
    - Over 45 years (OUT)

4. How many children have you given birth to?
    - None
    - One
    - Two
    - Three
    - Four
    - Five or more
5. Do you have an immunological condition? If so, which one? (If you have more than one of these conditions, tick the one that is most prominent)
    - Rheumatoid arthritis
    - Systemic lupus
    - Crohn's disease
    - Ulcerative colitis
    - Axial spondyloarthritis
    - Psoriatic arthritis
    - None (OUT)
    - Other (OUT)
6. Are you currently taking any medication for your condition?
    - Yes
    - No

Next, we would like to ask you a few questions around your visits to your doctor.

7. Which doctor(s) did you visit during the last two years for your condition? (please tick all that apply)
    - GP
    - Gynaecologist
    - Rheumatologist
    - Gastroenterologist
    - Immunologist
    - Dermatologist
    - Other
8. During any of your last three medical appointments, did you discuss any of the following topics in relation to your condition? (please tick all that apply)
    - Employment
    - Emotional wellbeing
    - Social life
    - Having children/pregnancy [if ticked, option 9 of Q11 was hidden]
    - Sex life
    - Sports activities
    - Leisure/holiday
    - Independent living
    - Family life
    - Finances

Finally, we would like to ask you about family planning (having children), and how you discuss this during your medical appointment.

9. Are you considering having a child/another child?
    - Yes
    - No
10. Do you consider your condition a point of concern for family planning (i.e. for your plans of having another child)?
    - Yes
    - No
11. Have you ever discussed your concerns around your condition and family planning with a healthcare professional (specialist, GP or nurse)? (please tick all that apply)
    - Yes, with my GP
    - Yes, with my gynaecologist
    - Yes, with my paediatrician
    - Yes, with my rheumatologist
    - Yes, with my gastroenterologist
    - Yes, with my immunologist
    - Yes, with my dermatologist
    - Yes, with a nurse
    - No, I haven't discussed this [this option will not appear if FPP is ticked in Q8; if ticked only Q16-23 subsequently shown]
    - Other

12. When was the last time you discussed your concerns around your condition and family planning with a healthcare professional (specialist, GP or nurse)?
    - Less than six months ago
    - Between six months and two years ago
    - More than two years ago
    - Don't remember
13. Over the last five years, how frequently did you have a discussion on your concerns around your condition and family planning with a healthcare professional (specialist, GP or nurse)?
    - Every visit
    - Most visits
    - Occasionally, during some visits
    - Just once
    - Never
    - Don't remember
14. Who initiated the last discussion around your condition and family planning?
    - I did
    - The doctor or nurse did
    - Don't remember
15. To what extent did that discussion settle concerns? (please rate on a scale from 0 to 10 where 0 = no, the discussion didn't settle my concerns at all, and 10 = yes, the discussion completely settle my concerns)

16. Do you intend to make family planning a discussion point during your next medical appointment? (omitted in UK)
    - Yes, definitely
    - Yes, probably
    - Maybe
    - No, probably not
    - No, definitely not

Additional questions for Phase 2 questionnaire

17. Which of the issues listed below prevented you from discussing your concerns around your condition and family planning during your medical appointments? (maximum 2)
    - Not enough time on behalf of my doctor or other healthcare professional
    - I forgot to bring up my concerns
    - I feel the healthcare professionals I am seeing are unable to help me here
    - The healthcare professionals I am seeing are reluctant to enter into this discussion
    - I am very worried that bringing up my concerns will trigger a change in my medication, which will make symptoms worse
    - Other

18. What type of healthcare professional (specialist, GP or nurse) are you primarily seeing in relation to your condition? (only 1 allowed)

- GP
- Gynaecologist
- Paediatrician
- Rheumatologist
- Gastroenterologist
- Immunologist
- Dermatologist
- Nurse
- Other

19. What type of healthcare professional (specialist, GP or nurse) are you primarily seeing in relation to family planning and pregnancy? (only 1 allowed)

- GP
- Gynaecologist
- Paediatrician
- Rheumatologist
- Gastroenterologist
- Immunologist
- Dermatologist
- Nurse
- Other

20. If you discussed your concerns around family planning and your condition with several healthcare professionals (specialists, GP or nurse), how consistent would you say the answers were? (please rate on a scale from 0 to 10 where 0 = the answers were not consistent at all, and 10 = the answers were very consistent)

21. Which channels are you using to find information about family planning as impacted by your condition? (please tick all that apply)

- Family and friends
- Fellow patients
- Other pregnant women and mothers
- Twitter
- Facebook
- Specific condition related websites
- Specific pregnancy related websites
- Health blogs
- Specific condition related forums (online)
- Specific pregnancy related forums (online)
- TV
- Magazines or e-magazines
- Books or e-books
- DVDs/CDs
- Patient organisations
- Radio
- Health and wellness clubs
- Religious groups
- Condition related groups (not online)
- Other

22. Which channels are you using to engage (comment, discuss, post, share, like) in discussions around family planning as impacted by your condition? (please tick all that apply)

- Family and friends
- Fellow patients
- Other pregnant women and mothers
- Twitter
- Facebook
- Specific condition related websites
- Specific pregnancy related websites
- Health blogs
- Specific condition related forums (online)
- Specific pregnancy related forums (online)
- Patient organisations
- Health and wellness clubs
- Religious groups
- Condition related groups (not online)
- Other

23. What is in your opinion the best way to bring up the topic of family planning and your condition during a medical appointment?
    - I would like a healthcare professional (specialist, GP or nurse) to initiate the discussion
    - I would like a healthcare professional (specialist, GP or nurse) to provide me with some informational materials about family planning and my condition
    - I would prefer to initiate the discussion myself
    - I would prefer not to have such discussion [GO TO END]
    - Other [GO TO END]
24. How often would you like the topic of family planning be brought up during your medical appointments?
    - Once is enough
    - At every visit
    - When changing my medication
    - When taking decisions that could have an impact on my family planning
    - Regularly, at least once a year
    - Every time when my condition is stable enough to become pregnant

BMJ open

Family Planning and Pregnancy Issues for Women with Systemic Inflammatory Diseases: Patient and Physician Perspectives

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004081.R1
Article Type:	Research
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Family Planning and Pregnancy Issues for Women with Systemic Inflammatory Diseases: Patient and Physician Perspectives

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Abstract

Objectives: To identify family planning and pregnancy (FPP) issues for female patients of child-bearing age living with a chronic inflammatory disease and to assess whether current clinical practice routinely provides adequate support to alleviate these concerns.

Setting: Multinational survey and an analysis of online patient activity.

Participants: Premenopausal women (aged 20-45 years of age; N=969) were surveyed in USA, UK, Germany, France, Italy and Spain. Rheumatologists were surveyed in Germany (N=50), France (N=50), Italy (N=50) and the USA (N=100) and gastroenterologists were also surveyed in the USA (N=100).

Primary and Secondary Outcome Measures: Two online surveys were undertaken to identify FPP issues for both physicians and patients. The surveys examined the frequency of dialogue on these topics between physicians and patients, alongside assessment of patient satisfaction regarding these conversations. Online analysis identified key themes for patient discussion outside their doctors' office/clinic/surgery.

Results: 32-56% of physicians spontaneously reported having talked about FPP with their female patients of child-bearing age. When prompted, the majority of rheumatologists (74-92%) and gastroenterologists (74%) reported having discussed conception/pregnancy with female patients; however, less than half reported consulting their patient's treating GP/gynaecologist about these topics.

The majority of patients reported their FPP-related concerns are not adequately addressed/settled during their medical appointments. Furthermore, only 30-40% of patients considered advice/information to be consistent across multiple healthcare professionals.

Key online FPP-related patient discussions included: disease state, adverse effects, treatment, switch behaviour and wash-out requirements.

Conclusions: Female patients who live with chronic inflammatory disease have important FPP concerns. The majority of patients, however, do not feel that their FPP concerns are adequately addressed in current clinical practice and report that they receive inconsistent advice from the various healthcare professionals who manage different aspects of their care. There is a clear need for provision of up-to-date and consistent information/support to female patients.

Article Summary

Article Focus:

- To identify key family planning and pregnancy (FPP) issues for female patients of child-bearing age who live with a chronic inflammatory disease and to assess whether current clinical practice routinely provides adequate support to alleviate these concerns.

Key Messages:

- Female patients of child-bearing years wish to discuss FFP issues in relation to their disease with their physicians but the majority of female patients who live with chronic inflammatory disease feel that their concerns are not adequately addressed.
- Physicians should initiate discussion of FPP issues with their female patients, particularly those receiving immunosuppressive treatment up to the ages of 50, and establish their expectations and concerns.
- Treating physicians should work to maintain this dialogue, at least once per year or when treatment changes, and align the advice offered to their female patients of child-bearing age with that from other physicians involved in their care.

Strengths and Limitations:

- Strengths: investigation of both patient and physician perspectives, involvement of specialists from different areas of interest and cross-cultural investigation.
- Limitations: absence of formal survey validation, reliance upon patient self-reporting, complications associated with delivery of the survey in local languages and possible bias in netnography research due to regional differences in language usage.

Introduction

Autoimmune and inflammatory diseases often affect women of reproductive age. Although RA becomes more common as patients age,[1] women are increasingly choosing to start their family later in life and treatments to control RA are now often started at a younger age. Moreover, even though only a minority proportion of RA patients are women of child-bearing age,[2] the high prevalence of the disease means that it does impact a significant number of young women. Many other inflammatory diseases, including ankylosing spondylitis (AS),[3 4] Crohn's disease (CD),[5 6] inflammatory bowel disease (IBD)[7] and systemic lupus erythematosus (SLE),[8] also affect a younger population and thus have a direct effect on women of child-bearing age.

Pregnancy and child rearing are important facets of life for most women. Now that improved therapies for inflammatory diseases have enabled better physical function and quality of life, many women who previously would have felt too ill to consider child-bearing are now better able to fulfil desires for family life. Family planning and pregnancy (FPP) are also important issues for this patient population as these disease states have been linked to an increased risk of adverse pregnancy outcomes,[9-11] including increased risk of preterm birth,[12] difficulty carrying to full term[13] and a possible reduction in fertility,[14 15] although there is conflicting evidence regarding the impact of inflammatory diseases on fertility.[16 17] Due to the impact on pregnancy outcomes, expert advice is to achieve and maintain stable low disease activity prior to conception and throughout pregnancy.[18-20] Some anti-inflammatory treatment options can be potentially hazardous for pregnant women to take as drugs can pass across the placenta and may affect the foetus.[21] Methotrexate, a common RA treatment, can be damaging to foetal development (at least at high doses)[22 23] whilst other disease-modifying anti-rheumatic drugs such as leflunomide have been shown to cause malformations in animal studies.[24]

However, use of medications during pregnancy is not always contraindicated and an individual risk-benefit discussion should be undertaken between the patient and expert physician to provide the best management of both the disease and the pregnancy.[25] Inadequate dissemination of appropriate advice describing which drugs may be continued can lead to women unnecessarily forgoing potentially helpful medications and thus suffering throughout pregnancy, with the increased risk of further complications to both mother and child due to the effects of active disease.[26] Furthermore, patients are increasingly seeking additional information on the internet,[27] while a recent analysis of information regarding medication safety on active internet sites has noted an inadequate evidence base for the advice often provided and inconsistent guidance.[28] It is clear that communication of reliable and consistent information is required to enable the correct treatment of these women before and during pregnancy, and while breast-feeding. Education and information should be shared by healthcare professionals dealing with these diseases, medications and situations on a daily basis. Accurate, consistent information must be communicated to women considering or entering pregnancy in order to support patients through this delicate journey.

Two surveys were undertaken to investigate some of these issues, one of physicians and another of female patients, to identify the key concerns of both groups related to the topics of FPP in inflammatory disease. The surveys were designed to gauge whether there is a gap in the communication between what healthcare professionals provide in terms of information/support and what patients feel that they receive. The patient survey also investigated where patients go to seek additional information. Two key objectives of the study were to examine the proportion of physicians who discuss FPP issues with their female patients of child-bearing age and the proportion of patients who have discussed these

topics, in the context of their condition, with their healthcare professional. The survey also assessed the proportion of patients who feel that their concerns on this topic have been satisfactorily addressed by these discussions. Here we aim to communicate the insights gained from this investigation to clinicians treating women of child-bearing age, who live with chronic inflammatory conditions, in order to provide advice on how best to support these patients.

Methods

This study complied with the ICC/ESOMAR, EphMRA, ABPI, MRS and BHBIA market research codes of conduct, ensuring the anonymity and confidentiality of all participants. Respondents were paid a nominal amount, calculated using fair market value guidance, to compensate for the time and effort of completing the survey.

Physician Survey

The online physician questionnaire was delivered in two phases, the first phase (baseline) was distributed in July 2012 (Europe) and September 2012 (USA), and the second phase was distributed in November 2012 in both Europe and USA. The survey was delivered in the local language and translations were checked for consistency against the original in English by native speakers with fluency in both languages (the complete Physician Questionnaire can be found online in Appendix 1). The questionnaire was designed to elicit both spontaneous (open-ended question) and prompted (closed question in which FPP topics were an option among other answering categories) responses. Participants were recruited from the WorldOne Physician Panel. Rheumatologists were surveyed in four countries: Germany (N=50), France (N=50), Italy (N=50) and the USA (N=100). Gastroenterologists were surveyed in the USA (N=100). Responses were compared between phases using two-sided z-tests with significance level 0.05, which corresponds to a confidence interval of 95%.

Participating physicians had to meet the following criteria: 3 to 30 years of experience, ≥50% patient-facing time, had not participated in medical research within their specialist area in the past month, were not currently a clinical investigator for a pharmaceutical manufacturer and were not currently active in medical research or advertising (to avoid inclusion of respondents motivated only by receipt of payment). Physicians with Rheumatology as their primary specialty had to meet the following additional criteria: treat ≥20 RA patients per month and have ≥10 patients on biologics per month. Physicians with Gastroenterology as their primary specialty had to meet the following additional criteria: treat ≥8 CD patients per month and have ≥2 patients on biologics per month. These selection criteria were applied to ensure participating physicians had sufficient experience treating patients with systemic inflammatory disease in order to provide informative results, while also seeking to include physicians with a range of experience in order to investigate routine clinical practice.

Patient Survey

The online patient questionnaire was designed according to standard market research survey methodology, including scaling questions and avoiding skewed questions. The questionnaire was delivered in the local language and translations were checked for consistency against the original in English by native speakers with fluency in both languages (the complete Patient Questionnaire can be found online in Appendix 2). The questionnaire was targeted at premenopausal women (age was self-declared and the survey excluded women under 20 and over 45 years of age; see Question 3 Patient Survey). A professional recruitment agency was used to recruit patients from the GlobalTestMarket and MySurvey online survey panels. Respondents were screened according to age, gender and disease (all self-reported) and those who were <20 or >45 years old, male, or not suffering from RA,

CD or lupus were excluded. Recruited patients were then sent a link to an online survey, which was followed up by a short telephone interview at a pre-arranged time.

The patient questionnaire was delivered in two phases and was distributed in six countries (USA, UK, Germany, France, Italy and Spain). The first phase (baseline) consisted of 16 questions and was disseminated to patients between 17th July and 15th August 2012. There were 1,069 respondents to the first phase which covered patients with RA, SLE, CD and ulcerative colitis (UC). The second phase consisted of the original 16 questions from the first phase plus an additional 8 questions included in order to avoid so-called 'false positives' (i.e. covered topics included in other questions to test consistency of response) and to provide greater insight into patients' experience in terms of medical care and needs. The second phase elicited 969 responses and was distributed between 13th October and 16th November 2012 to patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA), in addition to RA, SLE, CD and UC patients. All responses were anonymous. The patients who were invited to participate in the two survey phases were not identical, although there may have been some overlap (responses were anonymous therefore the extent of overlap could not be determined).

Netnography Research

Online discussions (English language only) relating to FPP issues were investigated using two approaches: social media monitoring, and search engine landscape/content analysis (SELA).

Social media monitoring was undertaken by identifying categories of interest (defined as: 'ulcerative colitis', 'systemic lupus erythematosus', 'rheumatoid arthritis', 'colitis ulcerosa', 'lupus', 'regional enteritis', 'Crohn's disease') and keywords of interest (defined as:

'pregnancy', 'miscarriage', 'birth control', 'miscarriages', 'fertile', 'family planning', 'gestation', 'pregnant', 'fertility', 'pregnancy disease evolution', 'disease transfer to baby', 'breastfeeding', 'breast feeding', 'conception', 'conceived' and 'placental transfer'), and then combining keywords together with the categories of interest to ensure coverage of all topics of interest.

SELA methodology involved identification of keywords (including generic keywords/keyword phrases and specific keywords/keyword phrases), assessment of keyword search volume and ranking of individual sites in search engine results. The 'click through rate' was combined with the 'monthly search volume' to estimate the 'share of attention index'. The final keyword pool included the categories 'colitis ulcerosa', 'ulcerative colitis', 'Crohn's disease', 'lupus', 'rheumatoid arthritis', 'regional enteritis' and 'systemic lupus erythematosus', and the following FPP-related keywords 'gestation', 'birth control', 'pregnancy', 'fertility', 'miscarriage' and 'family planning'.

Results

Physician Survey

Many rheumatologists and gastroenterologists spontaneously reported having discussed FPP-related topics with their female patients of child-bearing age; reports were consistent across all countries studied (Figure 1A). Interestingly, the number of US gastroenterologists who discussed these topics with their female patients increased significantly between the first and second Phases of the survey (Figure 1A). This was particularly true for fertility, pregnancy and/or family planning issues specifically, in which the percentage of US gastroenterologists discussing these topics increased from 67% to 79% between the two Phases (significant difference, 95% confidence level; N=100 for both survey phases); however there was no difference in European practice, with levels remaining at 60%.

When prompted, the majority of rheumatologists (74-92%) and gastroenterologists (74%) reported having discussed conception/pregnancy with female patients of child-bearing age. However, less than half of these physicians discussed FPP related issues with their patient's treating GP (i.e. primary care physician) or gynaecologist (Figure 1B and Figure 1C; survey Phase 2 data shown; see Questions 20 and 21 Physician Survey Appendix 1).

When seeking additional information regarding FPP, community rheumatologists and gastroenterologists reported currently relying on presentations and educational events at congresses, other healthcare professionals and key opinion leaders as their preferred sources of information.

Patient Survey and Netnography Analysis

Patients reported that the frequency of FPP-related conversations during their medical appointments was lower than their discussions about emotional well-being and employment (Figure 2A), although most female patients of child-bearing age reported discussing these issues at some point during their care pathway (Figure 2B).

Patients currently on medication for the treatment of their condition reported being more concerned about FPP issues than those not receiving medication, with 63% of those on medication reporting that pregnancy was a concern compared to only 32% of patients not receiving medication. In addition, the female age group with most concerns related to FPP was between the ages of 30 and 34 (Figure 2C; survey Phase 2 data shown, similar trend observed in Phase 1). Concern was high between the ages of 25 and 39 but decreased in patients aged between 40 and 45.

Patients were asked when they would prefer to discuss the topics of FPP. The survey revealed patients prefer to discuss these issues in the context of their disease and treatment whenever a decision is made that could have an impact on their family planning or ability to become pregnant (Figure 3A). Approximately a quarter feel that one conversation with their healthcare professional on this topic is enough, although some would like to discuss these topics at every visit. Furthermore, approximately a third of patients prefer to initiate conversations on this topic themselves or to obtain information from their healthcare professional when appropriate to their individual situation.

Patients gave a range of reasons for not discussing FPP concerns with their healthcare provider, with the most common reason being that they forgot to mention it (Figure 3B). Other important reasons identified as barriers for discussing FPP was the impression that the healthcare professional either did not have time for discussions or that they were not the correct physician to provide advice on these topics. Importantly, some patients also reported that they choose to not discuss FPP issues as they were reluctant to change medication. Very few patients felt that their healthcare professional was reluctant to discuss these topics. Over a quarter of respondents indicated that they had 'other' reasons for not discussing these issues with their doctor (Figure 3B). A higher proportion (39%) of patients aged 40-45 years recorded 'other' reasons for not discussing FPP issues with their doctor, compared to younger patients ('other' was recorded by 21.7% of 20-24 year olds, 18.3% of 25-29 year olds, 18.7% of 30-34 year olds and 25.6% 35-39 year olds).

Patients report a preference for seeking information regarding FPP from their gynaecologist (Figure 4A), whereas disease specialists (e.g. rheumatologist or gastroenterologist) are their key contact point for management of their chronic condition (Figure 4B). GPs/primary care physicians were also identified by patients as central to their discussions of both FPP and

their chronic condition (Figure 4A-B). It should be noted, however, that patient reports of a preference for one specialist over another regarding FPP discussions could be expected to vary by country given differences in treatment practices. For example, in the USA patients may commonly visit a gynaecologist/obstetrician for all pregnancy care whereas in the UK the patient's GP and local midwife may oversee most of their pregnancy planning and management. In addition, when responding to the survey some, but not all, patients may have regarded the terms 'obstetrician' and 'gynaecologist' as interchangeable based on their own experience.

Other than their doctors' office/clinic/surgery, patients reported researching and discussing information regarding FPP through multiple channels (Figure 4C): predominantly on disease-related websites and with family and friends. In addition, patients reported that specific condition-related forums/patient organisations did not play a prominent part in their search for online information on these topics. A number of key themes, such as discussions around disease state, adverse effects, treatment, switch behaviour and wash-out requirements, emerged after following online patient activity. Other themes noted were patient emotions and feelings, interactions with healthcare professionals, how best to identify the correct healthcare professional for their treatment, concerns about inconsistent advice, infertility, sexuality and conception, disease carry-over to the baby, placental transfer of treatments and breastfeeding.

Importantly, approximately 30-55% of female patients reported that their concerns relating to FPP are not adequately addressed or settled during their medical appointments (data from patient survey Phase 2). Some variability in this response was observed across countries, with 30% of patients from the USA, 34% from Italy, 35% from Spain, 39% from the UK, 43% from France and 54% from Germany reporting their concerns were not settled

(data from patient survey Phase 2). Patients also reported that consistency of advice and information given by multiple healthcare professionals, including nurses, was low with only about 30-40% of patients reporting consistent advice. Again, responses to this question varied across countries with 33% of patients reporting consistent advice from Spain and the UK, 36% from Germany and Italy, 40% from the USA and 41% from France (data from patient survey Phase 2). Inconsistent advice was reported by about 30-50% of patients overall: 27% from Italy, 32% from Spain, 38% from France, 41% from the USA, 44% from Germany and 49% from the UK (remaining patients selected a neutral response to this question; data from patient survey Phase 2).

Discussion

The investigation described here was carried out to illuminate some of the issues surrounding FPP for female patients of child-bearing age who live with chronic inflammatory diseases. Recently it was reported that almost half of female IBD patients feel their disease and/or treatment influences their decisions about FPP but despite this about two thirds had not discussed these issues with their doctor.[29] The results from the current study confirmed that FPP are considered important issues by this group of female patients and that there are key gaps in communication which result in inconsistent advice and subsequent patient concern/confusion. Importantly, the majority of female patients of child-bearing age reported that current clinical practice does not adequately address their concerns related to FPP in inflammatory disease.

Some clinical recommendations for the management of inflammatory disease during pregnancy have been published[18-20 25 30] and advise that clinical remission/stable low disease activity be achieved prior to conception and maintained throughout pregnancy using appropriate therapy as needed. However, in the current study few patients reported

discussing FPP at the point their condition was stable enough to become pregnant, suggesting a gap in necessary communication from physicians to patients regarding the need to control disease activity prior to conception, the impact of disease activity on pregnancy outcomes and the need to adjust medications during pregnancy. Indeed, a general lack of patient knowledge regarding continued use of medication during pregnancy was highlighted recently by a survey of female IBD patients which revealed a widespread, but inaccurate, belief that all medications needed to be stopped during pregnancy.[29] Respondents to the current patient survey also reported that inconsistencies in advice regarding the use of anti-inflammatory and immunosuppressive medications during pregnancy are common. Together, these results suggest a need for continuing education of all specialists involved in the care of women with inflammatory disease in order to ensure women understand the implications of their condition and treatment on FPP. Congress presentations and associated education events were identified by physicians, specifically rheumatologists and gastroenterologists, as their currently preferred source of information and continuing education – which may also be applicable to other specialists. As such, these events should be actively targeted to maximise and improve continued education. This could, for example, include hosting discussion forums between specialists involved in different aspects of care for these patients at international and national congresses. Timely discussion of FPP issues is also an important consideration given a high percentage of pregnancies are unplanned.[31]

GPs/primary care physicians and gynaecologists were identified by patients as frequently central to their discussions on FPP issues, although research has previously shown that 41% of GPs do not initiate discussion of FPP with female patients affected by IBD.[29] Importantly a gap in communication was identified between these physicians and the specialists who treat chronic inflammatory diseases. As such, improved cross-specialty communication should be

strongly encouraged, particularly for discussions regarding planning and treatment guidelines. This could involve establishment of cross-specialty teams within hospitals/centres of excellence to co-ordinate care of pregnant women living with systemic inflammatory disease. A recent survey of GPs in Ireland did show that the majority of GPs report seeking additional advice on FPP issues, in relation to their female IBD patients, from tertiary specialists[29] so improved education for all specialties and fostering communication should assist dissemination of information and consistent advice for patients. Furthermore, all of those involved in the care of female patients of child-bearing age who live with chronic inflammatory disease, not only the immunological disease specialists, should be exposed to continued education on this topic. Another recent survey of rheumatologists and obstetricians showed that there is variability in advice given to patients concerning the use of specific medication during pregnancy.[32] This highlights a need for consistency amongst clinicians to achieve quality patient care. Development of cross-specialty international guidelines/consensus papers by relevant expert physicians may help bridge these gaps in communication. Furthermore, publication of evidence-based discussions of the risks and benefits of medication use and disease activity control during pregnancy in women with inflammatory diseases by relevant medical societies could provide an easily accessible resource for physicians and patients alike. These could be in the form of "white papers" and accompanying patient information pieces, published in the scientific literature and online, to provide consistent education and advice for cross-specialty physicians and their patients.

In order to improve the dissemination of information regarding FPP to patients, it is important to identify when patients prefer to receive such information and also why this information may not be adequately communicated. Patient preference regarding timing of discussions about FPP varied. This variability may be due to the personal nature of this topic, differences in retention of information and differences in healthcare services/societal

norms across different countries. Patients did, however, generally report that they wished to discuss FPP-related issues with their specialist physician (i.e. rheumatologist or gastroenterologist) every time a decision was made that could impact upon their FPP. As such, healthcare professionals should routinely consider any issues that affect fertility or pregnancy and offer to have a conversation with their patient regarding these issues at every clinic visit, unless it is known not to be relevant. It may also be useful to clarify patient expectations for support and advice during these discussions. Patients on medication were more concerned about FPP issues than those not receiving medication, as were female patients between the ages of approximately 25 and 40. The high level of concern in both of these groups highlights these patients as key populations requiring additional consideration, although it could be argued that all women of child-bearing age should be targeted for such communications.

The most common reason patients offered to explain why they did not raise FPP with their healthcare provider was that they forgot to mention it during their consultation. Many also stated they avoided such discussion as they did not want to change their medication, implying that a fear of destabilising their disease could influence the preparedness of patients to discuss FPP topics. Other key reasons identified were the impression that their physician did not have time for the discussion or that they felt their treating physician was not the correct physician to consult on these topics. Consequently, physicians should consider periodically raising the issue themselves, particularly when treatment decisions or disease activity could impact FPP plans. Notably over a quarter of respondents indicated that they had 'other' reasons for not discussing these issues with their doctor. It is possible that this high response was due to patient demographics (e.g. age, social background or current use of contraception) and patients considering their family already complete. Indeed, a higher proportion of older patients recorded 'other' reasons for not discussing FPP issues

with their doctor compared to younger patients. Patient emotions was an important theme identified for online discussions, perhaps particularly relevant for those with a history of miscarriage/stillbirth or infertility problems, and it should also be considered that such associations could be a factor underlying why some patients reported that they did not discuss FPP with their physician for 'other' reasons.

Of key importance, many female patients of child-bearing age reported that they did not feel that their concerns relating to FPP in the context of their disease were adequately addressed during their medical appointments. There was some variability in patient response across countries to this question, suggesting that cultural differences and differences in healthcare system structure may contribute to the variability in patient satisfaction. However, it is clear that there can be a definite improvement in the response to these issues and all healthcare professionals should consider how they could increase such communication and support to their patients. This could include provision of better patient educational material and advice on reliable and up-to-date websites containing FPP-related information. Indeed, patients reported that they frequently sought information online, although specific condition-related forums/patient organisations did not appear to be common sources of this information. Furthermore, the online landscape was fragmented by disease area, with no specific resource (beyond "Motherisk"; www.motherisk.org) that provides FPP guidance on common autoimmune conditions and medication use affecting women in the reproductive age group. As such, development of a single site with consistent up-to-date guidance covering topics identified by patients as key interests would probably be of great value. Alternatively patient and/or physician organisations could incorporate more detailed information and advice on their websites to offer improved support to concerned patients and the various physicians involved in their care during pregnancy. Another key improvement would be increased dialogue, by telephone, letters or e-mail, between the varied physicians involved in an

individual patient's care in order to provide coordinated advice and support. Together these measures would aim to improve patient support and satisfaction.

It should be noted that this study does have some limitations. Two important limitations of the patient survey were an absence of formal survey validation and the reliance upon self-reporting of diagnosis by patients. It should also be considered that patients who are willing and motivated to complete a questionnaire may differ significantly from the overall patient population. Furthermore, even though the surveys were translated into local languages, differences in terminology and healthcare system structure exist across countries which could impact pooling of results; for example, the terms obstetrician and gynaecologist could be understood as being interchangeable in some countries but distinctly different specialties in others meaning patient interpretation of the survey could vary. The physician survey may also suffer related issues. In addition, the physician survey was only delivered to gastroenterologists in the USA and did not investigate the activities of these physicians in other countries. The range of experience amongst physicians was also broad which, although providing good coverage of routine clinical practice, could be complicated by differences in attitudes between physicians of different generations. A limitation of the current study is an inability to tease out any potential influence these factors may have on variation in the results. The netnography research may have been limited by use of keywords common to one country/region but different in others (e.g. 'fertility' vs 'infertility') which could have restricted comprehensive analysis of the online landscape and patient discussions. Finally, this study did not investigate the related concerns of men suffering from inflammatory disease who may be using chronic medication and also considering a family; indeed this population is often understudied and may need improved support.

In summary, FPP are extremely important issues for female patients of child-bearing age who live with chronic inflammatory disease. A summary of key considerations, highlighted by the results from the current study, for all physicians involved in the treatment of this often neglected group of patients is presented in Figure 5. It is clear that female patients of child-bearing age do wish to discuss these issues with their physicians although expectations regarding frequency of discussion and their preferred physician for advice vary considerably. Currently it appears that more can be done to provide these patients with consistent and co-ordinated information regarding their disease and how it, and associated treatments, could affect conception or pregnancy. Results from this study suggest physicians should regularly initiate discussion of these topics with their female patients of child-bearing age, particularly those on chronic medication or when changes to the treatment plan could impact pregnancy outcome, in order to improve patient support. In addition, greater cross-speciality communication between physicians involved in different aspects of the patient's care, from gastroenterologists and rheumatologists to gynaecologists/obstetricians and GPs, is needed to improve the consistency of advice offered to this often overlooked patient population.

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Competing Interests Statement

EC has previously been reimbursed by UCB Pharma for consultation services; MEBC has previously been reimbursed by UCB Pharma for consultation services; DSP is an employee of UCB Pharma; SM is an employee of UCB Pharma; CG declared no competing interests.

Author Contributions

EC: substantial contribution to conception and design, interpretation of data, drafting and critical revision of the manuscript, and final approval of the manuscript for submission.

MEBC: substantial contribution to conception and design, interpretation of data, drafting and critical revision of the manuscript, and final approval of the manuscript for submission.

DSP: substantial contribution to conception and design, interpretation of data, drafting and critical revision of the manuscript, and final approval of the manuscript for submission.

SM: substantial contribution to conception and design, acquisition, analysis and interpretation of data, critical revision of the manuscript, and final approval of the manuscript for submission.

CG: substantial contribution to conception and design, interpretation of data, drafting and critical revision of the manuscript, and final approval of the manuscript for submission.

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Figure 1. Frequency of physician-initiated discussions regarding FPP issues with female patients and their GPs or gynaecologists (survey Phase 2 data shown in B and C)

Abbreviations: Ga = gastroenterologist; Rh = rheumatologist. *p<0.05 compared to Phase 1 (two-sided z-test with significance level 0.05)

Figure 2. Patient reported (patient survey) topics of discussion with specialist physicians, the frequency of patient-initiated FPP discussion and the importance of FPP issues stratified by patient age (data from survey Phase 2 shown in C)

Figure 3. Patient preference for frequency of discussions relating to FPP issues and identification of issues that prevented discussion (data from patient survey Phase 2 shown)

Figure 4. Patient preference for choice of healthcare provider for discussions of their condition and FPP issues, and their preferred source of additional information (outside doctors' office/clinic/surgery) relating to both their condition and FPP issues (data from patient survey Phase 2 shown)

Figure 5. FPP-related considerations for practicing physicians treating female patients of child-bearing age who live with chronic inflammatory disease: key messages from the survey of current clinical practice and patient perceptions.

Family Planning and Pregnancy Issues for Women with Systemic Inflammatory Diseases: Patient and Physician Perspectives

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Author Contributions

EC: substantial contribution to conception and design, interpretation of data, drafting and critical revision of the manuscript, and final approval of the manuscript for submission.

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Abstract

Objectives: To identify family planning and pregnancy (FPP) issues for female patients of child-bearing age living with a chronic inflammatory disease and to assess whether current clinical practice routinely provides adequate support to alleviate these concerns.

Setting: Multinational survey and an analysis of online patient activity.

Participants: Premenopausal women (aged 20-45 years of age; N=969) were surveyed in USA, UK, Germany, France, Italy and Spain. Rheumatologists were surveyed in Germany (N=50), France (N=50), Italy (N=50) and the USA (N=100) and gastroenterologists were also surveyed in the USA (N=100).

Primary and Secondary Outcome Measures: Two online surveys were undertaken to identify FPP issues for both physicians and patients. The surveys examined the frequency of dialogue on these topics between physicians and patients, alongside assessment of patient satisfaction regarding these conversations. Online analysis identified key themes for patient discussion outside their doctors' office/clinic/surgery.

Results: 32-56% of physicians spontaneously reported having talked about FPP with their female patients of child-bearing age. When prompted, the majority of rheumatologists (74-92%) and gastroenterologists (74%) reported having discussed conception/pregnancy with female patients; however, less than half reported consulting their patient's treating GP/gynaecologist about these topics.

The majority of patients reported their FPP-related concerns are not adequately addressed/settled during their medical appointments. Furthermore, only 30-40% of patients considered advice/information to be consistent across multiple healthcare professionals.

Key online FPP-related patient discussions included: disease state, adverse effects, treatment, switch behaviour and wash-out requirements.

Conclusions: Female patients who live with chronic inflammatory disease have important FPP concerns. The majority of patients, however, do not feel that their FPP concerns are adequately addressed in current clinical practice and report that they receive inconsistent advice from the various healthcare professionals who manage different aspects of their care. There is a clear need for provision of up-to-date and consistent information/support to female patients.

Article Summary

Article Focus:

- To identify key family planning and pregnancy (FPP) issues for female patients of child-bearing age who live with a chronic inflammatory disease and to assess whether current clinical practice routinely provides adequate support to alleviate these concerns.

Key Messages:

- Female patients of child-bearing years wish to discuss FFP issues in relation to their disease with their physicians but the majority of female patients who live with chronic inflammatory disease feel that their concerns are not adequately addressed.
- Physicians should initiate discussion of FPP issues with their female patients, particularly those receiving immunosuppressive treatment up to the ages of 50, and establish their expectations and concerns.
- Treating physicians should work to maintain this dialogue, at least once per year or when treatment changes, and align the advice offered to their female patients of child-bearing age with that from other physicians involved in their care.

Strengths and Limitations:

- Strengths: investigation of both patient and physician perspectives, involvement of specialists from different areas of interest and cross-cultural investigation.
- Limitations: absence of formal survey validation, reliance upon patient self-reporting, complications associated with delivery of the survey in local languages and possible bias in netnography research due to regional differences in language usage.

Introduction

Autoimmune and inflammatory diseases often affect women of reproductive age. Although RA becomes more common as patients age,[1] women are increasingly choosing to start their family later in life and treatments to control RA are now often started at a younger age. Moreover, even though only a minority proportion of RA patients are women of child-bearing age,[2] the high prevalence of the disease means that it does impact a significant number of young women. Many other inflammatory diseases, including ankylosing spondylitis (AS),[3 4] Crohn's disease (CD),[5 6] inflammatory bowel disease (IBD)[7] and systemic lupus erythematosus (SLE),[8] also affect a younger population and thus have a direct effect on women of child-bearing age.

Pregnancy and child rearing are important facets of life for most women. Now that improved therapies for inflammatory diseases have enabled better physical function and quality of life, many women who previously would have felt too ill to consider child-bearing are now better able to fulfil desires for family life. Family planning and pregnancy (FPP) are also important issues for this patient population as ~~multiple studies have linked~~ these disease states have been linked to an increased risk of adverse pregnancy outcomes,[9-11] including increased risk of preterm birth,[12] ~~decreased chance of conceiving,[12]~~ difficulty carrying to full term[13] and a possible reduction in fertility,[14 15] although there is conflicting evidence regarding the impact of inflammatory diseases on fertility.[16 17] ~~increasing the risk of other potential complications.[9-11]~~ Due to ~~this~~ the impact on pregnancy outcomes, expert advice is to achieve and maintain stable low disease activity prior to conception and throughout pregnancy.[18-20] Some anti-inflammatory treatment options can be potentially hazardous for pregnant women to take as drugs can pass across the placenta and may affect the foetus.[21] Methotrexate, a common RA treatment, can be damaging to foetal

development (at least at high doses)[22 23] whilst other disease-modifying anti-rheumatic drugs such as leflunomide have been shown to cause malformations in animal studies.[24]

However, use of medications during pregnancy is not always contraindicated and an individual risk-benefit discussion should be undertaken between the patient and expert physician to provide the best management of both the disease and the pregnancy.[25] Inadequate dissemination of appropriate advice describing which drugs may be continued can lead to women unnecessarily forgoing potentially helpful medications and thus suffering throughout pregnancy, with the increased risk of further complications to both mother and child due to the effects of active disease.[26] Furthermore, patients are increasingly seeking additional information on the internet,[27] while a recent analysis of information regarding medication safety on active internet sites has noted an inadequate evidence base for the advice often provided and inconsistent guidance.[28] It is clear that communication of reliable and consistent information is required to enable the correct treatment of these women before and during pregnancy, and while breast-feeding. Education and information should be shared by healthcare professionals dealing with these diseases, medications and situations on a daily basis. Accurate, consistent information must be communicated to women considering or entering pregnancy in order to support patients through this delicate journey.

Two surveys were undertaken to investigate some of these issues, one of physicians and another of female patients, to identify the key concerns of both groups related to the topics of FPP in inflammatory disease. The surveys were designed to gauge whether there is a gap in the communication between what healthcare professionals provide in terms of information/support and what patients feel that they receive. The patient survey also investigated where patients go to seek additional information. Two key objectives of the

study were to examine the proportion of physicians who discuss FPP issues with their female patients of child-bearing age and the proportion of patients who have discussed these topics, in the context of their condition, with their healthcare professional. The survey also assessed the proportion of patients who feel that their concerns on this topic have been satisfactorily addressed by these discussions. Here we aim to communicate the insights gained from this investigation to clinicians treating women of child-bearing age, who live with chronic inflammatory conditions, in order to provide advice on how best to support these patients.

Methods

This study complied with the ICC/ESOMAR, EphMRA, ABPI, MRS and BHBIA market research codes of conduct, ensuring the anonymity and confidentiality of all participants. Respondents were paid a nominal amount, calculated using fair market value guidance, to compensate for the time and effort of completing the survey.

Physician Survey

The online physician questionnaire was delivered in two phases, the first phase (baseline) was distributed in July 2012 (Europe) and September 2012 (USA), and the second phase was distributed in November 2012 in both Europe and USA. The survey was delivered in the local language and translations were checked for consistency against the original in English by native speakers with fluency in both languages (the complete Physician Questionnaire can be found online in Appendix 1). The questionnaire was designed to elicit both spontaneous (open-ended question) and prompted (closed question in which FPP topics were an option among other answering categories) responses. Participants were recruited from the WorldOne Physician Panel. Rheumatologists were surveyed in four countries: Germany (N=50), France (N=50), Italy (N=50) and the USA (N=100). Gastroenterologists

were surveyed in the USA (N=100). Responses were compared between phases using two-sided z-tests with significance level 0.05, which corresponds to a confidence interval of 95%.

Participating physicians had to meet the following criteria: 3 to 30 years of experience, ≥50% patient-facing time, had not participated in medical research within their specialist area in the past month, were not currently a clinical investigator for a pharmaceutical manufacturer and were not currently active in medical research or advertising (to avoid inclusion of respondents motivated only by receipt of payment). Physicians with Rheumatology as their primary specialty had to meet the following additional criteria: treat ≥20 RA patients per month and have ≥10 patients on biologics per month. Physicians with Gastroenterology as their primary specialty had to meet the following additional criteria: treat ≥8 CD patients per month and have ≥2 patients on biologics per month. These selection criteria were applied to ensure participating physicians had sufficient experience treating patients with systemic inflammatory disease in order to provide informative results, while also seeking to include physicians with a range of experience in order to investigate routine clinical practice.

Patient Survey

The online patient questionnaire was designed according to standard market research survey methodology, including scaling questions and avoiding skewed questions. The questionnaire was delivered in the local language and translations were checked for consistency against the original in English by native speakers with fluency in both languages (the complete Patient Questionnaire can be found online in Appendix 2). The questionnaire was targeted at premenopausal women (age was self-declared and the survey excluded women under 20 and over 45 years of age; see Question 3 Patient Survey). A professional recruitment agency was used to recruit patients from the GlobalTestMarket and MySurvey

online survey panels. Respondents were screened according to age, gender and disease (all self-reported) and those who were <20 or >45 years old, male, or not suffering from RA, CD or lupus were excluded. Recruited patients were then sent a link to an online survey, which was followed up by a short telephone interview at a pre-arranged time.

The patient questionnaire was delivered in two phases and was distributed in six countries (USA, UK, Germany, France, Italy and Spain). The first phase (baseline) consisted of 16 questions and was disseminated to patients between 17th July and 15th August 2012. There were 1,069 respondents to the first phase which covered patients with RA, SLE, CD and ulcerative colitis (UC). The second phase consisted of the original 16 questions from the first phase plus an additional 8 questions included in order to avoid so-called 'false positives' (i.e. covered topics included in other questions to test consistency of response) and to provide greater insight into patients' experience in terms of medical care and needs. The second phase elicited 969 responses and was distributed between 13th October and 16th November 2012 to patients with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA), in addition to RA, SLE, CD and UC patients. All responses were anonymous. The patients who were invited to participate in the two survey phases were not identical, although there may have been some overlap (responses were anonymous therefore the extent of overlap could not be determined).

Netnography Research

Online discussions (English language only) relating to FPP issues were investigated using two approaches: social media monitoring, and search engine landscape/content analysis (SELA).

Social media monitoring was undertaken by identifying categories of interest (defined as: 'ulcerative colitis', 'systemic lupus erythematosus', 'rheumatoid arthritis', 'colitis ulcerosa', 'lupus', 'regional enteritis', 'Crohn's disease') and keywords of interest (defined as: 'pregnancy', 'miscarriage', 'birth control', 'miscarriages', 'fertile', 'family planning', 'gestation', 'pregnant', 'fertility', 'pregnancy disease evolution', 'disease transfer to baby', 'breastfeeding', 'breast feeding', 'conception', 'conceived' and 'placental transfer'), and then combining keywords together with the categories of interest to ensure coverage of all topics of interest.

SELA methodology involved identification of keywords (including generic keywords/keyword phrases and specific keywords/keyword phrases), assessment of keyword search volume and ranking of individual sites in search engine results. The 'click through rate' was combined with the 'monthly search volume' to estimate the 'share of attention index'. The final keyword pool included the categories 'colitis ulcerosa', 'ulcerative colitis', 'Crohn's disease', 'lupus', 'rheumatoid arthritis', 'regional enteritis' and 'systemic lupus erythematosus', and the following FPP-related keywords 'gestation', 'birth control', 'pregnancy', 'fertility', 'miscarriage' and 'family planning'.

Results

Physician Survey

Many rheumatologists and gastroenterologists spontaneously reported having discussed FPP-related topics with their female patients of child-bearing age; reports were consistent across all countries studied (Figure 1A). Interestingly, the number of US gastroenterologists who discussed these topics with their female patients increased significantly between the first and second Phases of the survey (Figure 1A). This was particularly true for fertility, pregnancy and/or family planning issues specifically, in which the percentage of US gastroenterologists discussing these topics increased from 67% to 79% between the two

Phases (significant difference, 95% confidence level; N=100 for both survey phases); however there was no difference in European practice, with levels remaining at 60%.

When prompted, the majority of rheumatologists (74-92%) and gastroenterologists (74%) reported having discussed conception/pregnancy with female patients of child-bearing age. However, less than half of these physicians discussed FPP related issues with their patient's treating GP (i.e. primary care physician) or gynaecologist (Figure 1B and Figure 1C; survey Phase 2 data shown; see Questions 20 and 21 Physician Survey Appendix 1).

When seeking additional information regarding FPP, community rheumatologists and gastroenterologists reported currently relying on presentations and educational events at congresses, other healthcare professionals and key opinion leaders as their preferred sources of information.

Patient Survey and Netnography Analysis

Patients reported that the frequency of FPP-related conversations during their medical appointments was lower than their discussions about emotional well-being and employment (Figure 2A), although most female patients of child-bearing age ~~(up to 85%)~~ reported discussing these issues at some point during their care pathway (Figure 2B).

Patients currently on medication for the treatment of their condition reported being more concerned about FPP issues than those not receiving medication, with 63% of those on medication reporting that pregnancy was a concern compared to only 32% of patients not receiving medication. In addition, the female age group with most concerns related to FPP was between the ages of 30 and 34~~, with >60% of these patients reporting concerns~~ (Figure 2C; survey Phase 2 data shown, similar trend observed in Phase 1). Concern was

high between the ages of 25 and 39 ~~(57-63%)~~ but decreased ~~to 44%~~ in patients aged between 40 and 45.

Patients were asked when they would prefer to discuss the topics of FPP. The survey revealed ~~that approximately 35% of~~ patients prefer to discuss these issues in the context of their disease and treatment whenever a decision is made that could have an impact on their family planning or ability to become pregnant (Figure 3A). Approximately a quarter feel that one conversation with their healthcare professional on this topic is enough, although ~~approximately 17%~~some would like to discuss these topics at every visit. Furthermore, approximately a third of patients prefer to initiate conversations on this topic themselves ~~(30-40% patients)~~ or to obtain information from their healthcare professional when appropriate to their individual situation ~~(15-35% patients)~~.

Patients gave a range of reasons for not discussing FPP concerns with their healthcare provider, with the most common reason being that they forgot to mention it (Figure 3B). Other important reasons identified as barriers for discussing FPP was the impression that the healthcare professional either did not have time for discussions or that they were not the correct physician to provide advice on these topics. Importantly, some patients also reported that they choose to not discuss FPP issues as they were reluctant to change medication. Very few patients felt that their healthcare professional was reluctant to discuss these topics. Over a quarter of respondents indicated that they had 'other' reasons for not discussing these issues with their doctor (Figure 3B). A higher proportion (39%) of patients aged 40-45 years recorded 'other' reasons for not discussing FPP issues with their doctor, compared to younger patients ('other' was recorded by 21.7% of 20-24 year olds, 18.3% of 25-29 year olds, 18.7% of 30-34 year olds and 25.6% 35-39 year olds).

Patients report a preference for seeking information regarding FPP from their gynaecologist (Figure 4A), whereas disease specialists (e.g. rheumatologist or gastroenterologist) are their key contact point for management of their chronic condition (Figure 4B). GPs/primary care physicians were also identified by patients as central to their discussions of both FPP and their chronic condition (Figure 4A-B). It should be noted, however, that patient reports of a preference for one specialist over another regarding FPP discussions could be expected to vary by country given differences in treatment practices. For example, in the USA patients may commonly visit a gynaecologist/obstetrician for all pregnancy care whereas in the UK the patient's GP and local midwife may oversee most of their pregnancy planning and management. In addition, when responding to the survey some, but not all, patients may have regarded the terms 'obstetrician' and 'gynaecologist' as interchangeable based on their own experience.

Other than their doctors' office/clinic/surgery, patients reported researching and discussing information regarding FPP through multiple channels (Figure 4C): predominantly on disease-related websites and with family and friends. In addition, patients reported that specific condition-related forums/patient organisations did not play a prominent part in their search for online information on these topics. A number of key themes, such as discussions around disease state, adverse effects, treatment, switch behaviour and wash-out requirements, emerged after following online patient activity. Other themes noted were patient emotions and feelings, interactions with healthcare professionals, how best to identify the correct healthcare professional for their treatment, concerns about inconsistent advice, infertility, sexuality and conception, disease carry-over to the baby, placental transfer of treatments and breastfeeding.

Importantly, approximately 30-55% of female patients reported that their concerns relating to FPP are not adequately addressed or settled during their medical appointments (data from patient survey Phase 2). Some variability in this response was observed across countries, with 30% of patients from the USA, 34% from Italy, 35% from Spain, 39% from the UK, 43% from France and 54% from Germany reporting their concerns were not settled (data from patient survey Phase 2). Patients also reported that consistency of advice and information given by multiple healthcare professionals, including nurses, was low with only about 30-40% of patients reporting consistent advice. Again, responses to this question varied across countries with 33% of patients reporting consistent advice from Spain and the UK, 36% from Germany and Italy, 40% from the USA and 41% from France (data from patient survey Phase 2). Inconsistent advice was reported by about 30-50% of patients overall: 27% from Italy, 32% from Spain, 38% from France, 41% from the USA, 44% from Germany and 49% from the UK (remaining patients selected a neutral response to this question; data from patient survey Phase 2).

Discussion

The investigation described here was carried out to illuminate some of the issues surrounding FPP for female patients of child-bearing age who live with chronic inflammatory diseases. Recently it was reported that almost half of female IBD patients feel their disease and/or treatment influences their decisions about FPP but despite this about two thirds had not discussed these issues with their doctor.[29] The results from the current study confirmed that FPP are considered important issues by this group of female patients and that there are key gaps in communication which result in inconsistent advice and subsequent patient concern/confusion. Importantly, the majority of female patients of child-bearing age reported that current clinical practice does not adequately address their concerns related to FPP in inflammatory disease.

Some clinical recommendations for the management of inflammatory disease during pregnancy have been published[18-20 25 30] and advise that clinical remission/stable low disease activity be achieved prior to conception and maintained throughout pregnancy using appropriate therapy as needed. However, in the current study few patients reported discussing FPP at the point their condition was stable enough to become pregnant, suggesting a gap in necessary communication from physicians to patients regarding the need to control disease activity prior to conception, the impact of disease activity on pregnancy outcomes and the need to adjust medications during pregnancy. Indeed, a general lack of patient knowledge regarding continued use of medication during pregnancy was highlighted recently by a survey of female IBD patients which revealed a widespread, but inaccurate, belief that all medications needed to be stopped during pregnancy.[29] Respondents to the current patient survey also reported that inconsistencies in advice regarding the use of anti-inflammatory and immunosuppressive medications during pregnancy are common. Together, these results suggest a need for continuing education of all specialists involved in the care of women with inflammatory disease in order to ensure women understand the implications of their condition and treatment on FPP. Congress presentations and associated education events were identified by physicians, specifically rheumatologists and gastroenterologists, as their currently preferred source of information and continuing education – which may also be applicable to other specialists. As such, these events should be actively targeted to maximise and improve continued education. This could, for example, include hosting discussion forums between specialists involved in different aspects of care for these patients at international and national congresses. Timely discussion of FPP issues is also an important consideration given a high percentage of pregnancies are unplanned.[31]

GPs/primary care physicians and gynaecologists were identified by patients as frequently central to their discussions on FPP issues, although research has previously shown that 41% of GPs do not initiate discussion of FPP with female patients affected by IBD.[29] Importantly a gap in communication was identified between these physicians and the specialists who treat chronic inflammatory diseases. As such, improved cross-specialty communication should be strongly encouraged, particularly for discussions regarding planning and treatment guidelines. This could involve establishment of cross-specialty teams within hospitals/centres of excellence to co-ordinate care of pregnant women living with systemic inflammatory disease. A recent survey of GPs in Ireland did show that the majority of GPs report seeking additional advice on FPP issues, in relation to their female IBD patients, from tertiary specialists[29] so improved education for all specialties and fostering communication should assist dissemination of information and consistent advice for patients. Furthermore, all of those involved in the care of female patients of child-bearing age who live with chronic inflammatory disease, not only the immunological disease specialists, should be exposed to continued education on this topic. Another recent survey of rheumatologists and obstetricians showed that there is variability in advice given to patients concerning the use of specific medication during pregnancy.[32] This highlights a need for consistency amongst clinicians to achieve quality patient care. Development of cross-specialty international guidelines/consensus papers by relevant expert physicians may help bridge these gaps in communication. Furthermore, publication of evidence-based discussions of the risks and benefits of medication use and disease activity control during pregnancy in women with inflammatory diseases by relevant medical societies could provide an easily accessible resource for physicians and patients alike. These could be in the form of "white papers" and accompanying patient information pieces, published in the scientific literature and online, to provide consistent education and advice for cross-specialty physicians and their patients.

In order to improve the dissemination of information regarding FPP to patients, it is important to identify when patients prefer to receive such information and also why this information may not be adequately communicated. Patient preference regarding timing of discussions about FPP varied. This variability may be due to the personal nature of this topic, differences in retention of information and differences in healthcare services/societal norms across different countries. Patients did, however, generally report that they wished to discuss FPP-related issues with their specialist physician (i.e. rheumatologist or gastroenterologist) every time a decision was made that could impact upon their FPP. As such, healthcare professionals should routinely consider any issues that affect fertility or pregnancy and offer to have a conversation with their patient regarding these issues at every clinic visit, unless it is known not to be relevant. It may also be useful to clarify patient expectations for support and advice during these discussions. Patients on medication were more concerned about FPP issues than those not receiving medication, as were female patients between the ages of approximately 25 and 40. The high level of concern in both of these groups highlights these patients as key populations requiring additional consideration, although it could be argued that all women of child-bearing age should be targeted for such communications.

The most common reason patients offered to explain why they did not raise FPP with their healthcare provider was that they forgot to mention it during their consultation. Many also stated they avoided such discussion as they did not want to change their medication, implying that a fear of destabilising their disease could influence the preparedness of patients to discuss FPP topics. Other key reasons identified were the impression that their physician did not have time for the discussion or that they felt their treating physician was not the correct physician to consult on these topics. Consequently, physicians should consider periodically raising the issue themselves, particularly when treatment decisions or

disease activity could impact FPP plans. Notably over a quarter of respondents indicated that they had 'other' reasons for not discussing these issues with their doctor. It is possible that this high response was due to patient demographics (e.g. age, social background or current use of contraception) and patients considering their family already complete. Indeed, a higher proportion of older patients recorded 'other' reasons for not discussing FPP issues with their doctor compared to younger patients. Patient emotions was an important theme identified for online discussions, perhaps particularly relevant for those with a history of miscarriage/stillbirth or infertility problems, and it should also be considered that such associations could be a factor underlying why some patients reported that they did not discuss FPP with their physician for 'other' reasons.

Of key importance, many female patients of child-bearing age reported that they did not feel that their concerns relating to FPP in the context of their disease were adequately addressed during their medical appointments. There was some variability in patient response across countries to this question, suggesting that cultural differences and differences in healthcare system structure may contribute to the variability in patient satisfaction. However, it is clear that there can be a definite improvement in the response to these issues and all healthcare professionals should consider how they could increase such communication and support to their patients. This could include provision of better patient educational material and advice on reliable and up-to-date websites containing FPP-related information. Indeed, patients reported that they frequently sought information online, although specific condition-related forums/patient organisations did not appear to be common sources of this information. Furthermore, the online landscape was fragmented by disease area, with no specific resource (beyond "Motherisk"; www.motherisk.org) that provides FPP guidance on common autoimmune conditions and medication use affecting women in the reproductive age group. As such, development of a single site with consistent up-to-date guidance covering topics

identified by patients as key interests would probably be of great value. Alternatively patient and/or physician organisations could incorporate more detailed information and advice on their websites to offer improved support to concerned patients and the various physicians involved in their care during pregnancy. Another key improvement would be increased dialogue, by telephone, letters or e-mail, between the varied physicians involved in an individual patient's care in order to provide coordinated advice and support. Together these measures would aim to improve patient support and satisfaction.

It should be noted that this study does have some limitations. Two important limitations of the patient survey were an absence of formal survey validation and the reliance upon self-reporting of diagnosis by patients. It should also be considered that patients who are willing and motivated to complete a questionnaire may differ significantly from the overall patient population. Furthermore, even though the surveys were translated into local languages, differences in terminology and healthcare system structure exist across countries which could impact pooling of results; for example, the terms obstetrician and gynaecologist could be understood as being interchangeable in some countries but distinctly different specialties in others meaning patient interpretation of the survey could vary. The physician survey may also suffer related issues. In addition, the physician survey was only delivered to gastroenterologists in the USA and did not investigate the activities of these physicians in other countries. The range of experience amongst physicians was also broad which, although providing good coverage of routine clinical practice, could be complicated by differences in attitudes between physicians of different generations. A limitation of the current study is an inability to tease out any potential influence these factors may have on variation in the results. The netnography research may have been limited by use of keywords common to one country/region but different in others (e.g. 'fertility' vs 'infertility') which could have restricted comprehensive analysis of the online landscape and patient

discussions. Finally, this study did not investigate the related concerns of men suffering from inflammatory disease who may be using chronic medication and also considering a family; indeed this population is often understudied and may need improved support.

In summary, FPP are extremely important issues for female patients of child-bearing age who live with chronic inflammatory disease. A summary of key considerations, highlighted by the results from the current study, for all physicians involved in the treatment of this often neglected group of patients is presented in Figure 5. It is clear that female patients of child-bearing age do wish to discuss these issues with their physicians although expectations regarding frequency of discussion and their preferred physician for advice vary considerably. Currently it appears that more can be done to provide these patients with consistent and co-ordinated information regarding their disease and how it, and associated treatments, could affect conception or pregnancy. Results from this study suggest physicians should regularly initiate discussion of these topics with their female patients of child-bearing age, particularly those on chronic medication or when changes to the treatment plan could impact pregnancy outcome, in order to improve patient support. In addition, greater cross-speciality communication between physicians involved in different aspects of the patient's care, from gastroenterologists and rheumatologists to gynaecologists/obstetricians and GPs, is needed to improve the consistency of advice offered to this often overlooked patient population.

Acknowledgements

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Figure 1. Frequency of physician-initiated discussions regarding FPP issues with female patients and their GPs or gynaecologists (survey Phase 2 data shown in B and C)

Abbreviations: Ga = gastroenterologist; Rh = rheumatologist. *p<0.05 compared to Phase 1 (two-sided z-test with significance level 0.05)

Figure 2. Patient reported (patient survey) topics of discussion with specialist physicians, the frequency of patient-initiated FPP discussion and the importance of FPP issues stratified by patient age (data from survey Phase 2 shown in C)

Figure 3. Patient preference for frequency of discussions relating to FPP issues and identification of issues that prevented discussion (data from patient survey Phase 2 shown)

Figure 4. Patient preference for choice of healthcare provider for discussions of their condition and FPP issues, and their preferred source of additional information (outside doctors' office/clinic/surgery) relating to both their condition and FPP issues (data from patient survey Phase 2 shown)

Figure 5. FPP-related considerations for practicing physicians treating female patients of child-bearing age who live with chronic inflammatory disease: key messages from the survey of current clinical practice and patient perceptions.

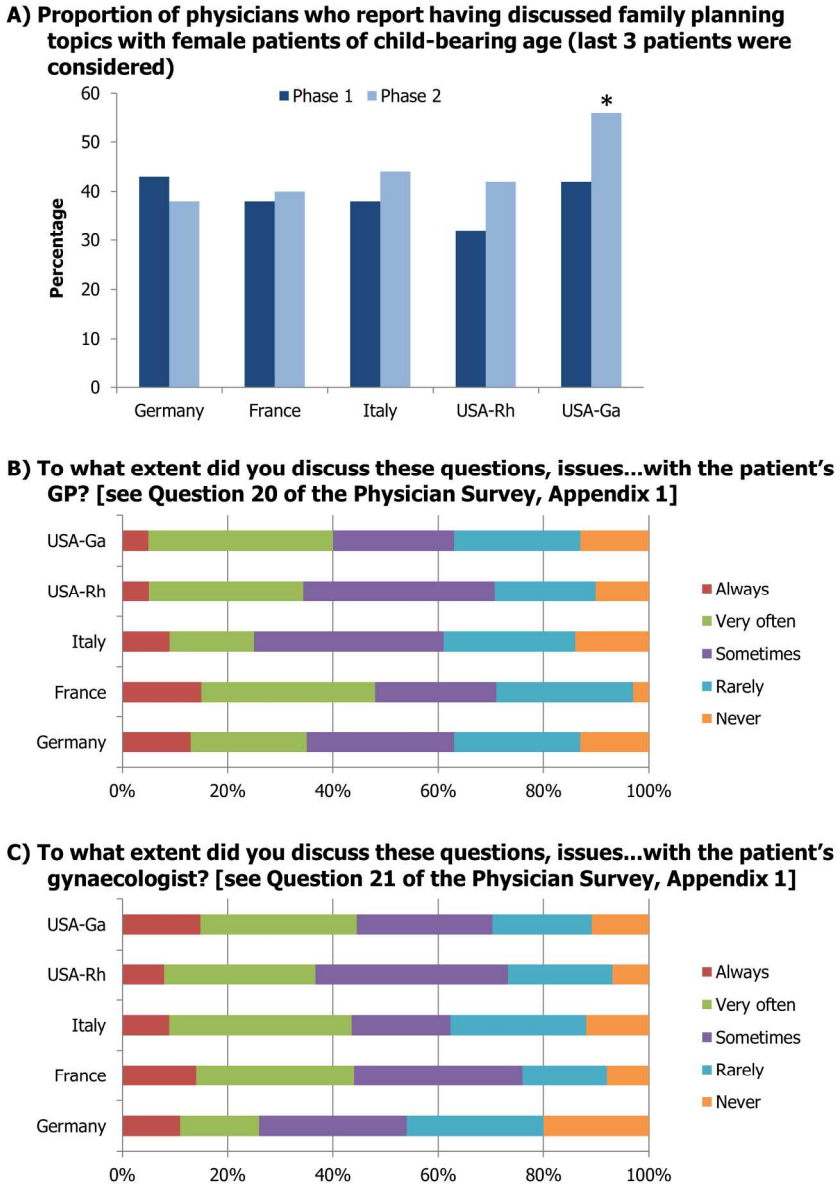

Figure 1. Frequency of physician-initiated discussions regarding FPP issues with female patients and their GPs or gynaecologists (survey Phase 2 data shown in B and C) Abbreviations: Ga = gastroenterologist; Rh = rheumatologist. *p<0.05 compared to Phase 1 (two-sided z-test with significance level 0.05)
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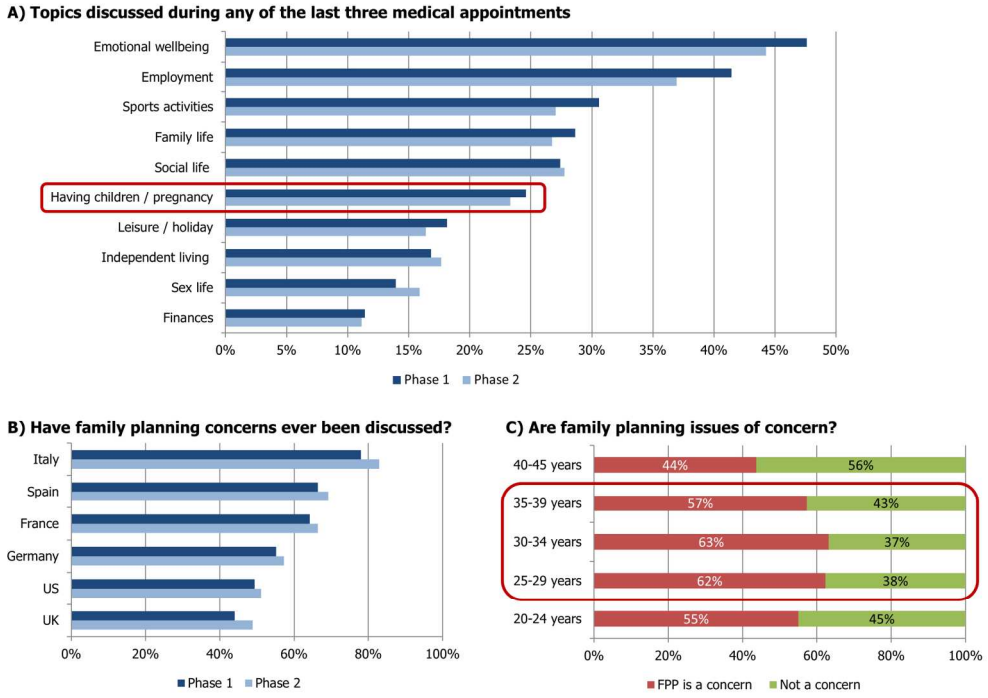

Figure 2. Patient reported (patient survey) topics of discussion with specialist physicians, the frequency of patient-initiated FPP discussion and the importance of FPP issues stratified by patient age (data from survey Phase 2 shown in C).
180x128mm (300 x 300 DPI)

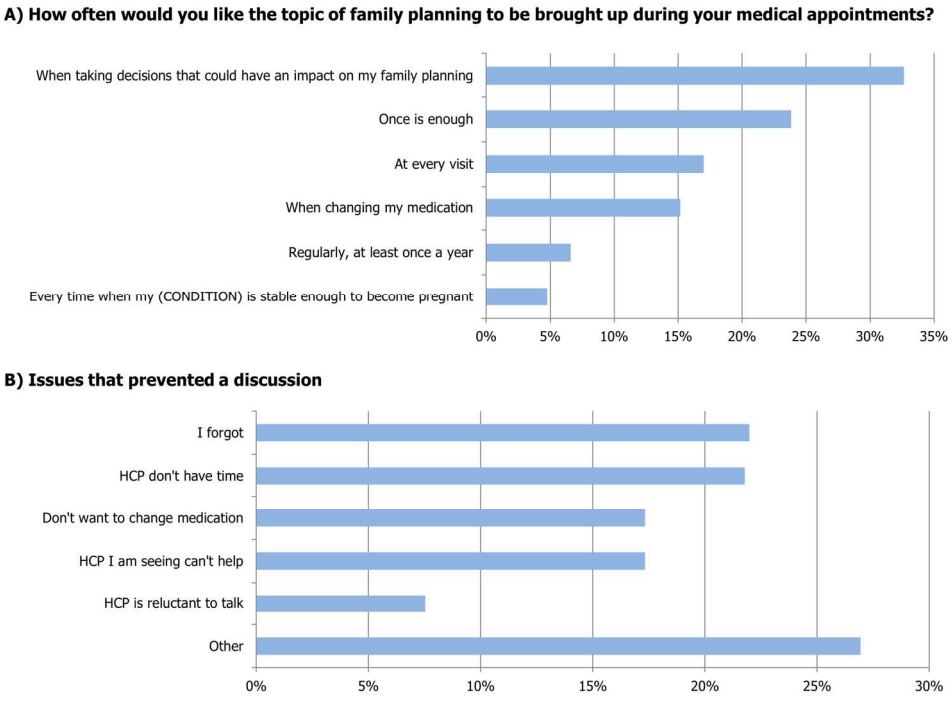

Figure 3. Patient preference for frequency of discussions relating to FPP issues and identification of issues that prevented discussion (data from patient survey Phase 2 shown).
180x126mm (300 x 300 DPI)

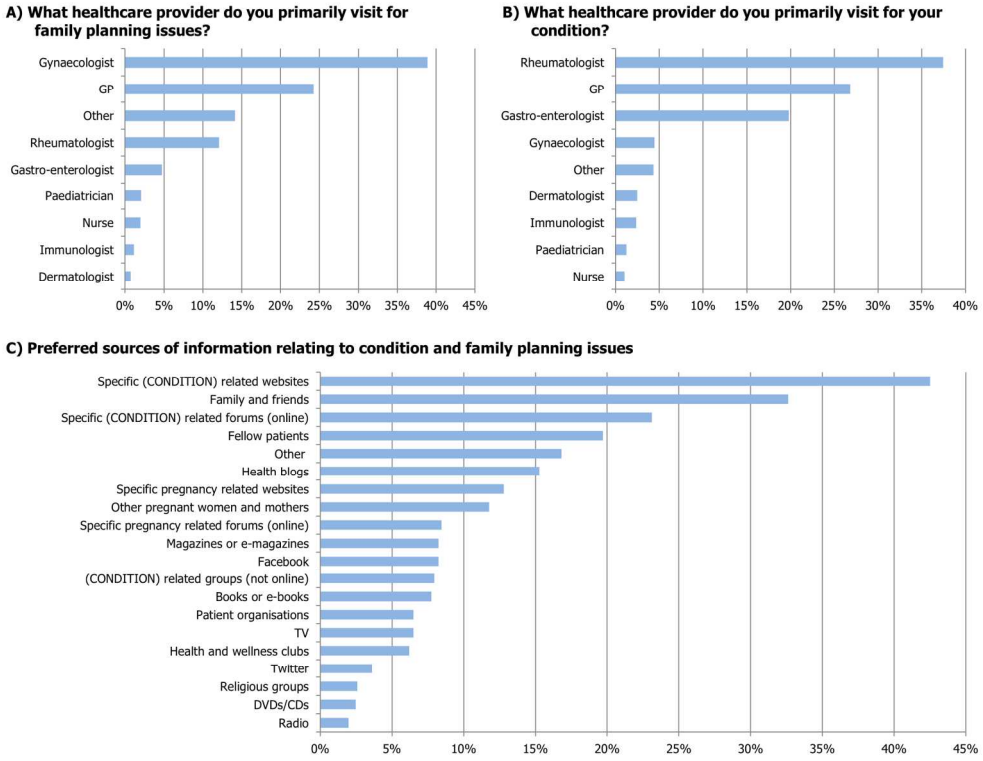

Figure 4. Patient preference for choice of healthcare provider for discussions of their condition and FPP issues, and their preferred source of additional information (outside doctors' office/clinic/surgery) relating to both their condition and FPP issues (data from patient survey Phase 2 shown).
180x138mm (300 x 300 DPI)

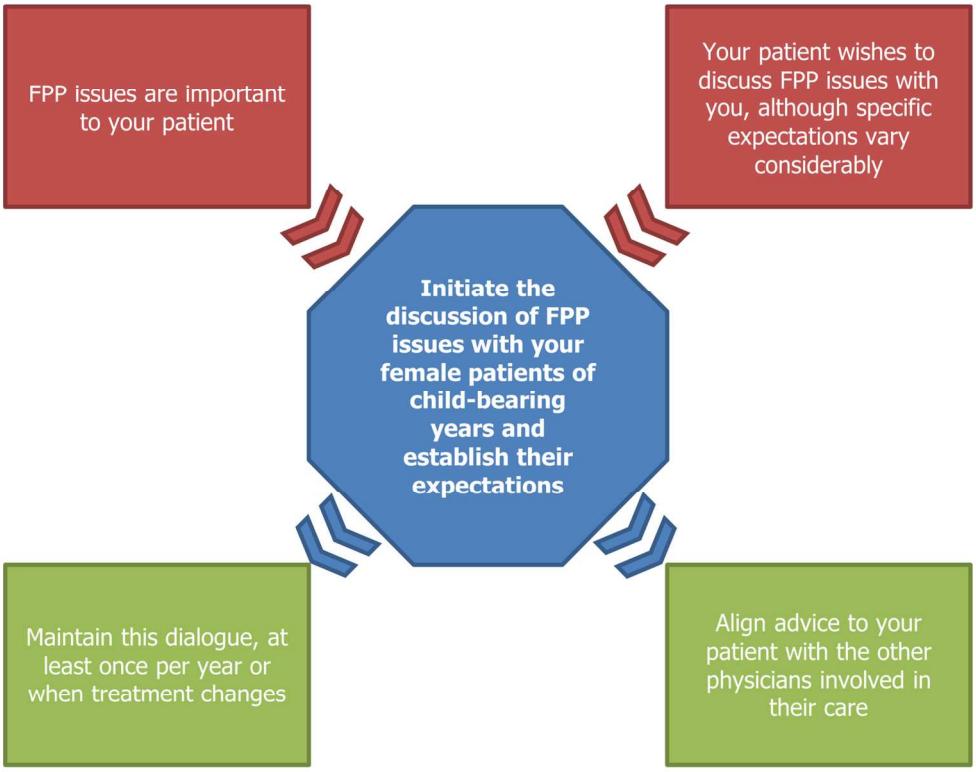

Figure 5. FPP-related considerations for practicing physicians treating female patients of child-bearing age who live with chronic inflammatory disease: key messages from the survey of current clinical practice and patient perceptions.
145x117mm (300 x 300 DPI)

Appendix 1

Physician Survey Questionnaire

Overview – survey flow

1. Participant profiling and screening
2. Implicit measurement of impact FPP
3. Communication testing
4. Explicit measurement of FPP related conversations

Thank you for your interest in our study. Before we begin, we would like to assure you that we act in accordance with the ESOMAR, EphMRA, ABPI, MRS and BHBIA codes of conduct regarding anonymity and confidentiality.

Any information you disclose will be treated in the strictest confidence and the results are pooled so none of the answers are attributable to individual respondents.

First we would like to ask you a few qualifying questions. This will take less than 1 minute. The questionnaire takes some 20 minutes to complete and covers the domain of Rheumatoid Arthritis/Crohn's Disease.

The market research is being conducted on behalf of a pharmaceutical company. The market research study itself is strictly non-promotional. The company commissioning this research has no access whatsoever to information regarding respondents.

If you have any problems or questions filling out this questionnaire, please feel free to contact us at support@leadphysician.com.

- ❑ I hereby agree to proceed with the questionnaire on this basis. **STOP if not selected**

The participant should agree to treat with the utmost confidentiality all data and information to which he is made privy in light of and/or as a result of his participation in this study.

The participant expressly guarantees that he will not divulge said information or data, nor will third parties be granted access. He will not publish or reproduce the information, nor will he exploit it in any other way.

Only public information or information that the participant may also obtain via other legitimate means than through participation in this study are not subject to this obligation of confidentiality.

This obligation is irrevocable and remains in effect as long as the information is to be considered confidential and has, therefore, not been made public by the authorized party or parties.

- ❑ Yes, I expressly and unconditionally accept the above obligation of confidentiality. **STOP if not selected**

ADVERSE EVENT REPORTING: We have been asked to provide our client with details of adverse events divulged during the course of this market research. Although this is an online survey and the information you provide will of course be treated in confidence, we are still under an obligation to report any information on adverse events in specific patients, even if you have already reported said event to the company or the regulatory authorities. In this case you will be contacted with a request to waive the confidentiality provided under the market research codes of conduct specifically for this particular adverse event. All other information you provide during the course of the survey will remain confidential.

- ❑ I hereby confirm to have been informed that the organiser of the survey is under the obligation to collect and report all information on adverse events linked to the client's product as recorded by me during the course of this research. **STOP if not selected**

[Parameters to be recorded from panel database:

- *Age*
- *Gender*
- *Region*
- *No Clinical investigation or pharmaco/biotech manufacturer (not in US)]*

PARTICIPANT PROFILING AND SCREENING

1. What is your primary specialty?

Question type: Single response

- ❑ Gastroenterology (US only) =GASTROENTEROLOGIST
- ❑ Rheumatology = RHEUMATOLOGIST
- ❑ Internal medicine specialized in rheumatology (Germany only) = RHEUMATOLOGIST
- ❑ Internal medicine not specialized in rheumatology (Germany only) **STOP**
- ❑ Other specialty **STOP**

[Gastroenterologists get questions personalized to Crohn's Disease, Rheumatologists to Rheumatoid Arthritis.]

2. How long have you been IN PRACTICE since qualifying as a specialist?

[Question type: Open comment - numeric

Max score allowed: 50 ("Years" - next to box)]

[ ]

[If < 3 or > 30 => STOP]

3. What percent of your working time is dedicated to treating patients?

[Question type: Open comment - numeric

0 to 100%]

☐ % is dedicated to treating patients **[STOP if less than 50%]**

4. In an average month, approximately how many different patients do you see for <u>all disorders and conditions</u> and for whom you are personally involved in making treatment decisions? Please count each patient once, not the number of visits.

[Question type: Open comment - numeric

Max score allowed: 1000]

[STOP if <20]

☐

5. In an average month, approximately how many different patients do you see for <u>Rheumatoid Arthritis</u> (for Rheumatologists)/ <u>Crohn's Disease</u> (for Gastroenterologists) and for whom you are personally involved in making treatment decisions? Please count each patient once, not the number of visits.

[Question type: Open comment - numeric

Max score allowed: number at S4

Number needs to be lower or equal than in previous question.]

[STOP if < 20 RA patients or < 8 CD patients]

☐

6. In an average month, approximately how many different patients with Rheumatoid Arthritis (for Rheumatologists)/ Crohn's Disease (for Gastroenterologists) do you see that are on biologic treatment?

[Question type: Open comment - numeric

Max score allowed: Number in S5

Number needs to be lower or equal than in previous question]

[STOP if < 10 RA patients or < 2 CD patients]

7. What type of practice do you have? (tick only one)

[Question type: Single response]

- ❑ Office only *[STOP in France]*
- ❑ Hospital only
- ❑ Office and hospital *[(don't show in Germany)]*

8. What is the size of hospital where you carry out your regular practice?

[Question type: Single response]

[Show only if 'hospital' or 'office and hospital' was selected in q0]

- ❑ More than 700 beds
- ❑ 400 to 700 beds
- ❑ Less than 400 beds

9. Have you taken part in a market research study in the area of Rheumatoid Arthritis (for Rheumatologists)/ Crohn's Disease (for Gastroenterologists) in the last month?

[Question type: Single response]

- ❑ Yes ***[STOP]***
- ❑ No

10. What percentage of your Rheumatoid Arthritis/Crohn's Disease patient base can be attributed to the following categories?

[Question type: Open comment - numeric

Should add up to 100%]

Male younger than 45 years old	%
Male 45 years or older	%
Female younger than 45 years old	%
Female 45 years or older	%

IMPLICIT MEASUREMENT OF IMPACT FPP

In the following questions we would like to talk about the topics you discussed with your moderate to severe Rheumatoid Arthritis/Crohn's Disease patients.

Obviously, most of the conversations are about clinical topics, but from now on we would like you to think about **non clinical nor treatment related topics**.

11. Please think back about your last 6 *[3: IF Q10_1 OR Q10_2=0]* male patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease that were initiated on treatment by you. Which topics did you discuss with these patients?

Please bear in mind to mention non clinical and non-treatment related topics.

[Question type: Open comment – text]

	Last 3 patients younger than 45 years old *[only show if Q10 "Male younger than 45 years old" > 0]*	Last 3 patients of 45 years or older *[only show if Q10 "Male 45 years or older" > 0]*
Male patient 1		
Male patient 2		
Male patient 3		

12. Please think back about your last 6 *[3: IF Q10_3 OR Q10_4=0]* female patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease that were initiated on treatment by you. Which topics did you discuss with these patients?

Please bear in mind to mention non clinical and non-treatment related topics.

[Question type: Open comment – text]

	Last 3 patients younger than 45 years old *[only show if Q10 "Female younger than 45 years old" > 0]*	Last 3 patients of 45 years or older *[only show if Q10 "Female 45 years or older" > 0]*
Female patient 1		
Female patient 2		
Female patient 3		

13. Please think back about your last male patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease that were initiated on treatment by you.

Other than disease related topics, which of the following topics did you discuss with these patients?.

[Question type: Multiple response]

[Randomisation: Yes]

LAST 3 MALE PATIENTS YOUNGER THAN 45 YEARS *[only show if Q10 "Male younger than 45 years old" > 0]*

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)
- ❑ None of the above

LAST 3 MALE PATIENTS OF 45 YEARS OR OLDER *[only show if Q10 "Male 45 years or older" > 0]*

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)
- ❑ None of the above

14. Below, we have listed the topics you discussed with your last male patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease.

Please select the 5 topics you spent most time on, and rank them by attributing a score between 1 and 5, where 1 indicates the topic you spent most time on.

[PN: Show text before each part of question and adjust number of topics selected when less than 5]

[Question type: ranking (top 5)

Randomisation: Yes]
[Filter: only show options selected in Q13]

LAST 3 MALE PATIENTS YOUNGER THAN 45 YEARS (max 5)

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)

LAST 3 MALE PATIENTS OF 45 YEARS OR OLDER (max 5)

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)

15. Please think of your last male patient with whom you discussed conception / having children.

Who initiated this discussion on conception / having children?

[Question type: Single response]

[Filter: only show if "Conception / having children" is selected in Q0]

- ❑ I initiated this discussion
- ❑ The patient initiated this discussion
- ❑ I don't remember who initiated this discussion

16. Please think back about your last female patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease that were initiated on treatment by you.

Other than disease related topics, which of the following topics did you discuss with these patients?

[Question type: Multiple response]

[Randomisation: Yes]

LAST 3 FEMALE PATIENTS YOUNGER THAN 45 YEARS *[only show if Q10 "Female younger than 45 years old" > 0]*

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)
- ❑ None of the above

LAST 3 FEMALE PATIENTS OF 45 YEARS OR OLDER *[only show if Q10 "Female 45 years or older" > 0]*

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)
- ❑ None of the above

17. Below, we have listed the topics you discussed with your last female patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease.

Please select the 5 topics you spent most time on, and rank them by attributing a score between 1 and 5, where 1 indicates the topic you spent most time on.

[PN: Show text before each part of question and adjust number of topics selected when less than 5]

[Question type: ranking (top 5)]

[Randomisation: Yes]
[Filter: only show options selected in Q16]

LAST 3 FEMALE PATIENTS YOUNGER THAN 45 YEARS (max 5)

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)

LAST 3 PATIENTS OF 45 YEARS OR OLDER (max 5)

- ❑ Ability to gain/maintain employment
- ❑ Emotional wellbeing of the patient
- ❑ Social life of the patient
- ❑ Conception / having children
- ❑ Sex life
- ❑ Sports activities
- ❑ Leisure / holiday
- ❑ Independent living of the patient
- ❑ Family life
- ❑ Finances
- ❑ Other (please specify)

18. Please think of your last female patient with whom you discussed conception / having children.

Who initiated this discussion on conception / having children?

[Question type: Single response]

[Filter: only show if "Conception / having children" is selected in Q6]

- ❑ I initiated this discussion
- ❑ The patient initiated this discussion
- ❑ I don't remember who initiated this discussion

QUESTIONS REGARDING FPP MANAGEMENT

In the next chapter, we would like to ask you some questions regarding the Family Planning and Pregnancy management of your patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease.

19. How often do you consult the following channel(s) in order to look for extra information regarding Family Planning and Pregnancy issues?

[Question type: Single response]

[Randomise options]

	Always	Very often	Sometimes	Rarely	Never
Congresses/meetings	❑	❑	❑	❑	❑
Medical Science Liaison (MSL)	❑	❑	❑	❑	❑
Sales representative	❑	❑	❑	❑	❑
Industry-sponsored symposia or meetings	❑	❑	❑	❑	❑
Company websites with disease management education	❑	❑	❑	❑	❑
Social media (e.g. Facebook, LinkedIn, Twitter) for your profession (please specify):	❑	❑	❑	❑	❑
Other healthcare professionals (peers)	❑	❑	❑	❑	❑
Expert opinion blogs (please specify):	❑	❑	❑	❑	❑
Physician communities (please specify):	❑	❑	❑	❑	❑
KOLs (Key Opinion Leaders)	❑	❑	❑	❑	❑
Online consultation	❑	❑	❑	❑	❑
Other (please specify):	❑	❑	❑	❑	❑

The family planning and/or pregnancy related issues, questions… your patients with moderate to severe Rheumatoid Arthritis/Crohn's Disease could have, might also be relevant for their other treating physicians.

[Filter: only show if "Conception / having children" is selected in Q0 or Q0]

20. To what extent do you discuss these questions, issues… with the patient's GP?

[Question type: Single response]

[Filter: only show if "Conception / having children" is selected in Q0 or Q0]

1 Never discuss with patient's GP	2	3	4	5 Always discuss with patient's GP
❑	❑	❑	❑	❑

21. To what extent do you discuss these questions, issues… with the patient's gynaecologist?

[Question type: Single response]

[Filter: only show if "Conception / having children" is selected in Q0]

1 Never discuss with patient's gynaecologist	2	3	4	5 Always discuss with patient's gynaecologist
❑	❑	❑	❑	❑

Appendix 2

Patient Survey Questionnaire

1. Please specify the country where you live:
    - United States
    - United Kingdom
    - France
    - Italy
    - Germany
    - Spain
    - Other (OUT)
2. Please specify your gender:
    - Male (OUT)
    - Female
3. Please specify your age:
    - Under 20 years (OUT)
    - 20-24 years
    - 25-29 years
    - 30-34 years
    - 35-39 years
    - 40-45 years
    - Over 45 years (OUT)

4. How many children have you given birth to?
    - None
    - One
    - Two
    - Three
    - Four
    - Five or more
5. Do you have an immunological condition? If so, which one? (If you have more than one of these conditions, tick the one that is most prominent)
    - Rheumatoid arthritis
    - Systemic lupus
    - Crohn's disease
    - Ulcerative colitis
    - Axial spondyloarthritis
    - Psoriatic arthritis
    - None (OUT)
    - Other (OUT)
6. Are you currently taking any medication for your condition?
    - Yes
    - No

Next, we would like to ask you a few questions around your visits to your doctor.

7. Which doctor(s) did you visit during the last two years for your condition? (please tick all that apply)
    - GP
    - Gynaecologist
    - Rheumatologist
    - Gastroenterologist
    - Immunologist
    - Dermatologist
    - Other
8. During any of your last three medical appointments, did you discuss any of the following topics in relation to your condition? (please tick all that apply)
    - Employment
    - Emotional wellbeing
    - Social life
    - Having children/pregnancy [if ticked, option 9 of Q11 was hidden]
    - Sex life
    - Sports activities
    - Leisure/holiday
    - Independent living
    - Family life
    - Finances

Finally, we would like to ask you about family planning (having children), and how you discuss this during your medical appointment.

9. Are you considering having a child/another child?
    - Yes
    - No
10. Do you consider your condition a point of concern for family planning (i.e. for your plans of having another child)?
    - Yes
    - No
11. Have you ever discussed your concerns around your condition and family planning with a healthcare professional (specialist, GP or nurse)? (please tick all that apply)
    - Yes, with my GP
    - Yes, with my gynaecologist
    - Yes, with my paediatrician
    - Yes, with my rheumatologist
    - Yes, with my gastroenterologist
    - Yes, with my immunologist
    - Yes, with my dermatologist
    - Yes, with a nurse
    - No, I haven't discussed this [this option will not appear if FPP is ticked in Q8; if ticked only Q16-23 subsequently shown]
    - Other

12. When was the last time you discussed your concerns around your condition and family planning with a healthcare professional (specialist, GP or nurse)?
    - Less than six months ago
    - Between six months and two years ago
    - More than two years ago
    - Don't remember
13. Over the last five years, how frequently did you have a discussion on your concerns around your condition and family planning with a healthcare professional (specialist, GP or nurse)?
    - Every visit
    - Most visits
    - Occasionally, during some visits
    - Just once
    - Never
    - Don't remember
14. Who initiated the last discussion around your condition and family planning?
    - I did
    - The doctor or nurse did
    - Don't remember
15. To what extent did that discussion settle concerns? (please rate on a scale from 0 to 10 where 0 = no, the discussion didn't settle my concerns at all, and 10 = yes, the discussion completely settle my concerns)

16. Do you intend to make family planning a discussion point during your next medical appointment? (omitted in UK)
    - Yes, definitely
    - Yes, probably
    - Maybe
    - No, probably not
    - No, definitely not

Additional questions for Phase 2 questionnaire

17. Which of the issues listed below prevented you from discussing your concerns around your condition and family planning during your medical appointments? (maximum 2)
    - Not enough time on behalf of my doctor or other healthcare professional
    - I forgot to bring up my concerns
    - I feel the healthcare professionals I am seeing are unable to help me here
    - The healthcare professionals I am seeing are reluctant to enter into this discussion
    - I am very worried that bringing up my concerns will trigger a change in my medication, which will make symptoms worse
    - Other

18. What type of healthcare professional (specialist, GP or nurse) are you primarily seeing in relation to your condition? (only 1 allowed)

- GP
- Gynaecologist
- Paediatrician
- Rheumatologist
- Gastroenterologist
- Immunologist
- Dermatologist
- Nurse
- Other

19. What type of healthcare professional (specialist, GP or nurse) are you primarily seeing in relation to family planning and pregnancy? (only 1 allowed)

- GP
- Gynaecologist
- Paediatrician
- Rheumatologist
- Gastroenterologist
- Immunologist
- Dermatologist
- Nurse
- Other

20. If you discussed your concerns around family planning and your condition with several healthcare professionals (specialists, GP or nurse), how consistent would you say the answers were? (please rate on a scale from 0 to 10 where 0 = the answers were not consistent at all, and 10 = the answers were very consistent)

21. Which channels are you using to find information about family planning as impacted by your condition? (please tick all that apply)

- Family and friends
- Fellow patients
- Other pregnant women and mothers
- Twitter
- Facebook
- Specific condition related websites
- Specific pregnancy related websites
- Health blogs
- Specific condition related forums (online)
- Specific pregnancy related forums (online)
- TV
- Magazines or e-magazines
- Books or e-books
- DVDs/CDs
- Patient organisations
- Radio
- Health and wellness clubs
- Religious groups
- Condition related groups (not online)
- Other

22. Which channels are you using to engage (comment, discuss, post, share, like) in discussions around family planning as impacted by your condition? (please tick all that apply)

- Family and friends
- Fellow patients
- Other pregnant women and mothers
- Twitter
- Facebook
- Specific condition related websites
- Specific pregnancy related websites
- Health blogs
- Specific condition related forums (online)
- Specific pregnancy related forums (online)
- Patient organisations
- Health and wellness clubs
- Religious groups
- Condition related groups (not online)
- Other

23. What is in your opinion the best way to bring up the topic of family planning and your condition during a medical appointment?
    - I would like a healthcare professional (specialist, GP or nurse) to initiate the discussion
    - I would like a healthcare professional (specialist, GP or nurse) to provide me with some informational materials about family planning and my condition
    - I would prefer to initiate the discussion myself
    - I would prefer not to have such discussion [GO TO END]
    - Other [GO TO END]
24. How often would you like the topic of family planning be brought up during your medical appointments?
    - Once is enough
    - At every visit
    - When changing my medication
    - When taking decisions that could have an impact on my family planning
    - Regularly, at least once a year
    - Every time when my condition is stable enough to become pregnant