

**HEALTH OUTCOMES STUDY PROTOCOL - QUALITATIVE RESEARCH**

UNIQUE IDENTIFIER	HO-16-17264
FULL TITLE	<b>Qualitative research to characterize the patient experience of nasal polyps</b>
ABBREVIATED TITLE	<i>Qualitative research to categorize nasal polyps</i>
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13/04/2017	V2_0	Comments from client incorporated
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30/10/2017	V7_0	<ul style="list-style-type: none"> <li>• Errors with study quotas corrected and study quotas broadened to allow for smoother recruitment.</li> <li>• New exclusion criteria added to ensure that the criteria was aligned with that of the client's clinical trial.</li> <li>• Interview length extended to 120 mins and incentive increased to \$200 to ensure that all concepts could be covered in interviews.</li> </ul>

Description: *Qualitative research to categorize nasal polyps*

Unique Identifier: HO-16-17264

**SPONSOR SIGNATORY**

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Description: *Abbreviated Title*

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### **Investigator Protocol Agreement Page**

- I confirm agreement to conduct the study in compliance with the protocol.
- I acknowledge that I am responsible for overall study conduct. I agree to personally conduct or supervise the described clinical study.
- I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations. Mechanisms are in place to ensure that site staff receives the appropriate information throughout the study.

Investigator Name:

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Investigator Signature

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Date (DD-MMM-  
YYYY)

## PROTOCOL SYNOPSIS

Unique Identifier	HO-16-17264
Abbreviated Title	Qualitative research to categorize nasal polyps
GSK Product	Mepolizumab
Rationale	<p>GlaxoSmithKline (GSK) is embarking on a clinical program to assess treatment of severe, recurrent nasal polyps with an anti-interleukin-5 (anti-IL5) (mepolizumab). Patient symptomatic endpoints will form the basis for the assessment of treatment benefit of nasal polyp therapies. Currently, there is a lack of published qualitative data regarding nasal polyps to understand the symptoms (specific symptoms, duration, frequency, severity) or health-related quality of life (HRQoL) impacts for patients, as well as the patient decision-making process in electing for surgery and their pre- and post-surgical experience to treat nasal polyps. In line with regulatory requirements,<sup>1,2</sup> the patient experience of nasal polyps will need to be characterized. Additionally, there is a requirement to evaluate existing symptomatic endpoints with respect to relevance and comprehensiveness within this population to inform GSK's clinical outcome assessment (COA) strategy for this trial. To address this unmet need GSK would like to conduct a qualitative research study with adult patients with nasal polyps to explore the disease experience from the patient perspective and to debrief existing symptomatic PROs (including overall and single item VAS's and the SNOT-22), via patient interviews and real-time data capture. This protocol details the methods and procedures that will be used in the conduct of this study.</p>
Objectives (Primary, Secondary)	<p><b><u>Primary</u></b> To explore the symptom, impact and surgery experience of patients with severe, recurrent nasal polyps and obtain patient feedback regarding the adequacy of the SNOT-22 and GSK VAS assessments (in terms of relevance and comprehensiveness) in assessing disease experience in nasal polyps.</p> <p><b><u>Secondary</u></b> <b>Combined concept elicitation (CE) and cognitive debriefing (CD) interviews</b> <i>Concept elicitation objectives:</i></p>

	<p>To identify through open-ended questioning the concepts that are important to patients with severe, recurrent, nasal polyps, who have been treated with surgery and the language they use to describe their disease experience. The main areas of exploration will be the symptoms with particular attention paid to the frequency, severity, duration and bother of each symptom, patients' surgical decision-making and surgical/treatment experience and the functional and HRQoL impact experienced by patients.</p> <p><b><u>Cognitive debriefing objectives:</u></b></p> <p>To cognitively test and explore the content and face validity of existing PRO instruments (single item VAS and SNOT-22) via assessment of the relevance and appropriateness of the items included in the instruments and the participants' ability to read, and consistently understand the instrument item wording, instructions, response option and recall period.</p> <p><b><u>Real-time data capture app</u></b></p> <p>To explore the patient experience of the symptoms, HRQoL impacts and treatment of nasal polyps and any day-to-day variability that exists in these experiences in 'real time' using smartphone/tablet app based technology.</p>
Study Design	<p>This is a cross-sectional qualitative study comprising the conduct of semi-structured combined CE and CD telephone interviews (each 120 minutes in duration) with US (n=20) and German (n=10) adults with severe, recurrent nasal polyps. The combined CE and CD interviews aim to investigate the patient experience of nasal polyps, and the relevance and understanding of existing PRO instruments (e.g. VAS and SNOT-22). In addition to the interview, the study includes a real-time data capture task conducted with 10 of the 20 US participants over a 10-day period using smartphone/tablet app-based technology. Five of the ten participants (50%) will take part in the app task prior to their interview and the remaining five participants (50%) will take part in the app task following their interview.</p> <p>This study will be conducted by Adelphi Values, an independent research agency specializing in health outcomes research, on behalf of GSK.</p>
Study Population and Sampling Methods	<p>A sample of 20 US-English speaking patients and 10 German patients will be recruited, giving a collective sample of 30 patients. Recruitment will be facilitated by third-party vendors in</p>

both US and Germany (MedQuest Global in US and Zeste in Germany). A purposive approach to sampling using recruitment quotas outlined in section 3.2.2 in Table 1 and Table 2 will be employed to ensure that patients with a broad range of demographic and clinical characteristics are recruited.

#### **Inclusion criteria**

To participate in the interview aspect of this study, patients must meet the following criteria:

- Participant has a clinical diagnosis of **bilateral nasal polyps** as diagnosed by endoscopy or CT scan;
- Participant is aged 18 or over;
- Participant has severe nasal polyps symptoms defined as an patient-reported nasal obstruction VAS score of >5 (see Appendix 1);
- Participant has had at least **one previous surgery in the past ten years** for the **removal of nasal polyps**. Surgery in this case is defined as any procedure involving instruments with resulting incision and removal of polyp tissue from the nasal cavity (polypectomy);
- Participant is currently an eligible candidate for polypectomy defined by:  
An overall patient-reported VAS symptom score of >7.(**Appendix 2**), **AND**

An endoscopic bilateral nasal polyp score of at least 5 out of a maximum score of 8 (with a minimum score of 2 in each nasal cavity). (

Appendix 3);

- Participant has symptoms consistent with chronic rhinosinusitis;
- Participant is currently receiving intranasal corticosteroids for the management of their nasal polyps;
- Participant is willing to participate in the study and provide informed consent;
- Participant is an English speaker and is able to read, write and fully understand the English language;
- Participant is willing to and able to attend and participate in a 120-minute interview to discuss their experiences of nasal polyps and obtain their feedback on several symptom/impact questionnaires.

In addition to meeting the interview criteria, those participants invited to take part in the real-time data capture will also be required to meet the following criteria:

- Participant owns/or has access to either a smartphone (iOS

	<p>or android) or tablet which has video, audio/microphone and photographic capabilities and access to either the Apple app store or google play store to download the app;</p> <ul style="list-style-type: none"> <li>Participant is willing and able to take part in the real-time data application task and respond to a series of questions/tasks fielded to them via the application over the course of 10 days;</li> </ul> <p style="text-align: center;">AND</p> <p>Is willing to respond to some brief questions following the real-time data capture task about their experience of using the app and completing the tasks, either during their interview or in a 5-10 minute telephone call following completion of the task.</p> <ul style="list-style-type: none"> <li>Participant has stated that they would feel comfortable recording short videos of themselves and providing audio commentary in response to questions/tasks.</li> </ul> <p><b>Exclusion criteria</b> Patients will not be eligible to participate in the study if they meet any of the following criteria:</p> <ul style="list-style-type: none"> <li>Participant has received oral or injectable systemic corticosteroids in the last 4 weeks (28 days) for the management of their nasal polyps</li> <li>Participant has a diagnosis of cystic fibrosis;</li> <li>Participant has a diagnosis of eosinophilic granulomatosis with polyangitis (also known as Churg Strauss syndrome), Young's, Kartagener's or dyskinetic ciliary syndromes;</li> <li>Participant has a diagnosis of antrochoanal polyps;</li> <li>Participant has a diagnosis of nasal septal deviation occluding one nostril;</li> <li>Participant has had acute sinusitis or upper respiratory tract infection in the last two weeks;</li> <li>Participant has ongoing rhinitis medicamentosa (rebound or chemical induced rhinitis);</li> <li>Participant has had an asthma exacerbation requiring admission to hospital in the last four weeks;</li> <li>Participant is currently or has previously taken part in a clinical trial for nasal polyps;</li> <li>Participant is unwilling or unable to comply with the requirements of the study or has a physical or mental condition or learning difficulties that, in the opinion of the physician, may affect the participant's ability to participate in the study, the responses he/she might provide or their ability to provide consent.</li> </ul>
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<p>Data Source</p>	<p>This study will consist of combined concept elicitation and cognitive debriefing interviews, which will last for 120 minutes in total. All participants (20 participants from the US and 10 participants from Germany) will all complete these interviews. Ten of the 20 US participants (50%) will also complete a 10-day real-time data capture app task and provide feedback about their experience of completing this task.</p> <p>No endpoints are specified or feature as part of this study.</p>
<p>Data Analysis Methods</p>	<p><b>Descriptive socio-demographic and clinical characteristics</b>  Socio-demographic and clinical characteristics for participant collected from the demographics form and CRF respectively will be summarized using descriptive statistics (e.g. n vales, means, ranges, percentages etc. where relevant).</p> <p><b>Analysis of interviews</b>  All interviews will be audio-recorded, and along with audio real-time data capture app task responses, transcribed/translated verbatim. Transcripts will be analyzed using thematic analysis methods and qualitatively coded using Atlas.Ti software. The Adelphi Values project team will create the initial code list, and each transcript would be assessed and participant comments that pertain to the main research questions would be highlighted. The code list will be updated iteratively during the coding process. The CE interview data will be analyzed in accordance with the principle of conceptual saturation as fully outlined in section 4.</p> <p><b>Descriptive statistics for the SNOT-22 and visual analogue scales</b>  The data collected from the SNOT-22 and visual analogue scales during the CD interview will be scored by Adelphi Values and summarized using descriptive statistics (e.g., n values, mean scores, ranges and percentages). Information relating to the distribution of responses will be summarized in addition to any missing data. The data will be presented in tabular or graphical format, whichever is deemed most appropriate at the time of reporting the findings.</p> <p><b>Real-time data capture analysis</b></p>

	<p>Responses to the real-time data capture data will be collected using a variety of methodologies (e.g., video, audio, text and photographic responses with captions). For audio responses these will be transcribed.</p> <p>Participants' responses to questions/tasks in the real-time data capture activity and post-activity questions administered via telephone will be analyzed in the same way using Atlas.Ti for the qualitative interviews as outlined above. Video, free text photographic and transcribed audio responses will be entered into Atlas Ti and assigned codes in the same manner as the verbatim interview transcripts to tag/code what their content conveys. For any questions/tasks fielded to participants as part of the app with multiple choice or numerical responses options, descriptive analysis of these items will be performed and reported (e.g. mean item score, ranges etc.).</p> <p>The interview and app task results will be used to inform the further development of a conceptual model for nasal polyps, previously constructed based on literature review activity only. The qualitative analysis will also be used help summarize the content validity of the reviewed PRO instruments and their suitability for use with patients with nasal polyps.</p>
<p>Sample Size and Power</p>	<p>Where the goal of qualitative research is to provide comprehensive understanding of complex phenomena (e.g. the holistic experience disease from the patient/caregiver perspective), it is recommended that sample sizes are determined based on the concept of 'conceptual saturation' where no new concepts are identified with repeated data collection. Past research and experience suggests that conceptual saturation can typically be achieved in as few as 12 individual interviews in a relatively homogenous population.<sup>3,4</sup> Taking the above into account, a total of 20 participants from the US and a total of 10 from Germany will be interviewed (total sample= 30).</p>
<p>Limitations</p>	<p>As the study has been designed using best practice methodology advocated by the Food and Drug Administration for exploratory qualitative studies used to support clinical measurement strategies, the foreseen risk/limitations of the study are minimal but include the following:</p>

	<ul style="list-style-type: none"><li>• <b>Selection of participants:</b> potential bias is always possible when selecting interviewees; however, as outlined in sections 3.2.1 and 3.2.2 eligibility criteria and recruitment quotas will be employed to ensure the participant sample is as diverse and representative as possible given the overall study size (n=30).</li><li>• <b>Generalizability of data:</b> The participant sample (n=30) is relatively small as the planned research is primarily exploratory in nature. The sample size is typical of qualitative studies conducted in this context. Nevertheless, the findings obtained from the participant interviews cannot be extrapolated or generalized to the wider population with nasal polyps; however, they will be relevant to GSK target nasal polyp population for their planned Phase III clinical trial.</li><li>• <b>Real-time data capture:</b> The eligibility criteria for the real-time data capture task and information included within the consent form (Appendix 5) will aim to ensure that those participants who take part in this activity are willing to take part over a period of ten days and that they would feel comfortable in providing responses using a variety of methods including video, audio, photographic and/or free text responses. As this methodology is exploratory and ethnographic in nature the quality of completion and the comprehensiveness of participant responses cannot be guaranteed. This said however, the participants will be contactable both via the app and also via email and/or telephone during the completion of the app task and as such the project researchers will endeavor to encourage the completion of all task in as thorough manner as possible (e.g. provide reminders to participants to complete their task or probes/examples if they are unsure of how to respond to a task/question).</li><li>• <b>Conceptual saturation:</b> Whilst conceptual saturation can typically be achieved in a sample of 12 in a relatively homogenous population, a potential limitation of the study is that conceptual saturation is not achieved across the 20 interviews. Should conceptual saturation not be achieved, discussion will be held with GSK to determine whether additional interviews should be conducted in</li></ul>
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	order to achieve saturation.
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## ABBREVIATIONS

AE	Adverse Event
AV	Adelphi Values
CD	Cognitive Debriefing
CE	Concept Elicitation
COA	Clinical Outcomes Assessment
CRF	Case Report Form
ENT	Ear, Nose and Throat
GSK	GlaxoSmithKline
HRQoL	Health-Related Quality of Life
ICF	Information Consent Form
PRO	Patient-Reported Outcome
SNOT	Sino-Nasal Outcomes Test
US	United States
VAS	Visual Analogue Scales

## 1 INTRODUCTION/BACKGROUND

Nasal polyps is considered to be a subgroup of chronic rhinosinusitis and is defined as a chronic inflammatory disease of the nose and sinuses.<sup>5</sup> Nasal polyps is characterized by the presence of two or more of the following symptoms: watery rhinorrhea from the nose (anterior), postnasal drainage (posterior), nasal obstruction and a temporary or in extreme cases permanent decreased sense of smell (anosmia).<sup>6</sup> The standard of care for patients with severe nasal polyps includes intranasal steroids, oral corticosteroids and surgery. However, there are currently no established criteria for surgery; candidacy for surgery is considered on the basis of level of nasal obstruction, symptom severity, impacts to the patient and the perceived risks/benefits of surgery.

The patient experience of nasal polyps is typically assessed via clinical interview and review of clinical history and the use of existing patient-reported outcome instruments (PROs). PRO instruments used with patients with nasal polyps typically include single item visual analogue scales (VAS), whereby patients are asked to evaluate overall symptom severity, or the severity of individual symptoms of nasal polyps along a continuum, typically of 10cm or 100 mm whereby 0 represents 'no symptom' and '10 or 100 represents 'as bad as you can imagine', Scores of 0-3 (or 0-30) are defined as mild disease, >3-7 (or >30-70) as moderate disease and >7-10 (or >70-100) as severe disease.<sup>5</sup> Historically, these items have not been developed based on patient characterization and therefore there is a need to understand the appropriateness of these measures for use within this population. The Sino-Nasal Outcomes Test (SNOT-22) is also used frequently within clinical research and as a clinical trial endpoint to measure health-related quality of life associated with rhinosinusitis with or without nasal polyps. The SNOT-22, a derivative of the SNOT-20, is a modification of the 31-Item Rhinosinusitis Outcome Measure (RSOM), containing 22 nose, sinus, and general health-related quality of life (HRQoL) items. Within the SNOT-22 patients are required to indicate the level of to which each listed nasal, sinus or HRQoL experience has been affected on a 6-point scale ranging from 0 (No problem) to 5 (Problem as bad as it can be) and also identify the five most important items affecting their health.<sup>7</sup> Existing evidence supports the psychometric validity of the SNOT-22 among patients with rhinosinusitis; with evidence of high reliability and sensitivity to clinical change.<sup>8</sup> Preliminary searches, however, suggest that evidence regarding the content validity of the SNOT-22 may be lacking.

GlaxoSmithKline (GSK) is embarking on a clinical program to assess treatment of severe, recurrent nasal polyps with an anti-interleukin-5 (anti-IL5) (mepolizumab). Patient symptomatic endpoints will form the basis for the assessment of treatment benefit of nasal polyp therapies. Currently, there is a lack of published qualitative data regarding nasal polyps to understand the symptoms (specific symptoms, duration,

frequency, severity) or health-related quality of life (HRQoL) impacts for patients, as well as the patient decision-making process in electing for surgery and their pre- and post-surgical experience to treat nasal polyps. In line with regulatory requirements,<sup>1,2</sup> the patient experience of nasal polyps will need to be characterized. Additionally, as described above, there is a requirement to evaluate existing symptomatic endpoints with respect to relevance and comprehensiveness within this population to inform GSK's clinical outcome assessment (COA) strategy for this trial.

To address this unmet need GSK would like to conduct a qualitative research study with adult patients with nasal polyps to explore the disease experience from the patient perspective and to debrief existing symptomatic PROs (including overall and single item VAS's and the SNOT-22), via patient interviews and real-time data capture. This protocol details the methods and procedures that will be used in the conduct of this study.

## **2 OBJECTIVES**

### **2.1 Primary**

To explore the symptom, impact and surgery experience of patients with severe, recurrent nasal polyps and obtain patient feedback regarding the adequacy of the SNOT-22 and GSK VAS assessments (in terms of relevance and comprehensiveness) in assessing disease experience in nasal polyps.

### **2.2 Secondary**

#### **Combined concept elicitation (CE) and cognitive debriefing (CD) interviews:**

To identify through open-ended questioning the concepts that are important to patients with severe, recurrent, nasal polyps, who have been treated with surgery and the language they use to describe their disease experience. The main areas of exploration will be the symptoms with particular attention paid to the frequency, severity, duration and bother of each symptom, patients' surgical decision-making and surgical/treatment experience and the functional and HRQoL impact experienced by patients.

To cognitively test and explore the content and face validity of existing PRO instruments (single item VAS and SNOT-22) via assessment of the relevance and appropriateness of the items included in the instruments and the participants' ability to read, and consistently understand the instrument item wording, instructions, response option and recall period. The CD interviews will:

- Explore participants' ability to read and consistently understand the item wording, instructions, response options and recall period of the overall and single item VAS and SNOT-22.
- Explore the relevance and appropriateness of all of the items covered by the instruments based on the symptom experience of patients with nasal polyps.
- Verify if the key concepts identified in the concept elicitation phase of the study are adequately assessed by the PRO instruments (confirmation of face validity) and if any gaps exist, provide recommendations for how these could be addressed.
- Explore what level of change in symptoms and/or impacts the patients might consider meaningful. (E.g. what level of change they might consider noticeable and important in response to treatment, and how changes on the item scores might relate to changes in their experience in their symptoms and/or functional impacts.

**Real-time data capture application:**

To supplement the CE section of the interviews with additional data regarding the patient experience of nasal polyps in 'real time' using smartphone/tablet app based technology. Real-time data capture uses a smart-phone or web-based application allowing the patient to communicate about their experience of nasal polyps in real-time as they go about their daily lives via varying video, audio, photographic and text responses.

Real-time data capture will be used to field a series of questions/tasks to patients with nasal polyps to:

- Explore the patient experience of the symptoms, HRQoL impacts and treatment of nasal polyps and any day-to-day variability that exists in these experiences in 'real time'.

Note: This is a low-interventional study – participants will not be asked to change their treatment as part of this study.

### **3 RESEARCH METHODOLOGY**

#### **3.1 Study Design**

This is a cross-sectional qualitative study comprising the conduct of semi-structured combined CE and CD telephone interviews (each 120 minutes in duration) conducted in with US and German adults with severe, recurrent nasal polyps. In addition to the interview, the study includes a real-time data capture task conducted with US participant only over a 10-day period using smartphone/tablet app-based technology. The combined CE and CD interviews aim to investigate the patient experience of nasal

polyps, and the relevance and understanding of existing PRO instruments (e.g. VAS and SNOT-22).

A total of 20 adult participants from the US with severe, recurrent, nasal polyps, who have received nasal polyp removal surgery in the past 10 years, will participate in the study as well as 10 patients of the same characteristic in Germany. In qualitative research, sample size estimation is based on projections of the number of participants needed to reach conceptual saturation (i.e., the point in the data collection process after which no new information is elicited). Past evidence in the literature suggests that conceptual saturation can be achieved in as few as 12 individual interviews in a relatively homogenous population.<sup>7,8</sup> As such, it is anticipated that conceptual saturation will be achieved within 20 interviews.

This study comprises two qualitative research activities outlined in the sections below: combined CE and CD qualitative interviews and real-time data capture.

#### **Combined CE and CD interviews (120 minutes)**

Twenty participants for the US and 10 from Germany (total sample= 30 participants) will be invited to part in combined CE and CD interviews. The CE component of the interview will explore participants' experience of living with severe, recurrent nasal polyps with particular focus on participants' symptoms, impacts and treatment/surgical experiences relating to their condition and the terminology used to describe their experiences. Following CE, participants will complete the CD component of the interview. Participants will complete the existing PRO instruments (overall symptom VAS, single item VAS and SNOT-22) as part of a 'think aloud' process in which they will be asked to speak aloud their thoughts as they read the instructions and complete the questions. Participants will also be probed upon their experience of completing the instruments/items and the relevance and participant understanding of the instrument items, instructions, recall period and response options. Further details regarding the conduct of the combined CE and CD interviews are provided in section 3.3.

#### **Real-time data capture application (10 days)**

All 20 US patients will be invited to take part in an app-based real world data capture activity. It is anticipated that of the 20 interview participants, a sub-set of ten will meet the inclusion criteria for this task. Therefore, the first ten patients to meet the criteria will make up the sample for this task. Five of the ten participants (50%) will take part in the app task prior to their interview and the remaining five participants (50%) will take part in the app task following their interview. Using this methodology, identified participants will be asked to download an app to their smartphone or tablet. Data capture will be conducted over a 10 day period and during this time participants will receive a series of questions/tasks via the application that they can response to in real-time, designed to

explore the experience of nasal polyps. The task will aim to explore the patient experience of the symptoms, HRQoL impacts and treatment of nasal polyps and any day-to-day variability that exists in these experiences in 'real time'. Participants will be able to provide responses to the questions/tasks fielded to them using a variety of methodologies including video, audio, text and photographic responses with captions. Further details regarding conduct of the real-time data application component are provided in section 3.3.

### **3.2 Study Population**

Twenty adult participants in the US, and 10 participants in Germany with severe, recurrent nasal polyps who have received nasal polyp surgery in the past 10 years prior to screening will take part in this study. Of these 30 participants, 10 of the 20 US participants (50%) will also complete the real-time data capture app task. The real-time data capture app task will not be conducted in Germany.

MedQuest Global, a recruitment agency, will assist in recruiting participants from a minimum of two geographically diverse sites in the US (e.g., East Coast, West Coast, Southern states). Zeste, a recruitment agency in Germany will assist with the recruitment of the German sample across 1-2 sites. Both agencies will recruit participants using the same methodology outlined below.

Participants will be recruited through a combination of primary care physicians/general practitioners and ear, nose and throat (ENT) specialists. Physicians will identify suitable participants for the study using the case report form (CRF) (Appendix 4). Participants identified by their physician will be provided with two copies of the information and consent form (ICF) to read and sign to indicate informed consent/assent if they wish to participate in the study (Appendix 5) – one for the participant to keep and one that the recruitment agency will send to AV. Participants will be given the opportunity to consider the information provided in the ICF and to ask the recruitment agencies/recruiting physician or AV any questions about the ICF before providing their informed consent. If the participant verbally agrees to take part and also signs the ICF, they will be informed that their name and contact information will be passed to the respective recruitment agencies in each country who will contact them to screen them into the study and collect demographic information about each participant (Appendix 6), ensuring study quotas are met for obtaining a representative sample as outlined in section 3.2.2. No information will be passed to the recruitment agencies until verbal and informed consent has been obtained from the participant. After informed consent has been obtained, the participant's physician will release the CRF data to the respective recruitment agencies in each country (Appendix 4); confirming that the participant meets the study inclusion requirements, and providing additional information about the participant's clinical condition and medical history. MedQuest Global will be responsible for ensuring that

any US participant who opts in to take part in the real-time data capture activities meets the criteria as outlined in section 0.

If the participant meets the criteria for inclusion in the study section 3.2.1.1 the recruiter will organize enrolment into the app task (where applicable) and schedule a time for the participant to attend the 120-minute interview visit. Of the 10 US participants who elect to take part in the app task five will complete the app task prior to their scheduled interview, and the remaining five will complete the app task after their interview. For the five US participants who complete the app task prior to their interview they will be asked about their experience of completing the app task at the end of the interview. For the five US participants who complete the app task after their interview, a separate a brief telephone call (approximately 5-10 minutes) will be scheduled with the participant to ask them brief questions about their experience. The questions relating to the participant experience of completing the app task are provided in Appendix 7.

In terms of compensating participants for their involvement in the study the following compensation structure will be employed:

#### **Payments to participants for their participation**

US participants will receive \$200 upon completion of the 120-minute interview. Those participants who also complete real-time data capture will receive an additional payment of \$200. German participants will each receive €200 following completion of the interview. All payments will be paid via bank transfer or amazon voucher.

### **3.2.1 Eligibility Criteria**

Participants eligible for enrolment in the study must meet the following inclusion and exclusion criteria, which are broadly reflective of GSK's clinical trial population.

#### **3.2.1.1 Inclusion Criteria**

Participants will be required to meet the following inclusion criteria to be eligible for inclusion in the study.

1. Participant has a clinical diagnosis of **bilateral nasal polyps** as diagnosed by endoscopy or CT scan;
2. Participant is aged 18 or over;
3. Participant has severe nasal polyps symptoms defined as a patient-reported nasal obstruction VAS score of >5 (Appendix 1);
4. Participant has had at least **one previous surgery in the past ten years** for the **removal of nasal polyps**. Surgery in this case is defined as any procedure involving instruments with resulting incision and removal of polyp tissue from the nasal cavity (polypectomy);

5. Participant is currently an eligible candidate for polypectomy defined by:

a) An overall patient-reported VAS symptom score of  $>7$ . (**Appendix 2**), **AND**

An endoscopic bilateral nasal polyp score of at least 5 out of a maximum score of 8 (with a minimum score of 2 in each nasal cavity). (

- b) Appendix 3);
- 6. Participant has symptoms consistent with chronic rhinosinusitis;
- 7. Participant is currently received intranasal corticosteroids for the management of their nasal polyps;
- 8. Participant is willing to participate in the study and provide informed consent;
- 9. Participant is an English speaker and is able to read, write and fully understand the English language;
- 10. Participant is willing to and able to attend and participate in a 120-minute interview to discuss their experiences of nasal polyps and obtain their feedback on several symptom/impact questionnaires.

### **Inclusion criteria for real-time data capture**

In addition to meeting the standard inclusion criteria outlined in section 3.2.1.1, those participants invited to take part in the real-time data capture will also be required to meet the following criteria:

- 1. Participant owns/or has access to either a smartphone (iOS or android) or tablet which has video, audio/microphone and photographic capabilities and access to either the Apple app store or google play store to download the app;
- 2. Participant is willing and able to take part in the real-time data application task and respond to a series of questions/tasks fielded to them via the application over the course of 10 days;

AND

Is willing to respond to some brief questions following the real-time data capture task about their experience of using the app and completing the tasks, either during their interview or in a 5-10 minute telephone call following completion of the task

- 3. Participant would feel comfortable recording short videos of themselves and providing audio commentary in response to questions/tasks.

### **3.2.1.2 Exclusion Criteria**

Any participant presenting with any of the following will not be included in the study.

- 1. Participant has received oral or injectable systemic corticosteroids in the last 4 weeks (28 days) for the management of their nasal polyps
- 2. Participant has a diagnosis of cystic fibrosis;

3. Participant has a diagnosis of eosinophilic granulomatosis with polyangiitis (also known as Churg Strauss syndrome), Young's, Kartagener's or dyskinetic ciliary syndromes);
4. Participant has a diagnosis of antrochoanal polyps;
5. Participant has a diagnosis of nasal septal deviation occluding one nostril;
6. Participant has had acute sinusitis or upper respiratory tract infection in the last two week;
7. Participant has ongoing rhinitis medicamentosa (rebound or chemical induced rhinitis);
8. Participant has had an asthma exacerbation requiring admission to hospital in the last four weeks;
9. Participant is currently or has previously taken part in a clinical trial for nasal polyps;
10. Participant is unwilling or unable to comply with the requirements of the study or has a physical or mental condition or learning difficulties that, in the opinion of the physician, may affect the participant's ability to participate in the study, the responses he/she might provide or their ability to provide consent.

### **3.2.2 Sampling**

Twenty adult participants in the US, and 10 participants in Germany with severe, recurrent nasal polyps who have received nasal polyp surgery in the past 10 years prior to screening will take part in this study. Of these 30 participants, 10 of the 20 US participants (50%) will also complete the real-time data capture app task. The real-time data capture app task will not be conducted in Germany.

In addition to meeting the inclusion/exclusion criteria outlined in section 3.2.1, AV will employ a purposive approach to sampling to ensure patients with a range of demographic, educational and clinical characteristics are recruited. To achieve representation of demographics and clinical characteristics within the sample, sampling quotas will be employed. Overall sampling quotas for the US are detailed in Table 1 and for Germany outlined in Table 2. German demographic data is not collected in regards to ethnicity and race separately, and thus, the quotas have been adjusted to fit the norm in Germany. Quotas may be relaxed if recruitment proves challenging. The clinical and demographic information to support the achievement of these quotas will be captured using the clinician-completed case report form (CRF) and patient-completed demographic form.

**Table 1: Quotas for US participants (n=20)**

Participant characteristics		Adults		Total
		18-45	46+	
<b>Age</b>		≥6	≥6	≥12
<b>Gender</b>	Male	≥2	≥2	≥6
	Female	≥2	≥2	≥6
<b>Ethnicity</b>	Hispanic or Latino (of any race)			≥6
	Non-Hispanic or Latino			≥6
<b>Race</b>	White			≥4
	Black/African American			≥4
	Multi-racial			≥2
	Other race/ethnicities <ul style="list-style-type: none"> <li>• Asian or Pacific Islander</li> <li>• Native American or Alaska native</li> <li>• North African or Middle Eastern</li> <li>• Other (specified by participant)</li> </ul>			≥2
<b>Education</b>	Some high school			≥3
	College or higher			≥3
<b>Polypectomy surgery</b>	In past 2 years			≥6
	In past 3-10			≥6

**Table 2: Quotas for German participants (n=10)\***

Participant characteristics		Adults		Total
		18-45	46+	
<b>Age</b>		≥3	≥3	≥6
<b>Gender</b>	Male	≥2	≥2	≥4
	Female	≥2	≥2	≥4
<b>Race</b>	White Caucasian			≥4
	Non-Caucasian			≥2
<b>Education</b>	Some high school (German equivalent)			≥3
	College or higher (German equivalent)			≥3
<b>Polypectomy surgery</b>	In past 2 years			≥3
	In past 3-10			≥3

\*Note that German quotas have no ethnicity category as this is not typically collected in German. The race category is also simplified in line with what is typically expected in Germany.

### **3.3 Data Source / Data Collection**

All recruited participants will take part in a 120-minute telephone interview. A semi-structured interview guide will be used to guide the conduct of the CE interview section and CD interview section and will ensure that all topics of interest are discussed (Appendix 7). The interview guide is designed to be used as a guide, not as a script to be read verbatim. The interviewer will therefore be flexible in the order of questioning, following the lead of the participant and asking appropriate questions when topics of interest arise. All interviews will be audio recorded and transcribed verbatim for the purpose of analysis. Any identifiable information (e.g. participant or doctor's names) will be removed from the transcripts such that they are fully anonymized.

#### **Concept elicitation (55 minutes)**

During the CE section of the interview participants will be asked a series of broad open-ended questions designed to encourage them to talk openly and as spontaneously as possible about their experience of having nasal polyps and how it affects their life. In addition to speaking open-endedly about their experiences, participants will be asked more focused questions designed to probe on issues that they may not have mentioned during the course of the interview or concepts/statements that require additional clarification. Asking probe questions in a dynamic and 'as required' fashion information will be important for ensuring all study objectives are met and all study questions and topics of interest are explored, thus supporting the identification of the concepts that are most important to patients and the terminology they use to describe their experiences.

#### **Cognitive debriefing (60 minutes)**

During the CD section of the interview participants will be asked to complete the PRO instruments using a 'think aloud' process in which they will be asked to speak aloud their thoughts as they read the instructions, item and complete the questions. After completion of each 'think aloud' exercise, participants will take part in in-depth CD centered on their experience of completing the instruments, with particular focus on the relevance and understanding of the items, instructions, response options and recall period. In addition, the participants will be encouraged to discuss what level of change in their symptoms would they consider meaningful and important and how this would relate to changes on the items scores.

The questionnaires (Appendix 8) that will be used in the cognitive debriefing task will be sent to participants in the mail in advance of their interview by the recruitment agency. Participants will not be required to complete these until instructed to during the interview. Following the interview, participants will be asked to send the questionnaires

back to the recruitment agency using a stamped addressed envelope which will be supplied to them.

### **Real-time data capture**

All 20 US patients will be invited to take part in an app-based real world data capture activity. It is anticipated that of the 20 interview participants, a sub-set of ten will meet the inclusion criteria for this task. Five of the ten participants (50%) will take part in the app task prior to their interview and the remaining five participants (50%) will take part in the app task following their interview. Eligible participants will receive instruction and supporting documentation on how to download and access the application via their smartphone or tablet. Participants will be required to take part in the real-time data capture exercise over the course of 10 days and during this time a series of approximately 10 questions/tasks will be fielded to participants via the application to explore the experience of the symptoms, HRQoL impacts and treatment of nasal polyps and any day-to-day variability that exists these experiences in 'real time'. Some questions/tasks may be issued daily over the 10 days and others may be issued once. Examples of the types of questions that might be asked to participants via the application are documented in Appendix 9. Each task will take no longer than 5-10 minutes to complete and participants will be able to provide responses to the questions/tasks fielded to them using a variety of methodologies including video, audio, text and photographic responses.

Once recorded, the participants can submit their responses via Wi-Fi or 3/4G and they will become immediately viewable on a response dashboard for the study researchers to track and analyses. The AV research team would be able to interact with participants via the dashboard (e.g. add new tasks, send reminders to complete a task), monitor compliance and review and run reports on received responses to questions/tasks. All data from the dashboard would be downloaded and stored by Adelphi Values. As part of this process any video or photographic data whereby the participant's face was visible would be blurred/redacted.

Germany participants will not be invited to take part in the real-time data capture app task.

For those participants who elect to take part in the app task and complete this activity prior to their interview, participants will also be asked a series of general questions at the end of their interview about their experience of the app and completing the tasks/questions over the 10-day period. For those participants who take part in the app task after their interview the same questions included in the interview about the app task will be asked during a separate brief telephone call (approximately 5-10 minutes) conducted upon completion of the app task.

Adelphi Values' qualitative interviewers who are experienced in conducting interviews with adult participants will conduct the interviews. Each interviewer will participate in a comprehensive briefing meeting to ensure that they are fully familiar with the interview guide and can anticipate difficulties that may arise during the interview. The AV project team will also be responsible for the content and management of the real-time data capture application.

### **3.3.1 Endpoints**

As this study is a low-interventional, qualitative interview study, there are no formal endpoints. Data from the interviews will be used to supplement a provisional conceptual model that has been developed from a review of qualitative literature of nasal polyps, exploring the symptoms and quality of life impacts of nasal polyps. Patients will be asked to complete the SNOT-22 questionnaire and overall and single item VAS assessment during the interview; however this is purely for cognitive debriefing purposes to explore the relevance and patients understand of the content of the assessments.

#### **3.3.1.1 Primary Endpoint**

Not applicable

#### **3.3.1.2 Secondary Endpoint(s)**

Not applicable

### **3.4 Sample Size / Power Calculations**

Where the goal of qualitative research is to provide comprehensive understanding of complex phenomena (e.g. the holistic experience disease from the patient/caregiver perspective), it is recommended that sample sizes are determined based on the concept of 'conceptual saturation' where no new concepts are identified with repeated data collection. Past research and experience suggests that conceptual saturation can typically be achieved in as few as 12 individual interviews in a relatively homogenous population.<sup>3,4</sup>

Taking the above into account, a total of 20 participants from the US and a total of 10 from Germany will be interviewed (total sample= 30).

### **3.5 Hypotheses**

As this qualitative research study is exploratory in nature no formal hypotheses are required.

## **4 DATA ANALYSIS CONSIDERATIONS**

### **Descriptive socio-demographic and clinical characteristics**

Socio-demographic and clinical characteristics for participant collected from the demographics form and CRF respectively will be summarized. Ratio data (e.g., age) will be summarized using totals (n values), means, min/max (range) statistics and where relevant standard deviations and medians. Similarly, categorical data (e.g., gender, ethnicity, race, education levels) will be summarized using totals (n values) and percentages to represent the sample in each sub-category. Descriptive data will be summarized in tabular format.

### **Analysis of interviews**

All interviews will be audio-record and transcribed/translated verbatim. All identifiable information (e.g. participants', interviewer's and doctors' names) will be removed from the transcripts to make them anonymous and all participants will be assigned a unique participants identification code (ID).

Qualitative analysis of verbatim transcripts for the semi-structured interviews will be conducted using thematic analysis methods (CE interview data) and framework analysis (CD interview data). All interview data will be audio-recorded, transcribed and entered into ATLAS.Ti, a software package which is designed to facilitate the storage, coding, and analysis of qualitative data. This program allows the researcher to code data at different levels of analysis and search for coded data using Boolean operators. ATLAS.Ti software allows traditional qualitative analysis of transcripts, but facilitates an easier break-down and management of qualitative data into groups and assign 'codes'. Each transcript would be assessed and participant comments that pertain to the main research questions would be highlighted. Axial coding enables the relationship between concepts to be explored.

The AV project leader will review the analysis of the first two interviews with the project researcher and create a coding scheme to be used throughout the analysis process (each highlighted statement will eventually be coded). After analyzing each transcription, the coded statements are then moved into their relevant domains. A list of participant statements would be generated for each domain, all of which will contain a prefix comprising the participant's designated ID number and the corresponding transcript page from which the statement was derived. Of note, whilst the frequency of participants mentioning a particular issue may be reported, quantitative analysis of this data would not occur, since that is not the purpose of qualitative research and the sample sizes are too small to utilize the data meaningfully in a quantitative or statistical fashion.

In assessing the adequacy of the qualitative research to explore the patients' experience of nasal polyps, Adelphi Values will assess whether conceptual saturation has been obtained for the CE component of the qualitative interviews (i.e. that a point has been reached at which no substantially new themes or descriptions of the concept and no new terms are being introduced by patients). Assessment of conceptual saturation is important to ensure that all concepts of importance to participant have been elicited in the interviews and is a key means of justifying the adequacy of sample sizes used in qualitative research studies. If saturation has not been reached, additional concepts important to patients may not have been captured. The process for determining saturation involves comparison of sets of transcripts to identify any consistency or inconsistencies in the pattern elicited concepts and themes. This typically involves comparison of the findings from sets of consecutive interviews. Specifically, for this sample of 30 participants (20 in the US and 10 in Germany), five sets of six interviews will be compared. If new concepts and themes are emerging in the final set of interviews then this suggests that conceptual saturation has not been achieved and further interviews may be necessary and would be discussed with GSK.

### **Descriptive statistics for the SNOT-22 and visual analogue scales**

The SNOT-22 and VAS assessments completed as part of the CD interviews will be scored by Adelphi Values using the instrument scoring instructions. For the collected VAS assessments the research team will measure the vertical line bisection and record the corresponding score which will be factored into the instrument scoring. Instrument total scores and items scores and data from the VAS (ratio data) will be summarized using totals (n values), means and min/max statistics. At the item level the distribution of participant responses (categorical data) will be summarized using totals (n values) and percentages to represent the proportion of the sample selecting each response option. Any missing data at the item level will be summarized using total (n values) and percentages. Where relevant, data will be presented in tabular or graphical format, whichever is deemed most appropriate based on the content at the time of reporting of findings.

### **Real-time data capture analysis**

Responses to the real-time data capture data will be collected using a variety of methodologies (e.g., video, audio, text and photographic responses with captions). For audio responses these will be transcribed.

Participants responses to questions/tasks in the real-time data capture activity will be analyzed in the same way using Atlas.Ti for the qualitative interviews as outlined above. Video, free text photographic and transcribed audio responses will be entered into Atlas.Ti and assigned codes in the same manner as the verbatim transcripts to tag/code

what their content conveys. For any questions/tasks fielded to participants as part of the app with multiple choice or numerical responses options, descriptive analysis of these items will be performed and reported (e.g. mean item score, ranges etc.). For those participants who complete the app task after their interview, they will answer a series of questions via telephone about their experience of this activity. This data would also be audio-recorded, transcribed verbatim and analyzed in the same way as the interview and app task data.

The interview and app task results will be used to inform the further development of a conceptual model for nasal polyps, previously constructed based on literature review activity only. The qualitative analysis will also be used help summarize the content validity of the reviewed PRO instruments and their suitability for use with patients with nasal polyps.

### **Reporting**

Adelphi Values will prepare a single report, detailing the findings from the CE and CD interviews and real-time data capture. Within the report, anonymized patient quotes will be reported. Findings from the study may also be published in peer-reviewed journals. Again, however, only anonymized information will be reported.

## **5 LIMITATIONS**

As the study has been designed using best practice methodology advocated by the Food and Drug Administration for exploratory qualitative studies used to support clinical measurement strategies, the foreseen risk/limitations of the study are minimal but include the following:

- **Selection of participants:** potential bias is always possible when selecting interviewees; however, as outlined in sections 3.2.1 and 3.2.2 eligibility criteria and recruitment quotas will be employed to ensure the participant sample is as diverse and representative as possible given the overall study size (n=30).
- **Generalizability of data:** The participant sample (n=30) is relatively small as the planned research is primarily exploratory in nature. The sample size is typical of qualitative studies conducted in this context. Nevertheless, the findings obtained from the participant interviews cannot be extrapolated or generalized to the wider population with nasal polyps; however, they will be relevant to GSK target nasal polyp population for their planned Phase III clinical trial.
- **Real-time data capture:** The eligibility criteria for the real-time data capture task and information included within the consent form (Appendix 5) will aim to ensure that those participants who take part in this activity are willing to take part over a period of ten days and that they would feel comfortable in providing responses using a variety of methods including video, audio, photographic and/or free text

responses. As this methodology is exploratory and ethnographic in nature the quality of completion and the comprehensiveness of participant responses cannot be guaranteed. This said however, the participants will be contactable both via the app and also via email and/or telephone during the completion of the app task and as such the project researchers will endeavor to encourage the completion of all task in as thorough manner as possible (e.g. provide reminders to participants to complete their task or probes/examples if they are unsure of how to respond to a task/question).

- **Conceptual saturation:** As outlined in section 4 the CE component of the interviews will be analyzed according to the principles of conceptual saturation to assess that all concepts of importance have been elicited. Whilst conceptual saturation can typically be achieved in a sample of 12 in a relatively homogenous population, a potential limitation of the study is that conceptual saturation is not achieved across the 30 interviews. Should conceptual saturation not be achieved, discussions will be held with GSK to determine whether additional interviews should be conducted in order to achieve saturation.

## **6 STUDY CONDUCT, MANAGEMENT & ETHICS**

### **6.1 Ethics Committee/IRB Approval**

This study will be submitted to an independent ethical review board in the US for review and approval prior to any study related activities and fieldwork being conducted. The German component of this study will be submitted for ethical approval to the Freiburger Ethik-Kommission International (FEKI) board in Germany.

### **6.2 Informed Consent**

Each participant will be given full oral and written information about the nature, purpose, possible risk and benefit of the study. The participant will be given the opportunity to ask questions and allowed time to consider the information provided. Participants will also be notified of their right to discontinue their participation in the study at any time. The participant's signed and dated informed consent will be obtained using the information and consent form (ICF) (Appendix 5) before any medical information is accessed (i.e. before completion of the CRF, Appendix 4), before the participant is contacted by the recruitment agencies, and before they are asked to perform any study related activities. The participant will be provided with the ICF (Appendix 5), be allowed to read it, and given the opportunity to ask the study investigator or recruitment agencies any questions. Copies of the ICF will be signed by the recruitment agencies and the participant, with the participant given one copy to take away for their records.

### **6.3 Data Protection**

The ICF (Appendix 5) explains that the transcribed data will be stored in a computer database in a folder that is password protected for 15 years by Adelphi Values. Confidentiality of this data will be maintained in accordance with HIPAA legislation. The database will be de-identified; participants will be assigned a participant ID number in place of their name and any identifiable data will be made anonymous – such as place names, family members, etc. If participants participate in the app task, for some questions/tasks they will have the option to submit video, picture, audio and text responses. In these situations all visible faces will be blurred/redacted following analysis and prior to storage, to ensure anonymity.

The ICF also explains that for data verification purposes, authorized representatives of GSK, AV, a regulatory authority or an IRB may require direct access to parts of the hospital or practice records relevant to the study including participants' medical history. The ICF further explains that in the event that a medical emergency should occur at the time of interview, the interviewer is permitted to break confidentiality and pass information onto persons such as medical personnel, in order for the participant to receive medical treatment.

With regard to the real-time data app task, the ICF also explains that if participants choose to participate in the app task, for some questions/tasks they will have the option to submit video, photograph, audio and text responses. If they choose to take part in the app task and choose to submit videos of themselves or pictures, full anonymity of the data cannot be guaranteed if their face is visible in the recordings and images that are uploaded to Adelphi Values. If they consent to participate in the real-time data app task they agree that full anonymity of the data cannot be guaranteed. However, any data submitted via the real-time data capture task will not be shared with any individuals outside of the project team. For each app question/task they will have the option of how they respond (e.g. video, audio, photograph/text). Full anonymity and confidentiality can be guaranteed for any data files, written documents or reports that are produced about the data collected.

### **6.4 Personally Identifiable Information (PII)**

Participant data will be handled in accordance to the data protection information provided in section 6.3. All participant data (study forms, transcripts and responses to the real-time data task) will be de-identified and participants will be assigned a participant ID number. This ID number will be used to label the electronic data files and documents relevant to each participant and will be used to reference participant data in the reporting of the study findings (e.g. study reports, presentations, publications).

## 6.5 Adverse Event (AE), Pregnancy Exposure, and Incident Reporting

As this is a low-interventional study that does not involve an investigational product the occurrence of adverse events is anticipated to be none to extremely low. Adverse event reporting will be managed in line with the study-specific pharmacovigilance plan (sPVP) that will be completed and filed internally at GSK. If a participant mentions during the interview any adverse event (AE) or product complaint, whether it is considered serious or not, experienced whilst taking a product produced by GSK, this must be reported to the pharmacovigilance department at GSK. The interviewer will complete an adverse event monitoring report form (**Error! Reference source not found.**) at the end of the interview that will capture information regarding the reportable event and the GSK product involved and the role of the person reporting the event. As part of this process the interviewer will seek the participant's permission to include their contract details and the contact details of their physician on the form; however, should a participant not choose to include their contact details on the AE form, they will be informed that the AE still has to be reported, but will be done so anonymously. Any completed forms will be sent to the designated contact at GSK within 24 hours of awareness of the adverse event or adverse drug reaction.

## 7 EXTERNAL INVOLVEMENT

### 7.1 Third Party Supplier

Supplier	Address	Staff contact details
Adelphi Values (Company conducting the study)	Adelphi Mill Grimshaw Lane Bollington Macclesfield SK10 5JB	Senior Lead: PPD PPD Project Lead: PPD PPD Researcher: PPD PPD Project administrator: PPD PPD
MedQuest Global (Recruiter)	MedQuest Global 30460 Cartagena Place, Castaic, CA 91384	PPD
Zeste Germany (Recruiter)	Zeste Research Stockheimerstrasse 297647 Willmars, Germany	
Transperfect	Transperfect	

(Transcription agency)	Three Park Avenue 39th Floor New York, NY 10016	PPD
LumiGlobal (App vendor)	LumiGlobal Lumi USA 510 First Avenue North Suite 222 Minneapolis USA MN 55403	

## 7.2 External Expert/Health Care Professionals (Consultants & Research PIs)

Not applicable

## 8 REFERENCES

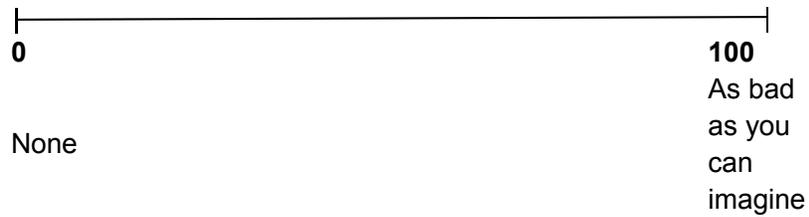
1. US Food and Drug Administration. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims. 2009.
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## 9 APPENDICES

### Appendix 1: Patient-reported nasal obstruction VAS

The following question should be completed by the participant. Recruited participants are required to have an **overall symptom score of >50**.

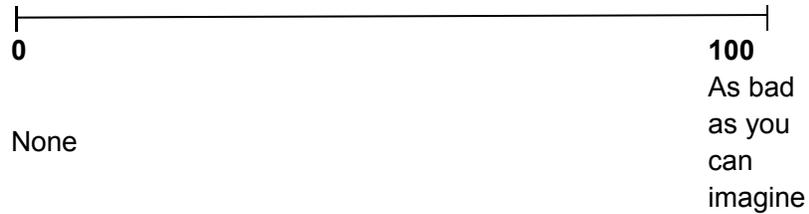
**Please rate your nasal obstruction at its worst over the previous 24 hours.**



## Appendix 2: Patient-reported overall symptom VAS

The following question should be completed by the participant. Recruited participants are required to have an **overall symptom score of >70**.

**Please rate your nasal polyps symptoms at their worst over the previous 24 hours.**

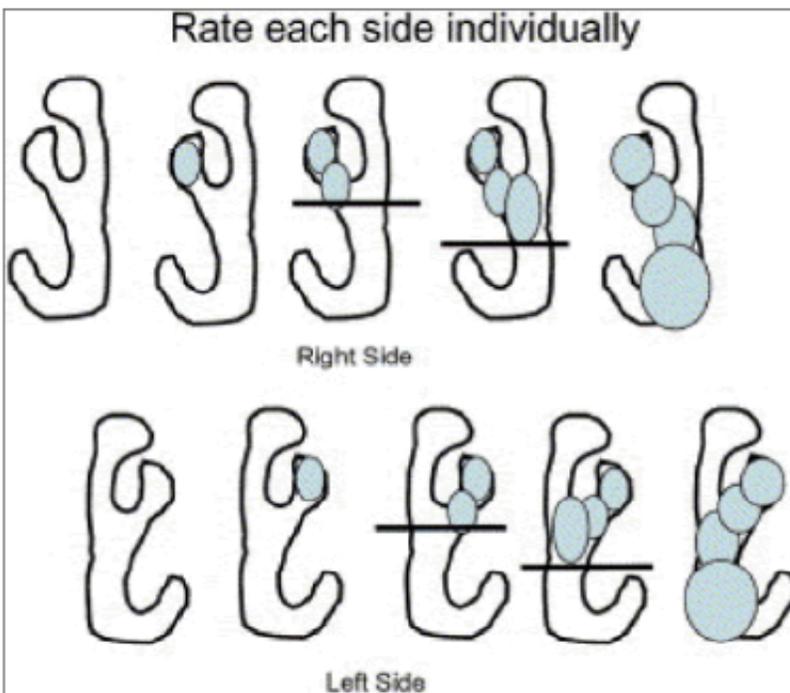


### Appendix 3: Clinician-reported endoscopic nasal polyp scoring

Recruited patients should have an endoscopic bilateral nasal polyp score of **at least 5 out of a maximum score of 8 (with a minimum score of 2 in each nasal cavity)** to be eligible for participation in the study.

Clinicians will be asked to provide confirmation of each nasal cavity rating as part of the case report form.

Polyp Score	Polyp size
0	No polyps
1	Small polyps in the middle meatus not reaching below the inferior border of the middle concha
2	Polyps reaching below the lower border of the middle turbinate
3	Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle concha
4	Large polyps causing almost complete congestion/obstruction of the inferior meatus



**Appendix 4: Case Report Form**

**PARTICIPANT CASE REPORT FORM (CRF)**

**TO BE COMPLETED BY THE RECRUITING PHYSICIAN**

**(Please complete a separate form for each patient recruited to the study)**

<u>Physician Details</u>	
Name (printed):	_____
Date of form completion:	<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">/___/___ Month</div> <div style="text-align: center;">/___/___ Day</div> <div style="text-align: center;">/___/___ Year</div> </div>
What is your job title/field of specialty?	
Please specify: _____	
Please sign here: _____	

INCLUSION CRITERIA		
	Yes	No
1. Participant has received oral or injectable systemic corticosteroids in the last 4 weeks (28 days) for the management of their nasal polyps	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
2. Participant has a clinical diagnosis of <b>bilateral nasal polyps</b> as diagnosed by endoscopy or CT scan.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
3. Participant is aged 18 or over.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
4. Participant has severe nasal polyp symptoms as defined as a patient-reported nasal obstruction Visual Analogue Score (VAS) of >5 (Please ask patient to complete Appendix 1 of this protocol).	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
5. Participant has had at least <b>one previous surgery</b> in the <b>past ten years</b> for the <b>removal of nasal polyps</b> . Surgery in this case is defined as any procedure involving instruments with resulting incision and removal of polyp tissue from the nasal cavity (polypectomy).	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
6. Participant is currently an eligible candidate for polypectomy defined by:		
c) An overall patient-reported VAS symptom score of >7 ( <b>Appendix 2</b> of this protocol).	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
<b>AND</b>		
d) An endoscopic bilateral nasal polyp score of at least 5 out of a maximum score of 8 (with a minimum score of 2 in each nasal cavity) (	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>

ADELPHI VALUES

INCLUSION CRITERIA		
	Yes	No
e) Appendix 3 of this protocol).		
7. Participant has symptoms consistent with chronic rhinosinusitis.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
8. Participant is currently receiving intranasal corticosteroids for management of their nasal polyps.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
8. Participant is willing to participate in the study and provide informed consent.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
9. Participant is an English speaker and is able to read, write and fully understand the English language.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
10. Participant is willing to and able to attend and participate in a 120-minute interview to discuss their experiences of nasal polyps and give feedback on several symptom/impact questionnaires.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>

⚡ If **ONE** of the above answers is **NO**, the patient **CANNOT** be included in the study

EXCLUSION CRITERIA		
	Yes	No
1. Participant has a diagnosis of cystic fibrosis.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
2. Participant has a diagnosis of eosinophilic granulomatosis with polyangiitis (also known as Churg Strauss syndrome), Young's, Kartagener's or dyskinetic ciliary syndromes).	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
3. Participant has a diagnosis of antrochoanal polyps.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
4. Participant has a diagnosis of nasal septal deviation occluding one nostril.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
5. Participant has acute sinusitis or upper respiratory tract infection or has had had acute sinusitis or upper respiratory tract infection in the last two weeks.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
6. Participant has ongoing rhinitis medicamentosa (rebound or chemical induced rhinitis).	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
7. Participant has had an asthma exacerbation requiring admission to hospital in the past four weeks.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
8. Participant is currently or has previously taken part in a clinical trial for nasal polyps.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
9. Participant is unwilling or unable to comply with the requirements of the study or has a physical or mental condition or learning difficulties that, in the opinion of the physician, may affect the participant's ability to participate in the study, the	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>

ADELPHI VALUES

	Yes	No
responses he/she might provide or their ability to provide consent.		

↪ If **ONE** of the above answers is **YES**, the patient **CANNOT** be included in the study

↪ If all inclusion criteria are **YES** and all exclusion criteria are **NO** please include the participant in the study

**INFORMATION ABOUT THE PARTICIPANT'S NASAL POLYPS**

1. When was the participant first diagnosed with bilateral nasal polyps?

\_\_\_\_\_/\_\_\_\_ (month, year)

2. Please specify which methods were used to support the participant's diagnosis with nasal polyps:

Endoscopy <sub>1</sub>

CT scan <sub>2</sub>

Nasoscope investigation <sub>3</sub>

MRI scan <sub>4</sub>

Other diagnosis tool (please state) <sub>5</sub>

---

3. Please indicate which of the following symptoms the participant experienced with their nasal polyps (tick as many as apply):

Nasal blockage/obstruction/congestion <sub>1</sub>

Nasal discharge (anterior) <sub>2</sub>

Post nasal drip (anterior discharge) <sub>3</sub>

Facial pain <sub>4</sub>

Facial pressure <sub>5</sub>

Reduction or loss of smell <sub>6</sub>

Reduction or loss of taste <sub>7</sub>

Sleep apnea <sub>8</sub>

Snoring <sub>9</sub>

Other symptom type (please state) <sub>10</sub>

---

4. Please indicate the number of surgeries the patient has received to **remove** their nasal (polypectomy), the date of surgery and the extent of the surgery received.

ADELPHI VALUES

Surgery Number	Date of surgery (MM/DD/YYYY)	Type of nasal polyp surgery (e.g. polypectomy, functional endoscopic sinus surgery with polypectomy or balloon sinuplasty with polypectomy etc.)

5. Please indicate what treatments (drug and non-drug treatments) the participant is currently receiving (or has previously received) for their nasal polyps.

	Current medications		Past medications		
Treatments (for medications, generic or trade name is acceptable)  Please specify type and dose	Medication in current use? (✓)	Medication start date (MM/DD/YYYY)	Medication NOT in current use, BUT used in the past? (✓)	Medication start date (MM/DD/YYYY)	Medication end date (MM/DD/YYYY)
<b>Nasal corticosteroids</b>  (e.g., Flutisone, Budesonide, Flunisolide, Mometasone etc.)					

ADELPHI VALUES

Treatments (for medications, generic or trade name is acceptable)  Please specify type and dose	Current medications		Past medications		
	Medication in current use? (✓)	Medication start date (MM/DD/YYYY)	Medication NOT in current use, BUT used in the past? (✓)	Medication start date (MM/DD/YYYY)	Medication end date (MM/DD/YYYY)
<b>Oral corticosteroids</b> (e.g., Prednisone)					
<b>Injectable corticosteroids</b> (e.g., Prednisone)					

ADELPHI VALUES

Treatments (for medications, generic or trade name is acceptable)  Please specify type and dose	Current medications		Past medications		
	Medication in current use? (✓)	Medication start date (MM/DD/YYYY)	Medication NOT in current use, BUT used in the past? (✓)	Medication start date (MM/DD/YYYY)	Medication end date (MM/DD/YYYY)
Other treatment type (please specify)					

6. Please indicate which surgical **nasal** treatments (**which did not include the removal of polyps**) that the patient has previously received.

Other nasal and/or sinus surgery ( <u>Non-polyp removal surgeries</u> )	Dates of previous surgeries (please list all dates if the surgery has been performed more than once)
(e.g., balloon sinuplasty without polypectomy, nasal stent insertion)	

**GENERAL HEALTH STATUS INFORMATION**

7. Does the participant currently have any chronic diseases or conditions in addition to bilateral nasal polyps?

<sub>1</sub> Yes                      <sub>0</sub> No

If **YES**, please indicate the disease(s) or condition(s) below. For each comorbidity, please indicate the category of the chronic disease or condition the participant has and the specific diagnosis.

<u>Chronic Disease/Condition</u>	<u>Please specify diagnosis</u>
<input type="checkbox"/> <sub>1</sub> Cardiovascular	
<input type="checkbox"/> <sub>2</sub> Urological/Nephrological	
<input type="checkbox"/> <sub>3</sub> Dermatological	
<input type="checkbox"/> <sub>4</sub> Endocrinological/Nutritional	
<input type="checkbox"/> <sub>5</sub> Gastroenterological	
<input type="checkbox"/> <sub>6</sub> Gynecological	
<input type="checkbox"/> <sub>7</sub> Psychiatric	
<input type="checkbox"/> <sub>8</sub> Stomatological (diseases of the mouth)	
<input type="checkbox"/> <sub>9</sub> Ophthalmological	
<input type="checkbox"/> <sub>10</sub> Hematological	
<input type="checkbox"/> <sub>11</sub> Pneumological/Pulmonary	
<input type="checkbox"/> <sub>12</sub> Rheumatological	
<input type="checkbox"/> <sub>13</sub> Neurological	
<input type="checkbox"/> <sub>14</sub> Allergy	
<input type="checkbox"/> <sub>15</sub> Otorhinolaryngological (ear, nose, throat)	
<input type="checkbox"/> <sub>16</sub> Other (e.g. obesity)	

8. Is the participant currently taking treatment(s) for any other disease or condition?

<sub>1</sub> Yes

<sub>0</sub> No

9. If yes, please give the name of the condition and the treatment received.

<u>Disease or Condition</u>	<u>Treatment</u>
<input type="checkbox"/> <sub>1</sub>	
<input type="checkbox"/> <sub>2</sub>	
<input type="checkbox"/> <sub>3</sub>	
<input type="checkbox"/> <sub>4</sub>	
<input type="checkbox"/> <sub>5</sub>	
<input type="checkbox"/> <sub>6</sub>	

10. How would you rate the participant's general health?

Excellent <sub>1</sub>

Very Good <sub>2</sub>

Good <sub>3</sub>

Fair <sub>4</sub>

Poor <sub>5</sub>

Once you have a participant who has agreed to participate in the study and who meets the selection criteria, please send a signed copy of this form

to **MedQuest** by fax  PPD for the attention of:  PPD

Should you have any questions, please contact  PPD on  PPD

**THANK YOU FOR COMPLETING THIS FORM**

Approved:

## Appendix 5: Information and consent form

### INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

**Name of Research Study:** Qualitative research to characterize the patient experience of nasal polyps

**Study #:** GK7818A

**Sponsor:** GlaxoSmithKline

**Study Doctor Name:** PPD

**Research Site Address(es):** Adelphi Values  
290 Congress Street  
7th Floor  
Boston, MA  
02210

**Daytime telephone number(s):** PPD

**24-hour contact number(s):** PPD

You should keep a copy of this form. If you have any questions or problems during the study, call the phone number(s) above.

#### **What is the purpose of this form?**

The purpose of this form is to help you decide if you want to be in the research study. It is up to you to decide if you want to take part in this study. You should take part in this study only if you want to.

Before you decide if you want to take part in this research study, it is important that you read the information below.

This form may use words you do not understand. Please ask the person who gave you this form to explain any words or procedures that you do not clearly understand.

If you sign this form, it means that you agree to take part in this study. This form describes what the study is about and what will happen. It also tells you about the risks and benefits of the study.

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You can change your mind about taking part in this study at any time. You may leave the study at any time, even if you have signed this form. You do not have to give a reason.

Please ask any questions you have.

You may talk with your family, friends, and your doctor to help you make your decision. You can take as much time as you like to make this decision.

The sponsor (Glaxo SmithKline) is paying for this research study and the research will be carried out by Adelphi Values (a health research company). Your study doctor will be paid by the sponsor.

When deciding to take part in a research study you should know:

- The main goal of medical care is to help you.
- The main goal of a research study is to gain information to help patients in the future.
- Being in this study does not replace your regular medical care.

### **Why is this study being done?**

The purpose of this research study is to learn more about the experiences of individuals living with nasal polyps, and how having nasal polyps affects individuals in their daily life.

To do this, we would like to conduct interviews with individuals with nasal polyps to understand their experience of nasal polyps. As part of this interview, we would also like you to complete a number of questionnaires about your experience of nasal polyps and give your opinion on whether they are easy to understand and complete, and relevant to your experience of nasal polyps. As an optional activity, we would also like a sub-set of ten individuals with nasal polyps to complete a series of activities via a free app downloaded to their smartphone or tablet.

This study will involve approximately 20 subjects from the United States and 10 subjects from Germany.

### **What will I need to do as part of the study?**

You are invited to take part in the following research activities:

1. **Nasal polyp interview:** Participants will take part in a 120-minute telephone interview about their experience of living with nasal polyps. During the first half of the interview you will be asked to discuss the symptoms of nasal polyps that you experience, how they affect you, and your experience of any treatment/surgery you have received.

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For the second half of the interview, participants will be asked to complete a number of questionnaires about their experience of nasal polyps. You will be asked about the relevance of the questionnaires to your experience of nasal polyps and your ability to understand and complete the questionnaires.

2. **(OPTIONAL) App task:** Participants will be invited to download a free application (app) to their personal smartphone or tablet. Participants will be asked to complete approximately 10 questions/tasks via the app over a 10-day period. The questions/tasks will explore the participants' experience of the symptoms, impacts and treatments of nasal polyps and any day-to-day changes that the participant experiences, in 'real time' as participants go about their daily lives. Participants will be required to complete some questions/tasks once during the 10 days and other questions/tasks will need to be completed daily. Each task will take no longer than 5-10 minutes to complete and participants will be able to provide video, audio, text, multiple choice and photographic responses to the questions/tasks. Participants will also be asked to complete a 5-10 minute phone call following completion of the app task to provide feedback about their experiences of completing the app task.

**SUBJECTS WHO AGREE TO TAKE PART IN THIS RESEARCH STUDY ARE  
REQUIRED TO TAKE PART IN ACTIVITY 1 BUT ACTIVITY 2 IS OPTIONAL**

**What are the study procedures?**

Before you decide whether to be in this study, you should think about how the study activities will affect your schedule. If you agree to be in this study, you will need to sign this form before you take part in any study activities.

If your doctor thinks you are suitable for this study, he or she will ask you to read this form and sign 2 copies of it – one for you to keep and one which will be kept by the company doing the research (Adelphi Values). If you sign this form and would like to take part, then your name will be passed to a recruitment agency – MedQuest Global Marketing Research. Your clinician will complete a short form about your nasal polyps and associated medical history and provide this to the recruitment agency. The recruitment agency will contact you to collect some background information from you such as your age, gender, race, and ethnicity and schedule the interview at a time that is convenient for you. The recruitment agency will also ask you if you would like to participate in the optional app task, and explore if you are a suitable to take part in this activity.

**Interview procedure:** Interviews will be conducted by a trained Adelphi Values researcher by telephone. The interviews will be audio-recorded. If you do not consent to the interview being audio-recorded, then you cannot take part in the study as it is essential that we have an accurate record of the interviews.

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The questionnaires you will provide feedback on during the interview will be sent to you in the mail in advance of your interview by the recruitment agency. You will not be required to complete these until instructed to during the interview. Following your interview you will be asked to send the questionnaires back to the recruitment agency using a stamped addressed envelope which will be supplied to you.

**(OPTIONAL) app task procedure:** If you have opted to participate in the app task, some participants will be asked to complete this before their interview and other participants will be asked to complete it after their interview. You will be provided with instructions from the recruitment agency or Adelphi Values on how download the free app, create a username and password login, work the app and complete the tasks over the 10-day period. The app is free to download/install however costs may be incurred if you download or upload any information from the app using your data allowance. We recommend using WiFi or enabling the 'WiFi only' mode in settings on your device to submit your responses as this uses the internet and not your data allowance. This will be further explained in the instructions, should you take part in the app task. Some questions/tasks may need to be completed on the same day and others may be completed at any time over the 10-day period. Participants will be required to complete some questions/tasks once during the 10 days and other questions/tasks will need to be completed daily.

Questions may be multiple choice questions or free text answer questions such as:

*"Please rate the severity of your nasal polyp symptoms today using the 0-100 scale below"*

Tasks may require video, audio or photographic responses such as:

*"Record a short audio, video or written response telling us about your symptoms today and how they have affected you."*

You will receive messages on your smartphone/tablet when you have a new question/task to complete, and will be told how long you have to complete this task. For most tasks you will have one day to complete them at a time of your choosing but the completion time for other tasks may vary. Your responses will be submitted automatically via Wi-Fi or 3/4G and they will become immediately available to study researchers. The researchers will be able to track your responses and interact with you via the app over the course of the 10 days if you need help or have any questions. Following completing of the app task, you will be asked about your experiences of using the app and completing the tasks. If you were selected to complete the app task following your interview, you will be contacted by telephone and asked about your experiences, this will take 5-10 minutes. If you were selected to complete the app task

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prior to interview, you will be asked about your experience of the app task during your interview.

If you choose to take part in the app task, your responses to questions/task will need to be visible to members of Adelphi Values (the company conducting this research on behalf of the study sponsor) and the study sponsor (Glaxo SmithKline) and will be included in study reports and presentations to the study sponsor. Please note that any data submitted will not be used outside of this study or published online for example on Facebook or video sharing websites such as YouTube.

### **How will my information be protected?**

All information that you provide will be kept strictly confidential. Your name and contact information will remain with Adelphi Values and will only be accessible to the research staff.

The audio-recording of the interviews and any audio or video responses to the optional app task will be transcribed (typed up word for word). All information collected during this study will be assigned a unique ID number. Any identifiable information including names and addresses that are reported in the interviews will be removed during the transcribing and analysis process. All information collected during this study (e.g. paperwork, data files and reports produced about the data) will be used for the purpose of this study only and will be kept confidential and anonymized. If information about this study is published, your name will not be given.

If you choose to participate in the app task, please note that for some questions/tasks you will have the option to submit video, picture, audio and text responses. If you choose to take part in the app task and choose to submit videos of yourself or pictures, anonymity of the data cannot be guaranteed if your face is visible in the recordings and images that are uploaded. If you consent to participate in the real-time data app task you agree that full anonymity of the data cannot be guaranteed. This data however will still be labelled and stored with your unique ID number. For each app question/task you will have the option of how you respond (e.g. video, audio, photograph/text).

Your interview transcripts, app task responses, audio recordings and study paperwork will be stored on Adelphi Values' computer system in a folder that is password protected so only the research staff will have access to it. It will be archived in this way for 15 years by Adelphi Values. Prior to the storage of any video/photographic app-task responses, any data whereby your face is visible will be blurred so that this data is anonymized..

The U.S. Food and Drug Administration (FDA), Copernicus Group Independent Review Board (IRB), GlaxoSmithKline, and other federal and regulatory agencies as required may sometimes request to look at the study information of those who participate in the study. By signing this consent form, you are authorizing such access. A court of law

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could order medical records shown to other people, but that is unlikely. Therefore, should this scenario occur, full confidentiality cannot be guaranteed.

**Adverse event reporting:** As part of Adelphi Values' agreement with the study sponsor (GlaxoSmithKline), if during the interviews you mention a bad effect/problem that you have experienced while using a product made by GlaxoSmithKline, Adelphi Values must report this back to them. This is so they can monitor and learn more about the safety of their medicines. By consenting to take part in this study you agree to such information being passed on to the sponsor anonymously. You will be identified only by a study participant number.

**What are the risks or discomforts of the study?**

There is no risk of physical harm directly related to completing an interview as part of this study. There is the potential risk of loss of confidentiality should you opt to take part in the video task as part of the app task which is explained in the section: 'How will my information be protected?'

**Are there any benefits?**

You will have no direct medical benefit from your participation in this study. Participation in the study will contribute to information about the experience of nasal polyps, the suitability of the reviewed questionnaires for use in clinical trials and may benefit others in the future.

**Will I be paid to take part?**

You will receive \$200 upon completion of the 120-minute interview. If you chose to take part in the optional app task, you will receive an additional payment of \$200. Payments will be paid by electronic bank transfer or amazon voucher.

**Are there any costs?**

You will not incur any costs to take part in this study. If you take part in the optional app task, you may incur data usage charges when downloading/uploading data. We recommend setting your device to 'WiFi only' if you are concerned about using your mobile data allowance. Submitting your responses by WiFi will be free of charge and not use your data allowance.

**What are the alternatives?**

You do not have to take part in this research study.

**What if I am hurt or get sick in the study?**

If you are hurt or get sick during the study, you should call your doctor. Neither GlaxoSmithKline nor Adelphi Values have a program in place to provide other compensation in the event of an injury. Since this is a telephone interview, there is no risk of injury. No risks are associated with the app-task; however, it is expected that participants will be sensible when completing and submitting tasks required and that

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these are done in a safe environment, thus reducing any possibility of risk. Participating in this study does not restrict your right to seek legal assistance. You do not waive any legal rights by signing this Subject Information and Consent Form and HIPAA Authorization.

**Do I have to take part in the study?**

Taking part in this study is your choice. There will not be any penalty or loss of benefits to you if you decide not to take part or if you leave the study early.

**Could I be withdrawn from the study?**

Your doctor or the study sponsor, may withdraw you from the study without your consent for the following reasons:

- if you do not follow the study procedures as instructed,
- if the study is canceled by the FDA or the sponsor.

The sponsor, the FDA or the IRB may decide to stop the study at any time. You may leave the study at any time.

**Who can answer my questions about this research?**

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

Please call Copernicus Group IRB at **PPD** (toll free) if:

- You want to talk to someone about the study other than the study staff;
- You cannot reach the research team;
- You have questions about your rights as a research subject.

# Informed Consent Form and HIPAA Authorization Template

## SUBJECT'S STATEMENT OF CONSENT

Qualitative research to characterize the patient experience of nasal polyps

Please indicate by **ticking (✓)** the activities you consent to taking part in.  
Please note that the app task is **optional**.

1. I would like to take part in the 120-minute nasal polyp interview to talk about my experience of nasal polyps and provide feedback on a number of questionnaires that assess my experience of nasal polyps.
2. (OPTIONAL) In addition to the interview I would also like to take part in the 10-day app task about my experience of nasal polyps and answer some questions about my experience of taking part in this activity. I confirm I have access to a smartphone or tablet to take part in this activity.

I consent to take part in the research study. This study and the information in this consent form have been explained to me. I have read all pages of this form. I have had an opportunity to ask questions and they have been answered to my satisfaction. I have been told that I have not given up any legal rights. I will receive a copy of this signed and dated consent form.

I voluntarily agree to take part in this research study.

---

**Printed Name of Subject**

---

**Signature of Subject**

**Date**

The information about the study was described to the subject in language he/she understood.

---

**Printed Name of Person Obtaining Consent**

---

**Signature of Person Obtaining Consent**

**Date**

# Informed Consent Form and HIPAA Authorization Template

## HIPAA AUTHORIZATION

Federal regulations give you certain rights related to your health information. These include the right to know who will receive the information and how it will be used. The study doctor must obtain your authorization (permission) to use or release any health information that might identify you.

- **What information may be used and shared?**

The study doctor and study staff will use and share your health information as part of this research study. This may include your name, address, telephone number or other facts that could identify the health information as yours.

Examples of the information that may be used are:

- Medical records (from any doctor, hospital or other healthcare provider)
- Information created or collected during the research. This could include your medical history, and dates or results from any physical exams, laboratory tests or other tests.

- **Who will receive information about you?**

The study doctor and study staff will share your personal health information with:

- the sponsor, including persons or companies working for or with the sponsor
- Copernicus Group Independent Review Board
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- other regulatory agencies

- **Why will this information be used and/or given to others?**

The sponsor and the groups above will use your health information:

- to complete this research

# Informed Consent Form and HIPAA Authorization Template

- to evaluate the results of the study
- to check that the study is being done properly
- to obtain marketing approval for new products resulting from this research

- **Is my health information protected after it has been given to others?**

Your health information may be further shared by the groups above. If shared by them, the information will no longer be covered by this Authorization. These groups are committed to keeping your health information confidential.

- **What if I decide not to allow the use of my health information?**

You do not have to sign this form. If you do not sign this form, you cannot take part in this research study.

- **May I withdraw or revoke (cancel) my permission?**

YES. You may withdraw your permission to use and disclose your health information at any time. You can do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in the research study.

- **What happens if I want to withdraw my authorization?**

Information that has already been gathered may still be used and given to others. If you withdraw your permission, no new health information will be gathered unless you have a side effect related to the study.

If you withdraw from the study but do not withdraw your Authorization, new health information may be collected until this study ends.

- **Will my authorization expire?**

If you do not withdraw this Authorization, it will remain in effect.

If the research site is located in <sup>PPD</sup> [redacted] or <sup>PPD</sup> [redacted] this authorization will expire on 31 Dec 2060.

There is no expiration of this authorization except for research conducted in the states listed above.

# Informed Consent Form and HIPAA Authorization Template

- **May I review or copy the information obtained or created about me?**

YES. You have the right to review and copy your health information. However, your access to this information may be delayed until the study is complete.

Your decision to withdraw your Authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

## **AUTHORIZATION**

By signing this form, I allow the use or disclosure of my health information. I will receive a signed and dated copy of this Authorization.

---

**Printed Name of Subject**

---

**Signature of Subject**

**Date**

Date:  /  / 2017  
MM DD

Center Number: /\_\_\_/\_\_\_/

Participant N°: /\_\_\_/\_\_\_/



**Appendix 6: Patient Demographic Form**

ADELPHI VALUES

**DEMOGRAPHICS FORM**

This form is to be completed by the recruitment agency  
(Please complete a separate form for each participant recruited)

**ACTIVITIES**

Please ask the participant which activities they would like to take part in:

- 60-minute interview ONLY <sub>1</sub>
- 60-minute interview AND 10-day app activity and follow-up call to provide feedback \* <sub>2</sub>

If the participant does not want to participate in the app task, please skip straight to the demographic questions section below.

\*If the participant **DOES** want to take part in the app task, please ensure that they meet the following inclusion criteria

INCLUSION CRITERIA FOR APP TASK	YES	NO
4. Participant owns/or has access to either a smartphone (iOS or android) or tablet which has video, audio/microphone and photographic capabilities and access to either the Apple app store or google play store to download the app;	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>1</sub>
5. Participant is willing and able to take part in the real-time data application task and respond to a series of questions/tasks fielded to them via the application over the course of 10 days.  AND  Is willing to respond to some brief questions following the real-time data capture task about their experience of using the app and completing the tasks, either during their interview or in a 5-10 minute telephone call following completion of the task	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>
6. Participant has stated that they would feel comfortable recording short videos of themselves and providing audio commentary in response to questions/tasks.	<input type="checkbox"/> <sub>1</sub>	<input type="checkbox"/> <sub>2</sub>

Date:   /   / 2017  
MM DD

Center Number: /\_\_\_/\_\_\_/

Participant N°: /\_\_\_/\_\_\_/



ADELPHI VALUES

👉 If **ONE** of the above answers is **NO**, the patient **CANNOT** be included in the app task aspect of the study.

**DEMOGRAPHICS QUESTIONS**

Please complete the following questions for all participant irrespective of which research activities they would like to take part in.

1. How old are you? |\_\_|\_\_| years

2. What is your gender?

Male <sub>1</sub>

Female <sub>2</sub>

3. How long have you have you been experiencing symptoms of nasal polyps?

\_\_\_\_\_years\_\_\_\_\_ months

4. At what age were you first diagnosed with nasal polyps by a physician?

\_\_\_\_\_ years\_\_\_\_\_ months

5. Who diagnosed your nasal polyps?

Ear, nose and throat (ENT) specialist <sub>1</sub>

GP/Family doctor <sub>2</sub>

Other (please specify)\_\_\_\_\_ <sub>3</sub>

6. What is your ethnicity? (please check which applies)

Hispanic or Latino (of any race) <sub>1</sub>

Non-Hispanic or Latino <sub>2</sub>

7. What is your race? (please check one box only)

White <sub>1</sub>

Black/African American <sub>2</sub>

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- Asian or Pacific Islander  3
- Native American or Alaska native  4
- North African or Middle Eastern  5
- Multi-racial  6
- (Please specify) \_\_\_\_\_
- Other  7
- (Please specify) \_\_\_\_\_

**8. What is your highest level of education?**

- Grade school  1
- Some high school  2
- High school diploma or GED  3
- Some years of college  4
- Certificate program  5
- College or university degree (2 or 4 year)  6
- Graduate or professional degree  7
- Other (please specify) \_\_\_\_\_  8

**9. What is your current living status? (please check all that apply)**

- Living alone  1
- Living with husband/wife/partner  2
- Living with parents  3
- Living with your children  4
- Living with other family members  5
- Living with your friends  6
- Other (please specify) \_\_\_\_\_  7

**10. How would you describe your work status (Please check all that apply)**

- Working full-time  1

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Working part-time

\_2

Retired

\_3

Unemployed

\_4

Student

\_5

Other (please specify) \_\_\_\_\_

\_6

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**11. What is your approximate annual income?**

Under \$25,000 \_1

\$25,000 to \$50,000 \_2

\$50,000 to \$75,000 \_3

\$75,000 to \$100,000 \_4

More than \$100,000 \_5

Prefer not to answer \_6

**12. How would you rate your health in general?**

Excellent \_1

Very Good \_2

Good \_3

Fair \_4

Poor \_5

**Recruitment Quotas**

In addition to meeting the inclusion/exclusion criteria please ensure the following quotas are met by the sample:

Participant characteristics		Adults		Total
		18-45	46+	
<b>Age</b>		≥6	≥6	≥12
<b>Gender</b>	Male	≥2	≥2	≥6
	Female	≥2	≥2	≥6
<b>Ethnicity</b>	Hispanic or Latino (of any race)			≥6
	Non-Hispanic or Latino			≥6
<b>Race</b>	White			≥4
	Black/African American			≥4
	Multi-racial			≥2
	Other race/ethnicities <ul style="list-style-type: none"> <li>• Asian or Pacific Islander</li> <li>• Native American or Alaska native</li> <li>• North African or Middle Eastern</li> <li>• Other (specified by participant)</li> </ul>			≥2
<b>Education</b>	Some high school			≥3
	College or higher			≥3
<b>Polypectomy surgery</b>	In past 2 years			≥6
	In past 3-10			≥6

**Recruiter:** If the participant meets the inclusion criteria for the study and is appropriate based on the sample quotas above please schedule the participant for an interview.

**Appendix 7: Combined concept elicitation and cognitive debriefing patient interview guide**

# 1. Interview objectives and overview

## [Note to interviewer]:

The overall objective of this interview is to explore patients' experience of severe, recurrent nasal polyps via the conduct of concept elicitation interviews and to obtain feedback from patients on a series of patient-reported outcome (PRO) instruments designed to assess the symptom and impact experience of nasal polyps via the conduct of cognitive debriefing interviews.

The concept elicitation phase will facilitate the identification of concepts of disease experience that are important to adult patients with nasal polyps and the language they use to talk about the concepts and describe those concepts. The main areas of exploration will be the symptoms experienced by patients. In particular we are interested in the intensity, frequency and duration of each symptom, how bothersome or intrusive each symptom is to each patient, and whether/ how the collective symptom experience of nasal polyps has any impact on the patient's quality of life.

The cognitive debriefing phase will assess a number of PROs including the following:

Sino-Nasal Outcome Test (SNOT-22);

Visual analogue scales (VAS) proposed for use in GSK phase III trial:

Nasal obstruction VAS;

Nasal discharge VAS;

Throat mucus VAS;

Loss of smell VAS;

Facial pain VAS;

Overall VAS symptom score.

The relevance and appropriateness of the each of the items covered by each instrument will be assessed during the cognitive debriefing interview, as will patients' ability to read and consistently understand the item wording, instructions, response options and recall period of each instrument. The cognitive debriefing phase will also investigate how patients define a meaningful change in score, for each item of each instrument.

- **Aim of the concept elicitation phase**

Explore the symptoms experienced by adults with nasal polyps, with particular attention paid to the frequency, intensity, duration of each symptom and how bothersome it is.

Explore the language used by adult nasal polyp patients to describe their disease experience.

Explore how each symptom (individually and collectively) affects the patients' quality of life.

- **Aim of the cognitive debriefing phase**

- Evaluate the relevance of the PRO instruments to nasal polyp patients.

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- Evaluate the patients' ability to read and consistently understand the content of the collection of PRO instruments, such as the item wording, instructions, response options and recall period.
- Investigate how patients define a meaningful change in score, for each item of each of the instruments.

*(PRO instruments include: SNOT-22, Nasal obstruction VAS, Nasal discharge VAS, Throat mucus VAS, Loss of smell VAS, Facial pain/pressure VAS and an overall severity of condition VAS scale).*

- **Overview of the interview process**

The interview should be conducted as follows:

1. **Introduction to the study:** Introduce Adelphi Values to the patient. Explain the objectives and the process of the interview.
2. **Consent:** Ensure the patients' written informed consent to participate has been obtained prior to beginning the interview. Also obtain the patients' verbal consent for the interview to be audio-recorded.
3. **Interview:** In the interviews you should ask the patient questions in an open-ended exploratory manner. Lead the patient as little as possible in this part of the interview.

The interview is divided into the following sections:

1. Introduction to the study (5 minutes)
2. Experience of nasal polyps (55 minutes)
3. Cognitive debriefing of the collection of PRO instruments (60 minutes)

In total, the interview should take approximately **120 minutes.**

## 2. Role of the interviewer and instructions

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### The role of the interviewer before the interview:

1. Check that the patient's clinician has completed the CRF and screener and that the patient meets the inclusion and exclusion criteria.
2. Check the patient has provided written informed consent and provided verbal consent for the interview to be audio-recorded.

### The role of the interviewer during the interview

- **Digital Audio recording.** Ensure that the comments of the patient throughout the interview are clearly recorded on the audio-recording. Audio recordings will be transcribed verbatim. Check the volume settings and positioning of the audio recorder to ensure the clarity of the audio recording prior to the interview making sure recordings are clearly audible. Check that the audio recorder has enough battery power for the duration of the interview. Avoid rustling papers near the recorder or jostling the recorder during the interview as this will lead to inaudible responses.

### The role of the interviewer is to **inquire** and **support**:

Do not give your own point of view

Be patient and accept silence during open-ended questioning to make sure the patient has time to think about her/his response

Help the patient stick to the topics intended in the guide (but not necessarily in the order presented in the guide)

Help the patient avoid repeating himself or herself

Help the patient cross-reference and make connections that they would not do spontaneously

Ask the patient to clarify any comments that you are not certain you understood and for the benefit of the recording

Ask the patient to explain any vague reference or comment that is pertinent to the research question

**Most importantly:** avoid biasing or leading the patient

**As much as possible your questions should be open-ended and general rather than specific – use suggested probes to follow-up on topics of interest if not adequately discussed in response to the open questions.**

**It is very important that you do not lead the patient with your questions or remarks.** Ask all questions in as open-ended a manner as possible; take care not to bias the patient's response one way or the other. Below for most questions, we have provided a number of possible probes that should help the patient explain his or her thinking when s/he is talking about the topics of interest. These probes are

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**optional** and do not have to be asked if, when asked the initial question, the patient provides a fully elaborated response and addresses the topics noted in the probes. The probes are only provided for use when the patient finds it difficult to answer your questions, if s/he is reluctant to speak at length about experiences or if key topics of interest have not been elicited spontaneously. You may have to invent your own probes or reword the probes indicated in the interview guide; this is fine. As a fully trained and experienced interviewer we rely on your judgment as to when more information is required from the patient and for you to probe as appropriate.

POSSIBLE NON-LEADING PROBES MIGHT INCLUDE:

- Can you describe exactly how that feels?
- Tell me more about that.
- How does that affect you?
- Can you talk more about \_\_\_\_\_?
- How often does that happen?
- How long does that last?
- Is there anything that makes it better or worse?

During the interview, it is not essential for you to ask the questions in exactly the way that they are written in this guide and for some interviewees it may be necessary for you to reword questions as a means to enable open-discussion. If you reword a question; however, you should be sure to avoid biasing the patient’s response. If a topic has been covered sufficiently in an earlier part of the discussion it is not necessary to go over it again later if this topic comes up later in the interview guide.

If the patient directs any questions to you that are of a medical nature, please explain that you are not a medical professional and that the patient should direct any medical queries to his or her doctor or nurse.

**Using the interview guide**

Throughout this guide we have coded the questions and instructions so that it is clear which questions are required and which are probes and do not necessarily need to be asked. The code is as follows:

<i>Blue font</i>	These are instructions to you
	These are statements that you are to read aloud word-for-word
<b>1.</b>	Questions prefixed by a specific number must be posed to all patients
•	All probes are bulleted – these do not need to be used specifically but are included to assist you in drawing further information from the patients

**Adverse event reporting**

If the respondent mentions an adverse event experienced while taking a product made by the sponsor company, or a product you suspect is a product made by the sponsor company, whether it is considered serious (see definitions below) or not, you should make a note of it and at the end of the interview go through the ‘**Adverse Event Form**’. At this time please state the following to the patient:

🗣️ *“During the interview you mentioned a problem that you experienced while taking [product name]. The sponsor of this research needs to collect information about their products in order to continue making them as safe and effective as possible. Every report they receive contains potentially useful information. I would like to spend a couple of minutes with you now to collect some more details. Is that OK with you?”*

**If yes** *“Thank you. The information you provide will be sent to the study sponsor, who may wish to contact your doctor for further information. If you agree to provide your doctor’s name, this will not be linked in any way to your other responses given during the interview. Are you happy to provide the name of your doctor?”*

(If the respondent subsequently says no, then go to the ‘If no’ section)

**If no** *“OK that’s fine. However, as the information you were given about this study explained, we do have to report this problem to the sponsor. This will be done anonymously, and none of your personal details will be shared with them.”*

You should complete the **‘Adverse Event Form’** with as much detail as you can retrieve.

Remember, an Adverse Event must be reported when the following are present:

**PREP – Patient, Reporter, Event, Product**

**1. A Patient or group of patients**

- Identifiers such as age, age group, birth date, gender, role, profession should be collected if available, if not the event should still be reported.

**2. An identifiable Reporting source**

- Information that identifies the reporter, establishing knowledge of the reportable event in an identifiable consumer.
- A reporter can be a patient, doctor, patient’s parent, friend, colleague or caregiver.

**3. An adverse Event**

- Description of at least one event or product complaint.

**4. A suspect Product**

- This must be one of the products being marketed by the company that we are doing research for.

**Remember:** The event need not have a causal relationship with the treatment or usage.

An adverse event is:

***“Any untoward medical occurrence in a patient administered a sponsor medicinal product and which does not necessarily have to have a causal relationship with this treatment. An adverse event can be any unfavorable and unintended sign (e.g. an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.”***

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An adverse event can also be revealed through follow up on a product complaint (PC). For these purposes a PC is a complaint specific to the product itself, or packaging, as opposed to its effect on the patient. Examples include damaged or missing tablets; wrong strength or color of tablets; damaged packaging; a label that cannot be read; a liquid that should be clear but is cloudy or contains unexpected particles; a bent needle, a broken syringe; a missing patient information leaflet or the identification of a potentially counterfeit medicine.

Cases where a woman is pregnant or breastfeeding while taking a company's medicine also need to be collected even if no AE is specifically cited. In these instances, it is important to capture whether or not there were any complications during the pregnancy or any congenital abnormalities occurring in the baby.

A **serious adverse event** (which should be reported to the FDA) is any undesirable experience associated with the use of a medical product in a patient when the patient outcome is:

### **Death**

Report if you suspect that the death was an outcome of the adverse event, and include the date if known.

### **Life-threatening**

Report if suspected that the patient was at substantial risk of dying at the time of the adverse event, or use or continued use of the device or other medical product might have resulted in the death of the patient.

### **Hospitalization (initial or prolonged)**

Report if admission to the hospital or prolongation of hospitalization was a result of the adverse event. Emergency room visits that do not result in admission to the hospital should be evaluated for one of the other serious outcomes (E.g., life-threatening; required intervention to prevent permanent impairment or damage; other serious medically important event).

### **Disability or permanent damage**

Report if the adverse event resulted in a substantial disruption of a person's ability to conduct normal life functions, i.e., the adverse event resulted in a significant, persistent or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities and/or quality of life.

### **Congenital anomaly/birth defect**

Report if you suspect that exposure to a medical product prior to conception or during pregnancy may have resulted in an adverse outcome in the child.

### **Required intervention to prevent permanent impairment or damage (devices)**

Report if you believe that medical or surgical intervention was necessary to preclude permanent impairment of a body function, or prevent permanent damage to a body structure, either situation suspected to be due to the use of a medical product.

### **Other serious (important medical events)**

Report when the event does not fit the other outcomes, but the event may jeopardize the patient and may require medical or surgical intervention (treatment) to prevent one of the other outcomes.

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Examples include allergic bronchospasm (a serious problem with breathing) requiring treatment in an emergency room, serious blood dyscrasias (blood disorders) or seizures/convulsions that do not result in hospitalization. The development of drug dependence or drug abuse would also be examples of important medical events.

### 3. Interview introduction (5 minutes)

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This interview should last approximately **120 minutes**.

#### **INTRODUCE YOURSELF AS WORKING FOR ADELPHI VALUES**

- 🗣️ *“My name is \_\_\_\_\_ and I work for a company called Adelphi Values. Adelphi Values is a research company which works with pharmaceutical companies to develop questionnaires for use in clinical studies to assess the impact of health conditions on people’s lives. GlaxoSmithKline, the sponsor of this study, would like to explore individuals’ experience of nasal polyps to find out more about the symptoms experienced and how the condition affects their lives.”*

#### **EXPLAIN THE AIM AND PROCESS OF THE INTERVIEW TO THE PATIENT**

- 🗣️ *“We would like to talk to you about your experience of living with nasal polyps, particularly the symptoms you experience and how having nasal polyps may impact you. This part of the interview will take approximately 55-minutes.”*
- 🗣️ *“We would also like to obtain your opinion of a number of questionnaires, including their relevance to nasal polyps and your understanding of their content. This part of the interview will take approximately 60-minutes.”*
- 🗣️ *When we’re finished with the interview, you will receive a payment of \$200 to thank you for your time and your participation in the interview.”*

#### **REASSURE THE PATIENT OF CONFIDENTIALITY**

- 🗣️ *“Your name and contact information will remain with Adelphi Values and will only be accessible to researchers directly involved with this project. Any information you provide will be reported in a way that protects your privacy by avoiding any mention of your name or other information that could identify you.*

#### **AUDIO-RECORDING THE INTERVIEW**

- 🗣️ *“The interview today will be audio-recorded to enable us to pay careful attention to what you say and to make certain we accurately capture the information that you provide to us during the interview. After the interview the audio-recording will be transcribed (written out).”*
- 🗣️ *“An anonymized recording or written version of the interview may be shared with the study sponsor. This means that we will take any information out of the interview that might identify you, like names or places, and any data that you provide will be assigned an ID number.”*
- 🗣️ *“Please try to speak relatively loudly so that your comments can be heard and are clear on the recordings.”*
- 🗣️ *“Please be honest in your responses and don’t be afraid to voice any opinions. We want to know about your experience and opinions, not those of your doctor or anyone else.”*
- 🗣️ *“If you do not understand a question, please ask for the question to be repeated and explained.”*

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💡 **IMPORTANT:** *“If you find any of the questions difficult to answer, please let me know. You do not have to answer any questions you do not want to. You may leave the interview at any point and you may decline to answer any question.”*

**At this point, turn on the audio-recorder and ask the patient the following questions:**

- 💡 *“Do you agree to participate in this interview?”*
- 💡 *“Do you agree to have this interview audio-recorded?”*
- 💡 *“Do you have any questions at this point?”*

## 4. Concept elicitation: exploration of the patient experience of nasal polyps (55 minutes)

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- Nasal polyp symptoms (35 minutes)**

🗣️ *“This is the first section of the interview where I will ask you general questions about your experience of having nasal polyps.”*

**[Note to the interviewer]:** First ask the participant how they refer to their condition and use this terminology in place of ‘nasal polyps’ throughout the interview.

**5. When you talk to your family or friends about your nasal condition, how do you refer to it? What do you call it? Is it ok to use this term throughout the interview?**

**[Interviewer]:** Enter term/s used \_\_\_\_\_

🗣️ *“We are now going to talk about the symptoms that you experience as a result of your nasal polyps.”*

**6. Tell me about your experience of nasal polyps.**

**7. Tell me about the symptoms that you experience related to your nasal polyps.**

**[Note to the interviewer]:** List down every symptom that the patient mentions spontaneously as a symptom that they experience. You can use the ‘symptom table’ below to record symptoms that the patient mentions spontaneously. If the symptom is not on the list, please write it down.

### SYMPTOM LIST

Symptom	Tick if mentioned spontaneously (✓)
Congestion	
Runny nose	
Nasal swelling	
Loss of smell	
Change in smell	
Nose bleed	
Post-nasal drip/throat mucus	
Nasal pain	
Nasal pressure	
Sneezing	
Visible polyps	

Symptom	Tick if mentioned spontaneously (✓)
Mucus/catarrh	
Nasal tightness	
Sinus blockage	
Sinus inflammation	
Sinus infections	
Difficult breathing	
Wheezing	
Cough	
Head/facial pressure	
Headache	
Dizziness	
Dry throat/mouth	
Loss of taste	
Distorted voice	
Ear congestion	
Illness and infection	
<b>Patient mentioned symptoms not currently in list:</b>	

**[Note to interviewer]:** Now ask the participant the following questions about each sign/symptom that they mentioned spontaneously. Allow the participant to answer spontaneously at first and only probe further if the participant is having difficulty discussing his/her experience or hasn't previously mentioned the probed topics. Please note that the probes are to be used as a guide and they may not all need to be asked.

**[Note to interviewer]: For each symptom mentioned ask the following questions:**

<b>Symptom description</b>	<ul style="list-style-type: none"> <li>• How would you describe this symptom? How does it make you feel?</li> <li>• Tell me about any additional words you use to describe this symptom, if at all.</li> </ul>
<b>Frequency</b>	<ul style="list-style-type: none"> <li>• How often do you experience this symptom?</li> <li>• Does the frequency vary/has it changed over time? Please tell me about this.</li> <li>• Does the frequency vary in the daytime versus the nighttime? Tell me about that.</li> <li>• Is it a constant symptom or does it come and go? Tell me about that.</li> </ul>
<b>Severity</b>	<ul style="list-style-type: none"> <li>• How would you describe the severity of this symptom?</li> <li>• Does the severity vary/has it changed over time? Please tell me about this?</li> <li>• Does the severity change in the daytime versus the nighttime? Time me about that</li> <li>• How would you describe mild, moderate and severe [insert symptom]?</li> </ul>
<b>Duration</b>	<ul style="list-style-type: none"> <li>• How long does this symptom typically last for?</li> <li>• Does the duration vary/has it changed over time? Please tell me about this.</li> </ul>
<b>Impacts</b>	<ul style="list-style-type: none"> <li>• How does this symptom affect you in your daily life?</li> <li>• How bothersome is this symptom for you? Please tell me more about that. <ul style="list-style-type: none"> <li>○ Physically?</li> <li>○ Doing your daily/usual activities?</li> <li>○ In doing things/relationships with family or friends?</li> <li>○ Emotionally?</li> <li>○ At school/work?</li> </ul> </li> </ul>
<b>Worsening / Improvement</b>	<ul style="list-style-type: none"> <li>• Tell me about anything that makes this symptom worse.</li> <li>• Tell me about anything that makes this symptom better.</li> </ul>
<b>Relation to other symptoms</b>	<ul style="list-style-type: none"> <li>• Do you experience this symptom on its own or at the same time as other symptoms? Please tell me more about that.</li> </ul>

**[TO INTERVIEWER]** Please probe on those symptoms in the ‘symptom list’ above, that were not spontaneously mentioned by the participant. Please assess relevance of the symptom first. If the participant experiences the symptom in question please ask the additional questions detailed in the table above.

**8. Have you ever experienced any of the following symptoms as part of your nasal polyps?**

**9. Are there any other symptoms of nasal polyps not already discussed that you have experienced? Please tell me about them.**

**10. Which of the symptoms that you described are the worst? Why?**

**11. Which of the symptoms that you described do you experience most frequently/least frequently?**

**12. Which of the symptoms that you described are most bothersome/least bothersome to you? Why?**

**13. Can you tell me about anything that makes your nasal polyp symptoms better?**

- *Medication?*
- *Coping strategies/lifestyle changes?*

**14. Can you tell me about anything that makes your nasal polyps worse?**

- *Does this affect specific symptoms or do your symptoms worsen equally? Tell me about this.*

- **Living with nasal polyps (10 minutes)**

 *"We are now going to talk about what it is like to live with nasal polyps."*

**15. Tell me what it is like to live with nasal polyps on a daily basis.**

- *How does nasal polyps affect you in your daily life?*
- *Tell me what a good day is like with your nasal polyps. Tell me what a bad day is like with your nasal polyps.*
- *Are there any things that you are not able or find difficult to do because of nasal polyps?*
- *Are there any things that you have to do differently because of nasal polyps? Please tell me about this.*
- *Which symptoms of nasal polyps have had the biggest impact on your life? Tell me why.*

**16. In what ways, if at all, has nasal polyps affected you physically?**

- *How has nasal polyps affected the physical activities you do? Please tell me about this.*
- *Do the physical impacts vary or change over time? (E.g. frequency, severity, duration).*
- *Which symptom(s) of your nasal polyps has the biggest impact on you physically? Why?*
- *Tell me about anything you do to cope with/manage the physical impacts of nasal polyps (e.g. have you made any changes to your life to accommodate these physical impacts?)*

**17. In what ways, if at all, has nasal polyps affected your sleep?**

- *Has nasal polyps affected your sleep quality? Tell me about that.*
- *Has nasal polyps affected how much sleep you can get in in a night? Tell me about that*
- *Which symptom(s) of your nasal polyps has the biggest impact on your sleep? Why?*
- *Tell me what you do to cope with the sleep impacts caused by your nasal polyps.*

**18. In what ways, if at all, has nasal polyps affected you emotionally/psychologically?**

- *Tell me about any emotional impacts you experience as a result of nasal polyps.*
- *Do the emotional impacts vary or change over time? (E.g. frequency, severity, duration).*
- *Which symptom(s) of your nasal polyps has the biggest impact on you emotionally? Why?*
- *Tell me about anything you do to cope with/manage the emotional impacts of nasal polyps*

**19. In what ways, if at all, has nasal polyps affected you in doing things with family and friends?**

- *Has nasal polyps affected your participation in social activities? Tell me about that*
- *Which symptom(s) of your nasal polyps has the biggest impact on your social life? Why?*
- *Has nasal polyps affected your relationships with family/friends? Tell me about that*
- *Which symptom(s) of your nasal polyps has the biggest impact on your relationships with others? Why?*

**20. In what ways, if at all, has nasal polyps affected your work activities?**

- *How do the nasal polyp symptoms that you discussed affect your work activities?*
- *Is there anything that you find challenging at work due to the nasal polyp symptoms that you experience? Please tell me about this.*
- *Have you ever had to take time off work because of your nasal polyps? Please tell me about this.*
- *Which symptom(s) of your nasal polyps has the biggest impact on your work activities? Why?*

**21. In what ways, if at all, has nasal polyps affected you financially?**

- **Treatment/surgical experiences (10 minutes)**

**22. How easy or difficult was it to choose to have surgery? Tell me about the things you considered in making your decision.**

- *When deciding whether to have nasal polyp surgery, which symptom(s) were those you wanted to be reduced the most by surgery?*

**23. Tell me about your experience of having nasal polyp surgery?**

- *What effect did surgery have on your symptoms and any impacts you experienced?*
- *How did having the nasal polyp surgery impact your life?*
- *What were the positives of having surgery (if any)?*
- *Were there any negatives or drawbacks of having surgery?*
- *Would you choose to have additional surgeries to remove your nasal polyps? Why/why not?*

**24. How have the treatments that you have taken for your nasal polyps impacted your life (if at all)? This may include prescribed, over-the-counter and alternative treatments.**

- *What was good about these treatments?*
- *What was bad about these treatments?*

**25. If you were to take a treatment for your nasal polyps, what would make you think that it was worth taking?**

- *How would the symptoms that you experience have to change?*
  - *What change would you like to see in the severity of your symptoms? (probe on the percentage decrease i.e. 50% less or 70% less)*
    - *What is the smallest change that you would be happy with?*
  - *What change would you like to see in how often you experience symptoms?*
    - *What is the smallest change that you would be happy with?*
  - *What change would you like to see in the length of time that your symptoms last for?*
    - *What is the smallest change that you would be happy with?*
  - *What change would you like to see in how bad your symptoms get?*
    - *What is the smallest change that you would be happy with?*
  - *How important is no longer experiencing symptoms at all?*
  - *Which symptoms would be most important to you to treat? Why?*
  - *How would these changes affect your life?*

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**26. Is there anything else you would like to tell me about your nasal polyps that we haven't already discussed?**

## 27. Think aloud cognitive debriefing (60 minutes)

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**[TO INTERVIEWER]** Ask the participant to read **aloud** the instructions, each item and the responses they choose for each questionnaire. After the participant has responded to each item ask the participant the corresponding questions in the table below. Ask the participant to complete **all** of the questions.

- 💡 *“For each instruction and question of each of the following questionnaires, I want you to read it out loud, and tell me what you are thinking when you are answering. Please tell me any thoughts or opinions you have on the instructions and questions as you read them and tell me why you selected the answer you did.”*
- 💡 *“After you respond to each question I am going to ask you some questions about each instruction/item. These will be about your understanding of the item and its relevance to your experience with nasal polyps. Additionally, I will ask you about the response options you selected for each assessment and what it would mean to you to select a different response option.”*
- 💡 *“You may decline to answer any question”*
- 💡 *“The questions I ask may be a bit repetitive, but they are important so that we can see how you understand each question.”*

**[TO INTERVIEWER]**

## Interviewer instructions

- You may need to keep reminding the participant to read and think aloud. Please have the patient read aloud the response they have chosen so this can be recorded.
- If the participant has difficulty reading a particular item, offer to read it for them and make a note of this.
- **Make sure you are non-judgmental in your tone** when probing. If the participant hesitates when answering, use one or more of the following probes, or similar questions to elicit comments from them. Please feel free to vary which ones you ask for each questionnaire item – rather than going through each one in rote fashion and getting one word answers. **Not every probe has to be used for every item/participant.**
- **Asking why:** if appropriate, probe further by asking the participant why they have answered the interview question in that way.
- If the patient has chosen to **skip a question** remember to ask why they have chosen to do so.
- If the patient has chosen “0” or “not applicable” option for any question ask why they have made this selection
  - Was the question not relevant? (e.g. they do not experience this symptom)
  - Is the question relevant, although they might not be currently experiencing this symptom?
- Wherever possible, please make brief notes in the empty boxes provided for each item to summarize:
  - How the question was **understood** by the participant?
  - Was the concept **relevant** to the participant?
  - How **easy/difficult** was it for the participant to choose their answer?
  - Why did they choose the answer they did? [please record their answers in the box below]

Date:  /  / 2017  
MM DD

Center Number: /\_\_\_/\_\_\_/

Participant N°: /\_\_\_/\_\_\_/



• **Cognitive debriefing of the SNOT-22**

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
<p><b>[INSTRUCTION 1]</b> Below you will find a list of symptoms and social/emotional consequences of your rhinosinusitis. We would like to know more about these problems and would appreciate your answering the following questions to the best of your ability. There are no right or wrong answers and only you can provide us with this information. Please rate your problems as they have been over the past <u>two weeks</u>. Thank you for your participation. Please do not hesitate to ask for assistance if necessary.</p>			
<p>In your own words, what is this instruction asking you to do? What does “social/emotional consequences” mean to you? What does “rhinosinusitis” mean to you? What does “problems” in relation to your condition mean to you?</p>		<p>What does “over the past two weeks mean to you”? How easy or difficult is it to remember your symptoms over the last two weeks? Do you think that it is appropriate to answer questions about your nasal polyps thinking back to the past two weeks? Tell me about that.</p>	
<p><b>[INSTRUCTION 2]</b> Considering how severe the problem is when you experience it and how often it happens, please rate each item below on how “bad” it is by selecting the number that corresponds with how you feeling using this scale.</p>			
<p>In your own words, what is this instruction asking you to do? What does “severe” mean to you? What does “how bad” mean to you? What does “how often it happens” mean to you? What does “corresponds with how you are feeling” mean to you?</p>	<p>Based on your experience of nasal polyps, do you think that how bad your symptoms are (severity) and how often you experience a symptom (frequency) can be assessed at the same time? Are they the same or different? Why?</p>		<p>How would you describe: “No problem” “Very Mild Problem” “Mild or Slight Problem” “Moderate Problem” “Severe Problem” “Problem as bad as it can be”</p>
<p><b>[QUESTION 1] Need to blow nose</b></p>			
<p>What does “need to blow nose” mean to you? Would you use any other words to describe this symptom?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “need to blow nose” separately, rather than together? Why?</p>	<p>What time frame were you thinking about when answering this question? Was it easy or difficult to remember over the past 2 weeks? Did you think about both how bad the symptom is and how often you experience it? Why/Why not?</p>	<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
	What would your severity based and frequency based scores be?		
<b>[QUESTION 2] Nasal blockage</b>			
<p>What does “nasal blockage” mean to you?</p> <p>Would you use any other words to describe this term?</p> <p>Is “nasal blockage” the same or different to “need to blow nose”? Why?</p>	<p>Do you experience this as part of your nasal polyps?</p> <p>Why did you choose an answer of [X]?</p> <p>Would your score be different if you were asked to rate the severity and frequency of your “nasal blockage” separately, rather than together? Why?</p> <p>What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why?</p> <p>What change in score would make a difference to you and why?</p>
<b>[QUESTION 3] Sneezing</b>			
<p>What does “sneezing” mean to you?</p> <p>Would you use any other words to describe this term?</p>	<p>Do you experience this as part of your nasal polyps?</p> <p>Why did you choose an answer of [X]?</p> <p>Would your score be different if you were asked to rate the severity and frequency of your “sneezing” separately, rather than together? Why?</p> <p>What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question?</p> <p>What change in score would make a difference to you and why?</p>
<b>[QUESTION 4]: Runny nose</b>			
<p>What does “runny nose” mean to you?</p> <p>Would you use any other words to describe this term?</p> <p>Is “runny nose” the same or different to “a need to blow nose”? Why?</p> <p>Is “runny nose” the same or different to “nasal blockage”? Why?</p>	<p>Do you experience this as part of your nasal polyps?</p> <p>Why did you choose an answer of [X]?</p> <p>Would your score be different if you were asked to rate the severity and frequency of your “runny nose” separately, rather than together? Why?</p>		<p>How easy or difficult was it for you answer this question? Why?</p> <p>What change in score would make a difference to you and why?</p>

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
	What would your severity based and frequency based scores be		
<b>[QUESTION 5] Cough</b>			
<p>What does “cough” mean to you? Would you use any other words to describe this term?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “cough” separately, rather than together? Why? What would your severity based and frequency based scores be?</p>	<p>What time frame were you thinking about when answering this question? Was it easy or difficult to remember over the past 2 weeks? Did you think about how bad the symptom is and how often you experience it? Why/Why not?</p>	<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>
<b>[QUESTION 6] Post-nasal discharge</b>			
<p>What does “post-nasal discharge” mean to you? Would you use any other words to describe this term? Is “post-nasal discharge” the same or different to “runny nose”? Why?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “post-nasal discharge” separately, rather than together? Why? What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>
<b>[QUESTION 7] Thick nasal discharge</b>			
<p>What does “thick nasal discharge” mean to you? Would you use any other words to describe this term? Is “thick nasal discharge” the same or different to “runny nose”? Why? Is “thick nasal discharge” the same or different to “post-nasal</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “thick nasal discharge” separately, rather than together? Why?</p>		<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
discharge"? Why?	What would your severity based and frequency based scores be?		
<b>[QUESTION 8] Ear fullness</b>			
<p>What does "ear fullness" mean to you? Would you use any other words to describe this term?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your "ear fullness" separately, rather than together? Why? What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>
<b>[QUESTION 9] Dizziness</b>			
<p>What does "dizziness" mean to you? Would you use any other words to describe this term?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your "dizziness" separately, rather than together? Why? What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>
<b>[QUESTION 10] Ear pain</b>			
<p>What does "ear pain" mean to you? Would you use any other words to describe this term? Is "ear pain" the same or different to "ear fullness"? Why?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your "ear pain"</p>	<p>What time frame were you thinking about when answering this question? Was it easy or difficult to remember over the past 2 weeks? Did you think about how bad the</p>	<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
	separately, rather than together? Why? What would your severity based and frequency based scores be?	symptom is and how often you experience it? Why/Why not?	
<b>[QUESTION 11] Facial pain/pressure</b>			
What does “facial pain” mean to you? What does “facial pressure” mean to you? Is “facial pain” the same or different to “facial pressure”? Why? Would you use any other words to describe these terms? Where on the face do you think about? Full face or specific areas? Tell me about that.	Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Do you think that it’s appropriate to assess facial pain and pressure in one question? Why/why not? Would your scores be different if you were asked to rate “facial pain” and “facial pressure” separately? Would your score be different if you were asked to rate the severity and frequency of your “facial pain” and “facial pressure” separately, rather than together? Why? What would your severity based and frequency based scores be for each?		How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?
<b>[QUESTION 12] Decreased sense of smell/taste</b>			
What does a “decreased sense of smell” mean to you? What does a “decreased sense of taste” mean to you? Would you use any other words to describe these terms?	Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Do you think that it’s appropriate to assess decreased sense of smell and taste in one question? Why/why not? Would your scores be different if you were asked to rate “decreased smell” and “decreased taste” separately?		How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
	<p>Would your score be different if you were asked to rate the severity and frequency of your “decreased sense of smell” and “decreased sense of taste” separately, rather than together? Why?</p> <p>What would your severity based and frequency based scores be for each?</p>		
<p><b>[QUESTION 13] Difficulty falling asleep</b></p>			
<p>What does difficult falling asleep mean to you?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “difficulty falling asleep” separately, rather than together? Why? What would your severity based and frequency based scores be?</p>	<p>What time frame were you thinking about when answering this question? Was it easy or difficult to remember over the past 2 weeks? Did you think about how bad the impact is and how often you experience it? Why/Why not?</p>	<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>
<p><b>[QUESTION 14] Wake up at night</b></p>			
<p>What does waking up at night mean to you?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “waking up at night” separately, rather than together? Why? What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
<b>[QUESTION 15] Lack of a good night's sleep</b>			
<p>What does "lack of good night's sleep" mean to you?</p> <p>Is "lack of good night's sleep" and "waking up at night" the same or different? Why?</p> <p>Is "lack of a good night's sleep" and "difficulty falling asleep" the same or different? Why?</p>	<p>Do you experience this as part of your nasal polyps?</p> <p>Why did you choose an answer of [X]?</p> <p>Would your score be different if you were asked to rate the severity and frequency of your "lack of good night's sleep" separately, rather than together? Why?</p> <p>What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why?</p> <p>What change in score would make a difference to you and why?</p>
<b>[QUESTION 16] Wake up tired</b>			
<p>What does "wake up tired" mean to you?</p>	<p>Do you experience this as part of your nasal polyps?</p> <p>Why did you choose an answer of [X]?</p> <p>Would your score be different if you were asked to rate the severity and frequency of "waking up tired" separately, rather than together? Why?</p> <p>What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why?</p> <p>What change in score would make a difference to you and why?</p>
<b>[QUESTION 17] Fatigue</b>			
<p>What does fatigue mean to you?</p> <p>Would you use any other words to describe this term?</p> <p>Is "fatigue" and "waking up tired" the same or different? Why?</p>	<p>Do you experience this as part of your nasal polyps?</p> <p>Why did you choose an answer of [X]?</p> <p>Would your score be different if you were asked to rate the severity and frequency of your "fatigue" separately, rather than together? Why?</p> <p>What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why?</p> <p>What change in score would make a difference to you and why?</p>

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
<b>[QUESTION 18] Reduced productivity</b>			
<p>What does “reduced productivity” mean to you? Would you use any other words to describe this term?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “reduced productivity” separately, rather than together? Why? What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>
<b>[QUESTION 19] Reduced concentration</b>			
<p>What does “reduced concentration” mean to you? Would you use any other words to describe this term? Is “reduced concentration” the same or different to “reduced productivity”? Why?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “reduced concentration” separately, rather than together? Why? What would your severity based and frequency based scores be?</p>		<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>
<b>[QUESTION 20] Frustration/restless/irritable</b>			
<p>What does “frustration” meant to you? What does “restless” mean to you? What does “irritable” mean to you? Would you use any other words to describe these words? Are these terms the same or different? Why?</p>	<p>Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate “frustration”, “restlessness” and “irritability” separately? What scored would they be? Would your score be different if you were asked to rate the severity</p>		<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
	and frequency of your “frustration” separately, rather than together? Why? What would your severity based and frequency based scores be?		
[QUESTION 21] Sad			
What does “sad” mean to you? Would you use any other words to describe this term?	Do you experience this as part of your nasal polyps? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “sadness” separately, rather than together? Why? What would your severity based and frequency based scores be?	What time frame were you thinking about when answering this question? Was it easy or difficult to remember over the past 2 weeks? Did you think about how bad the impact is and how often you experience it? Why/Why not?	How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?
[QUESTION 22] Embarrassed			
What does “embarrassed” mean to you? Would you use any other words to describe this term?	Do you experience this as part of your nasal polyps? ? Why did you choose an answer of [X]? Would your score be different if you were asked to rate the severity and frequency of your “sadness” separately, rather than together? Why? What would your severity based and frequency based scores be?		How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?

**General feedback on SNOT-22**

ADELPHI VALUES

🗨️ *We would also like to have your feedback on the questionnaire overall.*

**28. What do you think of the questionnaire in general?**

- *What did you like/dislike about the questionnaire?*
- *What did you find easy/difficult*

**29. Are there any symptoms or impacts that you experience due to your nasal polyps that you feel are missing from the questionnaire?**

**30. Do you have any further comments about this questionnaire that we haven't already discussed?**

Date:  /  / 2017  
MM DD

Center Number: /\_\_\_/\_\_\_/

Participant N°: /\_\_\_/\_\_\_/



• Cognitive debriefing of VAS scales

ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
<p><b>[NASAL OBSTRUCTION VAS] ‘Please rate your nasal obstruction at its worst over the previous 24 hours’</b>  <b>[SCALE] 0 (none) – 100 (as bad as you can imagine)</b></p>			
<p>What does “nasal obstruction” mean to you?            Would you use any other words to describe this term?            What does “at its worst mean to you”?            “What does “over the previous 24 hours mean to you”?            What does “0 none” mean to you?            What does “100 as bad as you can imagine none” mean to you?</p>	<p>Do you experience this as part of your nasal polyps?            Please mark your answer on the line.            What number from 0-100 does this line represent?            Does the severity of your nasal obstruction differ over 24 hours?</p>	<p>What time frame were you thinking about when answering this question?            Was it easy or difficult to remember over the past 2 weeks?</p>	<p>How easy or difficult was it for you answer this question? Why?            What change in score would make a difference to you and why?</p>
<p><b>[NASAL DISCHARGE VAS] ‘Please rate your nasal discharge at its worst over the previous 24 hours’</b>  <b>[SCALE] 0 (none) – 100 (as bad as you can imagine)</b></p>			
<p>What does “nasal discharge” mean to you?            Would you use any other words to describe this term?</p>	<p>Do you experience this as part of your nasal polyps?            Please mark your answer on the line.            What number from 0-100 does this line represent?</p>		<p>How easy or difficult was it for you answer this question? Why?            What change in score would make a difference to you and why?</p>

Date:  /  / 2017  
MM DD

Center Number: /\_\_\_/\_\_\_/

Participant N°: /\_\_\_/\_\_\_/



ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
<p><b>[MUCUS IN THROAT VAS] 'Please rate the feeling of mucus in the throat at its worst over the previous 24 hours'</b>  <b>[SCALE] 0 (none) – 100 (as bad as you can imagine)</b></p>			
<p>What does “mucus in the throat” mean to you?            Would you use any other words to describe this term?</p>	<p>Do you experience this as part of your nasal polyps?            Please mark your answer on the line.            What number from 0-100 does this line represent?            Does your experience of mucus in throat change in severity over 24 hours?</p>	<p>What time frame were you thinking about when answering this question?            Was it easy or difficult to remember over the past 2 weeks?</p>	<p>How easy or difficult was it for you answer this question? Why?            What change in score would make a difference to you and why?</p>
<p><b>[LOSS OF SMELL VAS] 'Please rate your loss of smell at its worst over the previous 24 hours'</b>  <b>[SCALE] 0 (none) – 100 (as bad as you can imagine)</b></p>			
<p>What does “loss of smell” mean to you?</p>	<p>Do you experience this as part of your nasal polyps?            Please mark your answer on the line.            What number from 0-100 does this line represent?            Does your experience of loss of smell change in severity over 24 hours?</p>		<p>How easy or difficult was it for you answer this question? Why?            What change in score would make a difference to you and why?</p>
<p><b>[FACIAL PAIN VAS] 'Please rate your facial pain or pressure at its worst over the previous 24 hours'</b>  <b>[SCALE] 0 (none) – 100 (as bad as you can imagine)</b></p>			
	<p>Do you experience this as part of your nasal polyps?            Please mark your answer on the line.            What number from 0-100 does this line represent?</p>		<p>How easy or difficult was it for you answer this question? Why?            What change in score would make a difference to you and why?</p>

Date:  /  / 2017  
MM DD

Center Number: /\_\_\_/\_\_\_/

Participant N°: /\_\_\_/\_\_\_/



ADELPHI VALUES

Understanding	Relevance	Recall period	Response Options
<p>[OVERALL VAS SYMPTOM SCORE] ‘Overall, please rate your nasal polyps symptoms at their worst over the previous 24 hours’</p> <p>[SCALE] 0 (none) – 100 (as bad as you can imagine)</p>			
<p>What does “overall symptoms” mean to you? Do you prefer the wording of this question, or the previous question? Why?</p>	<p>Do you experience this as part of your nasal polyps? Please mark your answer on the line. What number from 0-100 does this line represent?</p>		<p>How easy or difficult was it for you answer this question? Why? What change in score would make a difference to you and why?</p>

**General feedback on VAS scales**

🗣️ *We would also like to have your feedback on the VAS scales overall.*

**31. What do you think of the scales in general?**

- *What did you like/dislike about them?*
- *What did you find easy/difficult?*

**32. Any further comments about the VAS scales?**

## 33. General feedback on real-time data capture ADELPHI VALUES

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**[TO INTERVIEWER]** The following section should only be asked to participants if they have taken part in the real-time data capture task in addition to the interview.

 *"I would now like to ask you some question about your experience of completing the real-time data capture task*

### 34. Overall how did you find the app task?

- *What did you like/dislike?*
- *What did you enjoy? Was there anything you did not enjoy?*
- *Did you find the app easy or difficult to use? Tell me about that.*
- *Did you find it easy or difficult to submit your responses? Tell me about that.*

### 35. Was it easy or difficult to fit this into your daily routine? Tell me about that.

### 36. Please tell me about your experience of downloading the app?

- *Was this easy or difficult? Tell me about that.*
- *What did you think of the instructions you were provided with to download the app?*

### 37. What did you think of the types of tasks you were asked to complete? Tell me about that.

### 38. What did you think of the ways in which you could respond to tasks? (e.g. video recording, audio recording, photographs and text)

- *Was there a response method that you preferred? If so, why?*
- *Were there any response methods that you did not choose? Tell me about that.*

### 39. What did you think of the number of task you were asked to complete?

- *Were there too many/too few?*
- *On average, how long did each task take you to complete?*

### 40. Is there anything you'd change about the app task at all to make it better?

### 41. How did you find completing the app task before/after your interview?

- *Would you have preferred to take part in the app task before/after your interview instead? Why? Tell me about that.*
- *Would you have answered any of the app tasks/questions differently had you completed the app exercises before/after your interview instead?*

### THANK THE PARTICIPANT FOR HIS/HER PARTICIPATION

Finally I would like to thank you for taking part in this interview and sharing your experiences. If this discussion has given you any concerns about your condition or treatment please contact your doctor.

**Appendix 8: Questionnaires for use in cognitive debriefing interview****QUESTIONNAIRES**

This document contains a number of questionnaires for you to complete, during your telephone interview with Adelphi Values about your nasal polyps. Within this document you will see a series of images of the questionnaire in electronic format, designed for use on a smartphone. Although you will see the questionnaire in this format you will be required to provide your answers on paper in this document by checking the relevant answer.



**IMPORTANT:** This document is for use **DURING** your telephone interview **ONLY**. Please do not complete any of the questionnaires inside this document until you are told to do so during your telephone interview.

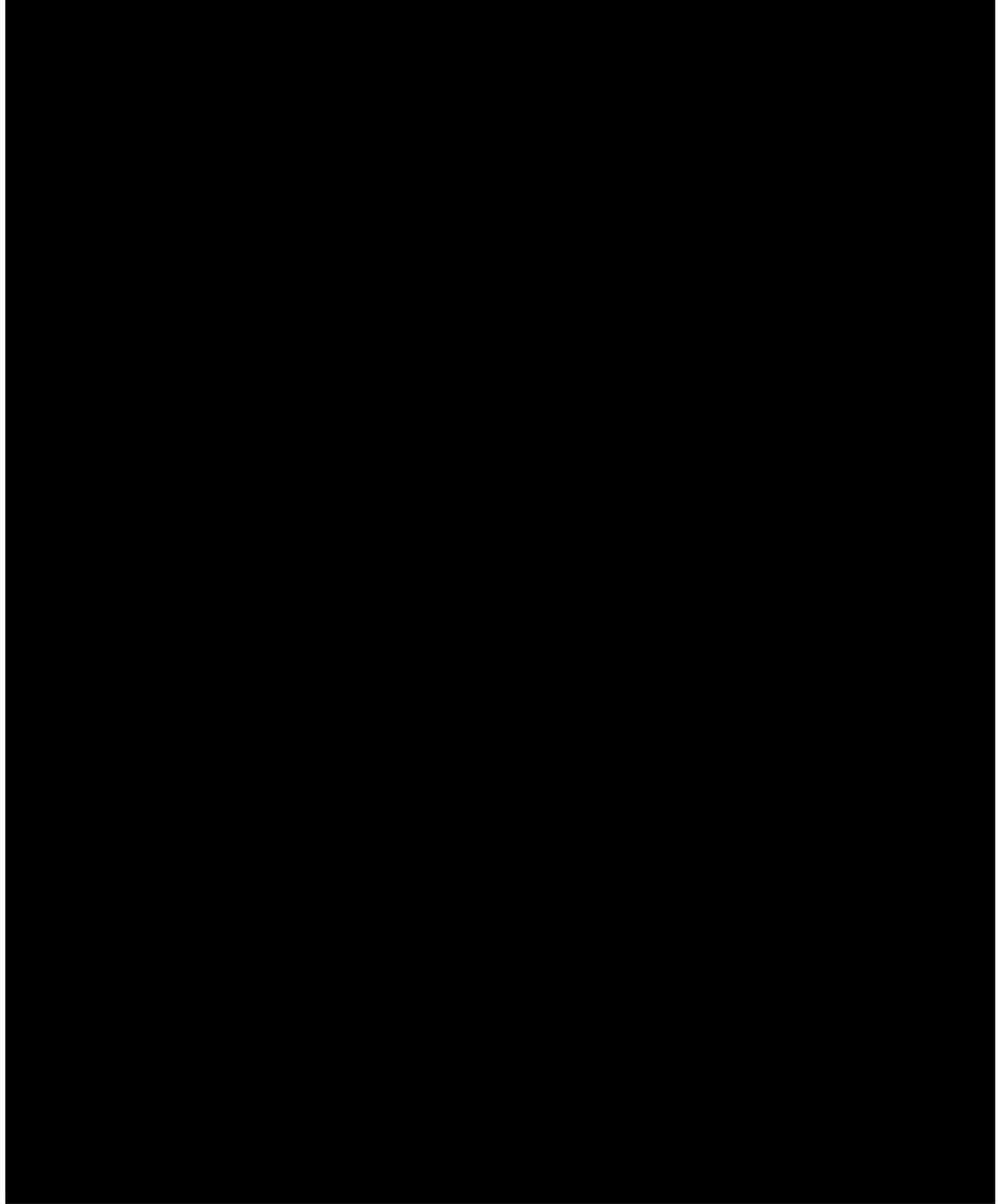
**Please keep this document and the pre-paid mail return envelope safe until your telephone interview.**

**Following the telephone interview, please mail this document to MedQuest (recruitment agency), using the pre-address and pre-paid mail envelope that has been provided.**

## Questionnaire 1: SNOT 22

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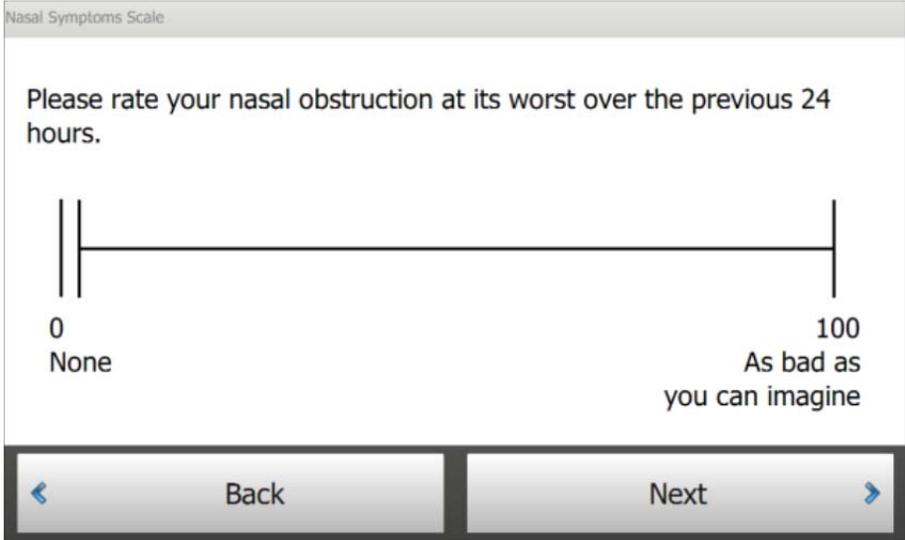
CCI - This section contained Clinical Outcome Assessment data collection questionnaires or indices, which are protected by third party copyright laws and therefore have been excluded.



# Questionnaire 2: Visual Analogue Scales

Instruction: For the following questions you are asked to rate your symptoms on a scale from 0 to 100. At the start of each rating scale you will see a single line (cursor). In electronic form on a smartphone form you would be asked to slide this line to a place on the 0-100 line that represents your answer.

Using a pen/pencil please mark on the 0-100 line using vertical line (|) where you would move the line (cursor) to that represents your answer.

A		Please write which number out of 100 your line represents
		

B	<p>Please rate your nasal discharge at its worst over the previous 24 hours.</p> <div data-bbox="269 615 1170 1152"><p>Nasal Symptoms Scale</p><p>Please rate your nasal discharge at its worst over the previous 24 hours.</p><p>0 None 100 As bad as you can imagine</p></div> <p>Back Next</p>	
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C	<p>Please rate the feeling of mucus in the throat at its worst over the previous 24 hours.</p> <div data-bbox="267 420 1169 955"><p>Nasal Symptoms Scale</p><p>Please rate the feeling of mucus in the throat at its worst over the previous 24 hours.</p><p>0 None</p><p>100 As bad as you can imagine</p><p>Back Next</p></div>	
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D	<p>Please rate your loss of smell at its worst over the previous 24 hours.</p> <div data-bbox="267 388 1172 928"><p>Nasal Symptoms Scale</p><p>Please rate your loss of smell at its worst over the previous 24 hours.</p><p>0 None 100 As bad as you can imagine</p><p>Back Next</p></div>	
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E	<p>Please rate your facial pain or pressure at its worst over the previous 24 hours.</p> <div data-bbox="267 422 1170 961"><p>Nasal Symptoms Scale</p><p>Please rate your facial pain or pressure at its worst over the previous 24 hours.</p><p>0 None</p><p>100 As bad as you can imagine</p><p>Back Next</p></div>	
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F	<p>Overall, please rate your nasal polyps symptoms at their worst over the previous 24 hours.</p> <div style="border: 1px solid gray; padding: 5px;"> <p>Nasal Symptoms Scale</p> <p>Overall, please rate your nasal polyps symptoms at their worst over the previous 24 hours.</p> <p style="text-align: center;">0 <span style="float: right;">100</span></p> <p style="text-align: center;">None <span style="float: right;">As bad as you can imagine</span></p> </div> <div style="display: flex; justify-content: space-between; margin-top: 10px;"> <span style="background-color: #ccc; padding: 5px 20px; border: 1px solid gray;">← Back</span> <span style="background-color: #ccc; padding: 5px 20px; border: 1px solid gray;">Next →</span> </div>	
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**Thank you for completing these questionnaires**

**Please put this completed document into the provided pre-addressed and pre-paid envelope, and mail it back to MedQuest.**

**Appendix 9: Example real-time data captures questions/tasks**

Example task/question	Comments/Rationale
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Example task/question	Comments/Rationale
<p><b>Introductory task/orientation to the device</b></p> <p><i>“Using video or audio, please describe your experience of living with nasal polyps.”</i></p>	<ul style="list-style-type: none"> <li>• Prior to commencing the formal app tasks/questions, in order to orient the participant to the device and the response modalities it is recommend that we include an introductory task for completion by the participants.</li> </ul>
<p><b>Nasal polyp description task</b></p> <p><i>“Please provide a written description of how you would describe nasal polyps to someone who had never heard of the condition.”</i></p>	<ul style="list-style-type: none"> <li>• In addition to understanding the patient experience of nasal polyps, additional value could be gained by getting patient to provide written description of their nasal polyps as if they were describing to someone who doesn’t know what nasal polyps are.</li> </ul>
<p><b>Assessment of global severity of nasal polyps</b></p> <p><i>“Please rate the severity of your nasal polyps today at their worst.”</i></p>	<ul style="list-style-type: none"> <li>• Asking questions such as these, on a daily basis will allow the day-to-day variability of the global severity of nasal polyps to be reported.</li> <li>• Responses to this daily question could be collected in a number of ways:               <ul style="list-style-type: none"> <li>○ Categorical response options (e.g. No symptoms through to Very severe)</li> <li>○ Numerical response scale (NRS)</li> <li>○ Implementation of the overall symptom VAS as intended for the Phase III trial. Due to variability in each participant’s screen size of their personal smart phone and the limitations of the app platform it won’t be possible to measure the VAS score as you would on paper or as would be on a provisioned electronic device. Here we would ask the participant to provide a response using a slider option (outlined in the table above) and also ask the participant to provide in a free text box the number the slider position represents.</li> </ul> </li> </ul>
<p><b>Assessment of global impact of nasal polyps</b></p> <p><i>“Please rate how much your nasal polyps affected your usual activities today”</i></p>	<ul style="list-style-type: none"> <li>• As per global severity assessment, asking questions such as these, on a daily basis will allow the day-to-day variability of the global impact of nasal polyps to be reported.</li> <li>• As described above, categorical, NRS or VAS a VAS sliding response scale could be used to respond to this task. In the case of the sliding scale VAS, a text box will also be provided for the patient to coordinate their sliding scale response to a number. .</li> </ul>
<p><b>Assessment of day in the life with nasal polyps</b></p> <p><i>“During the study period we would</i></p>	<ul style="list-style-type: none"> <li>• Participants would be asked to complete this question/task once or twice during the study period. Because this main study uses telephone interviews, questions such as these, using video/audio responses, will allow patients to give a more</li> </ul>

Example task/question	Comments/Rationale
<p><i>like to understand your experience of nasal polyps over one full day. You can choose any day during the 10-day period you would like complete this task. On your chosen day we would like you think about what you experienced, how it affected you and how you felt. You are encouraged to submit as many video or audio responses as you like as you move through your day.</i></p> <p><i>This may include submitting a response first thing in the morning to explain your experience of nasal polyps through the night (e.g. how you slept”.</i></p> <p><i>You could submit responses throughout your day as you go about your usual activities, explaining your experience of nasal polyps and how it affects you.</i></p> <p><i>You could also submit a response in the evening before bed describing your day’s experience with nasal polyps.</i></p> <p><i>These are just suggestion and you can submit any responses that you feel documents your experiences that day”</i></p>	<p>detailed description of their symptom and daily life experiences with nasal polyps and allow the researchers at AV further insight into their experience of the disease.</p>

Example task/question	Comments/Rationale
<p><b>Assessment of treatment experiences</b></p> <p><i>“Please take a photo(s) of the medications or remedies you use for your nasal polyps and provide a short text caption/description about what is shown in the photo(s) and what it means to you).”</i></p> <p><i>“Using video, audio or text response please describe which of these treatments (if any) you used today?</i></p> <p><i>What are the benefits you have seen today from these treatments?</i></p> <p><i>Is there anything you have disliked about your treatments today?”</i></p>	<ul style="list-style-type: none"> <li>• Treatments and surgical experiences and decisions for nasal polyps was discussed in both the qualitative literature and the patient blogs reviewed as part of an earlier nasal polyps literature review for GSK, and is included in the preliminary conceptual model. It is suggested that further detail regarding treatments and surgical decisions for nasal polyps is investigated using the app task.</li> </ul>
<p><b>Capturing feelings/emotions</b></p> <p><i>“During the 10-day period take photos of things that describe your experience of nasal polyps that day and how you felt. You can submit as many photographs as you like. For each photo submitted please provide a short text caption/description about what is shown in the photo and what it means to you.”</i></p> <p><i>“For each photo provided, please rate the importance of this photograph to you?” Why did you give it this number?</i></p>	<ul style="list-style-type: none"> <li>• A technique that has been utilised successfully in other AV studies is the implementation of creative exercises. Here, patients could be fielded creative question to ‘take a photo that best describes your feelings towards your nasal polyps today, and use the caption to explain why you chose this photo’. Again, this requires patient to consider their condition and experience of it differently and may allow for interesting insight. As part of this process patient could be asked to rank the importance of the photos submitted using a sliding scale. Ranking criteria could be discussed and drafted with input from GSK</li> </ul>

## Appendix 10: Adverse event form

ADELPHI VALUES

 <p><b>GSK Global Adverse Event, Pregnancy Exposure, and Incident Reporting Form for Epidemiology and Health Outcomes Studies</b></p> <p>To be completed in English</p> <p>Please send completed form to GSK within 24 hours of identifying the safety information via fax or e-mail to: Global CMG GCSP <span style="background-color: #00AEEF; color: white; padding: 2px;">PPD</span> or <span style="background-color: #00AEEF; color: white; padding: 2px;">PPD</span></p>
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Agency/Project details		
Activity type: Epidemiology <input type="checkbox"/> Health Outcomes <input type="checkbox"/>		
Project no./Activity ID:	Project title:	
Agency name:	Contact name:	
Address:		
Country:		
Tel. no:	Fax no:	E-mail:

Safety information		
Event no:	Respondent ID:	
When did the agency identify the safety information (day:month:year)?		
What GSK product is the safety information about?		
What indication (condition) was the product used for?		
Dose used:	Lot/Batch no:	Expiry date:
Describe the safety information disclosed during the research (include any verbatim text):		

<b>Information about the reporter (respondent) who disclosed the safety information</b>	
<b>Reporter:</b> Consumer <input type="checkbox"/> Doctor <input type="checkbox"/> Nurse <input type="checkbox"/> Pharmacist <input type="checkbox"/> Other (specify):	
<b>Which country does the reporter live in?</b>	
<b>Did the reporter consider the event was possibly related to the product use?</b> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	
<b>Is the reporter willing for GSK's safety team to contact them to discuss further?</b> Yes <input type="checkbox"/> No <input type="checkbox"/> If <u>No</u> , please complete just the reporter fields above. If <u>Yes</u> , please provide contact details below. For an HCP it is their contact details; for a patient it is their doctor's contact details:	
<b>Name:</b>	
<b>Address:</b>	
<b>Tel. no / E-mail:</b>	

<b>Information about the patient (person) or groups who used the product (may be the reporter or someone else)</b>	
<b>Gender:</b> Male <input type="checkbox"/> Female <input type="checkbox"/> Unknown <input type="checkbox"/>	<b>Individual/Multiple Patients:</b> Individual <input type="checkbox"/> Multiple <input type="checkbox"/>
<b>Age:</b>	If Multiple state number if known:
<b>Initials:</b>	<b>Other (date/year of birth, patient ID, etc):</b>
<b>Was the patient pregnant when using the product?</b> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown <input type="checkbox"/>	

<b>Agency signature and date:</b>	
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